INTERNATIONAL JOURNAL OF

Cardiovascular SCIENCES

INTERNATIONAL JOURNAL OF

Cardiovascular SCIENCES

ISSN 2359-4802 / IJCS ONLINE: ISSN 2359-5647

BIENNIUM BOARD 2020/2021

INTERNATIONAL JOURNAL OF
Cardiovascular
SCIENCES

INTERNATIONAL JOURNAL OF

Cardiovascular SCIENCES

SUMARY

• Review Article

• Viewpoint

• Letter to the Editor

• Case Reports

• See in the Next Edition

Pre-hospital Care for Suspected Stroke Patients, Cared for by Mobile Emergency Care Units in Northern Minas Gerais

Lorenn Lages Gusmão,[1] Israel Junior Borges do Nascimento,[1] Gabriel Almeida Silqueira Rocha,[1] João Antonio de Queiroz Oliveira,[1] Geisiane Sousa Braga Machado,[1] Izabella de Oliveira Antunes,[1] Romeu Vale Sant'anna,[2] Breno Franco Silveira Fernandes,[1] Ubiratam Lopes Correia,[3] Antonio Luiz Pinho Ribeiro,[1] Milena S. Marcolino[1]

Hospital das Clínicas da Universidade Federal de Minas Gerais,[1] Belo Horizonte, MG – Brazil
Hospital Risoleta Tolentino Neves,[2] Belo Horizonte, MG – Brazil
Núcleo de Educação Permanente (NEP) do SAMU,[3] Montes Claros, MG – Brazil.

Abstract

Background: Stroke management require rapid identification, assessment, and transport of patients to qualified health care centers. However, there is little description in the literature on the multiple challenges associated with the pre-hospital transport of suspected stroke patients.

Objective: To characterize the pre-hospital care provided to suspected stroke patients by the Brazilian Emergency Medical Service (SAMU in Portuguese), by means of a descriptive case study.

Methods: This is a descriptive study of a series of cases. Data from the SAMU regarding the responses to emergency calls from suspected stroke patients were collected. Independent reviewers confirmed the diagnostic hypothesis and all discordances were assessed using kappa statistics. Clinical data and transport times were described as frequency and proportion or central tendency and dispersion measures. Normality of continuous variable distribution was assessed using the Kolmogorov-Smirnov test. The Mann-Whitney U test was used for comparison of medians, with a 5% significance level.

Results: During the studied period, 556 suspected stroke patients were treated. The kappa index was 0.82 (95% CI 0.737 to 0.919) CI. In 74.7% of the cases, the symptom onset time was not recorded. The median time elapsed between the call for emergency services and the ambulance arrival was 18 minutes, and the median transport time was 38 minutes. A total of 34% of the patients were taken to referral hospitals for stroke.

Conclusion: This study revealed a low level of knowledge regarding the need to determine the exact time of symptom onset of suspected stroke patients. Also, the study showed the low rate of patients taken to referral hospitals. (Int J Cardiovasc Sci. 2021; 34(3):245-252)

Keywods: Epidemiology; Stroke; Preventive Health Services; Health Programs and Plans; Public Health; Health Policy.

Introduction

Strokes are one of the main causes of morbidity and mortality, functional disability, work absenteeism, and social-economic insecurity in Brazil and worldwide.[1] According to data provided by the World Stroke Organization (WSO), one in every six individuals in the world will have at least one stroke episode.[2] Another very relevant aspect is the monetary cost to public and private sectors related to stroke patients. An American study published by the Center for Disease Control (CDC) estimated that 34 billion dollars are spent annually on stroke-related expenses, including hospital stay, professional care team, pharmacotherapy, and indirect losses.[3] A recent study conducted at the Federal University of Goias estimated that the average national cost of hospital care of stroke patients has exceeded 1.5 billion Brazilian reals.[4] Thus, the clinical, epidemiological,

economic, and social impact of stroke triggers the need for studies on this topic in Brazil.

Due to its severity and epidemiological importance, stroke was included by the American Heart Association in the basic and advanced life support algorithms, requiring proper and specialized training in referral care centers.[5] Similarly, the Brazilian Department of Health created the "Line of Stroke Care" and defined it as a priority.[6,7] It refers to a dynamic, multidisciplinary monitoring system focused on rehabilitation, education, and care for patients and their caretakers, starting from hospital discharge, and on handling of expected clinical outcomes.[8] In 2008, the General Coordination of Urgency and Emergency of the Ministry of Health created a national stroke network, by means of the National Stroke Project, to include all levels of health care in the task force against stroke, thereby raising the public's awareness, pre-hospital care, hospital care, rehabilitation, and prevention.[9]

A key factor in the prognosis of stroke patients is the time elapsed between symptom onset and treatment. It is recommended the administration of thrombolytic drugs within three hours of symptom onset (with the possibility of extending up to four and a half hours in selected cases), and performance of thrombectomy procedures up to 24 hours after symptom onset, *i.e.*, during the hyperacute phase of stroke. In this sense, the pre-hospital care service plays a critical role in the prognosis of stroke patients, including an effective transport, symptom recognition and/or initial management of patients.[10] A study conducted in San Francisco involving trained paramedics, who participated in a training program designed to improve the recognition of stroke symptoms, and untrained paramedics, revealed that, after the program had been implemented, there was a significant increase in the identification of acute stroke patients.[11] Therefore, the creation of continued training programs for health care workers, especially pre-hospital care teams, is essential for the early detection of stroke cases and subsequent referral to specialized units. In Brazil, the Mobile Emergency Care Service (SAMU) has become key element in identifying suspected stroke, monitoring patients' vital functions, quick transport of patients to the appropriate care unit, and notifying this facility where the stroke patient will be admitted.[12]

Extended North Minas Gerais Region

Minas Gerais is the fourth largest state in Brazil by area (586,528 km²) and the second in population, with 19,597,330 inhabitants (10% of the Brazilian population) according to the last census (2010) conducted in the country.[13] Between January 2013 and June 2014, a total of 29,145 hospital admissions for stroke was registered in the state.[14] According to data from DATASUS database, the mortality rate due to cerebrovascular diseases is 52.3 per 100,000 inhabitants in Brazil, and of 51.8 per 100,000 inhabitants in Minas Gerais, which stands in the ninth position in the ranking position with the highest mortality rate from cerebrovascular diseases in Brazil.[14]

The state of Minas Gerais is divided into 12 macro-regions; the north region is the largest one, with a territory corresponding to that of the states of Santa Catarina and Alagoas combined, distances between cities of up to 500 kilometers, and extensive rural areas.[13] It includes 89 municipalities, with significant social inequality and low demographic density.[13] A study conducted by the Pan American Health Organization/WHO, in partnership with the Brazilian Department of Health and the Minas Gerais Department of Health, identified a higher risk of premature death from chronic degenerative diseases in Jequitinhonha and Northern Minas Gerais.[15] Among all the stroke cases registered in the state of Minas Gerais, 2,724 cases occurred in this region.[14]

The Inter-municipal Health Consortium of the Urgent Care Network of Northern Minas Gerais (CISRUN in Portuguese), integrates 86 of the 89 cities of the state, comprising approximately 1.6 million inhabitants. This service is based on 48 mobile units, of which 41 are basic health units (USB in Portuguese), in which patients are seen by two nurse technicians, and seven are advanced health care units (USA in Portuguese), consisting of a physician, a nurse, and a driver. These mobile units provide pre-hospital care over the region and make patient transport to the referral hospitals easier. Considering the important role played by the CISRUN in Northern Minas Gerais, as well as the epidemiological, clinical, and social-economic relevance of stroke, this study was designed to characterize the pre-hospital care provided by SAMU to suspected stroke patients in Northern Minas Gerais.

Methods

This is a descriptive study of a series of cases of suspected stroke patients provided by the SAMU of Northern Minas Gerais. Data were collected from the SAMU Registration Center, located in the area's main city, Montes Claros, by two trained researchers, from March to December 2014.

Cases of suspected stroke was identified by two independent reviewers (R.S. and B.X., experienced neurologists). In case of disagreement, an additional review was performed by the study coordinator (M.S.). Among suspected stroke patients, patients were classified by SAMU as emergency care (pre-hospital), therefore excluding patients associated with interhospital transport. The assessment included: (i) patient identification; (ii) date and time of symptom onset, SAMU call, SAMU ambulance arrival at the event location, SAMU ambulance departure from the event location, and SAMU ambulance arrival to its destination; (iii) code at departure: green, yellow, or red, which determine the event response priority as minimum, intermediate, or maximum, respectively;[16] (iv) activation motivation; (v) Glasgow coma scale;[17] (vi) Cincinnati pre-hospital stroke scale;[18] (vii) vital data; (viii) procedures conducted in the ambulance; (ix) development and/or complications; (x) diagnostic hypothesis; (xi) destination and current status.

For analysis of care profile, the following were calculated:

i) travel time to respond: refers to the time elapsed between call for ambulance and its arrival to the event location;

ii) patient travel time: time elapsed between ambulance departure from the event location and its arrival to destination (hospital facility), except for the cases in which a referral hospital was not informed (a time equal to zero was defined in these cases); and

iii) total response time: time elapsed between the call for an ambulance and its arrival at the destination (hospital facility), including the travel time for assistance, time spent at the event scene, and patient travel time.

Regarding the destination hospital, the authors observed if suspected stroke patients were transported to the local referral hospital listed in the Brazilian Stroke Network – *Irmandade Nossa Senhora das Mercês Santa Casa*, located in Montes Claros.[19]

This study was approved by the Research Ethics Committee of the Federal University of Minas Gerais (UFMG) in 2011 (approval number 065/11).

Statistical analysis

Normality of continuous variable distribution was tested with the Kolmogorov-Smirnov test. Since the distribution was not normal, the median was used as measure of central tendency, and the interquartile range as measure of dispersion. Categorical variables were described by absolute and relative frequencies. The Mann-Whitney U test was used for comparisons of the medians. The significance level for all tests was 5%. All analyses were performed using the IBM SPSS Statistics software for Windows, version 21.0 (Armonk, NY: IBM Corp.).

Results

During the study period, 556 consecutive suspected stroke patients were treated by the SAMU of northern Minas Gerais. Among them, 299 patients received pre-hospital care and comprise the study sample. Median patient age was 70 years old (interquartile range [IR] 60-81 years of age, varying between 19 and 101), and 51.2% of the patients were male. Regarding the motivation for the emergency call, the most frequent was motor impairment (54.8%), followed by speech impairment (42.1%) and facial asymmetry (33.1%) (Table 1).

In 74.7% of the cases, patients or family members were unable to define the time of symptom onset, and 8.7% called the emergency service after four hours of the symptom onset. For only 72.9% of the cases, the emergency call was assigned a red code, which denoted maximum priority in pre-hospital care. Results of the Cincinnati and Glasgow scales are provided in **Table 1**.

Median "travel time to respond" was 18 (14.0-33.0) minutes and median "patient travel time" was 12 (IR 6.0-23.5) minutes. Median "total response time" was 57 (IR 45.5-91.0) minutes (Table 2). There was no statistically significant difference in "travel time to respond" between the north macro-region and Montes Claros micro-regions. Table 2 reveals greater "patient travel time" and "total response time" for the calls originating from Montes Claros macro-region (p<0.01). Most patients (86.3%) received hospital care within four hours of the call.

Most treated patients were referred (99.0%) to hospital care; 110 patients were taken to the referral hospital for stroke care located in the respective macro-region, 22 were referred to other hospitals in Montes Claros, and 167 were referred to other health facilities in other cities. Among the patients who were not referred to hospital care, one was discharged at the event location, and two refused to receive treatment.

There was a high level of agreement between neurologists (1 and 2) in identifying suspected stroke (kappa = 0.82; 95% CI [0.737;0.919]) (Table 3).

Table 1 – Characterization of the sample treated by the SAMU of northern Minas Gerais (Minas Gerais, Brazil) regarding the pre-hospital care – motivation for the emergency call, time elapsed between symptom onset and service engagement, and clinical classification defined by the medical team (n=299)

Characteristics	n (%)
Age, years	70 (60-81)
Male	153 (51.2)
Motivation for the call	
Motor impairment	164 (54.8)
Speech impairment	126 (42.1)
Facial asymmetry	99 (33.1)
Visual impairment	6 (2.0)
Headache	14 (4.7)
Other neurological symptoms	11 (3.7)
Suspected stroke	83 (27.8)
Hemiparesis/hemiplegia	43 (14.4)
Lowered sensitivity	45 (15.1)
High blood pressure	13 (4.3)
Time elapsed between the symptom and the call to the emergency service	
Less than 4 hours	45 (15.0)
More than 4 hours	26 (8.7)
Not informed/Unknown	228 (76.3)
Activation code	
Green (low risk)	1 (0.3)
Yellow (intermediate risk)	73 (24.4)
Red (high risk)	218 (72.9)
Not informed	7 (2.3)
Cincinnati scale	
Informed	66 (22.1)
Glasgow scale	
Informed	291 (97.3)

Data expressed as number (%) or median (interquartile range)

Discussion

This study evaluated the profile of suspected stroke patients and of pre-hospital emergency care provided by the SAMU of north Minas Gerais in a large area that lacks sufficient health care resources. The results showed that stroke remains a disease associated with lack of knowledge by the residents in the area,

given that only 23.7% of the people were able to tell exactly the symptom onset time, and, among them, a little over half called SAMU within four hours of the symptom onset.

For the vast majority of patients, the total service time took place within the four hours. However, due to inexact reports on the time of symptom onset, the fact does not ensure the treatment was provided within the

Table 2 – Emergency response times of the pre-hospital care team

Time elapsed (min)	Total* (n=299)	From towns to Montes Claros* (n=170)	Outside Montes Claros* (n=129)	p-value
Travel time to respond †	18 (14.0-33.0)	19 (15.0-30.0)	17.5 (13.0-43.0)	0.174
Patient travel time‡	12 (6.0-23.5)	13 (9.0-20.0)	11 (5.0-31.0)	0.008
Total response time§	57 (45.5-91.0)	61 (49.0-78.0)	53 (40.5-118.0)	0.004

Comparison from towns to Montes Claros vs Outside Montes Claros (Mann-Whitney U test)
* Values expressed as median (interquartile range)
† Time between the call for the ambulance and its arrival to the destination
‡ Time between the ambulance departure from the event location and arrival to the destination. For those cases where patients were not taken to any referral hospital, the time was zero.
§ Time between the call to emergency and arrival of patient to the destination

Table 3 – Kappa statistics obtained between neurologists 1 and 2 in the evaluation of cases who called to the pre-hospital care service, SAMU of north Minas Gerais (n = 603)

Classification	Neurologist 1		
	Included	Excluded	Total
Neurologist 2			
Included	556	9	565
Excluded	4	34	38
Total	560	43	603

Kappa = 0.82 95% CI [0.737;0.919]

period recommended by international guidelines. In addition, most patients were not referred to a referral hospital for stroke care, following the Brazilian Department of Health guidelines.

As described in clinical and observation studies, most patients with suspected or confirmed stroke are admitted to emergency health care units within three hours of the symptom onset.[20] This fact may be related to the lack of knowledge about this condition, symptom onset during nighttime, patients living alone, among others.[21] A study conducted in the city of Belo Horizonte in 2018 detected that only 56.1% of participants were able to recognize signs of stroke in a pre-selected video.[22] In the north of Minas Gerais, considering the residents' low level of formal education, and the high poverty level, the lack of knowledge is probably even greater.[23]

In the aforementioned study, only 17 individuals (2.4%) knew about the use of thrombolytic drugs for treatment of acute stroke.[22]

Results also indicated a possible failure of SAMU to recognize emergency situations for many of the patients assisted. Among the 299 patients treated for suspected stroke in pre-hospital care, only 72.9% were assigned a red code, that is, maximum priority in treatment and transport. Considering that the exogenous administration of thrombolytics and the patient's prognosis depend on the time elapsed between symptom onset and the arrival at the hospital, this study observed that such variables might have affected the outcome of these patients. In April 2017, the Stroke System of the macro-region of north Minas Gerais was launched in the city of Montes Claros, to improve care provided to stroke patients,

reduce the average hospital stay for each patient, and to provide training and qualification for health care professionals, among others. Nevertheless, given that this implementation took place quite recently, it may be noted that descriptions of the results generated by such implementation are still scarce.[24]

The data provided reveal the importance of further discussing the establishment of priority at the SAMU system, prior to implementing a care line, as well as raising awareness and providing systematic qualification for the team. A study conducted in San Francisco compared awareness in recognizing acute stroke between trained and untrained paramedics before and after training. After training, a significant increase in sensitivity was detected among paramedics who had not been trained before.[11]

It is also important to emphasize the poor ability of the pre-hospital care team to recognize acute stroke and use the Cincinnati scale. Although its application is recommended by the Health Department and by the AHA in pre-hospital care, it has been reported that this scale was applied to only one in every 4.5 patients treated by SAMU. Its application is simple and for the detection of focal neurological deficits in the three parameters evaluated by this tool: motor skill, speech, and facial asymmetry. Despite recommendations, the use of the scale notified in only 20.2% of the responses, which can make the screening for stroke cases more difficult. Stroke sensitivity and specificity increase in direct proportion to the presence of these neurological alterations, making diagnosis and referral to specialized care units, and, therefore, early treatment, easier.

Regarding transport, despite the adversities that characterize the region – bad roads, long distances, river crossing on barges, and the interception of ambulances – the median transport time was adequate. However, some travels reached an extremely long time, possibly affecting patients' prognosis. The implementation of the stroke care line, with the use of telemedicine to make up for the insufficient number of neurologists in the area would be essential to enable a prompt response.[25] However, the consolidation of positive trajectories associated with telemedicine requires the creation of hubs with access to computed tomography scanners and the possibility of prescribing thrombolytics remotely. Therefore, the benefits of telemedicine are multiple and pertinent to the holistic care for stroke patients. Telemedicine-directed stroke care provides remote medical services (especially from neurologists and remote consultancy for the admitted cases), involving rural and remote areas, where financial resources are scarce.[26,27] Therefore, integration and articulation between mobile emergency care systems on the one hand, and reference hospitals for stroke care and telemedicine hubs on the other, are critical in achieving better results and prognosis associated with stroke cases.[28]

Another important aspect, in addition to an appropriate travel time, is the fact that the administration of thrombolytics is affected by the lack of precision in describing symptom development time. Thrombolysis is only indicated after four and a half hours after the onset of stroke symptoms and, in ischemic cases, there are systemic contraindications.[16] In our study, only 25.3% of the patients could report the exact time of symptom onset. This may be due to the occurrence of stroke during sleep and manifestation of symptoms on awakening (wake-up stroke), and to the fact that individuals and their social circle may not notice symptom onset, as they believe that such manifestations are temporary. In addition, among those patients who were aware of their symptoms, only 20.7% called the emergency ambulance service within four hours of symptom onset. Considering this time (from symptom onset to ambulance call) and the travel time of 38 minutes, treatment with thrombolytics would be contraindicated for most patients. The importance of raising residents' awareness, taking into account their sociocultural competencies becomes more evident, to ensure the identification of symptoms as early as possible. In addition, according to Brazilian data, a specialized and quick response increases the chances of a good prognosis and less sequelae.[29]

Some problematic aspects are observed when obstacles related to responding to and understanding stroke are analyzed. Initially, it is noticed that patients who live far from metropolitan areas, and those who are limited by logistics, and social and financial resources, are more likely to have a worse prognosis and higher morbidity and mortality rates.[26,27] Therefore, to make the identification of suspected stroke patients easier, it is suggested the use of a pre-hospital assessment tool in pre-hospital urgency and emergency services in Brazil and worldwide.

One of the limitations of this study is the absence of data about the clinical course of the patients, such

as the diagnostic confirmation of the reviewed cases, prognosis, and outcome. These data would help to identify additional endpoints and other clinical demands.

Despite these limitations, this study allowed for characterization of the care provided in an area with limited medical, social, and financial resources, revealing failures, such as difficulty in early identification of stroke signs by family members, and deficient health care, in disagreement with guidelines' recommendations. Results obtained in this study are useful for developing socio-educational actions and health promotion programs, improving emergency response systems, qualifying health care professionals involved in these systems, and for implementing strategies that may contribute to a faster, more effective and more appropriate care. In addition, the fact that the study was conducted on an intentional, rather than a probabilistic sample probably limits inference of the findings to other populations.

Conclusion

This study revealed a low level of knowledge regarding the need to determine and register the exact time of symptom onset of suspected stroke patients. Also, the study highlighted the low rate of patients taken to the referral hospitals of the northern macro-region of Minas Gerais. These observations indicate the need for interventions, with health promotion programs, for defining a standardized referral system and providing continued training for health care professionals. Intervention measures, such as socio-educational campaigns in primary health care centers, as well as health promotion in stroke-related engaged fiction , have become critical to facilitate early detection and intervention for stroke. Further studies are required to evaluate the clinical and economic impact of emergency

services in areas where resources are scarce, as is the northern macro-region of Minas Gerais.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Sources of Funding

This study was funded by FINEP.

Study Association

This study is not associated with any thesis or dissertation work.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the *Universidade Federal de Minas Gerais* under the protocol number 065/11. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

Author contributions

Conception and design of the research: Gusmão LL, Ribeiro TLP, Marcolino MS. Acquisition of data: Gusmão LL, Antunes I, Lopes U. Analysis and interpretation of the data: Gusmão LL, Nascimento IJB, Oliveira JAQ, Marcolino MS. Statistical analysis: Gusmão LL, Nascimento IJB, Oliveira JAQ. Obtaining financing: Ribeiro TLP, Marcolino MS. Writing of the manuscript: Gusmão LL, Nascimento IJB, Oliveira JAQ, Rocha GAS. Critical revision of the manuscript for intellectual content: Nascimento IJB, Antunes I, Fernandes BF, Sant'Anna RV, Oliveira JAQ, Lopes U, Ribeiro TLP, Marcolino MS.

References

1. Lotufo PA. Stroke in Brazil: a neglected disease. Sao Paulo Med J. 2005;123(1):3-4.

2. Kaste M. Every day is a world stroke day: act now, be a stroke champion and a torchbearer! Stroke. 2010;41(11):2449-50.

3. Centers for Disease Control and Prevention - CDC. Stroke Facts [database on the Internet]. 2017 [acesso em 25 Jun. 2019]. Disponível em: https://www.cdc.gov/stroke/facts.htm.

4. Brito GV. Acidente vascular cerebral no Brasil: estimativa contemporânea do custo da doença no período hospitalar [trabalho de conclusão de curso]. Brasília: Universidade Federal de Goiás; 2017.

5. Jauch EC, Cucchiara B, Adeoye O, Meurer W, Brice J, Chan YY, et al. Part 11: adult stroke: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation. 2010;122(18 Suppl 3):S818-28.

6. Brasil. Ministério da Saúde. Portaria n. 665, de 12 de abril de 2012. Diário Oficial da União 2012. [acesso em 20 Apr. 2020]. Disponível em : http://bvsms.saude.gov.br/bvs/saudelegis/gm/2012/PRT0665_12_04_2012.html.

7. Brasil. Ministério da Saúde. Secretaria de Atenção à Saúde. Departamento de Atenção Especializada. Coordenação-Geral de Média e Alta Complexidade.

8. Hospital Sírio Libanês. Protocolo gerenciado de Acidente Vascular Cerebral (AVC) [database on the Internet]; 2018. [acesso em 20 Apr. 2020]. Disponível em: https://www.hospitalsiriolibanes.org.br/institucional/gestao-da-qualidade/Documents/2018-11-01-protocolos/Protocolo%20Gerenciado%20de%20Acidente%20Vascular%20Cerebral/Protocolo %20AVC_VF.pdf.

9. Brasil. Ministério da Saúde. Departamento de Atenção Especializada, Coordenação Geral de Urgência e Emergência. Projeto Nacional de Atendimento à Doença Vascular Aguda. Brasília: OMS; 2008.

10. Tambara EM. Diretrizes para Atendimento Pré-Hospitalar no Acidente Vascular Cerebral;. Medicina Perioperatória. Rio de Janeiro: Sociedade de Anesteriologia do Estado do Rio de Janeiro; 2006. p. 77.

11. Smith WS, Corry MD, Fazackerley J, Isaacs SM. Improved paramedic sensitivity in identifying stroke victims in the prehospital setting. Prehosp Emerg Care. 1999;3(3):207-10.

12. Brasil. Ministério da Saúde. AVC: o que é, causas, sintomas, tratamentos, diagnóstico e prevenção; 2019. [acesso em 04 Set. 2020]. Disponível em: http://www.saude.gov.br/saude-de-a-z/acidente-vascular-cerebral-avc.

13. Instituto Brasileiro de Geografia e Estatística; 2010. [acesso em 20 Out. 2014]. Disponível em: http://www.ibge.gov.br/estadosat/perfil.php?sigla=mg.

14. Brasil. Ministério da Saúde. DATASUS. [acesso em 16 Set. 2014]. Disponível em: http://www2.datasus.gov.br/DATASUS/index.php.

15. Organização mundial da Saúde. Organização Pan-Americana da Saúde. Rede de Atenção à Urgência e Emergência na Macrorregião Norte de Minas Gerais: estudo de caso. Brasília: OMS; 2011.

16. Secretaria Municipal de Saúde de Franca SAMU. Protocolo Operacional Padrão. Franca - SP; 2012. 19 p.

17. Centers for Disease Control and Prevention. Glasgow Coma Scale. United States of America: Centers for Disease Control and Prevention; 2019. [acesso em 04 Abr. 2018]. Disponível em: https://www.cdc.gov/masstrauma/resources/gcs.pdf.

18. Kothari RU, Pancioli A, Liu T, Brott T, Broderick J. Cincinnati prehospital stroke scale: reproducibility and validity. Ann Emerg Med. 1999;33(4):373-8.

19. Rede AVC Brasil. Hospitais da Rede Brasil AVC; 2020. [acesso em 04 Abr. 2015]. Disponível em: http://www.redebrasilavc.org.br/para-profissionais-de-saude/hospitais-rede-brasil-avc2/.

20. American Academy of Neurology. Few Stroke patients fet to hospital in time for treatment [database on the Internet]; 2006 [acesso em 25 Jun. 2019]. Disponível em: https://www.aan.com/PressRoom/Home/PressRelease/334.

21. Ashraf VV, Maneesh M, PrAVCenkumar R, Saifudheen K, Girija AS. Factors delaying hospital arrival of patients with acute stroke. Ann Indian Acad Neurol. 2015;18(2):162-6.

22. Meira F, Magalhães D, Silva LS, Mendonça e Silva AC, Silva GS. Knowledge about stroke in Belo Horizonte, Brazil: a community-based study using an innovative video approach. Cerebrovasc Dis Extra. 2018;8(2):60-9.

23. Instituto de Pesquisa Econômica Aplicada. Programa das Nações Unidas para o desenvolvimento. Atlas de desenvolvimento humano do Brasil de 2013; 2013. [acesso em 25 Jun. 2019]. Disponível em: http://atlasbrasil.org.br/2013/.

24. Rede Urgência e Emergência CISRUN. Unidade da Rede AVC é inaugurada em Montes Claros; 2017 [acesso em 02 Set. 2019]. Disponível em: http://www.cisrun.saude.mg.gov.br/noticias/unidade-da-rede-avc-e-inaugurada-em-montesclaros/.

25. Breuer L, Schwab S. Telemedicine in stroke care. Med Klin Intensivmed Notfmed. 2017;112(8):687-94.

26. Joubert J, Prentice LF, Moulin T, Liaw ST, Joubert LB, Preux PM, et al. Stroke in rural areas and small communities. Stroke. 2008;39(6):1920-8.

27. Howard G, Kleindorfer DO, Cushman M, Long DL, Jasne A, Judd SE, et al. Contributors to the excess stroke mortality in rural areas in the United States. Stroke. 2017;48(7):1773-8.

28. Acker 3rd JE, Pancioli AM, Crocco TJ, Eckstein MK, Jauch EC, Larrabee H, et al. Implementation strategies for emergency medical services within stroke systems of care: a policy statement from the American Heart Association/American Stroke Association Expert Panel on Emergency Medical Services Systems and the Stroke Council. Stroke. 2007;38(11):3097-115.

29. Rocha MS, Almeida AC, Abath Neto O, Porto MP, Brucki SM. Impact of stroke unit in a public hospital on length of hospitalization and rate of early mortality of ischemic stroke patients. Arq Neuro-Psiquiatr. 2013;71(10):774-9.

EDITORIAL

AVC - Optimizing Pre-Hospital Care For A Time-Sensitive Disease

André Volschan

Hospital Pro-Cardíaco, Rio de Janeiro, RJ – Brazil.
Editorial referring to the article: Pre-hospital Care for Suspected Stroke Patients, Cared for by Mobile Emergency Care Units in Northern Minas Gerais

The care of patients with acute illnesses, in which the time to start treatment can have an important influence on the prognosis, requires a strategy based on well-defined structure and processes. Acute stroke is a disease whose prognosis is causally related to the length of care, and the possibility of implementing cerebral reperfusion therapies and neuroprotective measures. The recommendations suggest that the time should be optimized in the different phases of care, in the recognition of signs and symptoms, medical evaluation, computed tomography and thrombolysis, for patients who meet the criteria for their performance. The instruction of the population to identify the clinical manifestations of stroke, prioritizing the search for assistance, is an important step in this chain of treatment, which can modify the outcomes of this disease.[1]

As a result, access to treatment is another major challenge. Interventions that effectively demonstrated an impact on outcomes in acute ischemic stroke, need a structure that can be supported, in large part, by telemedicine, significantly increasing patient access. National experiences have shown important results in improving the rate of pharmacological thrombolysis and thrombectomy, when designing a service network strategy with the support of neurologists, neuroradiologists and neurointerventionists.

The complexity of the structures for the treatment of acute stroke requires a structured medical evaluation and the possibility of performing computed tomography. It is important to understand that smaller hospitals cannot offer this type of treatment and the identification of hospitals that can receive patients transferred from their homes or from other care units is valuable. The study by Mochari-Greenberger,et al.[2] showed that patients evaluated by the pre-hospital medical service managed to be seen and treated more quickly and efficiently considering the time of arrival at the emergency room, medical care, and thrombolysis rate.[2] The management of an assistance model based on the training of professionals and transport logistics brings benefits to patients in different forms of clinical outcome.

The study published by Gusmão et al.,[3] Pre-hospital Care for Suspected Stroke Patients, Cared for by Mobile Emergency Care Units in Northern Minas Gerais, analyzes the prehospital care of patients with suspected acute stroke (SAMU), in the north of the state from Minas Gerais, through the Mobile Emergency Care Service.[3] The services offer coverage over a wide geographical area, including rural areas, 299 patients with suspected acute stroke were observed, with a mean age of 70 years. The motivation of the call shows the motor deficit, the worsening of speech and facial asymmetry as the most frequent ones, reinforcing the importance of the Cinccinati Scale in the evaluation of these patients.[4] Approximately 25% of the calls did not have the activation of the red code by the service ambulance call, considered a top priority. After assessing the call motivations, all related to the risk situation, it is possible that there is an opportunity for improvement at this stage of the process. Likewise, the difficulty in describing the onset of signs and symptoms, described by 76.3% of patients, shows the need to instruct the population in the recognition of clinical manifestations so it would not delay the start of care. The response times measured at the time of calling, leaving the ambulance, and arriving at the destination hospital, showed, despite the large geographic area, excellent results with a "global

Keywords

Stroke/complications; Prognosis; Brain Ischemia/ diagnostic imaging; Hospitalization; Thrombolytic Therapy; Epidemiology.

Mailing Address: André Volschan
Hospital Pro-Cardíaco
Rua General Polidoro, 219. Postal Code: 22280-003, Rio de Janeiro, RJ – Brazil.
E-mail: andre.volschan@gmail.com

response time," described as the time between the call until the patient's arrival at the destination hospital, on average 57 minutes.

The great contribution of Gusmão's article is to identify, within the line of pre-hospital care for patients with acute stroke, opportunities for improvement in training, structure, and processes. The use of telemedicine, filling treatment gaps, as shown in national and international publications, can optimize the possibility of a part of this population to have access to reperfusion and brain protection strategies, which would mean the real utility of the care model.[5,6]

Therefore, the intervention in places with the possibility of improvement in the care process, with the incorporation of indicators related to clinical results, may be a suggestion to the authors for a future publication.

References

1. Ojike N, Ravenell J, Seixas A, Masters-Israilov A, Rogers A, Jean-Louis G, Ogedegbe G, McFarlane SI. Racial disparity in stroke awareness in the US: an analysis of the 2014 National Health Interview Survey. J Neurol Neurophysiol. 2016;7(2):1000365.

2. Mochari-Greenberger H, Xian Y, Hellkamp AS, Schulte PJ, Bhatt DL, Fonarow GC, et al. Racial/ ethnic and sex differences in emergency medical services transport among hospitalized US stroke patients: analysis of the national Get With The Guidelines-Stroke Registry. J Am Heart Assoc. 2015;4:e002099.

3. Gusmão LL, Nascimento IJB, Rocha GAS, Oliveira JAQ, Machado GSB, Antunes IO, Sant'anna RV, et al. Pre-hospital Care for Suspected Stroke Patients, Cared for by Mobile Emergency Care Units in Northern Minas Gerais. Int J Cardiovasc Sci.2021;34(3):245-252.

4. Kasner SE. Clinical interpretation and use of stroke scales. Lancet Neurol. 2006 Jul;5(7):603-12.

5. Hatcher-Martin JM, Adams JL, Anderson ER, Bove R, Burrus TM, Chehrenama M, et al. Telemedicine in neurology: Telemedicine Work Group of the American Academy of Neurology update. Neurology. 2020 Jan 7;94(1):30-8.

6. Carvalho VS Jr, Picanço MR, Volschan A, Bezerra DC. Impact of simulation training on a telestroke network. Int J Stroke. 2019 Jul;14(5):500-7.

Physical Activity Level, Anthropometric and Cardiovascular Profile Among Students in Sergipe State Attending Public Schools

Luan Morais Azevêdo,[1] Lucas Souza Santos,[2] Emerson Pardono,[2] Jeeser Alves Almeida,[3] Aldemir Smith Menezes[2,4]

Universidade de São Paulo (USP),[1] Escola de Educação Física e Esporte da Universidade de São Paulo (EEFE-USP), São Paulo, SP - Brazil.
Universidade Federal de Sergipe (UFS),[2] Programa de Pós-graduação em Educação Física, São Cristóvão, SE - Brazil;
Universidade Federal do Mato Grosso do Sul (UFMS),[3] Programa de Pós-Graduação em Saúde e Desenvolvimento na Região Centro Oeste, Campo Grande, MS - Brazil.
Instituto Federal de Educação, Ciência e Tecnologia de Sergipe (IFS),[4] Aracaju, SE – Brazil.

Abstract

Background: Cardiovascular diseases are the leading cause of mortality among adults. Evidence has shown that sedentary behaviors are the main preventable outcome, however, many sedentary children also become sedentary adults. Therefore, identifying potential risk factors as early as possible contributes to therapeutic success.

Objective: To achieve an anthropometric and cardiovascular mapping of school-age students from Sergipe State, Brazil.

Methods: A school-based cross-sectional study with a representative sample from public schools in the state of Sergipe (n= 4700). Anthropometric and blood pressure measurements were performed, and the Global School-based Student Health Survey was used to assess the physical activity level. An independent samples t-test was performed for all comparisons, and significance was established at 5% (p<0.05).

Results: Despite showing mean blood pressure values within reasonable limits (SBP = 114.1±12.4 mm Hg and DBP = 66.3±8.1 mm Hg), school-age students did not comply with global recommendations for health promotion. It was also observed a high rate of low body weight (42.6%), suggesting dietary compromises, which can interfere with the development of this population. In addition, only 7.3% of students met the minimum physical activity criteria proposed for maintaining their health status.

Conclusion: The findings of the present study emphasize the importance of maintaining Physical Education classes as an essential curricular component, since they provide several health benefits and ensure that this population reaches the minimum daily recommendations, preventing diseases in adult life. (Int J Cardiovasc Sci. 2021; 34(3):255-261)

Keywords: Students; Adolecents; Public Schools; Anthropometry; Exercise; Risk Factors; Hypertension; Sedentarism; Epidemiology; Prevalence.

Introduction

Data from the World Health Organization[1] show that systemic arterial hypertension (SAH) affects about 30% of the world population, and the Brazilian Society of Cardiology reports that about 3 to 5% of school-age individuals are hypertensive, which is attributed to the increased rates of obesity in this population[2]. Besides, most individuals who were hypertensive in childhood/adolescence remain hypertensive adults[3].

Mailing Address: Luan Morais Azevêdo
Escola de Educação Física e Esporte da Universidade de São Paulo
Laboratório de Hemodinâmica da Atividade Motora
Avenida Prof. Mello Moraes, 65. Postal Code: 05508-030, Butantã, São Paulo, SP – Brazil.
E-mail: luan.azvdo@gmail.com

SAH is a chronic non-communicable disease, in which biological, behavioral, and socioeconomic factors lead to blood pressure values higher than 120 and 80 mmHg for systolic (SBP) and diastolic (DBP) pressures, respectively[2,4,5]. However, strategies for the control and treatment of hypertension can be adopted to prevent it from remaining in adulthood.

These strategies include the promotion of public policies for prevention (primary care), pharmacological interventions (e.g. antihypertensive drugs), and non-pharmacological interventions, which include dietary changes[6] and physical exercise[7]. The latter were identified as the most effective and safe, because they did not show as many side effects when compared to pharmacological interventions, mainly in children. Besides, the effects of exercise may be as effective as those of antihypertensive drugs[8].

Therefore, the identification of risk factors associated with hypertension is essential for disease prevention and maintenance of quality of life in this population, reducing the burden on health care resources. In this sense, the present study aimed to identify the physical activity level and to trace the anthropometric and cardiovascular profile of a representative sample of school-age students attending public schools in the state of Sergipe, Brazil.

Methods

Characterization of the Study

A cross-sectional epidemiological study including students enrolled in public schools was conducted in the 8 geographic territories of the state of Sergipe, Brazil. The local Research Ethics Committee approved the present study under number 1522.876/2016/CEP/CONEP/CNS.

Research Field

The state of Sergipe is located in the northeastern region of Brazil and has a territorial area of 21,925,424 km², with approximately 2,298,696 inhabitants. In addition, the state is composed of 75 counties, being geographically divided into 8 territories. Each territory has similar characteristics for 15 variables and 79 indicators distributed in the following dimensions: economic-productive, social, political-institutional, socio-cultural, and environmental.

Considering the government actions that lead rural school-age students to study in the city (urban zone),

as well as the similarity in pedagogical proposals and organization within each territory, there is a reduction in the possibility of selection bias due to the equivalence of some characteristics of the sample. For these reasons, it is believed that the random selection of counties as well as of education units (territories) clearly represents the group of school-age students in the state of Sergipe. In this context, proportionality by territory, education unit size, school grades, and study shift justify the methodology adopted for sample selection (Table 1).

Population and Sample

Stratified random sampling was used to select the desired sample. First, the primary unit was determined by considering the minimum sample needed for the study and stratified proportionally to the territory and size of the school (1 = up to 199 students, 2 = 200-499 students, 3 = 500+ students). Besides, for all territories to be considered representatively with the 3 school sizes, an amount of 25% of the study units (160 study units) was established as a criterion, totaling 42 schools distributed in 30 counties. After this, the secondary unit consisted of schools selected according to school grade and study shift (day or evening), using a simple random process and considering 20 students per school grade.

It should be pointed out that to maintain sample representativeness, for reasons such as participant refusal, age above or below that established in this study, and/or not answering important questions (i.e., sex and age), 10% was added to the total desired sample.

Table 1 – Sample stratification by territories of the state of Sergipe (n = 4151)

Territory	n	%
Grande Aracaju	1043	25.1
Sul Sergipano	450	10.8
Agreste Sergipano	491	11.8
Centro Sul Sergipano	303	7.3
Leste Sergipano	300	7.2
Médio Sertão Sergipano	391	9.4
Baixo São Francisco	627	15.1
Alto Sertão Sergipano	546	13.2
Total	**4151**	**100**

Inclusion/Exclusion Criteria

Participants included students of both sexes, aged 14 to 19 years, who voluntarily joined the study, according to the following criteria: be regularly enrolled in the selected schools; be present at the time of the evaluation; and fill in the questionnaire adequately, reducing non-responses as much as possible. Students whose parents did not sign the negative consent form (Parental Passive Consent Form) and who did not answer questions such as sex and age were excluded.

Instrumentation and Data Collection

For anthropometric measurements, body mass and height measurements were used to estimate body mass index (BMI), and waist circumference (WC) and hip circumference (HR) were used to estimate the waist-to-hip ratio (WHR), following the WHO criteria and cut-off points[9]. Also, measurements of systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR) were performed using a calibrated and validated automated monitor (OMRON Healthcare brand, HEM-720, Kyoto – Japan)[10], adopting the Brazilian Society of Cardiology criteria and cut-off points[2].

The physical activity level was estimated from the Global School-based Student Health Survey (GSHS/WHO), using recommendations for each age group as criteria for analysis[11]. It should be pointed out that all procedures were performed by 2 trained evaluators/class, and each class teacher was asked to remain in class to maintain their well-being as well.

Statistical Procedures

Data were expressed using descriptive statistics, such as absolute and relative frequency for categorical variables and mean and standard deviation for continuous variables. Normality and heterogeneity were assessed by the Shapiro-Wilk and Levene tests, respectively. In order to verify differences between the sexes, Student t-test for independent samples was applied. Also, the criteria proposed by Cole et al.,[12] were adopted for BMI categorization. All procedures were performed using SPSS, version 22, and significance was established at p<0.05.

Results

A total of 4700 school-age students, of both sexes, were evaluated. However, due to non-compliance with some of the inclusion criteria, 549 of these were excluded from the sample, accounting for a final sample of 4151 individuals. The general characteristics of the study sample are shown in Table 2.

In general, students presented BMI in the "normal weight" category (22.1 ±4.0 kg/m²), WHR in the "low risk" category (0.8 ±0.1), and values within the reference range for both SBP (114.1 ±12.4 mmHg) and DBP (66.3 ±8.1 mmHg).

Table 3 shows the absolute and relative frequencies of school-age students who performed at least 60 min of moderate to vigorous physical activity. It can be observed that 83.5% (0 to 4 days) of the sample does not meet the recommendations proposed by the WHO and that only 7.3% engaged in moderate to vigorous physical activity for at least 60 min daily.

The same pattern was observed for both boys (42.9%) and girls (42.3%), with age ranging from 16 to 17 years, and compared to the BMI categories of the same age group, as well as among the other age groups (Table 4).

Table 5 shows blood pressure values stratified by sex and age groups. Significant differences were found between the sexes for SBP in all age groups. Regarding DBP, only the category "≤ 15 years" presented

Table 2 – General anthropometric and hemodynamic characteristics of the sample (n = 4151)			
	Mean	**±SD**	**95% CI**
Anthropometric			
Body Mass (kg)	59.5	12.4	59.1 – 59.9
Height (m)	1.6	0.1	1.63 – 1.64
Body Mass Index (kg/m²)	22.1	4.0	22.0 – 22.2
WC (cm)	72.3	8.8	72.0 – 72.5
HC (cm)	92.4	9.5	92.1 – 92.7
WHR	0.8	0.1	0.78 – 0.79
Cardiovascular			
SBP (mmHg)	114.1	12.4	113.7 – 114.5
DBP (mmHg)	66.3	8.1	66.0 – 66.5
HR (bpm)	82.2	12.9	81.8 – 82.6

WC: Waist Circumference; HC: Hip Circumference; WHR: Waist-Rip Ratio; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; HR: Heart Rate.

258

Azevêdo et al.
Health profile of school-aged students

Int J Cardiovasc Sci. 2021; 34(3):255-261

Original Article

Table 3 – Absolute and relative frequencies of days of physical activity of moderate to vigorous intensity stratified by age range (n = 4098)[a]		
	n	**%**
≤ 15 years		
0 day	226	5.5
1 to 2 days	287	7.0
3 to 4 days	125	3.1
5 to 6 days	63	1.5
7 days	47	1.1
16 - 17 years		
0 day	693	16.9
1 to 2 days	798	19.5
3 to 4 days	334	8.2
5 to 6 days	206	5.0
7 days	160	3.9
18 - 19 years		
0 day	339	8.3
1 to 2 days	460	11.2
3 to 4 days	160	3.9
5 to 6 days	104	2.5
7 days	96	2.3
Total	**4098**	**100**

[a] *difference between the initial sample due to missing cases in the analyzed variables.*

Table 4 – General BMI of the sample, stratified by age range and sex (n = 4141)[a]				
	Male		**Female**	
	n	**%**	**N**	**%**
≤ 15 years				
Low Weight	354	14.8	224	12.8
Normal Weight	90	3.8	44	2.5
Overweight	32	1.3	10	0.6
16 - 17 years				
Low Weight	1024	42.9	743	42.3
Normal Weight	205	8.6	115	6.6
Overweight	79	3.3	47	2.7
18 - 19 years				
Low Weight	450	18.9	451	25.7
Normal Weight	105	4.4	90	5.1
Overweight	47	2.0	31	1.8
Total	**2386**	**100**	**1755**	**100**

[a] *difference between the initial sample due to missing cases in the analyzed variables.*

Discussion

Several studies demonstrate the importance of physical activity, especially in the early stages of life, since it can promote increased academic performance[13], maintenance of glucose levels[14], lipid profile[15], and blood pressure[16], with consequent attenuation of diabetes, obesity, and hypertension, respectively. It also acts in the treatment and prevention of depression[17], among other benefits. Nevertheless, the present study found high rates of insufficient physical activity for both boys and girls, among school-age students in the state of Sergipe.

These indices reveal that Brazilian public policies appear to be ineffective in promoting health at the primary care level, addressing it only when issues reach a permanent status, which in turn leads to an excessive burden on the Brazilian public health system[18].

The "16 to 17 years" age group presented high rates of low body weight, both when compared to the other age categories, as well as between the sexes of the same

differences between the sexes, 65.6 ±8.1 mmHg vs. 63.7 ±7.6 mmHg, for boys and girls, respectively. The HR values were higher (p = 0.001) in boys of all age groups (Table 5).

After the BMI stratification, it was evidenced that the individuals with lower body mass had lower blood pressure values, 112.8 ±12.0 and 65.5 ±7.8 mmHg, respectively, for SBP and DBP, compared to normal weight (118.1 ±12.6 and 68.2 ±8.2 mmHg) and overweight (112.2 ±12.8 and 71.2 ±8.9 mmHg) individuals. Table 6 also shows the differences between SBP and DBP between normal weight (118.1 ±12.6 and 68.2 ±8.2 mmHg, respectively) and overweight students (122.2 ±12.8 and 71.2 ±8.9 mmHg, respectively).

Table 5 – Cardiovascular variables of the sample, stratified by age range and sex (n = 4151)					
	Boys		**Girls**		**p**
	Mean	**±SD**	**Mean**	**±SD**	
SBP (mmHg)					
≤ 15 years	108.9	10.8	116.2	12.1	0.001*
16 - 17 years	109.2	10.1	120.2	12.4	0.001*
18 - 19 years	111.0	10.9	122.3	11.4	0.001*
DBP (mmHg)					
≤ 15 years	65.6	8.1	63.7	7.6	0.001*
16 - 17 years	66.1	7.6	65.9	8.2	0.663
18 - 19 years	67.7	8.1	67.5	8.4	0.634
HR (bpm)					
≤ 15 years	87.3	12.0	80.8	13.0	0.001*
16 - 17 years	85.5	11.7	78.5	13.2	0.001*
18 - 19 years	83.9	11.6	74.7	12.0	0.001*

*SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; HR: Heart Rate. *p < 0.05.*

Table 6 – Cardiovascular variables of the sample, stratified by BMI categories (n = 4151)			
	Mean	**±SD**	**95% CI**
SBP (mmHg)			
Low Weight	112.8	12.0	112.3 – 113.2
Normal Weight	118.1[†]	12.6	117.1 – 119.0
Overweight	122.2[††]	12.8	120.6 – 123.8
DBP (mmHg)			
Low Weight	65.5	7.8	65.2 – 65.8
Normal Weight	68.2[†]	8.2	67.6 – 68.8
Overweight	71.2[††]	8.9	70.2 – 72.2
HR (bpm)			
Low Weight	82.1	13.0	81.7 – 82.6
Normal Weight	81.9	12.6	80.9 – 82.9
Overweight	83.5	11.6	81.8 – 85.1

SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; HR: Heart Rate. †p < 0.05 between Normal and Low Weight; ††p < 0.05 between Overweight and other categories.

260

Azevêdo et al.
Health profile of school-aged students

Int J Cardiovasc Sci. 2021; 34(3):255-261
Original Article

age category. The results of the present study differed partially from those obtained by Reuter et al.,[19] who found a high prevalence of overweight/obesity in school-age students in the city of Santa Cruz, Brazil (South region), with a higher susceptibility to cardiovascular risks compared to eutrophic students and those with low body weight. This fact evidences a discrepancy between the Brazilian South and Northeast regions. However, both presented increased risk factors in this population.

The study conducted by de Almeida Silva et al.,[20] showed a positive association between low consumption of fruits and vegetables and low levels of physical activity, which may have triggered the unfavorable nutritional status of the sample studied. Furthermore, the low consumption of fruits, vegetables, and legumes is associated with higher consumption of processed beverages, such as juices and soft drinks, which contain high sugar, sodium, food dyes, and preservatives, which in turn may contribute to cases of SAH.

Based on this premise, a study conducted in Belo Horizonte, state of Minas Gerais[21], evaluated the implementation and effectiveness of 2 programs to change the behavior of school-age students from 6 to 11 years old. After the implementation of the programs, the researchers observed a significant improvement in the behavior of students, who started to adopt a more active lifestyle. The results obtained by Ribeiro and Alves[21] reinforce the importance of public policies focused on primary care to avoid chronic diseases and comorbidities associated with these pathologies.

In the present study, the cardiovascular variables differed between the sexes and the BMI categories. Besides, low levels of physical activity associated with an inadequate diet can trigger chronic diseases, such as obesity and hypertension, which can persist into adulthood[3]. Furthermore, a meta-analysis conducted by Gonçalves et al.,[22] showed that the South region of Brazil has the highest prevalence of hypertension in adolescents (12.4%), followed by the Northeast (10%) and North (6.9%), while the Southeast and Midwest regions had the lowest scores, 4.3 and 3%, respectively. The Brazilian government can use the findings of Gonçalves et al.,[22] to direct health actions to mitigate these indices.

This study has some limitations, such as not using direct methods for measuring physical activity levels, although the instrument used presents high reliability in obtaining this variable in epidemiological studies, and the measurement of blood pressure in the classroom. However, the results obtained for this variable have high ecological validity, since they were obtained under real conditions of analysis.

Conclusions

Although no significant manifestations of obesity were revealed, students from the state of Sergipe showed insufficient levels of physical activity, despite the high levels of low body weight. Thus, after this epidemiological mapping, we suggest the development of strategies to increase physical activity in Physical Education classes, as well as health education policies for students in Sergipe State attending public schools to raise awareness of healthy habits that can contribute to the prevention of chronic diseases.

Author contributions

Conception and design of the research: Azevêdo LM, Santos LS, Pardono E, Almeida JA, Menezes AS. Acquisition of data: Azevêdo LM, Santos LS. Analysis and interpretation of the data: Azevêdo LM, Santos LS, Pardono E, Almeida JA, Menezes AS. Statistical analysis: Azevêdo LM, Santos LS, Pardono E, Almeida JA, Menezes AS. Writing of the manuscript: Azevêdo LM, Santos LS, Pardono E, Almeida JA, Menezes AS. Critical revision of the manuscript for intellectual content: Pardono E, Almeida JA, Menezes AS.

References

1. World Health Organization (WHO). A Global Brief on Hypertension. Geneva: 2013. 40 p.

2. Malachias M, Souza W, Plavnik F, Rodrigues C, Brandão A, Neves M, et al. VII Diretriz Brasileira de Hipertensão Arterial. Arq Bras Cardiol. 2016;107(3):1-103.

3. Chen X, Wang Y. Tracking of blood pressure from childhood to adulthood: A systematic review and meta-regression analysis. Circulation. 2008;117(25):3171–80.

4. Wang B, Liao C, Zhou B, Cao W, Lv J, Yu C, et al. Genetic contribution to the variance of blood pressure and heart rate: a systematic review and meta-regression of twin studies. Twin Res Hum Genet. 2015;18(2):158–70.

5. Perin MS, Cornélio ME, Rodrigues RCM, Gallani MCBJ. Caracterização do consumo de sal entre hipertensos segundo fatores sociodemográficos e clínicos. Rev Lat Am Enfermagem. 2013;21(5):1–9.

6. Tebar WR, Ritti-Dias RM, Farah BQ, Zanuto EF, Vanderlei LCM, Christofaro DGD. High blood pressure and its relationship to adiposity in a school-aged population: body mass index vs waist circumference. Hypertens Res. 2018;41(2):135-40.

7. Cornelissen VA, Smart NA. Exercise training for blood pressure: a systematic review and meta-analysis. J Am Heart Assoc. 2013;2(1):e004473.

8. Naci H, Salcher-Konrad M, Dias S, Blum MR, Sahoo SA, Nunan D, et al. How does exercise treatment compare with antihypertensive medications? A network meta-analysis of 391 randomised controlled trials assessing exercise and medication effects on systolic blood pressure. Br J Sports Med. 2018;bjsports-2018-099921.

9. World Health Organization. (WHO). Waist Circumference and Waist-Hip Ratio: Report of a WHO Expert Consultation. Geneva; 2008.39p.

10. Topouchian J, Agnoletti D, Blacher J, Youssef A, Ibanez I, Khabouth J, et al. Validation of four automatic devices for self-measurement of blood pressure according to the international protocol of the European Society of Hypertension. Vasc Health Risk Manag. 2011;7(1):709–17.

11. World Health Organization, (WHO). Global School-Based Student Health Survey (GSHS) CORE QUESTIONNAIRE MODULES. Geneva;2009;

12. Cole T, Bellizzi M, Flegal K, Dietz W. Establishing a standard definition for child overweight and obesity worldwide: international survey. BMJ. 2000;320(7244):1240-3.

13. de Greeff JW, Bosker RJ, Oosterlaan J, Visscher C, Hartman E. Effects of physical activity on executive functions, attention and academic performance in preadolescent children: a meta-analysis. J Sci Med Sport. 2018;21(5):501-7.

14. Wheeler MJ, Dempsey PC, Grace MS, Ellis KA, Gardiner PA, Green DJ, et al. Sedentary behavior as a risk factor for cognitive decline? A focus on the influence of glycemic control in brain health. Alzheimer's Dement Transl Res Clin Interv. 2017;3(3):291–300.

15. Yoon J-G, Kim S-H, Rhyu H-S. Effects of 16-week spinning and bicycle exercise on body composition, physical fitness and blood variables of middle school students. J Exerc Rehabil. 2017;13(4):400–4.

16. Cardoso CG, Gomides RS, Queiroz ACC, Pinto LG, da Silveira Lobo F, Tinucci T, et al. Acute and chronic effects of aerobic and resistance exercise on ambulatory blood pressure. Clinics (Sao Paulo). 2010;65(3):317–25.

17. Gujral S, Aizenstein H, Reynolds CF, Butters MA, Erickson KI. Exercise effects on depression: Possible neural mechanisms. Gen Hosp Psychiatry. 2017;49:2–10.

18. Bielemann RM, da Silva BGC, Coll C de VN, Xavier MO, da Silva SG. Burden of physical inactivity and hospitalization costs due to chronic diseases. Rev Saude Publica. 2015;49:75.

19. Reuter CP, Burgos LT, Camargo MD, Possuelo LG, Reckziegel MB, Reuter EM, et al. Prevalence of obesity and cardiovascular risk among children and adolescents in the municipality of Santa Cruz do Sul, Rio Grande do Sul. Sao Paulo Med J. 2013;131(5):323–30.

20. de Almeida Silva FM, Menezes AS, da Silva Duarte M de F. Consumption of fruits and vegetables associated with other risk behaviors among adolescents in Northeast Brazil. Rev Paul Pediatr (English Ed. 2016;34(3):309–15.

21. Ribeiro RQ, Alves L. Comparison of two school-based programmes for health behaviour change: the Belo Horizonte Heart Study randomized trial. Public Health Nutr. 2014;17(06):1195–204.

22. Gonçalves VSS, Galvão TF, de Andrade KRC, Dutra ES, Bertolin MNT, de Carvalho KMB, et al. Prevalence of hypertension among adolescents: systematic review and meta-analysis. Rev Saude Publica. 2016;50:27.

EDITORIAL

A Burden of Physical Inactivity in School-Age Students: The Early Beginning of Cardiometabolic Risk

Pedro Paulo da Silva Soares,[1,2] Gabriel Dias Rodrigues[1,2]

Laboratory of Experimental and Applied Exercise Physiology, Department of Physiology and Pharmacology, Fluminense Federal University,[1] Niterói, RJ - Brazil.
National Institute for Science & Technology - INCT Physical (In)activity & Exercise, CNPq,[2] Niterói, RJ - Brazil.
Editorial referring to the article: Physical Activity Level, Anthropometric and Cardiovascular Profile Among Students in Sergipe State Attending Public Schools

It is well-known that sedentarism has a close association with the risk of cardiovascular and metabolic diseases. The physical inactivity lifestyle contributes to the prevalence of obesity and hypertension in children, highlighting a big health problem since most individuals who were hypertensive and obese in childhood/adolescence become hypertensive and obese adults[1]. On the other hand, physical exercise is a frontline non-pharmacological strategy to control and treat hypertension, as well as to prevent obesity, which should be encouraged among children/adolescents to reduce cardiometabolic risk in adulthood[2]. In this context, the mapping of risk factors associated with hypertension at the early age should be considered a primary step to plan public policies for disease prevention and health promotion, reducing the burden on healthcare resources[3]. Both obesity and high blood pressure have multifactorial causes, among them low levels of physical activity in adults, children, and adolescents. It is of utmost relevance to investigate the prevalence of physical activity levels in scholars, mainly in a country such as Brazil, with enormous disparities among regions.

In the current issue of the International Journal of Cardiovascular Sciences, Azevêdo et al.[4] investigated physical activity levels, as well as the anthropometric and cardiovascular profile in school-age students attending public schools in the state of Sergipe, northeast of Brazil. The study reported high rates of physical inactivity for both boys and girls, and increased blood pressure in overweight school-age students. Regarding anthropometric profiles, intriguing data showed a high prevalence of low body weight in the age group from 16 to 17 years for both sexes. In contrast, a previous study found a high prevalence of overweight/obesity in school-age students in a city of the Brazilian South region[5], suggesting a discrepancy between the Brazilian South and Northeast regions that must be considered for Brazilian public policies in health promoting at the primary care level[3]. From a practical perspective, physical education classes, as well as the public schools' pedagogic programs, must work together for health promoting and health education[6], and physical activity should be encouraged to prevent cardiovascular risk starting from childhood to adult life.

Keywords

Sedentarism; Students; Exercise; Adolecents; Physical Activity; Risk Factors; Metabolic Diseases; Public Health.

Mailing Address: Pedro Paulo da Silva Soares, PhD
Laboratory of Experimental and Applied Exercise Physiology - Fluminense Federal University
Rua Professor Hernani Pires de Melo, 101. Postal Code: 24210-130, São Domingos, Niterói, RJ – Brazil.
E-mail: ppssoares@id.uff.br

References

1. Chen X, Wang Y. Tracking of blood pressure from childhood to adulthood: A systematic review and meta-regression analysis. Circulation. 2008; 117(25):3171–80.

2. Cornelissen VA, Smart NA. Exercise training for blood pressure: a systematic review and meta-analysis. J Am Heart Assoc. 2013; 2(1): e004473.

3. Bielemann RM, da Silva BGC, Coll C de VN, Xavier MO, da Silva SG. Burden of physical inactivity and hospitalization costs due to chronic diseases. Rev Saude Publica. 2015; 49:75.

4. Azevêdo LM, Santos LS, Pardono E, Almeida JA, Menezes AS. Physical Activity Level, Anthropometric and Cardiovascular Profile Among Students in Sergipe State Attending Public Schools. Int J Cardiovasc Sci.2021;34(3):255-261.

5. Reuter CP, Burgos LT, Camargo MD, Possuelo LG, Reckziegel MB, Reuter EM et al. Prevalence of obesity and cardiovascular risk among children and adolescents in the municipality of Santa Cruz do Sul, Rio Grande do Sul. Sao Paulo Med J. 2013; 131(5):323–30.

6. Rodrigues GD, Alves Junior ED. Perfil de qualidade de vida e atividade física habitual de adultos participantes das aulas de educação física da Educação de Jovens e Adultos. Rev Bras Prescrição Fisiol Exerc. 2016;10:62.

ORIGINAL ARTICLE

Risk Score for Prolonged Mechanical Ventilation in Coronary Artery Bypass Grafting

Fernanda Dallazen-Sartori,[1,2] Luciano Cabral Albuquerque,[3] João Carlos Vieira da Costa Guaragna,[3] Ellen Hettwer Magedanz,[1] João Batista Petracco,[3] Rodrigo Bodanese,[3] Mario Bernardes Wagner,[1] Luiz Carlos Bodanese[1,3]

Pontifícia Universidade Católica do Rio Grande do Sul - PUCRS,[1] Porto Alegre, RS - Brazil
Universidade Regional do Noroeste do Estado do Rio Grande do Sul - UNIJUÍ,[2] Ijuí, RS - Brazil
Hospital São Lucas Hospital,[3] Porto Alegre, RS - Brazil

Abstract

Background: Prolonged mechanical ventilation (MV) after cardiac surgery imposes a significant burden on the patient in terms of morbidity and financial hospital costs.

Objective: To develop a risk score model to predict prolonged MV in patients undergoing coronary artery bypass grafting (CABG) surgery.

Methods: This was a historical cohort study of 4165 adult patients undergoing CABG between January 1996 and December 2016. MV for periods ≥ 12 hours was considered prolonged. Logistic regression was used to examine the relationship between risk predictors and prolonged MV. The variables were scored according to the odds ratio. To build the risk score, the database was randomly divided into 2 parts: development data set (2/3) with 2746 patients and internal validation data set (1/3) with 1419 patients. The final score was validated in the total database and the model's accuracy was tested by performance statistics. Significance was established at p < 0.05.

Results: Prolonged MV was observed in 783 (18.8%) patients. Predictors of risk were age ≥ 65 years, urgent/emergency surgery, body mass index ≥ 30 kg/m², chronic kidney disease, chronic obstructive pulmonary disease, and cardiopulmonary bypass time ≥ 120 minutes. The area under the ROC curve was 0.66 (95% CI, 0.64-0.68; p<0.001), the Hosmer-Lemeshow chi-square test was χ^2: 3.38 (p=0.642), and Pearson's correlation was r = 0.99 (p<0.001), indicating the model's satisfactory ability to predict the occurrence of prolonged MV.

Conclusion: Selected variables allowed the construction of a simplified risk score for daily practice, which may classify the patients as having low, moderate, high, and very high risk. (Int J Cardiovasc Sci. 2021; 34(3):264-271)

Keywords: Respiration, Artificial; Myocardial Revascularization; Risk Factors; Thoracic Surgery; Coronary Artery Disease; Probability.

Introduction

Although there has been a substantial advance in the perioperative treatment of patients undergoing cardiac surgery, prolonged mechanical ventilation (MV) continues to be an important adverse outcome, with an incidence greater than 22%.[1,2] Prolonged MV has a notable impact on cardiac surgery outcome, increasing morbidity, hospital length of stay, and, consequently, hospital costs.[3-7]

In cardiac surgery, most patients receive mechanical ventilatory support, which should be withdrawn when the clinical situation is stabilized.[8] It should be considered that early extubation, within 8 to 12 hours after the patient's transfer to the postoperative ward, is associated with improved cardiovascular conditions.[9,10]

The construction of a risk score that incorporates pre- and intraoperative risk factors that seek to predict the need for prolonged MV, especially in coronary artery bypass grafting (CABG) surgery, may be useful for patient care. It is utterly important on the contemporary setting, where patient conditions become more complex due to aging and coexistence of multiple comorbidities.[3]

Several studies have identified factors that predict the need for prolonged MV. The most frequently associated factors are sex, type of surgery, arterial hypertension, chronic kidney disease, chronic obstructive pulmonary disease, cardiopulmonary bypass time, and reduced left ventricular ejection fraction.[6,8,11] Evaluation and monitoring of risk scores with their respective rates of postoperative complications and mortality are considered excellent indicators of the quality of hospital services.[6] It should be noted that specific risk scores for prolonged MV in patients undergoing CABG in clinical practice are limited since those available refer to combined cardiac surgery[3] or valve replacement surgeries.[12]

The development of a risk model to identify the need for prolonged MV would potentially help to select high-risk patients and the need for preventive measures to be taken. It would also help to better allocate postoperative care resources that may be adopted for recovery and rehabilitation after a surgical procedure.[6,10] Therefore, this study aimed to build a risk score model for prolonged MV in patients undergoing CABG.

Methods

This was a historical cohort observational study. The data were prospectively collected and inserted in the database of the Cardiac Surgery Postoperative Unit of Hospital São Lucas of PUCRS. We included 4165 patients who underwent isolated CABG with cardiopulmonary bypass between January 1996 and December 2016. The study followed the tenets of the Declaration of Helsinki and was approved by the institution's Research Ethics Committee under no. 2.231.168 and CAAE 72189417.5.0000.5336. Patients who underwent congenital heart surgery, valve replacement, or combined surgery and those who died during surgery or within the first 12 hours were excluded.

Variables initially included in the logistic regression model were age (classified as ≥ 65 years or < 65 years), sex (male and female), previous cardiac surgery, elective surgery, urgent/emergency surgery (included as a single variable and defined as intervention required within 48 hours), chronic obstructive pulmonary disease (clinically diagnosed by chest X-ray and/or spirometry) and/or on drug treatment (corticosteroid or bronchodilator), asthma (reported previous history and/or chronic use of bronchodilators), heart failure by functional class II versus III-IV (NYHA criteria),[13] current smoking, body mass index (classified as ≥ 30 kg/m², defined by specific

calculation for adults up to 59 years[14] and specific for adults aged 60 and over),[15] arterial hypertension, diabetes mellitus, previous myocardial infarction, previous stroke, chronic kidney disease (defined as hemodialysis and/or creatinine ≥ 1.5 mg/dL), preoperative use of beta-blockers, preoperative use of corticosteroids, left ventricular ejection fraction (classified as < 40% according to the Brazilian Guidelines for Chronic and Acute Heart Failure[13] and measured by echocardiography or myocardial scintigraphy), and cardiopulmonary bypass time (classified as ≥ 120 minutes).

The main outcome was prolonged MV time, defined as MV for ≥ 12 hours,[9,10] including patients who were continuously ventilated for ≥ 12 hours postoperatively and those who were intubated and then extubated and subsequently re-intubated, resulting in a total duration of ≥ 12 hours.

Anesthesia, cardiopulmonary bypass, and cardioplegia were conducted according to the standard procedures of Hospital São Lucas of PUCRS, as previously described.[16] After CABG, all patients were transferred to the postoperative intensive care unit.

Statistical Analysis

Distributional assumptions were assessed using the Kolmogorov-Smirnov test. Continuous data were described as mean and standard deviation. Categorical variables were presented as absolute counts and percentages. Univariate comparisons were conducted with the chi-square test or Fisher's exact test as appropriate.

To construct the risk score, the automatic random function within the select cases tool of SPSS was used, with a 1:2 distribution, so that the database was randomly divided into 2 portions: development data set (2/3), with 2746 patients, and internal validation data set (1/3), with 1419 patients.

The initial consideration of the variables followed a hierarchical model based on biological plausibility and external information (literature) on the relevance and power of the association between these potential risk factors and the occurrence of the outcome to be analyzed. Once these variables were listed, multiple logistic regression was used in a backward selection process and all variables with a level of significance p < 0.05 were maintained in the model. After that, a weighted risk score was built, based on the magnitude of the b coefficients of the logistic equation. After they were transformed (exp [b]) into odds ratios, the values were rounded to the closest whole number to create the score.[17]

The preliminary risk score was applied to the validation database and 2 performance statistics were obtained: area under the ROC (Receiver Operating Characteristic) curve, the Hosmer-Lemeshow chi-square goodness-of-fit test, and the consequent Pearson's coefficient of correlation between the observed events and those predicted by the model. The area under the ROC curve was calculated, indicating the model's satisfactory ability to predict the occurrence of MV.

Observing the appropriate performance of the preliminary model in validation process, databases (modeling and internal validation) were arranged to obtain the final risk score, that is, with the total sample of this study. In this process, variables that had been removed were not included, which simply resulted in the obtaining of more accurate estimates for the coefficients that had been previously calculated. A weighted risk score was created from this final model by rounding the adjusted odds ratio (OR) to the nearest integer. These values made it possible to construct the weighted risk score with punctuated variables according to the magnitude of its effect, and significance was established at $p < 0.05$.

The resulting logistic model presents direct estimates of outcome occurrence probability. This process is understood as more appropriate to obtain event estimates, although it has a certain degree of mathematical complexity for its use in daily medical practice. The use of the logistic model is more adequate for the prognosis of individual risk, mainly in patients with a very high risk in the additive model.[17]

Statistical analyses were performed using SPSS, version 22.0 (Chicago, IL, USA) and R for Windows, version 3.4.2 (R Development Core Team – www.r-project.org).

Results

A sample of 4165 patients with coronary artery disease underwent CABG. Mean age was 61.7 (SD, 9.9 years), 2807 (67.4%) were men, and 783 (18.8%) required prolonged MV. Table 1 shows the univariate analysis of the clinical characteristics of patients who required prolonged MV vs those who did not require MV. A multiple logistic regression model was fitted to the development data set, which consisted of 2746 patients. Eighteen variables were included, which resulted in 6 independent predictors of prolonged MV remaining in the model, considering statistical significance and clinical relevance. The resulting predictors were urgent

or emergency surgery (OR, 2.94; 95% confidence interval [CI], 2.07-4.18), chronic kidney disease (OR, 2.00; 95% CI, 1.55-2.59), age ≥ 65 years (OR, 1.86; 95% CI, 1.52-2.26), cardiopulmonary bypass ≥ 120 minutes (OR, 1.92; 95% CI, 1.48-2.48), body mass index ≥ 30 kg/m² (OR, 1.71; 95% CI, 1.33-2.21), and chronic obstructive pulmonary disease (OR, 1.46; 95% CI, 1.13-1.87).

The performance of the development model was tested on the internal validation data set and showed an area under the ROC curve of 0.64 (95% CI, 0.60-0.68) and a Hosmer-Lemeshow chi-square goodness of fit of χ^2: 1.85 (p = 0.870). The Pearson's correlation coefficient between observed and predicted events was r = 0.98 (p < 0.001). A final model was obtained from combining the development and validation data sets that resulted in the estimates presented in Table 2. In the total sample data set, the area under the ROC curve was 0.66 (95% CI, 0.64-0.68; p < 0.001), the Hosmer-Lemeshow chi-square goodness of fit was χ^2: 3.38 (p = 0.642), and the Pearson's correlation coefficient between observed and predicted events was r = 0.99 (p< 0.001).

A final risk score was obtained for each patient by adding the points presented in Table 3. The resulting risk score was then classified into 4 levels: low (0 to 1 point), medium (2 to 4 points), high (5 to 7 points), and very high risk (8 or more points), representing different probabilities for prolonged MV (Table 4). Figure 1 represents the calibration of the logistic model, and Figure 2 shows the area under the ROC curve of the risk model's predictive capacity for prolonged MV for the total sample data set.

Discussion

This study identified 6 risk predictors of prolonged MV in a population of patients who underwent CABG: urgent or emergency surgery, age (≥ 65 years), chronic kidney disease, body mass index (≥ 30 kg/m²), cardiopulmonary bypass time (≥ 120 minutes), and chronic obstructive pulmonary disease were significantly associated with prolonged MV. A clinical practice instrument was developed from these predictors to calculate the risk of MV in patients undergoing CABG.

The score was developed according to the choice of variables based on scientific evidence[6,9,10] and data available from our database records. Statistical resources were used to validate the results and allowed the score to be classified as low, medium, high, and very high risk of prolonged MV according to the values obtained. Many

Table 1 - Clinical characteristics of patients underwent coronary artery bypass grafting surgery

Clinical characteristics	Total sample (n = 4,165)	Without Prolonged MV (n = 3,382)	With Prolonged MV (n = 783)	p
Age ≥ 65 years	1,694/4,163 (40.7%)	1,264/3,380 (37.4%)	430/783 (54.9%)	< 0.001[a]*
Male	2,807 (67.4%)	2,283 (67.5%)	524 (66.9%)	0.767[a]
Asthma	90 (2.2%)	72 (2.1%)	18 (2.3%)	0.785[a]
COPD	653 (15.7%)	494 (14.6%)	159 (20.3%)	< 0.001[a]*
Smoking	1,345 (32.3%)	1,143 (33.8%)	202 (25.8%)	< 0.001[a]*
BMI ≥ 30 kg/m²	629 (15.1%)	483 (14.3%)	146 (18.6%)	0.003[a]*
Diabetes	1,430 (34.3%)	1,128 (33.4%)	302 (38.6%)	0.006[a]
Hypertension	3,220 (77.3%)	2,589 (76.6%)	631 (80.6%)	0.016[a]
CKD	537 (12.9%)	368 (10.9%)	169 (21.6%)	< 0.001[a]*
Previous stroke	307 (7.4%)	225 (6.7%)	82 (10.5%)	< 0.001[a]*
Previous MI	1,985 (47.7%)	1,606 (47.5%)	379 (48.4%)	0.662[a]
LVEF ≤ 40%	3,317/4,147 (80.0%)	2,744/3,369 (81.5%)	573/780 (73.5%)	< 0.001[a]*
NYHA Class I	2,673/4,087 (65.4%)	2,239/3,313 (67.6%)	434/774 (56.1%)	
NYHA Class II	868/4,087 (21.2%)	681/3,313 (20.6%)	187/774 (24.2%)	
NYHA Class III	434/4,087 (10.6%)	326/3,313 (9.8%)	108/774 (14.0%)	< 0.001[b]*
NYHA Class IV	112/4,087 (2.7%)	67/3,313 (2.0%)	45/774 (5.8%)	
Previous CS	98 (2.4%)	78 (2.3%)	20 (2.6%)	0.695[a]
Urgent/emergency CS	223 (5.4%)	134 (4.0%)	89 (11.4%)	< 0.001[a]*
CPB ≥ 120 minutes	551 (13.2%)	395 (11.7%)	156 (19.9%)	< 0.001[a]*

MV: mechanical ventilation; COPD: chronic obstructive pulmonary disease; BMI: body mass index; MI: myocardial infarction; LVEF: left ventricular ejection fraction; CKD: chronic kidney disease; NYHA: New York Heart Association; CS: Cardiac surgery; CPB: cardiopulmonary bypass. * p < 0.05 was deemed statistically significant; [a] chi-square tests; [b] Fisher's test.

Table 2 – Predictor variables of prolonged mechanical ventilation in patients who underwent coronary artery bypass grafting in the total sample database

Predictor variables	OR	95% CI	p
Urgent/emergency surgery	2.79	2.09 – 3.73	< 0.001
CKD	1.98	1.61 – 2.44	< 0.001
Age ≥ 65 years	1.91	1.62 – 2.24	< 0.001
CPB ≥ 120 minutes	1.75	1.42 – 2.16	< 0.001
BMI ≥ 30 kg/m²	1.49	1.21 – 1.84	< 0.001
COPD	1.43	1.16 – 1.76	0.001

OR: odds ratio; 95% CI: 95% confidence interval; CKD: chronic kidney disease; CPB: cardiopulmonary bypass; BMI: body mass index; COPD: chronic obstructive pulmonary disease. p < 0.05 was deemed statistically significant.

Table 3 - Risk score of prolonged mechanical ventilation in patients who underwent coronary artery bypass grafting

Predictor variable	Score
Urgent/emergency surgery	3
CKD	2
Age ≥ 65 years	2
CPB ≥ 120 minutes	2
BMI ≥ 30 kg/m²	1
COPD	1

CKD: chronic kidney disease; CPB: cardiopulmonary bypass; BMI: body mass index; COPD: chronic obstructive pulmonary disease.

patients undergoing CABG have multiple comorbidities and require adequate treatment to eliminate or reduce the risk of prolonged MV. The identification of these variables and their adequate stratification may provide important elements for different strategies to be followed, which can result in a favorable hospital stay and contribute to the improvement of clinical outcomes.[9]

In the present study, the definition used for prolonged MV was 12 hours or more and the incidence was 18.8%, which is lower than the results of studies by Cislagui et al.,[9,10] with the same criteria for prolonged MV. Patients requiring MV of 12 hours or more, compared to those requiring less than 12 hours, had higher mortality and morbidity, and longer hospital stays[18]. Therefore, the prolonged period of MV can be a marker of great impact and considered a predictor variable of hospital death.[8] When the threshold used for prolonged MV was 48 hours or more, the incidence was lower, from 2.6% to 7.3%.[6,8,11] In some studies using the 24-hour parameter, the need

for prolonged MV ranged from 4.9 to 29.4%[19,20] in patients undergoing cardiac surgery. The main predictor variables for prolonged MV identified in the present study are in agreement with literature findings.[8,10,11,19,21]

Urgent or emergency surgery was considered the variable with the greatest impact on prolonged MV, obtaining the highest value in the proposed score, with an odds ratio of 2.79 (95% CI, 2.09-0.73), and this condition adds 3 points to the risk score. The need for an intra-aortic balloon or more intense circulatory support offers limited opportunities to optimize the preoperative period and may be responsible for the high morbidity of prolonged MV. This outcome after cardiac surgery can be accurately predicted by readily available pre- and intraoperative information.[6]

Chronic kidney disease in predicting prolonged MV was the second most relevant variable in the present study, with an odds ratio of 1.98 (95% CI, 1.61-2.44), and this condition adds 2 points to the risk score. Compared to other studies, this variable associated with prolonged MV shows high odds ratio values, ranging from 1.57 to 5.53, possibly related to different evaluation parameters. Patients with chronic kidney disease have other comorbidities, such as systemic atherosclerosis, diabetes and hypertension, which contribute to the increased risk of complications in surgical procedures.[6,8,10,21,22]

Regarding the variable age ≥ 65 years, we obtained in the present study an odds ratio of 1.91 (95% CI, 1.62-2.24), and this condition adds 2 points to the risk score, which was higher compared to other studies with values of 1.06[8] and 1.04.[21] Also, Fitch et al.,[23] found that for each additional year of age, patients were less likely to be extubated early. Totonchi et al.,[11] found no association between increased age and delayed extubation. It can be considered that in the aging process there is a reduced physiological reserve associated with the development of pulmonary complications and increased morbidity and mortality.[8,24]

Table 4 - Risk score classification of prolonged mechanical ventilation (MV) in patients who underwent coronary artery bypass grafting

Risk score	Sample	Prolonged MV		Classification
		n	%	
0 to 1	1,856	207	11.2	low
2 to 4	1,997	444	22.2	medium
5 to 7	290	120	41.4	high
8 or more	22	12	54.5	very high
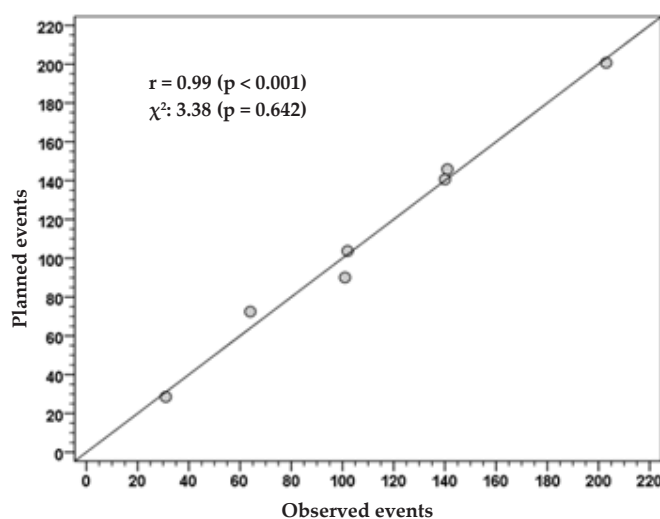
Figure 1 – Dispersion of points representing the outcome prolonged mechanical ventilation predicted and observed points
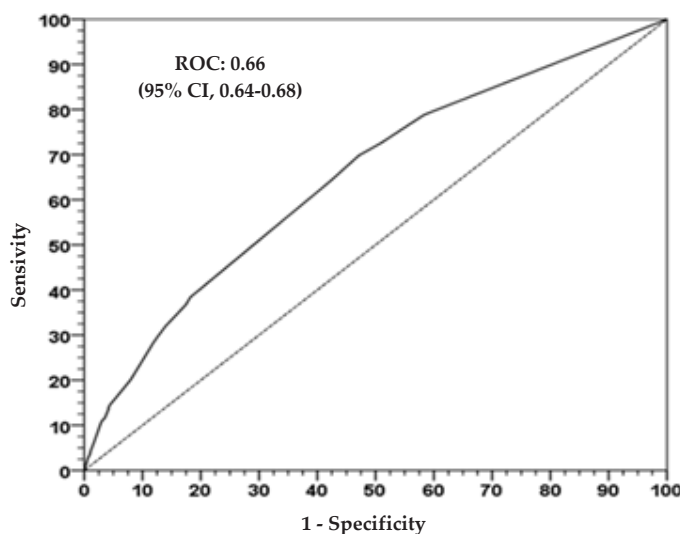
Figure 2 – Area under the Receiver Operational Characteristic (ROC) curve for predicting the occurrence of prolonged mechanical ventilation in the total data set

Cardiopulmonary bypass time was considered prolonged in our proposal (≥ 120 minutes), because beyond this limit, the complications inherent to procedure increase, and we obtained an odds ratio of 1.75 (95% CI, 1.42-2.16), condition that adds 2 points to the risk score. In view of the available data on prolonged cardiopulmonary bypass time in other studies, there are no differences regarding need for prolonged MV.[6,8,10] This technique provides an adequate surgical field, preserves functional characteristics of the heart, and provides safety for the surgical team, but when extubation is delayed, there is an increase in the intensity of inflammatory reactions and in the risk of respiratory problems.[5,19,25] Lung function and oxygenation are impaired in 20 - 90% of patients undergoing cardiac surgery with cardiopulmonary bypass.[26] Nozawa et al.,[27] consider that a cardiopulmonary bypass time greater than 120 minutes influences weaning from MV, and this is one of the factors that can increase surgical risk of patients.[27]

270

Dallazen-Sartori et al.
Prolonged mechanical ventilation risk score

Int J Cardiovasc Sci. 2021; 34(3):264-271
Original Article

Obesity classified as body mass index ≥ 30 kg/m² was also a predictor of prolonged MV with an odds ratio of 1.49 (95% CI, 1.21-1.84), and this condition adds 1 point to the risk score; a similar impact was found by Wigfield et al.,[22] A high body mass index possibly increases the risk of pulmonary complications due to restrictive changes,[28] increasing complexity of the surgical procedure and hindering postoperative pulmonary rehabilitation.[21] Obesity proved to be a risk factor for pulmonary embolism after cardiac surgery, a condition that increases the duration of mechanical ventilation.[29] The impact of obesity on prolonged MV, however, still needs further studies for better understanding.

Chronic obstructive pulmonary disease was the lowest impact variable in our study, with an odds ratio of 1.43 (95% CI, 1.16-1.76), and this condition adds 1 point to the risk score. Regarding literature data, we found similar values with odds ratios ranging from 1.45 to 2.65.[8,10] This disease is considered a prothrombotic condition due to increased blood viscosity and endothelial dysfunction, which may contribute to postoperative complications.[8,11,19]

Performance analysis of weighted risk scores showed an area under the ROC curve with the model's satisfactory ability to predict prolonged MV, in agreement with literature findings. [3,6,19]

Limitations

Our risk model was constructed and validated in a single institution, a large university hospital in southern Brazil. In addition, we evaluated the results of patients from the same geographical area and who may have peculiar and distinct characteristics compared to other regions of Brazil. Therefore, validation in an external population with new data from other institutions is important so that the score has wide clinical use and can predict prolonged MV to optimize care resources and reduce hospital stay and costs in patients undergoing CABG.

Implications

As the score is based on a clinical database, the system offers an estimate of surgical risk in the "real world". The score can be used to monitor deficiencies of the hospital facility, the multidisciplinary team (surgeon, anesthesiologist, and postoperative team), and of the surgical indication. The model is accurate enough to be routinely employed at Hospital São Lucas of PUCRS and to be tested with data from other institutions.

Conclusion

Preoperative predictors (urgent / emergency surgery, age ≥ 65 years, chronic kidney disease, body mass index (≥ 30 kg/m²), chronic obstructive pulmonary disease, and perioperative variable (cardiopulmonary bypass time (≥ 120 minutes) were associated with prolonged MV. This risk score could be useful to predict the risk of prolonged MV and allow classifying patients as low, medium, high, and very high-risk.

Author Contributions

Conception and design of the research: Dallazen-Sartori F, Guaragna JC, Bodanese LC. Acquisition of data: Dallazen-Sartori F, Guaragna JC, Magedanz EH, Bodanese LC. Analysis and interpretation of the data: Dallazen-Sartori F, Guaragna JC, Bodanese LC, Albuquerque LC, Wagner MB. Statistical analysis: Dallazen-Sartori F, Bodanese LC, Wagner MB. Writing of the manuscript: Dallazen-Sartori F, Guaragna JC, Bodanese LC, Wagner MB. Critical revision of the manuscript for intellectual content: Dallazen-Sartori F, Guaragna JC, Magedanz EH, Petracco JB, Bodanese R, Bodanese LC.

References

1. Branca P, McGaw P, Light RW. Risk factors associated with prolonged mechanical ventilation following coronary artery bypass surgery. Chest. 2001;119(2):537-46.

2. Rajakaruna C, Rogers CA, Angelini GD, Ascione R. Risk factors for and economic implications of prolonged ventilation after cardiac surgery. J Thorac Cardiovasc Surg. 2005;130(5):1270-7.

3. Reddy S, Grayson AD, Griffiths EM, Pullan DM, Rashid A. Logistic risk model for prolonged ventilation after adult cardiac surgery. Ann Thorac Surg. 2007;84(2):528-36.

4. Cohen AJ, Katz MG, Frenkel G, Medalion B, Geva D, Schachner A. Morbid results of prolonged intubation after coronary artery bypass surgery. Chest. 2000;118(1):1724-31.

5. Cordeiro AL, de Melo TA, Santos AM, Lopes GF. Time influence of mechanical ventilation on functional independence in patients submitted to cardiac surgery: literature review. Fisioter Mov. 2015;28(4):859-64.

6. Sharma V, Rao V, Manlhiot C, Boruvka A, Fremes S, Wąsowicz M. A derived and validated score to predict prolonged mechanical ventilation in patients undergoing cardiac surgery. J Thorac Cardiovasc Surg. 2016;153(1):108-15.

7. Mehaffey JH, Hawkins RB, Byler M, Charles EJ, Fonner C, Kron I, et al. Cost of individual complications following coronary artery bypass grafting. J Thorac Cardiovasc Surg. 2018;155(3):875-82.

8. Piotto, RF, Ferreira FB, Colósimo FC, da Silva GS, de Sousa AG, Braile DM. Independent predictors of prolonged mechanical ventilation after coronary artery bypass surgery. Rev Bras Cir Cardiovasc. 2012;27(4):520-8.

9. Cislaghi F, Condemi AM, Corona A. Predictors of prolonged mechanical ventilation in a cohort of 3,269 CABG patients. Minerva Anestesiol. 2007;73(12):615-21.

10. Cislaghi F, Condemi AM, Corona A. Predictors of prolonged mechanical ventilation in a cohort of 5123 cardiac surgical patients. Eur J Anaesthesiol. 2009;26(5):396-403.

11. Totonchi Z, Baazm F, Chitsazan M, Seifi S, Chitsazan M. Predictors of prolonged mechanical ventilation after open heart surgery. J Cardiovasc Thorac Res. 2014;6(4):211-6.

12. Wang C, Zhang GX, Lu FL, Li BL, Zou LJ, Han L, et al. A local risk prediction model for prolonged ventilation after adult heart valve surgery in a Chinese single center. Heart Lung. 2012;42(1):13-8.

13. Sociedade Brasileira de Cardiologia. Comitê Coordenador da Diretriz de Insuficiência Cardíaca. Diretriz Brasileira de Insuficiência Cardíaca Crônica e Aguda. Arq Bras Cardiol. 2018;111(3):436-539.

14. World Health Organization. (WHO) Obesity: preventing and managing the global epidemic. Report of a WHO consultation on obesity. Geneva; 1998.

15. Wellman NS. The Nutrition Screening Initiative. Nutr Rev. 1994;52(8Pt2):S44-S47.

16. Guaragna JCVC, Bodanese LC, Goldani MA. Proposed Preoperative Risk Score for Patients Candidate to Cardiac Valve Surgery. Arq Bras Cardiol 2010; 94(4):507-14

17. Zingone B, Pappalardo A, Dreas L. Logistic versus additive EuroSCORE. A comparative assessment of the two models in an independent population sample. Eur J Cardiothorac Surg. 2004; 26(6):1134-40.

18. Crawford TC, Magruder JT, Grimm JC, Sciortino C, Conte JV, Kim BS, et al. Early extubation: a proposed new metric. Semin Thorac Cardiovasc Surg. 2016;28(2):290-9.

19. Widyastuti Y, Stenseth R, Pleym H, Wahba A, Videm V. Pre-operative and intraoperative determinants for prolonged ventilation following adult cardiac surgery. Acta Anaesthesiol Scan. 2012;56(2):190-9.

20. Hefner JL, Tripathi RS, Abel EE, Farneman M, Galloway J, Moffatt-Bruce SD. Quality improvement intervention to decrease prolonged mechanical ventilation after coronary artery bypass surgery. Am J Crit Care. 2016;25(5):423-30.

21. Saleh HZ, Shaw M, Al-Rawi O, Yates J, Pullan DM, Chalmers JA, et al. Outcomes and predictors of prolonged ventilation in patients undergoing elective coronary surgery. Interact Cardiovasc Thorac Surg. 2012;15(1):51-6.

22. Wigfield CH, Lindsey JD, Munõz A, Chopra PS, Edwards NM, Love RB. Is extreme obesity a risk factor for cardiac surgery? An analysis of patients with a BMI ≥40. Eur J Cardiothorac Surg. 2006; 29(4):434-40.

23. Fitch ZW, Debesa O, Ohkuma R, Duquaine D, Steppan J, Schneider EB. A protocol-driven approach to early extubation after heart surgery. J Thorac Cardiovasc Surg. 2014;147(4):1344-50.

24. Britto RR, Viera DSR, Rodrigues JM, Prado LF, Parreira VF. Comparação do padrão respiratório entre adultos e idosos saudáveis. Rev Bras Fisioter. 2005;9(3):281-7.

25. Reddy SLC, Grayson AD, Oo AY, Pullan MD, Poonacha T, Fabri BM. Does off-pump surgery offer benefit in high respiratory risk patients? A respiratory risk stratified analysis in a propensity-matched cohort. Eur J Cardiothorac Surg. 2006;30(1):126-31.

26. Dyhr T, Laursen N, Larsson A. Effects of lung recruitment maneuver and positive end-expiratory pressure on lung volume, respiratory mechanics and alveolar gas mixing in patients ventilated after cardiac surgery. Acta Anaesthesiol Scand. 2002;46(6):717-25.

27. Nozawa E, Kobayashi E, Matsumoto ME, Feltrim MIZ, Carmona MJC, Auler Júnior JOC. Evaluation of factors that influence the weaning of patients on prolonged mechanical ventilation after cardiac surgery. Arq Bras Cardiol. 2003;80(3):301-10.

28. Qaseem A, Snow V, Fitterman N, Hornbake ER, Lawrence VA, Smetana GW, et al; Clinical Efficacy Assessment Subcommittee of the American College of Physicians. Risk assessment for and strategies to reduce perioperative pulmonary complications for patients undergoing noncardiothoracic surgery: a guideline from the American College of Physicians. Ann Intern Med. 2006;144(8):575-80.

29. Guaragna LP, Dall'Alba DP, Goulart PR, Guaragna JCVC, Bodanese LC, Magedanz EH, et al. Impact of obesity in morbity and mortality of patients submitted to myocardial revascularization surgery. Sci Med. 2008;18(2): 75-80.

EDITORIAL

Prolonged Ventilation after CABG: an Important Issue

Leonardo Secchin Canale

Instituto Nacional de Cardiologia, Rio de Janeiro, RJ – Brazil
Editorial referring to the article: Risk Score for Prolonged Mechanical Ventilation in Coronary Artery Bypass Grafting

Coronary artery bypass surgery (CABG) is the most commonly performed heart operation in most countries, and its mortality and morbidity results are one of the most studied and scrutinized in the world. As a large operation involving long surgical times, sternotomy and cardiopulmonary bypass, long-term postoperative ventilation is a dreaded possible complication. Failure to wean from the ventilator can result both as a consequence of previous risk factors and as a cause of future morbidity and mortality. Not only it impacts patients' well-being and recovery times, but also can lead to further complications such as lung infections, sepsis, loss of general muscle function and need for tracheostomy.[1]

Therefore, the current study of Dallazen-Sartori et al.[2] is a timely and useful attempt to better characterize the incidence and risk factors for the development of prolonged ventilation (PV) after CABG. As previous authors did before, the authors focus on preoperative and per-operative factors to try to expose, by multiple logistic regressions, which ones are causally associated to PV in order to construct a practical Risk Score. It is needless to stress the importance of such a study in our Brazilian population, which might behave differently from well-known previous reports[3] from other countries. Unfortunately, we still face a paucity of local and regional studies that would better represent our own results, outcomes and challenges. The situation when we need to base our decisions in external sources of data instead of using the national one happens very often. The current study by Dallazen-Sartori et al,[2] is an attempt to change that.

Keywords

Thoracic Surgery, Coronary Artery Bypass Surgery, Mechanical Ventilation, Grafting; Risk Factors.

The first aspect we should notice in the actual study is that PV is defined as longer than 12 hours of mechanical ventilation after arrival in the ICU. There is a divergence of definition in the current literature as to what constitutes "prolonged" need for ventilation. While the references provided by the authors indeed use 12 hours as the limit for PV definition, others[1-3] and the STS database use the threshold of 24 hours. By "lowering the bar" for the outcome studied, it will most certainly increase its incidence (in this study 18.8%) and we should keep that in mind when comparing results with previous studies. The advantage to utilize the 12-hour hallmark is that it may better represent the threshold where mortality and prolonged length of stay starts to climb.[4] Therefore, it has a strong case to be viewed as a quality mark of our operations.

Possible risk factors elected by the authors to be investigated were adequately based in previous reports. The total number of patients included in this analysis (4,165 patients) is much larger than in many other studies conferring a great advantage on the power to draw sound conclusions. The time frame of observation used, over 20 years, was probably needed to achieve the present large cohort. It should be noted that such a wide period of observation might result in two different phenomena. On one hand, it avoids a time period bias (by precluding a too short period of observation when events could be mistakenly represented). On the other hand, by including the operation performed almost 24 years ago, it might have included scenarios and practices of extra-corporeal bypass circulation use and postoperative critical care that are no more in vogue today.

While many studies[1,3-5] limit themselves to describe risk factors and their respective Odd Ratios to the PV outcome, Dallazen-Sartori et al,[2] went a step further to empirically create a practical risk score and validated it with its own population. This was previously performed

Mailing Address: Leonardo Secchin Canale
Rua das Laranjeiras, 374. Postal Code: 22240-006, Rio de Janeiro, RJ – Brazil.
E-mail: leonardo.canale@gmail.com

by Legaré et al.[6] 20 years ago when a simple additive risk score could predict a patient being ventilated for more than 24h with moderate precision. Differently from this Canadian previous risk score, Dallazen-cols.[2] were able to instill different weights to different risk factors and also present us with a ROC curve.

The six risk factors that emerged as independent predictors of PV from the multiple logistic regression model are sound and in accordance with previous studies in this theme. The construction of an additive risk score could easily differentiate four different risk groups. The current risk score should be tested by other institutions, which may behave slightly differently and start to become part of the preoperative evaluation of patients deemed candidates for CABG. One should notice that, when used in the preoperative setting, all but one variable (Bypass time) will be available for evaluation. The appropriate preop estimation on the risk of PV can affect our expectations and resource utilization of the postoperative period and even make us reconsider the decision to go on with the operation (in elective cases). It could be useful for clinicians and surgeons dealing with individual patients and possibly to ICU administrators in evaluating the quality of surgical and ventilation specific care.

References

1. Gumus F, Polat A, Yektas A, Totoz T, Bagci M, Erentug V, et al. Prolonged mechanical ventilation after CABG: risk factor analysis. J Cardiothorac Vasc Anesth. 2015 Feb;29(1):52-8. doi: 10.1053/j.jvca.2014.09.002.

2. Dallazen-Sartori F, Albuquerque LC, Guaragna JCVC, Magedanz EH, Petracco JB, Bodanese R, et al. Risk Score for Prolonged Mechanical Ventilation in Coronary Artery Bypass Grafting. Int J Cardiovasc Sci.2021;34(3):264-271.

3. Wise ES, Stonko DP, Glaser ZA, Garcia KL, Huang JJ, Kim JS, et al. Prediction of Prolonged Ventilation after Coronary Artery Bypass Grafting: Data from an Artificial Neural Network. Heart Surg Forum. 2017 Feb 24;20(1): E007-E014. doi: 10.1532/hsf.1566.

4. Crawford TC, Magruder JT, Grimm JC, Sciortino C, Conte JV, Kim BS, et al. Early Extubation: A Proposed New Metric. Semin Thorac Cardiovasc Surg. 2016 Summer;28(2):290-299. doi: 10.1053/j.semtcvs.2016.04.009.

5. Branca P, McGaw P, Light R. Factors associated with prolonged mechanical ventilation following coronary artery bypass surgery. Chest. 2001 Feb;119(2):537-46. doi: 10.1378/chest.119.2.537.

6. Légaré JF, Hirsch GM, Buth KJ, MacDougall C, Sullivan JA. Preoperative prediction of prolonged mechanical ventilation following coronary artery bypass grafting. Eur J Cardiothorac Surg. 2001 Nov;20(5):930-6. doi: 10.1016/s1010-7940(01)00940-x.

Athletes Health during Pandemic Times: Hospitalization Rates and Variables Related to COVID-19 Prevalence among Endurance Athletes

Fabricio Braga da Silva,[1,2] Beatriz Fonseca,[1] Fernanda Domecg,[1] Marcelo Riccio Facio,[1] Christiane Prado,[1] Leandro Toledo,[1] Walter Tuche[3]

Laboratório de Performance Humana (LPH),[1] Rio de Janeiro, RJ – Brazil.
Casa de Saúde São José,[2] Rio de Janeiro, RJ – Brazil.
Walter Tuche Assessoria Esportiva,[3] Rio de Janeiro, RJ – Brazil.

Abstract

Background: The SARS-COV2 pandemic has deeply affected the availability for training and competing for recreational and professional athletes. However, to date, the disease's course among the athletic population has not been *studied .

Objectives: To compare the observed and expected rates of hospitalization for COVID-19 and to establish relationships between demographics and sportive characteristics of an athletic sample, and the COVID-19 infection rate.

Material and Methods: This study uses cross-sectional data sampling through an online questionnaire to collect data from recreational and professional athletes. Based on self-reports, athletes were grouped in COVID-19 and Non-COVID-19 cases. To decrease detection bias for each four patients who reported being hospitalized, one additional virtual patient was added to the sample. The observed rate of hospitalization (ORH) was compared with age expected rate of hospitalization (ERH) from the literature data. A multivariate model (MM) was developed to establish independent relationships between the prevalence of COVID-19 cases and the variables mentioned above. The statistical significance level was defined for a p-value<0.05.

Results: Answers from 1,701 individuals were analyzed. The COVID-19 group was comprised of 99 (5.8%) individuals, four of whom reported having been hospitalized. ORH and ERH were respectively of 5.0% and 18.1% (p=0.001). In the MM female gender (OR=2.02, 95% CI 1.28 to 3.19), cycling (OR=2.91, 95% CI 1.58 to 5.39), swimming (OR=2.97, 95% CI 1.14 to 7.74), and triathlon (OR=2.10, 95% CI 1.13 to 3.91) were independently associated with a COVID-19 prevalence.

Conclusion: Self-reported rates of hospitalization for COVID-19 among athletes were much lower than expected. The prevalence of positive cases of COVID-19 was independently higher for cyclists, triathletes, and swimmers than for runners. (Int J Cardiovasc Sci. 2021; 34(3):274-283)

Keywords: COVID-19; Betacoronavirus, SARS-COV-2, Athletes; Exercise; Motor Activity; Hospitalization.

Introduction

Even before the SARS-COV2 pandemic had been declared by the World Health Organization (WHO), professional and recreational sportive events had already been cancelled worldwide. For the first time since the World War II, the Tokyo 2020 Olympic Games is at the top of this long list.[1]

Not only was competitive athletic life compromised, but the adoption of social distancing as countermeasure for SARS-COV2 spread, deeply affecting their availability to train due to the closing of indoors sport facilities and, in some places, even the prohibition of any kind of outdoor workout.[2,3]

While this paper is being written, the total number of COVID-19 cases worldwide has already surpassed

6 million individuals, with almost 400,000 deaths. The USA is the most highly affected country (more than 1.8 million cases), followed by Brazil (more than a half million cases).[4] Scientific production on COVID-19 has also increased as never before. More than 4,000 papers have already been published in the first five months of 2020, registered under the medical subheading "coronavirus infection".[5] Among these are a wide range of reviews, opinions, and letters, which approach the effects of the pandemic among athletes. However, to the best of our knowledge, no original article has addressed this subject so far.

There is a biological plausibility that athletes cardiorespiratory fitness is a protective feature against severe forms of COVID-19.[6-8] By contrast, the high intensity exercise usually performed by endurance athletes increases the rates of upper respiratory tract infection (URTI).[9] In this new environment, we do not know if one of these two statements will prevail.

Sports organizations worldwide have been discussing the right moment to return to their competitions.[10] Good practice protocols are being developed. Pre-participation screening for post COVID-19 athletes has also been published.[11-13] The knowledge used in the establishment of these guidelines stems from experts' opinions, scarce information about previous coronavirus outbreaks, and some analogies made with other viral respiratory infections. To date, no specific knowledge has been developed.

Understanding the course of COVID-19 among the athletic population is of utmost importance in order to guide decision-making at individual and community levels, regarding exercise and sportive activities.

The primary goal of this research is to compare the observed and the expected rates of hospitalization for COVID-19 in an athletic sample.

The secondary goal is to establish relationships between demographics and sportive characteristics of an athletic sample, and the COVID-19 infection rate.

Materials and Methods

A cross-sectional data sampling (snowball sampling)[14] was started by initially 78 out of 152 seeds, comprised of athletes and coaches belonging to the authors' (B.F. and E.G.) personal relationship. A google form link was sent by WhatsApp messaging, with a note explaining the importance of taking part in the survey and asking

receivers to share it with other athletes and coaches. Every five days another 20 seeds were reached using the same process until the required number of COVID-19 cases was met. As soon as the target sample size was reached, the sending of the form was discontinued.

The questionnaire was developed specially for this survey, using simple language, and took 5 to 7 minutes to be fully completed. Before the first question, individuals had to read and accept the informed consent form. The first question was *"Are you an endurance athlete? We consider an endurance athlete to be an individual who performs such sports as running, cycling, rowing, canoeing, triathlon, swimming, and workout 3 or more times per week with the goal of improving his sports performance"*.[15,16] Only the response "*Yes*" allowed the participant to continue the questionnaire. After some demographic and sports practice questions, individuals were sent to COVID-19 questions. The first one was "*Did you have COVID-19?*". Three possibilities of answer were offered: "*Yes, confirmed by laboratorial tests*"; "*No, I did not*"; or "*Maybe. I had COVID-19-like symptoms but didn't get to test for it*". The latter option was followed by the question *"In the list below, choose all the symptoms you presented"*. The list of symptoms represented the COVID-19-like symptoms score created by the Mozambique ministry of health and adapted by a Brazilian university.[17] The score is composed by the sum of the positive signs and symptoms: fever (5 points), headache (1 point), coryza and sneezes (1 point), sore throat (1 point), dry cough (3 points), breathlessness (10 points); malaise (1 points); diarrhea (1 point); loss of smell (3 points); any contact with individual previous diagnosis for COVID-19 (10 points). Three outputs were possible: High suspicion (≥20 points), Moderated suspicion (10 to 19 points), and Low suspicion (≤9 points).

The COVID-19 group consisted of athletes with reported laboratorial confirmation for COVID-19 and those with highly suspicious symptoms. All the others were included in the Non-COVID-19 group. The reason to include cases without reported laboratorial confirmation is the low availability of tests in Brazil.

Except for those who reported not having COVID-19, all others were guided to the question *"Were you hospitalized for COVID-19?"*. For those who answered *"Yes"*, the next question was *"Were you admitted to the Intensive Care Unit?"*.

As self-filling questionnaires were not able to detect lethal cases, we estimated based on local and literature

276

Silva et al.
Athletes health during pandemic times

Int J Cardiovasc Sci. 2021; 34(3):274-283

Original Article

data an in-hospital mortality of 20%. Considering the same mortality rate among athletes, to decrease this sampling bias, for every 4 patients who reported having been hospitalized, one additional virtual patient was added.

Based on the Center of Disease Control (CDC),[18] for each individual, a probability of hospitalization was attributed, based on the age group he belonged to. The lower limit of confidence interval was used to avoid the overestimation of an expected hospitalization rate. Thus, the following expected rates of hospitalization were used: 1.6% for <20 years old (yo), 2.5% for 20-29 yo, 14.3% for 30-39 yo, 20.8% for 40-49 yo, 21.16% for 50-59 yo, and 22.4 for ≥60 yo. The average value for the COVID-19 group was the expected hospitalization rate. Two comparisons were performed: one for all COVID-19 groups and another only for the reported cases confirmed by a laboratory.

The prevalence for COVID-19 (positive tests and highly suspicious symptoms) were compared by gender, age group, Brazilian geographic regions, athletic level, and type of sport.

Statistical Analysis and Ethics

The sample size was calculated by estimating 10% and 20% for observed and expected hospitalization rates, respectively. A power of 80% and an alfa error of 5% were assumed, using a single proportion test based on the normal approximation to the binomial distribution.[19] According to these parameters, a sample size of 86 COVID-19 cases was necessary.

Categorical variables were expressed as absolute values and percentages. Observed hospitalization rates were compared with the expected value (used as the null hypothesis value) by the test for one proportion. The 95% confidence interval (CI) for the observed hospitalization rate was calculated using three different techniques.[20,21] To stress the difference between the observed and expected rates of hospitalization, a same size simulated sample was created using the expected number of COVID-19 and non-COVID-19 cases and compared using the Chi-squared test.[22] All other proportions were compared using the Chi-squared or Fisher's exact tests. CI for zero proportions were calculated according to the Hanley et al.[23] method.

A multivariate logistic model was developed using positive a COVID-19 case as a dependent variable, and gender, age group, athletic level, sport, and geographic region as independent variables. Variables were included in the model when their p-value was ≤5% based on chi-

squared statistics, except for the age group, which was included despite statistical significance because of its acknowledged epidemiological value.

Variables were considered statistically significant when having a p-value below 5%. All of the analysis was performed using an SPSS™ version 22.0 for Windows™ (Statistical Package for Social Sciences, IBM SPSS, IL, USA).

This research is registered in the National Committee for Ethical Research (CONEP), logged under protocol number 32179220.3.0000.5253 (https://plataformabrasil.saude.gov.br/login.jsf). Ethical approval for this study was obtained from *Hospital Federal de Bonsucesso* (approval number 4.054.651).

Results

Figure 1 represents the individuals included in the analysis. The questionnaire was released on May 10, 2020, and was closed in May 25, 2020, having collected 1,869 answers. After removing duplicate answers and missing data. 1,701 answers could be related to a single athlete. Among them 99 (5.8%) athletes were included in the COVID-19 group (70 laboratory-confirmed cases and 29 highly suspicious cases) and 1,602 (%) in the non-COVID-19 group. Twenty of the 26 states and federal district were represented in this sample (Figure 2). Table 1 shows the distribution of gender, athletic level, age group, sport, and country's geographic region for all athletes, the COVID-19 group, and the non-COVID-19 group.

For the hospitalization analysis, as four athletes reported having been hospitalized (one cyclist and three triathletes), one virtual case was added to the analysis, thus achieving the rate of a 5% need for hospitalization among athletes. Based on NYC rates of hospitalization by age, the average expected hospitalization rate was 18.1±4.6% (SE of mean=0.46%) for the COVID-19 group. Figure 3-A shows the comparison between the expected and the three different types of 95% CI calculation for the observed rate of hospitalization (p=0.001). Even considering only the 70 laboratory-confirmed positive cases, the expected rate of hospitalization was significantly higher than that observed (Figure 3-B).

A 2x2 Chi-square analysis comparing the observed and expected hospitalization rates showed significant differences either for the entire Covid-19 group (expected-observed=13.1%[95% CI 4.26 to 22.23%], p=0.003) as compared to the laboratory-confirmed cases (expected-observed=11.5%[95% CI 0.354 to 22.78%], p=0.046).
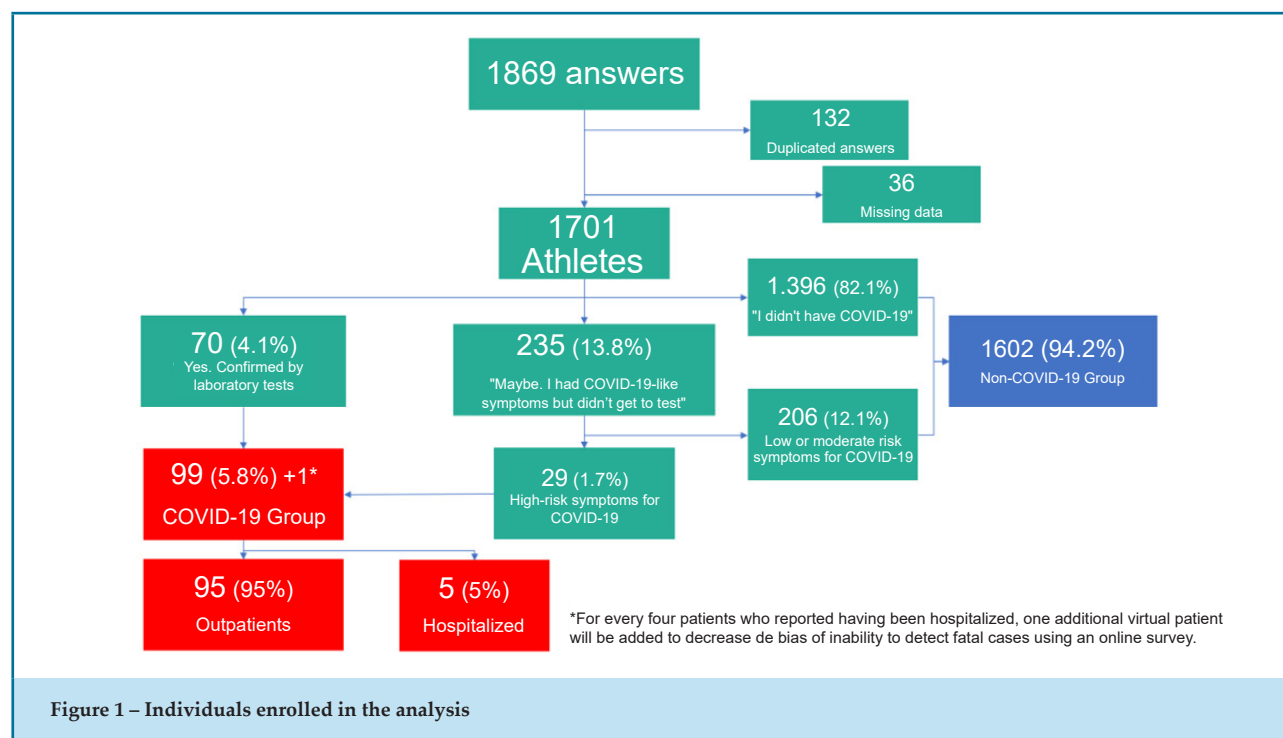
Figure 1 – Individuals enrolled in the analysis
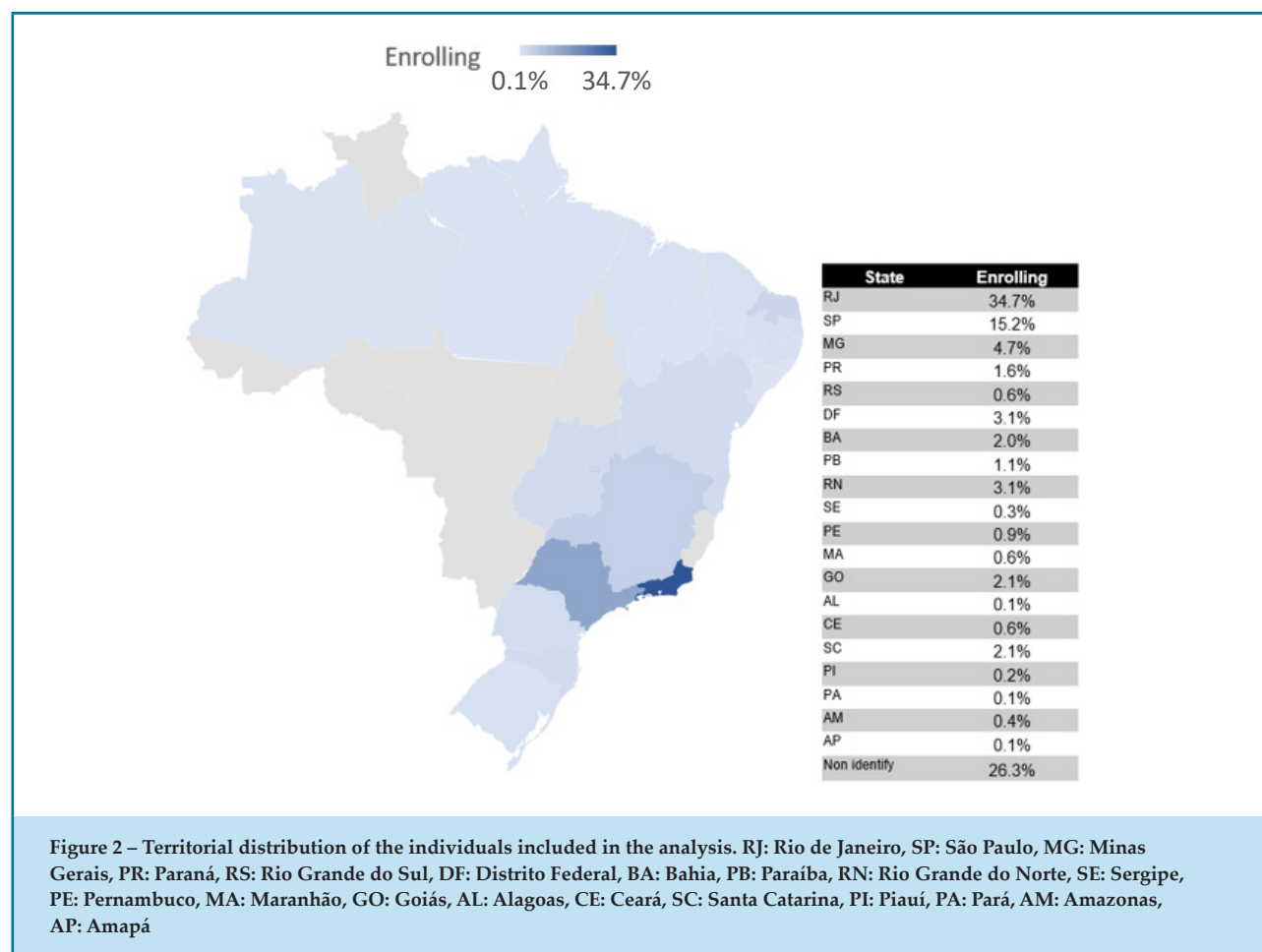
Figure 2 – Territorial distribution of the individuals included in the analysis. RJ: Rio de Janeiro, SP: São Paulo, MG: Minas Gerais, PR: Paraná, RS: Rio Grande do Sul, DF: Distrito Federal, BA: Bahia, PB: Paraíba, RN: Rio Grande do Norte, SE: Sergipe, PE: Pernambuco, MA: Maranhão, GO: Goiás, AL: Alagoas, CE: Ceará, SC: Santa Catarina, PI: Piauí, PA: Pará, AM: Amazonas, AP: Amapá

278

Silva et al.
Athletes health during pandemic times

Int J Cardiovasc Sci. 2021; 34(3):274-283
Original Article

Table 1 – Distribution of the individuals included in the analysis				
Name		Total (%)	Non-COVID-19 (%)	COVID-19 (%)
	N	1701	1602	99
Gender	Male	1181(69.4)	1124(95.2)	57(4.8)
	Female	520(30.6)	478(91.9)	42(8.1)
Sport	Running	516(30.3)	495(95.9)	21(4.1)
	Cycling	460(27)	423(92)	37(8)
	Swimming	73(4.3)	66(92.4)	7(9.6)
	Rowing/Canoeing	69(4.1)	68(98.6)	1(1.4)
	Triathlon	551(32.4)	518(94)	33(6)
	Others	32(1.9)	32(100)	0(0)
Age Group	< 20y	42(2.5)	42(100)	0(0)
	20-29y	121(7.1)	117(96.7)	4(3.3)
	30-39y	521(30.6)	489(93.9)	32(6.2)
	40-49y	631(37.1)	592(93.8)	39(6.2)
	50-59y	308(18.1)	291(94.5)	17(5.5)
	≥ 60y	78(4.6)	71(91)	7(9)
Regions	Southeast	930(54.7)	849(91.3)	81(8.7)
	South	73(4.3)	72(98.6)	1(1.4)
	Central	88(5.2)	88(100)	0(0)
	North-Northeast	162(95.9)	153(94.4)	9(5.6)
Athletic level	Amatheur	1632(95.9)	1535(94.1)	97(5.9)
	Professional	69(4.1)	67(97.1)	2(2.9)

Figures 4 A-E represent the intragroup comparisons for COVID-19 prevalence. Differences were found by gender (4.8 and 8.1%, respectively, for males and females; p=0.008); geographic region (8.7, 1.4, 0.0, and 5.6, respectively. for the Southeast, South, Midwest, and North/Northeast; p=0.003) and sport (4.1, 8.0, 9.6, 1.4, 6.0, and 0.0%, respectively, for running, cycling, swimming, rowing or canoeing, triathlon, among others) but not for age group or athletic level.

Table 2 shows the multivariate analysis for COVID-19 prevalence. The male gender, southeast region, running and age group ≥ 60 yo were used as reference categories for gender, geographic region, sport, and age group variables, respectively. After adjustment, the female gender (OR=2.02 95% CI 1.28 to 3.19), cycling (OR=2.91 95% CI 1.58 to 5.39), swimming (OR=2.97 95% CI 1.14 to 7.74), and triathlon (OR=2.10 95% CI 1.13 to 3.91) were independently associated with COVID-19 prevalence.

Discussion

In this research, the rate of observed hospitalization for COVID-19 was less than half of the expected rate. Cardiorespiratory fitness has already proven beneficial in myriads of diseases,[24,25] and it could be used as immunity protection until a vaccine is developed.[26] Regarding infectious diseases, exercise capacity is associated with reduction on morbidity and mortality in situations ranging from seasonal URTI[27] to post-operative complications resulting from major surgeries.[28]

Cardiorespiratory fitness has already shown benefits during viral outbreaks. Siu et al.[29] demonstrated that

Figure 3 – Expected and observed hospitalization rates for: A-all considered positive cases, and B-only laboratory confirmed cases

Figure 4 – Positives cases of COVID-19 per A-Gender; B-Athletic level; C-Age group; D-Geographic group and E-Sports
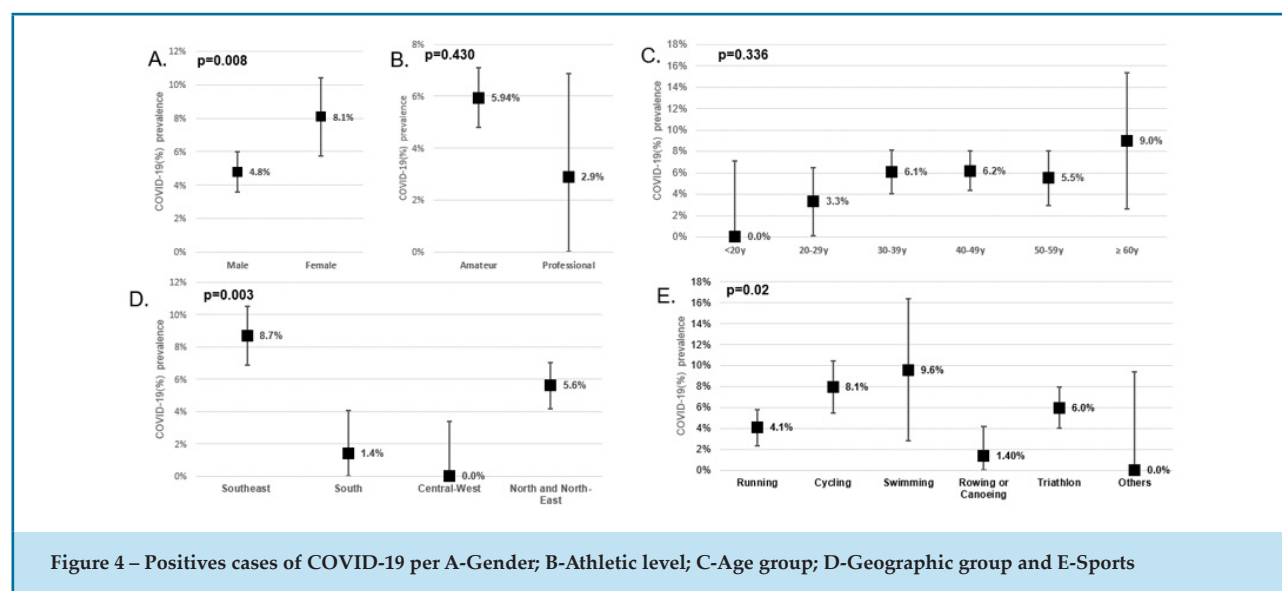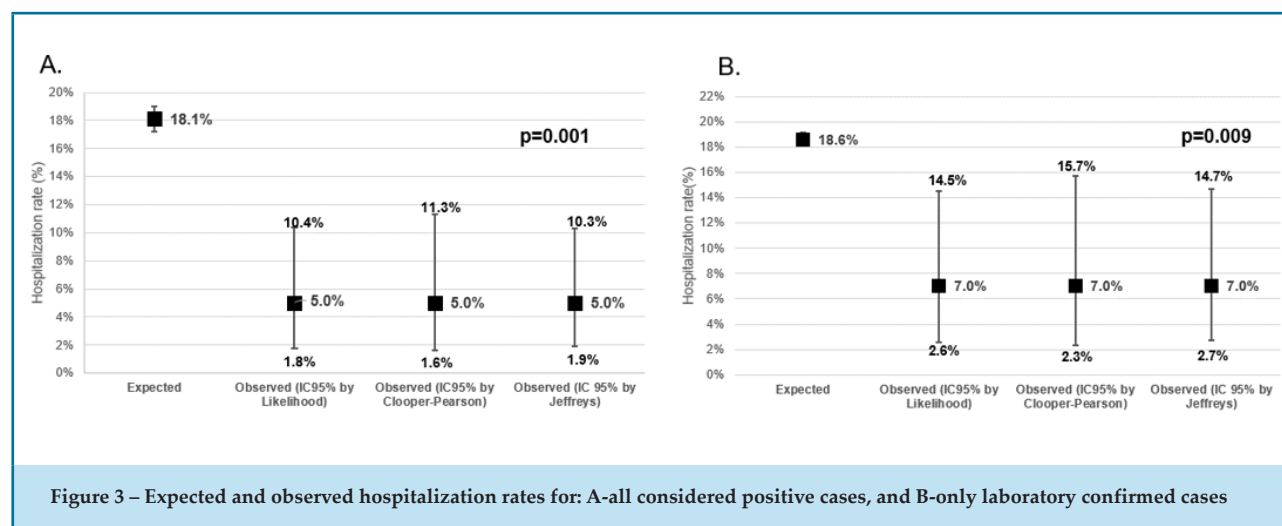
during 12 influenza seasons in Canada, moderately and highly active individuals younger than 65 yo had, respectively, 17% and 13% less outpatient visits for flu-like-symptoms than did their non-active counterparts. Wong et al. showed a 4.2% to 6.4% reduction in mortality by H1N1 and H3N1 influenza subspecies in the 1998 Hong-Kong outbreak.[30]

Despite the potential immunological infection windows described in athletes after high intensity training and competitions,[31,32] increasing the rate of URTI, there is no report of associating it to hard clinical endpoints. Indeed, there is some evidence that viral illnesses have little impact on training availability.[33,34]

Master athletes also have immunological benefits and documented reductions in respiratory infection rates.[35] Minuzzi et al. showed that senior athletes (mean age 53.2 yo) keep high cell and humoral post-exercise anti-inflammatory activity when compared to the controls.[36] Therefore, in a wide range of performance levels and ages, being an athlete seems to decrease the risk of respiratory infections, such as COVID-19, by approximately 28%.[26]

The prevalence of COVID-19 cases were 2 times higher among female athletes. Previous studies have already shown gender differences in terms of URTI in the athletic population. He et al. demonstrated that the number of respiratory illness days was higher (4.7 vs 6.8 days, p=0.02) and the duration of these episodes

280

Silva et al.
Athletes health during pandemic times

Int J Cardiovasc Sci. 2021; 34(3):274-283
Original Article

Table 2 – Multivariate analysis for COVID-19 prevalence				
	p value	OR	95% C.I	
			Lower bound	Upper bound
Gender				
Male		1.00		
Female	0.003	2.02	1.28	3.19
Region				
Southeast	0.28	1.00		
South	0.097	0.18	0.03	1.36
Midwest	1.00	0.00	0.00	
North and Northeast	0.255	0.65	0.31	1.36
Sport				
Running	0.01	1.00		
Cycling	0.001	2.91	1.58	5.39
Swimming	0.03	2.97	1.14	7.74
Rowing/Canoeing	0.443	0.45	0.06	3.48
Triathlon	0.02	2.10	1.13	3.91
Others	0.998	0.00	0.00	
Age Group				
≥ 60y	0.68	1.00		
50-59y	0.998	0.00	0.00	
40-49y	0.14	0.33	0.08	1.41
30-39y	0.365	0.65	0.26	1.65
20-29y	0.43	0.69	0.28	1.70
< 20y	0.191	0.52	0.20	1.39
Constant	0.00	0.06		

was longer (11.6 vs 15.5 days, p=0.03) in female than in male athletes. Although, the reasons behind it are not completely elucidated, it seems to be related to a decrease in oral-respiratory mucosal immunity.[37]

The differences in prevalence of COVID-19 positive case among sport modalities is a more complex subject. In this sample cycling, swimming and triathlon increased the odds of a COVID-19 case by 2 to 3-fold, when compared to running.

Nieman et al. compared the inflammatory and immunological response after three days of controlled overreaching between cyclists and runners, and their

impact in the URTI rate.[38] Despite a higher clinical and laboratory muscle damage and inflammatory response, no difference was found either in terms of frequency or in terms of severity of URTI. Williams et al. analyzed a cohort of more than 150,000 runners and walkers.[39] After a mean follow-up of 11.4 years, for each MET-hour/day increment in energy expenditure, a 10.5% reduction in pneumonia-related death was found. Although it cannot be affirmed that the sole effect is the result of running, we were unable to find any equivalent evidence for other sports.

As proposed by Gałązka-Franta et al., multiple factors are involved in the sport risk of respiratory infection.[40]

Inter-player relationships are one of the most important. This aspect during the pandemic time may well show how athletes and sportsmen complied to social distancing.

Measuring social distancing adherence is a difficult task. Even more complex is quantifying it among athletes. Google Mobility Reports, data regarding location tracking from mobile devices, is the closest one can come to a pattern of social distancing behavior in a specific community. Analyzing the mobility trends for potential exercise locations (national parks, public beaches, marinas, dog parks, plazas, and public gardens) offers the best available information about outdoor training, and hence social distance among athletes. Figure 5 shows mobility weekly trends in those areas in the 20 Brazilian states considered in this study, as compared to two other South American countries (Chile and Argentina) and two Europeans countries (Italy and Spain), from the beginning of March to the end of April. In addition to the fact that during this period these Brazilian regions underwent a 70% reduction in mobility,[41] this mobility reduction was considered low when compared to other countries. Therefore, it is suitable to assume that a non-negligible number of people continued to exercise outdoors.

Concerns about cyclists respiratory health caused by inhalation of fine and ultrafine particulate matter have already been raised by some studies.[42-45] Strak et al. found a significant change in lung function after cycling during rush hours.

If a cyclist (or even a triathlete during cycling training) inhales a great amount of air particles, respiratory SARS-COV2 infected droplets exhaled by another athlete in the same pack could also be inhaled. Blocken et al., in a simulated model, raised the possibility that droplets exhaled by a cyclist moving at 30km/h could travel in the air for up to 20m.[46,47] All this together could explain the increased odds for COVID-19 in cyclists and triathletes when compared to runners.

In this sample, 15.8% of the swimmers were older than 60 yo vs. 4.3% from other sports (p<0.001). Positive cases of COVID-19 were 9.0% in this age group and 5.7% at <60 yo. Not only is the severity of COVID-19 higher in the elderly, but the disease prevalence is as well. This could account for the independent relationship between COVID-19 cases and swimmers.

This study has a number of limitations. First, despite the measures to improve the sample's diversity, a true picture of the Brazilian population was not achieved. Not all pf the states were represented, and their proportions did not match Brazilian demographics. As a self-report survey, we could not guarantee that all individuals could self-recognize their symptoms nor understand what a laboratory-confirmed case is. However, Brazilian health agencies have been promoting educational campaigns to improve the recognition of symptoms and interpretations of test results. Unfortunately, there was also a lack local public data to compare the rates of hospitalization. Although some similarities were found between Brazilian and New York City data (mortality, mechanical ventilation, need for ICU), we could not guarantee the same for hospital admission rates. Athletes

Source: Google COVID-19 Community Mobility Reports (accessed: 05/31/2020)
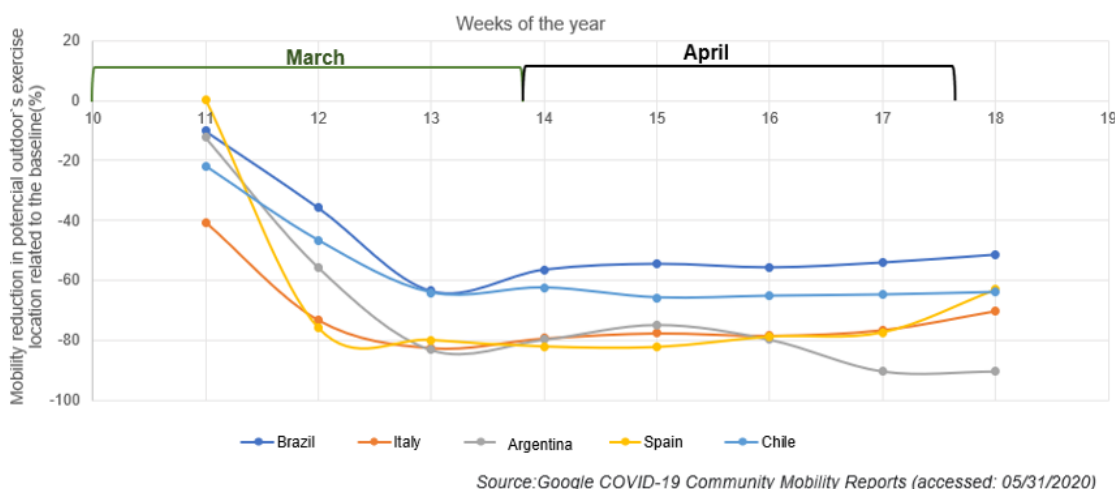
Figure 5 – Comparisons of mobility reduction among Brazil, Chile, Argentina, Italy, and Spain throughout March and April 2020

282

Silva et al.
Athletes health during pandemic times

Int J Cardiovasc Sci. 2021; 34(3):274-283
Original Article

hospitalized at the time when this survey was ongoing may have underestimated the rate of hospitalization among athletes. Finally, the numbers of variables related to infectiousness of SARS-COV-2 are much larger than we have collected here.

Conclusion

Based in this cross-sectional analysis of athlete self-reports, rates of hospitalization among these individials were much lower than expected. After adjustments, the COVID-19 prevalence was higher for cyclists, triathletes, and swimmers than for runners. No age, regional, or athletic level effects were found. Many social, biological, and environmental assumptions could explain these results. A great number of questions were raised by this research. In a world which claims to restore recreational and professional sports activities, answering these questions should be the aim of future studies.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Sources of Funding

Study Association

This study is not associated with any thesis or dissertation work.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of the *Hospital Federal de Bonsucesso* under the protocol number 4.054.651. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

Author Contributions

Conception and design of the research: Silva FB, T Walter. Acquisition of data: Silva FB, Fonseca B, Domecg F, Prado C, Facio MR, Toledo L. Analysis and interpretation of the data: Silva FB, Fonseca B. Statistical analysis: Silva FB. Critical revision of the manuscript for intellectual content: Silva FB.

References

1. Toresdahl BG, Asif IM. Coronavirus disease 2019 (COVID-19): considerations for the competitive athlete. Sports Health. 2020;12(3):221-4.

2. Timpka T. Sports health during the SARS-Cov-2 pandemic. Sports Med. 2020;50(8):1413-6.

3. Nyenhuis SM, Greiwe J, Zeiger JS, Nanda A, Cooke A. Exercise and fitness in the age of social distancing during the COVID-19 pandemic: J Allergy Clin Immunol Pract. 2020;8(7):2152-5.

4. Worldometer [Internet]. Coronavirus Update (Live): 6,206,037 Cases and 371,916 Deaths from COVID-19 Virus Pandemic.. [citado 31 maio 2020]. Disponível em:: https://www.worldometers.info/coronavirus/

5. PubMed [Internet]. "Coronavirus Infections"[Mesh] - Search Results - [citado 31 maio 2020]. Disponível em: https://pubmed.ncbi.nlm.nih.gov/?term=%22Coronavirus+Infections%22%5BMesh%5D&filter=years.2020-2020

6. Mohamed AA, Alawna M. Role of increasing the aerobic capacity on improving the function of immune and respiratory systems in patients with coronavirus (COVID-19): a review. Diabetes Metab Syndr Clin Res Rev. 2020;14(4):489-96.

7. Hamer M, Kivimäki M, Gale CR, Batty GD. Lifestyle risk factors for cardiovascular disease in relation to COVID-19 hospitalization: a community-based cohort study of 387109 adults in UK. medRxiv. 2020 May 13.

8. Ahmed I. COVID-19 - does exercise prescription and maximal oxygen uptake (VO2 max) have a role in risk-stratifying patients? Clin Med. 2020;20(3):282-4.

9. Hull JH, Loosemore M, Schwellnus M. Respiratory health in athletes: facing the COVID-19 challenge. Lancet Respir Med. 2020;8(6):557-8.

10. New York Times [Internet]. When are sports coming back from the coronavirus pandemic? [citado 12 maio 2020]. Disponível em: https://www.nytimes.com/article/coronavirus-sports-leagues-returning-canceled.html

11. Baggish BAL, Drezner JA, Kim JH, Martinez MW. Resurgence of sport in the wake of COVID-19 : cardiac considerations in competitive athletes. Br J Sports Med. 2020;54(19):1130-1.

12. Nieß A, Bloch W, Friedmann-Bette B, Grim C, Halle M, Hirschmüller A, et al. Position stand: return to sport in the current coronavirus pandemic (SARS-CoV-2 / COVID-19). Ger J Sport Med. 2020;71(5):E1–4.

13. Schellhorn P, Klingel K, Burgstahler C. Return to sports after COVID-19 infection. Eur Heart J. 2020 May 20;ehaa448. [Epub ahead of print].

14. Kirchherr J, Charles K. Enhancing the sample diversity of snowball samples: recommendations from a research project on anti-dam movements in Southeast Asia. PLoS One. 2018;13(8):e0201710.

15. McKinney J, Velghe J, Fee J, Isserow S, Drezner JA. Defining athletes and exercisers. Am J Cardiol. 2019;123(3):532-5.

16. MacMahon C, Parrington L. Not all athletes are equal, but don't call me an exerciser: response to Araujo and Scharhag. Scand J Med Sci Sports. 2017;27(8):904-6.

17. Comitê de Monitoramento do Coronavírus [Internet]. Medidas preventivas: orientações sobre o coronavírus nas crianças. [citado 12 maio 2020]. Disponível em: https://sites.unipampa.edu.br/coronavirus/prevencao/

18. Bialek S, Boundy E, Bowen V, Chow N, Cohn A, Dowling N, et al. Severe outcomes among patients with coronavirus disease 2019 (COVID-19) — United States, February 12–March 16, 2020. MMWR Morb Mortal Wkly Rep [Internet]. 2020 Mar 27;69(12):343-6. [citado 13 maio 2020] Disponível em: http://www.cdc.gov/mmwr/volumes/69/wr/mm6912e2. htm?s_cid=mm6912e2_w

19. Rosner B. Hypothesis testing: one-sample inference - one-sample inference for a binomial proportion . In: Fundamentals of biostatistics [Internet]. 4th ed. Belmont, Calif: Duxbury Press; 1995. p. 249-59. [citado 30 maio 2020]. Disponível em: https://iucat.iu.edu/iupui/1112772

20. Tony Cai T. One-sided confidence intervals in discrete distributions. J Stat Plan Inference. 2005 Apr 1;131(1):63-88.

21. Clopper CJ, Pearson ES. The use of confidence or fiducial limits illustrated in the case of the binomial Biometrika. 1934;26(4):404-13.

22. Newcombe RG, Altman DG. Proportions and their differences. In: Statistics with confidence. New Jersey: Wiley; 2000. p. 45–57.

23. Hanley JA, Lippman Hand A. If nothing goes wrong, is everything all right?: Interpreting zero numerators. JAMA. 1983 Apr 1;249(13):1743-5.

24. Pedersen BK, Saltin B. Exercise as medicine - evidence for prescribing exercise as therapy in 26 different chronic diseases. Scand J Med Sci Sport. 2015;25(Suppl 3):1–72.

25. Mandsager K, Harb S, Cremer P, Phelan D, Nissen SE, Jaber W. Association of cardiorespiratory fitness with long-term mortality among adults undergoing exercise treadmill testing. JAMA Netw Open. 2018;1(6):e183605.

26. Laddu DR, Lavie CJ, Phillips SA, Arena R. Physical activity for immunity protection: inoculating populations with healthy living medicine in preparation for the next pandemic. Prog Cardiovasc Dis. 2020 Apr 9. [Epub ahead of print].

27. Matthews CE, Ockene IS, Freedson PS, Rosal MC, Merriam PA, Hebert JR. Moderate to vigorous physical activity and risk of upper-respiratory tract infection. Med Sci Sports Exerc. 2002;34(8):1242-8.

28. Snowden CP, Prentis JM, Anderson HL, Roberts DR, Randles D, Renton M, et al. Submaximal cardiopulmonary exercise testing predicts complications and hospital length of stay in patients undergoing major elective surgery. Ann Surg. 2010;251(3):535-41.

29. Siu E, Campitelli MA, Kwong JC. Physical Activity and Influenza-coded outpatient visits, a population-based cohort study. PLoS One. 2012;7(6):e39518.

30. Wong CM, Lai HK, Ou CQ, Ho SY, Chan KP, Thach TQ, et al. Is exercise protective against influenza-associated mortality? PLoS One. 2008;3(5):e2108.

31. Valtonen M, Waris M, Vuorinen T, Eerola E, Hakanen AJ, Mjosund K, et al. Common cold in team Finland during 2018 Winter Olympic Games (PyeongChang): epidemiology, diagnosis including molecular point-of-care testing (POCT) and treatment. Br J Sports Med. 2019 Sep 1;53(17):1093-8.

32. Nieman DC, Wentz LM. The compelling link between physical activity and the body's defense system. J Sport Heal Sci. 2019;8(3):201-17.

33. Orhant E, Carling C, Cox A. A three-year prospective study of illness in professional soccer players. Res Sport Med. 2010 Jul;18(3):199-204.

34. Jaworski CA, Rygiel V. Acute illness in the athlete. Clin Sports Med. 2019;38(4):577-95.

35. Shephard RJ, Kavanagh T, Mertens DJ, Qureshi S, Clark M. Personal health benefits of masters athletics competition. Br J Sports Med. 1995 Sep 1;29(1):35-40.

36. Minuzzi LG, Rama L, Bishop NC, Rosado F, Martinho A, Paiva A, et al. Lifelong training improves anti-inflammatory environment and maintains the number of regulatory T cells in masters athletes. Eur J Appl Physiol. 2017 Jun 1;117(6):1131-40.

37. He CS, Bishop NC, Handzlik MK, Muhamad AS, Gleeson M. Sex differences in upper respiratory symptoms prevalence and oral-respiratory mucosal immunity in endurance athletes. Exerc Immunol Rev. 2014 Jan 1;20:8-22.

38. Nieman DC, Luo B, Dréau D, Henson DA, Shanely RA, Dew D, et al. Immune and inflammation responses to a 3-day period of intensified running versus cycling. Brain Behav Immun. 2014 Jul;39:180-5.

39. Williams PT. Dose-response relationship between exercise and respiratory disease mortality. Med Sci Sports Exerc. 2014;46(4):711-7.

40. Gałązka-Franta A, Jura-Szołtys E, Smółka W, Gawlik R. Upper respiratory tract diseases in athletes in different sports disciplines. J Hum Kinet. 2016;53:99-106.

41. Bergman NK, Fishman R. Mobility reduction and covid-19 transmission rates. medRxiv. 2020 Jun 2;2020.05.06.20093039.

42. Jarjour S, Jerrett M, Westerdahl D, Nazelle A, Hanning C, Daly L, et al. Cyclist route choice, traffic-related air pollution, and lung function: a scripted exposure study. Environ Health. 2013 Feb 7;12:14.

43. Park HY, Gilbreath S, Barakatt E. Respiratory outcomes of ultrafine particulate matter (UFPM) as a surrogate measure of near-roadway exposures among bicyclists. Environ Health. 2017 Feb 8;16:6.

44. Strak M, Boogaard H, Meliefste K, Oldenwening M, Zuurbier M, Brunekreef B, et al. Respiratory health effects of ultrafine and fine particle exposure in cyclists. Occup Environ Med. 2010 Feb 1;67(2):118-24.

45. Cole-Hunter T, Jayaratne R, Stewart I, Hadaway M, Morawska L, Solomon C. Utility of an alternative bicycle commute route of lower proximity to motorised traffic in decreasing exposure to ultra-fine particles, respiratory symptoms and airway inflammation - a structured exposure experiment. Environ Health. 2013 Apr 8;12:29.

46. Blocken B, Malizia F, Van Druenen T, Marchal T. Towards aerodynamically equivalent COVID-19 1.5 m social distancing for walking and running. [Preprint]. Disponível em: http://www.urbanphysics.net/Social%20 Distancing%20v20_White_Paper.pdf

47. Blocken B, Marchal T. Towards aerodynamically equivalent COVID-19 1.5 m social distancing for walking and running: questions and answers [Internet]. [citado 21 jun 2020]. Disponível em: http://www.urbanphysics. net/Questions_and_Answers.pdf

ORIGINAL ARTICLE

Potential Impact of the New American High Blood Pressure Guidelines on Hypertension Prevalence in a Primary Health Care Unit in Rio de Janeiro – the LapARC Study

Marcelle Guimarães de Oliveira,[1] Angélica Furriel de Almeida da Silva,[2] Taissa Lorena dos Santos,[2]
Mariana Loureiro Cunha,[2] Bruna Rosenbrock Ferreira Taveira,[2] Elizabeth Silaid Muxfeldt[2,3]

Universidade Federal do Estado do Rio de Janeiro, Escola de Medicina e Cirurgia, Hospital Universitário Gafree e Guinle,[1] Rio de Janeiro, RJ – Brazil.
Universidade Estácio de Sá, Curso de Medicina Campus Presidente Vargas, Estudo LapARC,[2] Rio de Janeiro, RJ – Brazil.
Universidade Federal do Rio de Janeiro, Faculdade de Medicina, Hospital Universitário Clementino Fraga Filho, ProHArt,[3] Rio de Janeiro, RJ - Brazil

Abstract

Background: The new American Heart Association guidelines for hypertension (HT) proposed a reduction of the diagnostic cut-off point, leading to a substantial increase in the prevalence of HT.

Objectives: To assess the prevalence of HT determined by the traditional criteria, the AHA criteria, and home blood pressure monitoring (HBPM) in a population of young adults attending a primary healthcare unit, and its association with cardiovascular risk.

Methods: A cross-sectional population study on adults aged from 20 to 50 years attending a primary healthcare unit, in Rio de Janeiro, Brazil. Sociodemographic and anthropometric data, cardiovascular risk factors, office blood pressure and HBPM were registered. The diagnosis of HT was defined by traditional criteria (office BP ≥ 140 x 90 mmHg) and by the new (AHA) criteria (office BP ≥ 130 x 80 mmHg). Bivariate analysis was used for comparisons between the two diagnostic criteria, and Kappa coefficient was used to assess the agreement in diagnosis between office BP and HBPM. The level of significance adopted was 5% (p<0.05).

Results: A total of 472 individuals were evaluated (male: 39%; mean age: 38.5 ± 8.7 years). The prevalence of HT was 23.5% and raised to 41.1% with the new AHA criteria. The prevalence of HT using HBPM was 25.5%, but the diagnostic agreement was low (kappa=0.028) with changes in diagnosis in 18% of the cases.

Conclusion: The prevalence of HT almost doubled with the new AHA diagnostic criteria for HT. HBPM seemed to be an important instrument in HT diagnosis in this population. (Int J Cardiovasc Sci. 2021; 34(3):284-293)

Keywords: Cardiovascular Diseases; Hypertension/diagnosis; Blood Pressure; Epidemiology; Primary Health Care.

Introduction

Hypertension (HT) is usually diagnosed as office blood pressure (BP) equal to or higher than 140 x 90 mmHg.[1,2] However, the new American Heart Association (AHA) guidelines recommended to reduce the diagnostic cut-off point for hypertension to ≥ 130 x 80 mmHg, leading to an increase in hypertension prevalencec.[3] Based on this, it is estimated that half of the general population would be considered hypertensive, with greater inclusion of young individuals. It is not clear, however, whether this will bring benefits in terms of leading to lifestyle changes and preventing cardiovascular (CV) events, or if it will simply increase the consumption of anti-hypertensive drugs. The new guidelines also reinforce the importance of blood pressure measurements outside the office, using Ambulatory Blood Pressure Monitoring (ABPM) or Home Blood Pressure Monitoring (HBPM).[1-3]

The LapARC study is a population cohort study that aims to evaluate and compare the prevalence of HT using the traditional criteria, the new AHA guidelines, and HBPM, as well as its association with CV risk in this population.

Methods

This is a cross-sectional population study of a cohort of 472 adults (20-50 years of age), selected from a total of 1,100

patients (43%) enrolled in CSE-Lapa, a school-based primary health center in Rio de Janeiro, Brazil.

Data Collection

In the first evaluation, sociodemographic characteristics (gender and age), physical inactivity (regular physical activity < 150 minutes/week), smoking (current smoking of at least one cigarette a day), previous diagnosis of hypertension, diabetes and dyslipidemia (total cholesterol > 190 mg/dL, LDL-cholesterol > 115 mg/dL, HDL-cholesterol < 40 mg/dL in men and < 46 mg/dL in women, triglycerides > 150 mg/dL or use of statin) were registered.[1,2] To assess obesity, the following anthropometric measurements were taken: weight and height for calculating Body Mass Index (BMI), abdominal circumference (midpoint between the lower costal margin and the iliac crest) and neck circumference (at the level of the cricothyroid cartilage).[1,2] The cut-off point used to assess obesity was BMI ≥ 30 kg/m². For abdominal obesity, we considered an abdominal circumference ≥ 88 cm in women and ≥ 102 cm in men, and for increased neck circumference, we used > 41 cm in women and > 43 cm in men.[1,2]

Blood Pressure Measurements

Office BP was measured using a digital oscillometric device (MicrolifeWatch BP03)[4] with a cuff suitable for the arm circumference, following the Brazilian Society of Cardiology guidelines.[2] The average readings obtained from two measurements was considered for analysis. The ankle-brachial index (ABI) was also calculated, as the ratio between the highest systolic BP taken from the lower limb to the highest systolic BP taken from the upper limb; an ABI ≥ 0.9 was considered normal.[1,2] The diagnosis of HT was defined by traditional criteria – office BP ≥ 140 x 90 mmHg[1,2] – and the new AHA criteria – office BP ≥ 130 x 80 mmHg, considering stage I, a systolic BP between 130 and 139mmHg and diastolic BP between 80 and 89 mmHg, and stage II ≥ 140 x 90 mmHg.[3]

Individuals were considered hypertensive when they previously knew their diagnosis (taking anti-hypertensive drugs or not) and had increased average office BP in two visits.

A subgroup of 218 individuals who were not using anti-hypertensive drugs underwent HBPM (HEM-705 CP, Omron Healthcare, Kyoto, Japan)[5], which is considered the gold standard for the diagnosis of HT. A 7-day protocol, with four daily measurements (two in the morning and two in the afternoon), was used.[6] The measurements taken on the first day were discarded and the average of the remaining six days was used in the analysis. Normal BP was defined as < 135 x 85 mmHg, following the Brazilian Guidelines on hypertension (traditional criteria).[2,6] Based on office BP and HBPM, individuals were classified in four phenotypes: (i) normotension with controlled office BP and HBPM, (ii) sustained HT with uncontrolled office BP and uncontrolled HBPM, (iii) white coat HT (WCHT) with increased office BP and controlled HBPM, and (iv) masked hypertension (MHT) with normal office BP and uncontrolled HBPM.

Electrocardiography (ECG)

Individuals underwent resting ECG to calculate voltage indexes for the diagnosis of left ventricular hypertrophy (LVH). The Solokow index was calculated by the formula SV1 + RV5 (cohort value ≥ 35mm) and the Cornell index by RaVL + SV3 (≥ 20 mm to women and ≥ 28mm to men).[1,2]

Statistical Analysis

The statistical analysis was made using the SPSS 19.0 (SPSS, Chicago, IL). Since it was a population study, a convenience sample was used. Data normality was verified using a histogram and a quantile-quantile (Q-Q) plot. Continuous variables showed normal distribution and were described as mean and standard deviation (SD). Bivariate analysis was used in the analysis of HT diagnosis by traditional criteria and by the new AHA guidelines, and comparisons were performed by unpaired Student's t test (continuous variables with normal distribution) and the χ2 test (categorical variables). The prevalence of the four hypertension phenotypes (normotension, sustained HT, WCHT and MHT) was calculated, and the agreement in HT diagnosis between the two methods was assessed by Kappa coefficient. One-Way ANOVA was used to evaluate differences in continuous variables between different groups, with p value calculated in relation to the normotensive group. The significance level adopted was 5% (p<0.05).

The variables sex, age > 39 years (mean age of the population), obesity, increased neck circumference, smoking, physical inactivity and the Sokolow-Lyon and Cornell indexes were examined in a multiple logistic regression model, and the HT diagnostic criteria (traditional

286

Oliveira et al.
Hypertension diagnosis in primary care

Int J Cardiovasc Sci. 2021; 34(3):284-293
Original Article

criteria, new AHA criteria and HBPM) were used as dependent variables. A step-by-step procedure was used to select the independent covariables (variables with p < 0.10 were selected to be added and remain in the models). The Hosmer-Lemeshow goodness-of-fit test and the area under the ROC curve were used to assess calibration and discrimination of the models. The results were presented as odds ratio (OR) and 95% confidence interval (CI).

Ethical considerations: The study was approved by the Research Ethics Committee of the institution and all participants signed an informed consent form.

Results

A total of 472 individuals were assessed; 186 (39%) were male, and mean age was 38.5 ± 8.7 years. Seventy-one (15%) patients reported previous diagnosis of hypertension, of which 62 (87%) were under pharmacological treatment, and 37 (52%) had good blood pressure control.

According to the traditional criteria, 109 (23%) individuals were considered hypertensive (stage II), and 192 individuals (41%) were hypertensive using the new criteria (stage I). These 83 "new" hypertensive patients according to the AHA criteria, were mostly men, less

sedentary, with increased neck circumference (Table 1). When compared with stage II hypertensive patients (n=109), stage I hypertensive subgroup was younger (38.3 ± 9.2 vs 43.0 ± 8.1 years; p <0.001), had a lower prevalence of abdominal obesity (27% vs 59%; p <0.001) and physical inactivity (27% vs 59%; p = 0.04), and lower BMI, neck circumference and Sokolow and Cornell indexes. They also had a lower (but not statistically significant) ABI compared with normotensive individuals (Table 2).

The prevalence of hypertension diagnosed by HBPM was 25.7% (n=56). Despite the similarity between the prevalence rates for office BP (23.1%) and for HBPM (25.7%), the diagnostic agreement was very low (Kappa coefficient = 0.028). In HBPM, we identified 167 normotensive individuals, 13 with sustained hypertension, 18 with WCHT and 20 with MHT. Therefore, in 17.5% of the cases (n=38), the diagnosis of HT changed with HBPM (Figure 1).

Individuals with WCHT were mostly men, had greater neck circumference and an increased Cornell index as compared with normotensive subjects. These patients showed not only increased office BP, but also increased home BP compared with normotensive individuals. Compared with sustained HT patients, individuals with WCHT had a lower BMI (28.1 ± 3.9 vs 30.9 ± 3.2 kg/m²,

Table 1 - Baseline characteristics of the total population and of normotensive and hypertensive groups according to the American Heart Association (AHA) and the traditional diagnostic criteria for hypertension

Characteristics	Total population (n=472)	Normotension (n=280)	Hypertension by AHA [a] (n=83)	Hypertension by traditional criteria [b] (n=109)
Male, n(%)	186 (39.4)	81 (28.9)	45 (54.2) ‡	60 (55.0) ‡
Obesity, n(%)[1]	115 (24.4)	51 (18.2)	19 (22.9)	45 (41.3) ‡
Abdominal obesity, n(%)[2]	177 (37.5)	91 (32.5)	22 (26.5)	64 (58.7) ‡
Increased neck circumference, n(%)[3]	53 (11.2)	12 (4.3)	9 (10.8) *	32 (29.4) ‡
Diabetes, n(%)	16 (3.4)	4 (1.4)	3 (3.6)	9 (8.3) †
Physical inactivity, n(%)	206 (43.6)	127 (45.4)	27 (32.5) *	52 (47.7)
Smoking, n(%)	68 (14.4)	39 (13.9)	16 (19.3)	13 (11.9)
Dyslipidemia, n(%)	85 (18.0)	47 (16.8)	12 (14.5)	26 (23.9)

[a] AHA criteria (BP ≥ 130 x 80 mmHg); [b] traditional criteria (BP ≥ 140 x 90 mmHg)
[1] Obesity: BMI > 30 kg/m²
[2] Abdominal obesity – increased abdominal circumference: >88 cm in women and >102 cm in men
[3] Increased neck circumference: >41 cm in women and >43 cm in men
Values are averages (SD) or absolute numbers and percentages,
χ2 test - p value calculated in relation to reference group (normotension)
* p< 0.05; † p< 0.01; ‡ p<0.001
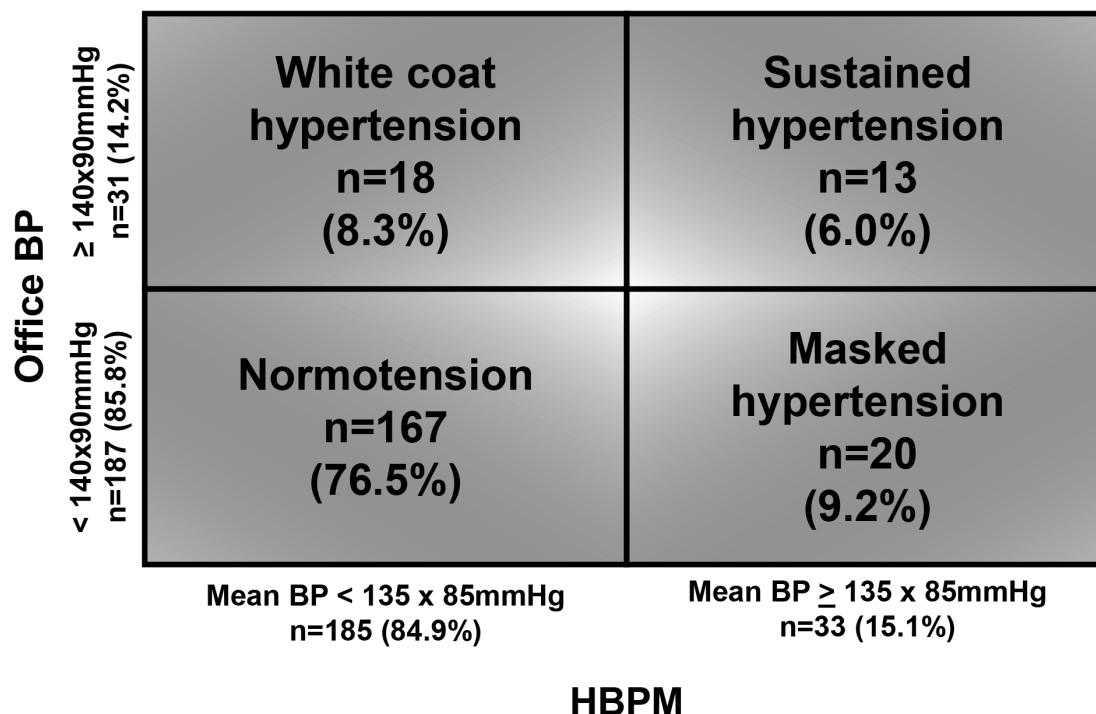
Figure 1 – Distribution of phenotypes of arterial hypertension diagnosed by office blood pressure (BP) and home blood pressure monitoring (HBPM)

p = 0.03). Except for office BP and home BP values, patients with MHT were similar in terms of CV risk factors compared with patients with sustained HT (Table 3).

In multiple logistic regression, obesity was independently associated with the diagnosis of HT, regardless of the diagnostic criteria, increasing the risk of developing HT by 2 to 3 times, and the only factor associated with the diagnosis of HT by HBPM. Increased neck circumference, male gender and older age were associated with the risk of HT by office BP (Table 4).

Discussion

The main finding of our study was the increase in the prevalence of HT from 23% by the traditional criteria (office BP criteria) to 41% by the new AHA criteria in a population of young adults. These patients, diagnosed with HT only by the AHA but not by the traditional criteria, have characteristics suggestive of higher CV risk, such as higher neck circumference and higher

voltage index on the ECG. Regarding the diagnosis of HT by HBPM, although the prevalence of HT was comparable to that by office BP, the concordance between the two methods was very low, with 18% of the participants having their diagnosis modified with home BP measurements.

Individuals classified as stage 1 by the new AHA guidelines did appear to have a higher CV risk compared to normotensive individuals, suggesting that the early diagnosis of this condition, in the context of primary care, in a younger population, may be important to reduce future risks. Studies in different countries have shown that diagnosis, treatment and control of HT are lower among young adults.[7,8] On the other hand, , when properly assisted and treated, these individuals are more likely to achieve blood pressure control when compared to the elderly. Changes in lifestyle are more feasible and effective in individuals with little endothelial injury and less arterial stiffness, denoting the relevance of the primary prevention strategy.[9]

288

Oliveira et al.
Hypertension diagnosis in primary care

Int J Cardiovasc Sci. 2021; 34(3):284-293
Original Article

Table 2 – Baseline characteristics of the individuals by blood pressure stages defined by the American Heart Association			
Blood pressure stage	**Variables** **average (SD)**	**95%CI**	**p value***
Age, years			
Normal (n=280)	36.6 (8.4)	35.6-37.6	Reference
Stage I (n=83)	38.3 (9.2)	36.2-40.3	0.37
Stage II (n=109)	43.0 (8.1)	41.4-44.5	< 0.001
Body mass index, kg/m²			
Normal (n=280)	26.1 (4.9)	25.5-26.7	Reference
Stage I (n=83)	27.2 (5.2)	26.1-28.4	0.28
Stage II (n=109)	29.7 (6.0)	28.6-30.9	< 0.001
Abdominal circumference, cm			
Normal (n=280)	84.4 (17.4)	82.3-86.4	Reference
Stage I (n=83)	88.3 (15.0)	85.0-91.6	0.17
Stage II (n=109)	99.6 (14.4)	96.8-102.3	< 0.001
Neck circumference, cm			
Normal (n=280)	34.8 (6.2)	34.1-35.6	Reference
Stage I (n=83)	37.8 (3.8)	37.0-38.6	< 0.001
Stage II (n=109)	39.9 (4.4)	39.0-40.7	< 0.001
Sokolow-Lyon Index, mm			
Normal (n=280)	17.2 (5.2)	15.9-18.5	Reference
Stage I (n=83)	20.0 (5.7)	17.7-22.3	0.09
Stage II (n=109)	20.9 (5.6)	19.1-22.6	0.004
Cornell Index, mm			
Normal (n=280)	10.4 (4.1)	9.3-11.4	Reference
Stage I (n=83)	12.7 (4.8)	10.8-14.7	0.05
Stage II (n=109)	13.0 (3.9)	11.7-14.2	0.009
Systolic blood pressure, mmHg			
Normal (n=280)	110 (18)	108-113	Reference
Stage I (n=83)	127 (8)	125-129	< 0.001
Stage II (n=109)	138 (16)	135-141	< 0.001
Diastolic blood pressure, mmHg			
Normal (n=280)	68 (12)	67-69	Reference
Stage I (n=83)	81 (5)	79-82	< 0.001
Stage II (n=109)	85 (10)	83-87	< 0.001
Pulse pressure, mmHg			
Normal (n=280)	42 (10)	41-43	Reference
Stage I (n=83)	47 (11)	44-49	0.004
Stage II (n=109)	53 (13)	51-55	< 0.001
Ankle-Brachial Index			
Normal (n=280)	1.15 (0.20)	1.12-1.17	Reference
Stage I (n=83)	1.14 (0.23)	1.10-1.19	1.00
Stage II (n=109)	1.11 (0.24)	1.06-1.16	0.43
*One-way ANOVA to assess the difference between groups			

Table 3 – Baseline characteristics of four blood pressure phenotypes, defined by office blood pressure and by home blood pressure monitoring (HBPM)

	Total population (n=218)	Normotension (n=167)	White coat hypertension (n=18)	Masked hypertension (n=20)	Sustained hypertension (n=13)
Cardiovascular Risk Factors					
Male, n(%) [a]	79 (36.2)	50 (29.9)	14 (77.8) [†]	8 (40.0)	7 (53.8)
Age, years [b]	39.5 (8.2)	39.1 (8.2)	39.8 (8.4)	40.3 (8.3)	43.2 (6.6)
Body mass index, kg/m²	27.6 (5.4)	26.9 (5.2)	28.1 (3.9)	30.8 (7.3) †	30.9 (3.2)
Obesity, n(%) [a]	45 (25.7)	34 (20.4)	5 (27.8)	10 (50.0) †	7 (53.0) [†]
Abdominal obesity[1], n(%) [a]	79 (36.2)	54 (32.3)	7 (38.9)	9 (45.0) *	9 (69.2) [†]
Increased neck circumference[2], n(%) [a]	18 (8.3)	7 (4.2)	4 (22.2) [‡]	4 (20.0) [‡]	3 (23.1) [‡]
Diabetes, n(%) [a]	9 (4.1)	5 (3.0)	1 (5.6)	1 (5.0)	2 (15.4)
Physical inactivity, n(%) [a]	101 (46.3)	79 (47.3)	4 (22.2)	11 (55.0)	7 (53.8)
Smoking, n(%) [a]	26 (11.9)	19 (11.4)	1 (5.6)	3 (15.0)	3 (23.1)
Dyslipidemia, n(%) [a]	46 (21.1)	36 (21.6)	5 (27.8)	3 (15.0)	2 (15.4)
Office BP, mmHg					
Systolic BP [b]	122 (14)	117 (10)	144 (5) [‡]	123 (13) [†]	149 (10) [‡]
Diastolic BP [b]	74 (9)	71 (7)	86 (7) [‡]	78 (9) [‡]	90 (9) [‡]
Pulse pressure [b]	47 (10)	45 (9)	58 (10) [‡]	45 (10)	49 (10) [‡]
HBPM, mmHg					
Systolic BP [b]	120 (12)	115 (9)	125 (8) [‡]	135 (9) [‡]	145 (9) [‡]
Diastolic BP [b]	74 (9)	71 (6)	75 (6) *	87 (7) [‡]	88 (9) [‡]
Pulse pressure [b]	46 (8)	45 (6)	49 (7) *	48 (9)	57 (12) [‡]
Electrocardiogram					
Sokolow-Lyon Index (mV) [b]	18.9 (5.6)	18.2 (5.4)	21.6 (4.5)	21.0 (7.2)	19.9 (6.1)
Cornell Index (mV) [b]	11.5 (4.4)	11.2 (4.2)	15.6 (3.6) [†]	9.3 (2.8)	12.3 (5.3)

[1] *Abdominal obesity: increased abdominal circumference: >88 cm in women and >102 cm in men*
[2] *Increased neck circumference: >41 cm in women and >43 cm in men*
BP: blood pressure
[a] *χ2 test (categorical variables)*
[b] *Unpaired Student's t test (continuous variables)*
* p< 0.05; † p< 0.01; ‡ p<0.001, p value calculated in relation to reference group (normotension)

When shedding light on the new AHA guidelines, it is noted that stage I hypertensive patients were previously labeled "prehypertensive" by the seventh report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure (JNC7).[10] This designation aimed to identify individuals at greater risk of developing HT and to intervene early

with the adoption of a healthy lifestyle. The term was intended to reduce therapeutic inertia, but paradoxically, less care was delivered.[10]

By reclassifying individuals, the AHA created a disease condition that affects people who were previously considered healthy. It is essential to note that the new definition may result in early diagnosis and prevention,

290

Oliveira et al.
Hypertension diagnosis in primary care

Int J Cardiovasc Sci. 2021; 34(3):284-293
Original Article

Table 4 - Multiple logistic regression for cofactors independently associated with hypertension by the traditional criteria, American Heart Association criteria, and home blood pressure monitoring (HBPM)

HT by traditional criteria (n=109)			
Cofactors	OR	95%CI	p-value
Male	2.48	1.46-4.22	0.001
Increased neck circumference	3.40	1.31-8.81	0.012
Obesity	2.45	1.39-4.30	0.002
Age > 39 years	3.77	2.18-6.49	< 0.001
HT by AHA criteria (n=83)			
Cofactors	OR	95%CI	p-value
Male	3.05	1.94-4.81	< 0.001
Increased neck circumference	3.91	1.24-12.4	0.02
Obesity	2.08	1.24-3.49	0.005
Age > 39 years	2.23	1.44-3.45	< 0.001
Sustained HT by HBPM (n=13)			
Cofactors	OR	95%CI	p-value
Male	1.38	0.57-3.33	0.48
Increased neck circumference	1.65	0.45-6.00	0.45
Obesity	3.07	1.28-7.36	0.012
Age > 39 years	1.46	0.62-3.48	0.39

Hosmer-Lemeshow goodness-of-fit test: p=0.604, area under the ROC curve 0.791 (95% IC 0.745-0.838).
Multiple logistic regression. The model was adjusted for sex, age > 39 years, obesity, increased neck circumference, smoking, physical inactivity, Sokolow-Lyon e Cornell indices.
HT: hypertension; AHA: American Heart Association; HBPM: Home Blood Pressure Monitoring; OR: Odds Ratio; CI: confidence interval.

more accurate screening for subclinical lesions and reduction in CV outcomes. Our study showed that these individuals have higher BMI, greater neck circumference and early changes in voltage indexes on the ECG when compared to normotensive individuals, pointing to a higher CV risk and greater chances of developing target organ damage, corroborating a possible positive effect in reducing BP cutoff point for hypertension.[3] However, these individuals now considered hypertensive (by the AHA criteria) would probably initiate pharmacological therapy earlier, and possibly experience more side effects, leading to higher costs to public health services,[11] in addition to a progressive reduction in treatment adherence. Vrijens et al.,[12] in a longitudinal study with electronic monitoring of medication, showed that after one year, half of the patients abandoned the pharmacological therapy.

Therefore, it is important to balance risks and benefits for this population. If, on the one hand, pharmacological therapy reduces CV risk and possible target organ lesions,[10] on the other, it may increase the likelihood of low output syndrome, and make hypertension management difficult.[3,11]

Home Blood Pressure Monitoring

The increasing importance of HBPM in primary care as a diagnostic and monitoring method for therapeutic response has been studied.[13-15] Currently, several guidelines[1,2] suggest that, whenever possible, ABPM or HBPM should be indicated at the time of diagnosis, and the AHA[3] recommends that HT diagnosis be based on elevated office BP followed by confirmatory ABPM or

HBPM. Compared with ABPM, HBPM is generally more accepted by patients and has a lower cost,[6,16] in addition to refining the diagnosis and having a higher predictive value of future CV events than office BP;[17] it is therefore considered a good option for underdeveloped countries.[13] We emphasize that the use of HBPM in primary care is recommended by the Brazilian Ministry of Health,[18] although in clinical practice it has not been used due to economic and logistical issues.

In our country, the diagnosis of HT is based on office BP because it is a simple and low-cost procedure,[2] despite the limitations of this method, especially in individuals with WCHT and MHT.[13,19] In the present study, despite the similar prevalence of HT diagnosed by office BP and HBPM, the diagnostic agreement was very low and, in almost 20% of the population, the diagnosis of HT has changed, which corroborates the importance of measuring BP out of the office, including in primary care.[13,14,18,20]

Analyzing individuals with WCHT in our study, we observed that despite normal home BP levels, they seem to present a higher CV risk associated with greater neck circumference, wider pulse pressure, and early elevation of the Cornell index, although still within normal ranges. Several studies have demonstrated a higher CV risk and higher risk for HT associated with WCHT.[21-23] This is in line with our results, which showed that individuals with WCHT have higher (but controlled) home BP levels compared with normotensive individuals (Table 3). They also showed higher Cornell voltage on ECG suggesting LVH, increased neck circumference suggesting a higher risk for obstructive sleep apnea and an increased office pulse pressure and HBPM that may reflect greater arterial stiffness, despite the younger age (Table 3). There is evidence to suggest the need to follow-up this group of patients, regarding lifestyle changes and the possibility of developing sustained hypertension.[1-3,9]

Analysis of MHT patients in our study revealed that, except for office BP, these patients behaved in a similar way to the sustained ones . A meta-analysis of 12 studies with 4,884 untreated individuals, 2,467 of whom were normotensive, 776 patients with MHT and 1,641 patients with sustained hypertension, showed an association between MHT and increased risk of LVH.[24] In another meta-analysis, the prognosis of individuals with WCHT was similar to that of normotensive individuals, while patients with MHT had a higher prevalence of subclinical lesions such as LVH, carotid wall thickening and microalbuminuria.[24] In the Finn-Home Study, a progressive increase in the incidence of CV events and total mortality in normotension, WCHT, MHT and sustained hypertension was observed,[25] while a recent study showed that individuals with MHT have twice the risk of developing LVH.[26] Possibly, the difficulty in detecting MHT and consequent lack of treatment contribute to this poor prognosis profile.

In our population, obesity was the common independent risk factor for the diagnosis of HT between the three diagnostic criteria (Table 4). A recent randomized clinical trial developed in several centers in Brazil showed that changes in eating habits had little impact on the secondary prevention of CV events,[27] but there are no studies demonstrating their long-term effects on reducing obesity and consequently CV risk.

It is also noteworthy that greater neck circumference increased the odds of having HT by almost four times, regardless of the diagnostic criteria system. Perhaps screening for sleep apnea in a younger population and initiating treatment and instituting treatment at earlier ages may reduce CV morbidity and mortality in the future; this has not yet been proven in patients with more severe HT and elderly patients using continuous positive airway pressure.[28]

Our study has two main limitations. Our sample was composed of young, economically active individuals, who self-reported as 'healthy'; these individuals do not usually seek health services. Although this group of individuals lived in an area covered by the CSE-Lapa, many were not even registered in the unit, which made it difficult to enroll these subjects in the study. Thus, most of our study population attended the CSE-Lapa, which generated a selection bias. This fact can be confirmed by the mean age of the cohort, which was higher than expected. Another limitation was the predominance of women (61.5%), apparently related to the well-recognized greater demand for healthcare services by women (including preventive tests, prenatal care etc.), while we know that in this age group (<50 years, men have higher CV risk than women. As it is a study with individuals aged between 20 and 50 years, the conclusions cannot be extrapolated to other age groups.

Conclusion

As expected, adopting the new AHA criteria caused a significant increase in the prevalence of HT in a population of young adults. However, it is not clear if these individuals would have a higher CV risk,

pointing to the need for future longitudinal studies. In addition, BP measurements outside the office would be important for a more accurate diagnosis of HT in primary care.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Sources of Funding

Study Association

This article is part of the thesis of course completion word submitted by Marcelle Guimarães de Oliveira, from Universidade Federal do Estado do Rio de Janeiro.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of the *Universidade Estácio de Sá* under the protocol number 50605215.4.0000.5284. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

Author Contributions

Conception and design of the research: Oliveira MG, Almeida da Silva AF, dos Santos TL, Muxfeldt ES. Acquisition of data: Oliveira MG, Almeida da Silva AF, dos Santos TL, Cunha ML, Taveira BRF, Muxfeldt ES. Analysis and interpretation of the data: Oliveira MG, Almeida da Silva AF, dos Santos TL, Muxfeldt ES. Statistical analysis: Muxfeldt ES. Obtaining financing :Muxfeldt ES. Writing of the manuscript: Oliveira MG, Almeida da Silva AF, dos Santos TL, Cunha ML, Taveira BRF, Muxfeldt ES. Critical revision of the manuscript for intellectual content: Oliveira MG, Muxfeldt ES.

References

1. Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension The Task Force for the management of arterial hypertension of the European Society of Cardiology (ESC) and the European Society of Hypertension (ESH). J Hypertens. 2018; 36(10):1935-2041.

2. Malachias MVB, Souza WKSB, Plavnik FL, Rodrigues CIS, Brandão AA, Neves MFT, et al. 7ª Diretriz Brasileira de Hipertensão Arterial. Arq Bras Cardiol 2016; 107(3Supl.3):1-83.

3. Whelton PK, Carey RM, Aronow WS, Casey DE Jr, Collins KJ, Dennison Himmelfarb C et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Hypertension 2018; 71(6):1269-324.

4. Cuckson AC, Reinders A, Shabeeh H, Shennan AH. Validation of the Microlife BP 3BTO-A oscillometric blood pressure monitoring device according to a modified British Hypertension Society protocol. Blood Press Monit 2002; 7(6):319-24.

5. Artigao LM, Llavador JJ, Puras A, López Abril J, Rubio MM, Torres C. Evaluation and validation of Omron Hem 705 CP and Hem 706/711 monitors for self-measurement of blood pressure. Aten Primaria. 2000;25(2):96-102.

6. Nobre F, Mion Júnior D, Gomes MAM, Barbosa ECD, Rodrigues CIS, Neves MFT et al. 6ª Diretrizes de Monitorização Ambulatorial da Pressão Arterial e 4ª Diretrizes Brasileiras de Monitorização Residencial da Pressão Arterial. Sociedades Brasileiras de Cardiologia, Hipertensão e Nefrologia. Arq Bras Cardiol 2018; 110(5 supl1):1-29.

7. Zhang Y, Moran AE. Trends in the Prevalence, Awareness, Treatment, and Control of Hypertension Among Young Adults in the United States, 1999 to 2014. Hypertension. 2017;70(4):736-42.

8. Mosha NR, Mahande M, Juma A, Mboya I, Peck R, Urassa M et al. Prevalence, awareness and factors associated with hypertension in North West Tanzania. Glob Health Action 2017; 10(1):1321279.

9. Precoma DB, Oliveira GMM, Simão AF, Dutra OP, Coelho OR, Izar MCO et al. Atualização da Diretriz Brasileira de Prevenção Cardiovascular da SBC-2019. Arq Bras Cardiol 2019; 113(4):787-891.

10. Verdecchia P, Angeli F. The Seventh Report of the Joint National Commitee on Prevention, evaluation, and treatment of high blood pressure: the weapons are ready. Rev Española de Cardiología, 2003; 56(9):843-7.

11. Bakris G, Sorrentino M. Redefining Hypertension — Assessing the New Blood-Pressure Guidelines. N Engl J Med. 2018; 378(6):497-9.

12. Vrijens B, Vincze G, Kristanto P, Urquhart J, Burnier M. Adherence to prescribed antihypertensive drug treatments: longitudinal study of electronically compiled dosing histories. BMJ 2008; 336(7653):1114-7.

13. Ndip Agbor V, Temgoua MN, Noubiap JJ. Scaling up the use of home blood pressure monitoring in the management of hypertension in low-income countries: A step towards curbing the burden of hypertension. J Clin Hypertens 2017; 19(8):786-9.

14. Kronish IM, Kent S, Moise N, Shimbo D, Safford MM, Kynerd RE, O'Beirne R, Sullivan A, Muntner P. Barriers to conducting ambulatory and home blood pressure monitoring during hypertension screening in the United States. J Am Soc Hypertens. 2017;11(9):573-80.

15. Abdullah A, Othman S. The influence of self-owned home blood pressure monitoring (HNPM) on primary care patients with hypertension: a qualitative study. BMC Fam Pract. 2011; 12:143.

16. Gosse P, Coulon P. Ambulatory or home measurement of blood pressure? J Clin Hypertens (Greenwich). 2009; 11:234-7.

17. Bliziotis IA, Destounis A, Stergiou GS. Home versus ambulatory and office blood pressure in predicting target organ damage in hypertension: a systematic review and meta-analysis. J Hypertens. 2012; 30(7):1289-99.

18. Brasil. Ministério da Saúde. Estratégias para o cuidado da pessoa com doença crônica: hipertensão arterial sistêmica. Brasília; 2013. (Cadernos de Atenção Básica, n.37)

19. Alessi A, Brandão AA, Paiva AMG, Nogueira AR, Feitosa A, Gonzaga CC, et al. I Posicionamento Brasileiro sobre Pré-Hipertensão, Hipertensão do Avental Branco e Hipertensão Mascarada: Diagnóstico e Conduta. Arq Bras Cardiol. 2014; 102(2):110-19.

20. Nobre F, Junior DM. Monitorização Ambulatorial da Pressão Arterial: Cinco Décadas de Mais Luzes e Menos Sombras Arq Bras Cardiol. 2016; 106(6):528-37.

21. Conen D, Ricker PM, Buring JE, Glynn RJ. Risk of cardiovascular events among women with high normal blood pressure or blood pressure progression: prospective cohort study. BMJ. 2007;335(7617):432-40.

22. Verdecchia P, Reboldi GP, Angeli F, Schillaci G, Schwartz JE, Pickering TG, et al. Short and long-term incidence of stroke in white coat hypertension. Hypertension. 2005;45(2):203-8.

23. Mancia G, Bombelli M, Facchetti R, Madotto F, Quarti-Trevano F, Polo Friz H, et al. Long-term risk of sustained hypertension in white-coat or masked hypertension. Hypertension. 2009;54(2):226-32.

24. Pierdomenico SD, Cuccurullo F. Prognostic value of white-coat and masked hypertension diagnosed by ambulatory monitoring in initially untreated subjects: an updated meta-analysis. Am J Hypertens. 2011;24(1):52-8.

25. Hanninen MR, Niiranen TJ, Puukka PJ, Johansson J, Jula AM. Prognostic significance of masked and white-coat hypertension in the general population: the Finn-Home Study. J Hypertens. 2012; 30(4):705-12.

26. Cuspidi C, Facchetti R, Quarti-Trevano F, Sala C, Tadic M, Grassi G, Mancia G. Incident Left Ventricular Hypertrophy in Masked Hypertension. Hypertension 2019; 4(1):56-62.

27. Weber B, Bersch-Ferreira ÂC, Torreglosa CR, Marcadenti A, Lara ES, da Silva JT et al. Implementation of a Brazilian Cardioprotective Nutritional (BALANCE) Program for improvement on quality of diet and secondary prevention of cardiovascular events: A randomized, multicenter trial.Am Heart J 2019; 215:187-97.

28. Drager LF, Lorenzi-Filho G, Cintra FD, Pedrosa RP, Bittencourt LR, Poyares D. et. al. 1º Posicionamento Brasileiro sobre o Impacto dos Distúrbios de Sono nas Doenças Cardiovasculares da Sociedade Brasileira de Cardiologia. Arq Bras Cardiol. 2018; 111(2):290-341.

ORIGINAL ARTICLE

Acute Blood Pressure Response to Different Resistance Programs in Trained Men

Ariani França Conceição,[1,2] Daniell Lima Muniz,[1,2] Clarcson Plácido Conceição dos Santos,[1,2] Ciro Oliveira Queiroz[1,2]

Escola Bahiana de Medicina e Saúde Pública (EBMSP),[1] Salvador, BA – Brazil.
Grupo de Estudos em Saúde e Performance Humana (GESPH),[2] Salvador, BA - Brazil

Abstract

Background: Resistance training is used in different exercise programs, with different objectives and different levels of physical fitness. Training-related variables, such as volume, rest time and intensity, can affect the response of blood pressure (BP), but studies on the effect of these variables on BP are still needed.

Objective: To evaluate the acute response of BP in trained individuals undergoing two different methods of resistance training.

Methods: The sample was divided into three groups: (1) the German volume training (GVT) (n= 15), which consisted of 10 series of 10 repetitions at 50% of 1-repetition maximum (RM) with intervals of 30 seconds; (2) the sarcoplasm stimulating training (SST) (n= 16), performed at 8 RM and 85% of 1-RM and interval of 10 seconds until failure, followed by removal of 20% of weight and repetition of the whole series (total of three sets), and the control group (CG) (n= 15) who underwent BP measurements only. The two-way repeated measures ANOVA was used for analysis of variations, and a p< 0.05 was considered statistically significant.

Results: In the within-group analysis, a significant lowering of systolic blood pressure (SBP) was found at 10 minutes (125.4±10.8 mmHg, p= 0.045) and 20 minutes (124.5±8.5 mmHg, p= 0.044) post-training compared with immediately after training. In the between-group comparison, higher SBP values were observed immediately after training in the SST group (142.1±28.2, p= 0.048) compared with the CG.

Conclusion: High-volume and high-intensity resistance training programs did not cause abnormal changes in blood pressure. (Int J Cardiovasc Sci. 2021; 34(3):294-299)

Keywords: Resistance Training; Exercise; Blood Pressure; Hypertension; Circuit Based Exercise; Exercise; Men; Rehabilitation.

Introduction

Aerobic and resistance exercises are broadly used for the maintenance and rehabilitation of cardiovascular health, and seen as one of the main non-pharmacological strategies for the prevention and treatment of systemic arterial hypertension (SAH). Resistance training (RT) was long considered a mere auxiliary tool of aerobic exercises for cardiovascular health rehabilitation, particularly for promoting musculoskeletal gain, but today, evidence suggests the efficacy of RT in modesty lowering blood pressure (BP) levels.[1-3]

This phenomenon, known as post-exercise hypotension, has an important role in the control of

blood pressure and cardiovascular risks, not only in hypertensive but also in normotensive individuals.[4,5] The effect of RT on reducing blood pressure levels can prevent the development of SAH in normotensive individuals.[4] However, there are can affect the response of BP during RT, such as exercise volume,[6,7] intervals between series[8,9], training methods[10] and intensity.[11]

Blood pressure response to exercise intensity and volume is not well established.[12] Studies have shown that moderate- and high-intensity exercises can lower BP levels and influence the duration of the hypotensive effect, but not its magnitude.[9-11] With regard to the volume of exercise, while some reports indicate that the

higher the volume of training, the longer the hypotensive effect,[6] others have suggested that high- and low-volume training have similar effects on BP.[11]

More advanced methods of RT have been developed over years, such as the German volume training (GVT)[13-15] and the sarcoplasm stimulating training (SST),[16,17] but no effect of these programs on BP have been reported so far. Thus, the objective of this study is to assess the acute response of BP to different methods of RT in trained individuals.

Methods

Study design and sample

This trial included male individuals aged 20-40 years, non-smokers, with at least one year of experience in RT. This was a convenience sample of 46 men, which was divided into three groups: SST (n= 16), and GVT (n= 15) and control group (CG) (n= 15).

The exclusion criteria were cardiometabolic diseases, use of medications that may influence the cardiovascular response, musculoskeletal disorders, and individuals who could not undergo the training protocol.

Participants were recruited through social media posts, flyers and telephone calls made to bodybuilding gyms in the city of Salvador, Bahia State, Brazil. Individuals were allocated consecutively in one of the groups, and were informed about the aims of the study, the exercise protocols and training methods. The study was approved by the Research Ethics Committee of Bahian School of Medicine and Public Health (EBMSP) (Certificate of Presentation for Ethical Consideration, CAAE, number 57573516.7.0000.5544). All participants signed an informed consent form.

Anthropometric measures

On the day before exercise, participants were instructed to refrain from high-intensity exercise, alcohol, caffeinated and energy drinks, and sleep from six to eight hours. On the study day, they were instructed to wear appropriate clothing and eat light meals in the period of two hours before the training.

Body weight and height were measured using a digital scale Welmy® (W200A, Brazil), and subsequently body mass index (BMI) was calculated.

Blood pressure measurements

An automatic sphygmomanometer - Microlife® (MAM BP3AC1PC, Brazil)- was used. The individuals rested in a supine position for five minutes, to stabilize pressure levels. After five minutes, blood pressure was measured in the pre-training stage, in a supine position, with head slightly tilted, in a quiet environment with a room temperature between 23°C and 25°C and dim light.[18] BP was then measured immediately after training, and every 10 minutes during the 50-minute rest period subsequently.

The one-repetition maximum test (1-RM)

The 1-RM test was used to determine the maximal weight each participant could lift with one repetition. First, the maximal number of repetitions of a given load (percentage of 1-RM) was determined of each participant. For this purpose, participants were first familiarized with the equipment and exercises to be performed. Then, there was a 3-5 minute warm up by performing repetitions of the muscle group to be tested using a light load. After a one-minute interval, participants performed three to five repetitions of a moderate-to-heavy load (60% to 80% of predicted 1-RM).

After an interval of two minutes, participants performed repetitions of the load close to the maximum estimated. After performing two-to-three additional repetitions of exercises for the upper limbs, the weight increased by 5 to 10% of predicted 1-RM. Based on these adjustments, the test would be repeated after an interval of three to five minutes. An attempt was considered valid if the test was performed according to the standardized instructions; if more than three attempts were needed, there was a one-day interval for repetition of the test.[19]

Training Protocol

German volume training

Participants performed 10 series of 10 repetitions, with an intensity of 50% of 1-RM, with a 30-second rest interval between the series. The test was conducted using leg press 45° (LP 45°) and bench press (BP).[14,20]

Sarcoplasm stimulating training

The SST session consisted of eight repetitions (of 85% of 1-RM) to failure, i.e., inability to complete a

full concentric repetition. After a 10-second interval, another set, using the same weight, was performed, so that the participant could make a higher number of repetitions. When a failed attempt occurred, there was an interval of 10 seconds.[16]

Subsequently, 20% of the weight was removed; participants made another series until failure, followed by one repetition. Then, another 20% of the weight was removed and the procedure was repeated.[16] The machines used were LP 45° and BP.[20]

The control group underwent BP measurements and did not participate in any of the exercise protocols.

Statistical analysis

The statistical package for social sciences (SPSS) software for Windows, version 14.0 was used for the statistical analysis. Continuous variables were described in average and standard deviation, and data normality was tested using the Kolmogorov-Smirnov test. The independent t-test was used for comparison of 1-RM averages and total weight training between the GVT and SST groups. The one-way ANOVA was used for comparison of mean age and BMI between the groups, and for within-group comparisons of the effect of exercise on systolic BP (SBP) and diastolic BP (DBP) (pre- vs. post-intervention). Then, the two-way repeated measures ANOVA was used for comparisons in the pre-and post-intervention periods.

The Bonferroni post-hoc test was used to identify significant differences, at the level of 5%.

Results

The characteristics of the sample are described in Table 1. No difference was observed in mean age, BMI or 1-RM (BP and LP 45°) between the groups. However, the total weight of training (LP 45° and BP) was significantly greater in the GVT than in the SST group (p = 0.001).

Data of SBP and DBP in the pre- and post-training periods are shown in Table 2. In the analyses of SBP, it was observed a significant lowering of SBP in the GVT group at 10 minutes (p= 0.045) and 20 minutes (p= 0.044) compared with immediately after training (0 minute). No difference was observed in any of the other time points. No difference was found for DBP in the GVT or SST groups.

Figure 1 shows the comparison of mean SBP and DBP between the three groups in all time points analyzed. Immediately after training, SBP was significantly higher than controls (p= 0.048); no other significant differences were found.

Discussion

The findings of this study showed that the different groups of trained individuals had different acute BP responses to exercises. The within-group comparisons revealed that, in the GVT groups, there was a significant rise in SBP immediately after training compared with 10 minutes and 20 minutes post-exercise.

In a study that compared the effect of different volumes of strength training on BP showed that a higher volume of training caused a more prolonged post-exercise hypotension.[6] Our results reinforce these

Table 1 – Characteristics of the study groups, composed of trained men undergoing German volume training (GVT, n=15), the sarcoplasm stimulating training (SST, n=15) and controls (n=15), Salvador, Bahia- Brazil, 2017-2018

Variables	CG (n=15) (mean ± SD)	GVT (n=15) (mean ± SD)	SST (n=16) (mean ± SD)	p
Age (years)	25.7 ± 4.9	28 ± 6.1	26.8 ± 4.5	0.587 [#]
BMI (kg/m²)	24. 7 ± 3.0	25.6 ± 2.5	25.6 ± 2.5	0.503 [#]
1-RM LP 45° (kg)	-	312.5 ± 63.1	315.6 ± 96.7	0.918 [$]
1-RM BP (kg)	-	89.1 ± 19.3	84.7 ± 18.5	0.522 [$]
Full charge LP 45° (kg)	-	16503.2 ± 3569.4	9382.9 ± 4012.4	0.001 [$*]
Full charge BP (kg)	-	4494.7 ± 1236.4	2159.0 ± 1067.1	0.001 [$*]

*CG: control group; GVT: German Volume Training; SST: Sarcoplasm Stimulating Training; 1-RM: one- repetition maximum test; LP 45°: leg press 45°; BP: bench press; $: Independent t-test; #: ANOVA; *: significant statistical difference*

Table 2 – Results of within-group comparisons of mean systolic blood pressure and diastolic blood pressure levels in the pre- vs. post-training in the German volume training (GVT, n=15), sarcoplasm stimulating training (SST, n=15) and control (n=15) groups

	Pre-training	0	10	20	30	40	50
CG (n=15)							
SBP mmHg	125.2 ± 7.3	124.6 ± 6.1	126 ± 5.4	125.1 ± 7.9	124.7 ± 7.6	126.5 ± 6.3	127.9 ± 12.5
DBP mmHg	69.1 ± 5.9	67.9 ± 5.8	69.1 ± 6.4	68.3 ± 4.7	71.5 ± 6	70.8 ± 7.9	71.7 ± 7.0
GVT (n=15)							
SBP mmHg	127.7 ± 9.4	137.8 ± 16.2*	125.4 ± 10.8*	124.5 ± 8.5*	126.7 ± 6.9	123.3 ± 8.8	124.9 ± 8.6
DBP mmHg	70.9 ± 9.2	72.5 ± 13.6	68.5 ± 8.2	67.2 ± 5.3	68.6 ± 7.5	65.3 ± 9.5	66.5 ± 6.9
SST (n=16)							
SBP mmHg	124.7 ± 9.2	142.1 ± 28.2	126.2 ± 10.5	126 ± 10.7	122.8 ± 10.5	123.1 ± 10.9	122.4 ± 8.9
DBP mmHg	72.1 ± 6.8	78.4 ± 19.7	66.6 ± 7.4	69.7 ± 9.2	68.5 ± 9.7	67.5 ± 7.9	67.6 ± 6.3

CG: control group; GVT: German volume training; SST: sarcoplasm stimulating training; SBP: systolic blood pressure; DBP: diastolic blood pressure; mmHg: millimeters of mercury: $p<0.05$ compared to immediately after training*
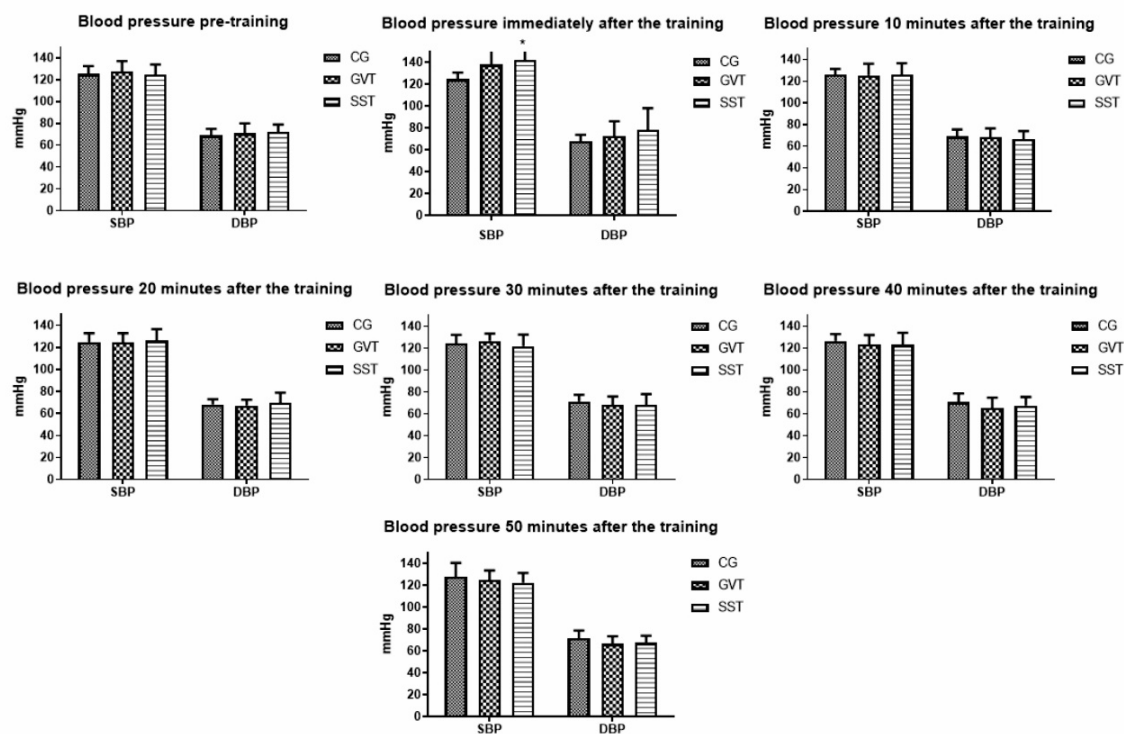
Figure 1 – Comparison of mean systolic blood pressure and mean diastolic blood pressure levels between the German volume training (GVT, n=15), sarcoplasm stimulating training (SST, n=15) and control (n=15) groups
*CG: control group; GVT: German Volume Training; SST: Sarcoplasm Stimulating Training; mmHg: millimeters of mercury; SBP: systolic blood pressure; DBP: diastolic blood pressure; * $p<0.05$ compared with the control group*

findings, since only GVT, which is an exercise program that involves sets and repetitions with high weights, showed significant hypotension after training. Our data differ from those previously published by Neto et al.,[11] who found similar responses of BP to trainings with different volumes.[11] However, the total training volume in our study was much higher than the total volume used in their study, which may explain the differences in the results.

Between-group analysis showed significantly higher SBP values in the SST immediately after training compared to the control group. However, despite this rise in BP levels, the higher intensity of the SST method (compared with the GVT) was not able to promote a significant lowering of BP during the post-exercise recovery period. This contrasts with previous studies reporting hypotensive effects of different resistance training intensities.[21-23]

Our data confirm the results of a study[24] that evaluated the effect of different intensities of exercise, and showed that not only low-intensity exercise (40% of 1-RM), but also the ones with high intensity (80% of 1-RM) caused systolic arterial hypotension in the post-exercise period.[24] However, we found a significant lowering of SBP only for the GVT method, which was performed at 50% of 1-RM (*i.e.*, low intensity).

The highest levels of SBP in the period immediately after training seen in the SST method can be justified by the high intensity and short interval between series (10 seconds vs 30 seconds for the GVT method). Thus, there was no time for recovery of pressure levels to start a new series, leading to higher cardiovascular stress. A clinical trial that compared the response of BP to different rest interval lengths showed that a two-minute interval could be more effective regarding post-exercise hypotension.[25] Although our trainings had shorter duration, the significant lowering of BP after the GVT may be explained by a longer rest interval between the series.[25]

Another hypothesis for the significantly rise in SBP levels immediately after the SST was the occurrence of fatigue in most of the repetitions. This is in line with the study by Polito and Farinatti,[26] who noticed that the highest BP elevations occurred when fatigue was reached after all repetitions.[26] Higher values of SBP was observed in the SST compared with the GVT group; in fact, the SST proposes that individuals perform the series until fatigue, which differs from the GVT, where fatigue occurred mostly in the last repetitions.

Regarding DBP, no significant effect by any of the methods was found. DBP levels remained below the

pre-training levels until the end of the analysis period. This result contrasts with the study showing that exercise with lower intensity would lower DBP for a short period, while exercises with higher intensity would not change acute DBP responses.[27]

One of the limitations in our study refers to the measurement of BP in the supine position. This is supported by the study[28] that evaluated the influence of posture on the recovery of BP and heart rate after resistance training in normotensive individuals. The study found greater hypotensive responses in the sitting position during recovery than in the supine position.[28] However, more studies are needed to support this hypothesis.

Our study group was composed of young male trained, normotensive adults. More studies are needed including female, older and hypertensive individuals. It is worth highlighting that studies on GVT and SST are still scarce in the literature, and that this is the first study to investigate the acute effects of these trainings on BP.

Conclusion

There was a significant lowering of SBP at 10 and 20 minutes after the GVT compared with the immediate post-training. The between-group analysis showed significantly higher SPB levels in the immediate post-training in the SST group compared with control group. High-volume RT of high-intensity-RT did not cause abnormal changes in BP.

Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

Author contributions

Conception and design of the research: Queiroz CO, Santos CPD, Conceição AF. Acquisition of data: Conceição AF, Queiroz CO, Santos CPD, Muniz DLC. Analysis and interpretation of the data: Conceição AF, Queiroz CO, Muniz, DLC. Statistical analysis: Conceição AF, Queiroz CO. Writing of the manuscript: Conceição AF, Queiroz CO. Critical revision of the manuscript for intellectual content: Queiroz CO.

References

1. Précoma DB, Oliveira GMM, Simão AF, Dutra OP, Coelho OR, Izar MCO, et al. Atualização da Diretriz de Prevenção Cardiovascular da Sociedade Brasileira de Cardiologia – 2019. Arq Bras Cardiol. 2019;113(4):787-891.

2. Herrod PJJ, Doleman B, Blackwell JEM, O'Boyle F, Williams JP, Lund JN, et al. Exercise and other nonpharmacological strategies to reduce blood pressure in older adults: a systematic review and meta-analysis. J Am Soc Hypertens. 2018;12(4):248–67.

3. Sharman JE, Gerche AL, Coombes JS. State of the art exercise and cardiovascular risk in patients with hypertension. Am J Hypertens. 2015; 28(2):147–58.

4. Pescatello, LS; Franklin, BA; Fagard, R; Farquhar, WB; Kelley, GA; Ray C. American College of Sports Medicine. Exercise and hypertension. Med Sci Sport Exerc. 2004; 36(3):533–53.

5. Pickering TG, Hall JE, Appel LJ, Falkner BE, Graves J, Hill MN, et al. Recommendations for blood pressure measurement in humans and experimental animals: Part 1: Blood pressure measurement in humans - A statement for professionals from the subcommittee of professional and public education of the American Heart Association Council on High Blod Pressure Research. Circulation. 2005;111(5):697–716.

6. Figueiredo T, Rhea MR, Peterson M, Miranda H, Bentes CM, Machado de Ribeiro dos Reis V, et al. Influence of number of sets on blood pressure and heart rate variability after a strength training session. J Strength Cond Res. 2015;29(6):1556–63.

7. Castinheiras-Neto AG, Costa-Filho IR, Farinatti PTV. Cardiovascular Responses to Resistance Exercise are Affected by Workload and Intervals between Sets. Arq Bras Cardiol. 2010;95(4):493–501.

8. Veloso J, Polito MD, Riera T, Celes R, Vidal JC, Bottaro M. Effects of rest interval between exercise sets on blood pressure after resistance exercises. Arq Bras Cardiol. 2010;94(4)512–8.

9. Rodriguez D, Nakazato K, Fleck S, Pontes Jr LF, Charro MA, Alegretti G, et al. Strength training methods does not affect post- exercise hypotension and heart rate variability. J Exerc Physiol online. 2017;20(5):36–51.

10. Neto VGC, Figueiredo T, Simões AD, Bezerra MG, Barguti STP, Bentes CM, et al. La influencia de la intensidad de la carga sobre la presión arterial después de una sesión de entrenamiento de fuerza. Apunt Med l'Esport. 2017;52(193):23–8.

11. Neto VGC, Fonseca EA, Damasco CAA, Oliveira RS, Bentes CM, Miranda H. [Hipotensão pós-treinamento de força realizado em sessões com diferentes intensidades]. Rev Bras Prescrição e Fisiol do Exerc. 2017;11(71):912–9.

12. Rivera CE, Jiménez MJ, Rojas SW, Herrera SA. Acute effects of exercise on blood pressure: a meta-analytic investigation. Arq Bras Cardiol. 2016;106(5):422–33.

13. Baker D. German Volume Training: an alternative method of high volume-load training for stimulating muscle growth. Perform Train J. 2009;8(1):10–3.

14. Amirthalingam T, Mavros Y, Wilson GC, Clarke JL, Mitchell L, Hackett DA. Effects of a modified German Volume Training program on muscular hypertrophy and strength. J Strength Cond Res. 2017;31(11):3109-19.

15. Gambassi BB, Queiroz C, Muniz D, Conceição A, Santos CE, Galvão V, et al. Acute effect of German Volume Training method on autonomic cardiac control of apparently healthy young. J Exerc Physiol online. 2019;22(2):49–57.

16. Prestes J, Foschini D, Marchetti P, Charro MA, Tibana R. Prescrição e Periodização do treinamento de força em academias. 2ª ed. Barueri: Manole; 2016.

17. Almeida FN, Lopes CR, Machado R, Oenning L, Crisp AH, Manuel N, et al. Acute effects of the new method sarcoplasma stimulating training versus traditional resistance training on total training volume, lactate and muscle thickness. Front Physiol. 2019;10:1–7.

18. Malachias M, Souza W, Plavnik F, Rodrigues C, Brandão A, Neves M, et al. 7TH Brazilian Guideline of Arterial Hypertension. Arq Bras Cardiol. 2016;107(supl 3):1-83.

19. Adams GM. Exercise Physiology Laboratory Manual. Boston; 1998.

20. Maior AS, Varallo ÂT, Matoso AG, Edmundo DA, Oliveira MM, Minari VA. [Resposta da força muscular em homens com a utilização de duas metodologias para o teste de 1RM]. Rev Bras Cineantropometria Desempenho Hum. 2007;9(2):177–82.

21. Casonatto J, Goessler KF, Cornelissen VA, Cardoso JR, Polito MD. The blood pressure-lowering effect of a single bout of resistance exercise: a systematic review and meta-analysis of randomised controlled trials. Eur J Prev Cardiol. 2016;23(16):1700–14.

22. Bentes CM, Costa PB, Neto GR, Costa G V, Salles BF de, Miranda HL, et al. Hypotensive effects and performance responses between different resistance training intensities and exercise orders in apparently health women.Clin Physiol Funct Imaging. 2014;35(5):185–90.

23. Figueiredo T, Willardson JM, Miranda H, Bentes CM, Reis VM, Simão R. Influence of load intensity on postexercise hypotension and heart rate variability after a strength training session. J Strength Cond Res. 2015;29(10):2941–8.

24. Rezk CC, Marrache RCB, Tinucci T, Mion D, Forjaz CLM. Post-resistance exercise hypotension, hemodynamics, and heart rate variability: influence of exercise intensity. Eur J Appl Physiol. 2006;98(1):105–12.

25. Figueiredo T, Willardson J, Mranda H, Bentes CM, Reis VM, Salles BF, et al. Influence of rest interval length between sets on blood pressure and heart rate variability after a strength training session performed by prehypertensive men. J Strength Cond Res. 2016;30(7):1813–24.

26. Polito M, Farinatti PTV. [Respostas de frequência cardíaca, pressão arterial e duplo produto ao exercício contra resistência - uma revisão da literatura]. Rev Port Ciências do Desporto. 2003;3(1):79–91.

27. Polito MD, Simão R,Senna WG, Farinatti PTV. Hypotensive effects of resistance exercises performed at different intensities and same work volumes. Rev Bras Med Esporte. 2003;9(2):69–73.

28. Farinatti PTV, Nakamura FY, Polito MD. Influence of recovery posture on blood pressure and heart rate after resistance exercises in normotensive subjects. J Strength Cond Res. 2009;23(9):2487–92.

Drug Profile and Therapeutic Adherence of African-Brazilians with Apparent Resistant Hypertension

Pedro Henrique Andrade Araújo Salvatore Barletta,[1] Júlia Lasserre Moreira,[2] Vitor Fernandes de Almeida,[2] Mateus Andrade Bomfim Machado,[2] Breno Lima de Almeida,[2] Tayla Samanta Silva dos Santos,[2] Yana Mendonça Nascimento,[2] Thaise Almeida Silva,[2] Roque Aras,[2] Cristiano Macedo[2]

Faculdade de Medicina da Bahia da Universidade Federal da Bahia,[1] Salvador, BA – Brazil.
Hospital Universitário Professor Edgard Santos (HUPES),[2] Salvador, BA – Brazil.

Abstract

Background: Resistant hypertension (RH) is manifested by the presence of blood pressure values resistant to antihypertensive therapy. RH is highly prevalent among black individuals, increasing cardiovascular risk in this population and requiring effective control of this comorbidity.

Objectives: To investigate the medication profile and therapeutic adherence in black people with apparent RH.

Methods: This is a cross-sectional study, with a convenience sample of individuals with apparent RH. Data were obtained from medical records. Therapeutic adherence was assessed using the Morisky Therapeutic Adherence Scale of 8 items (MMAS-8) and statistical analysis was performed using the SPSS, version 23. Significance was set at p <0.05.

Results: Of the 120 individuals, 90 (75%) were women and 72 (60%) were black. Mean SBP was 153.09 (SD 25.59) mm Hg and mean DBP, 90.82 (SD 16.91) mm Hg, with a statistical difference in relation to the target pressure for SBP. Regarding the medication profile, 79.2% of the individuals used the recommended regimen for RH (ACEI / ARB + Diuretic + CCB), with the fourth most used drug being beta-blockers. The average score in MMAS-8 was 6.62 (SD 1.38) points, with 19.2%, 50.0%, and 30.8% showing low, medium, and high adherence, respectively.

Conclusions: It was evidenced that two-thirds of the individuals did not have high therapeutic adherence and not all used the ideal regimen for the management of RH, nor full doses. Thus, most individuals were probably affected by pseudoresistance, which was initially diagnosed as apparent RH. (Int J Cardiovasc Sci. 2021; 34(3):300-306)

Keywords: Hypertension; African Continental Ancestry Group; Medication Adherence; Antihipertensive Agents; Blood Pressure; Drug Resistance.

Introduction

Systemic hypertension (SH) is an important risk factor for cardiovascular events, especially stroke, which justifies the relevance of its proper management. In a meta-analysis conducted by Sarki et al.,[1] the results showed a prevalence of 32.3% of SH, and Latin America was as one of the regions with the highest estimates (39.1%).[1] According to data from the American Heart Association, specifically in the African-American population, the prevalence of SH reaches 44.9% for black men, and 46.1% for black women.[2] A higher prevalence of SH in blacks was also identified in Brazilian studies.[3–5]

Despite this high prevalence, pressure control is achieved in most cases with the appropriate choice of antihypertensive drugs.[6] However, still 9-18% of individuals with SH have blood pressure levels resistant to pharmacological treatment, which characterizes resistant hypertension (RH).[6–8]

Mailing Address: Pedro Henrique Andrade Araújo Salvatore Barletta
Largo Terreiro de Jesus, s/n. Postal Code: 40026-010, Pelourinho, Salvador, BA – Brazil.
E-mail: pedro.barletta@hotmail.com

RH is defined as uncontrolled in-office blood pressure (≥ 140 / 90mm Hg) despite the use of 3 or more antihypertensive drugs in adequate doses, preferably including a diuretic. [6–9] Hypertension is also considered resistant when pressure control is obtained (< 140/90 mm Hg), but only with the use of 4 or more drugs.[6,7,9] In addition to the higher prevalence of RH in the black population, African-origin patients tend to have pressure levels that are more resistant to treatment.[7,10]

However, it is worth mentioning that for the definitive diagnosis of true RH, it is necessary to thoroughly check the patient's therapeutic adherence, since pseudoresistance is often due to poor adherence and / or inadequate therapeutic regimen.[6–8,11] In situations where the patient presents only blood pressure criteria and those referring to the number of antihypertensive drugs for the diagnosis of RH, but there is no exclusion of pseudoresistance after systematic verification of therapy and adherence, the diagnosis is of apparent resistant hypertension (apparent RH).[9]

Thus, in view of the morbidity and mortality associated with SH and the importance of an effective blood pressure control, we decided to investigate the drug profile and therapeutic adherence of black people with the diagnosis of apparent RH.

Methods

This is a cross-sectional descriptive study, which used a non-probabilistic convenience sample of black individuals who attended a reference outpatient clinic for the treatment of RH. Data were obtained from interviews and physical examinations, as well as the collection of information from medical records, using a standardized form approved by the Research Ethics Committee. Study participants signed a free and informed consent form, and were admitted based on the demand for assistance, as they went to the clinic for follow-up visits, from February 2014 to September 2017.

The individuals completed the questionnaire about life habits, medical history, therapeutic scheme used, and adherence to the proposed therapy while seated before blood pressure measurement. The individuals were instructed to empty their bladder before the measurement. Those who had ingested caffeinated drinks, smoked, or made physical effort, had their blood pressure measured in a minimum interval of 30 minutes.

After this initial resting moment, blood pressure was measured using a digital sphygmomanometer (Omron

Healthcare, BP785). The patient's bare arm was supported at the level of his precordium and the cuff was positioned 3 cm above the cubital fossa. For obese patients, the large size cuff was used (Omron Healthcare, HEM-CL24). Measurements were performed on both upper limbs, with an interval of 1 minute between them; the measurement with the highest mean arterial pressure [(2 x diastolic blood pressure + systolic blood pressure) / 3] was considered for record.

Information about the pharmacological prescription of each individual was obtained from medical records. Serum potassium (K +) and serum creatinine (Cr) levels were also obtained from medical records, for analysis of possible justification for not using drugs known to induce hyperkalemia.

The study included self-declared black or brown individuals who used 3 or more antihypertensive drugs, with pressure control not obtained, that is, systolic blood pressure (SBP) ≥ 140 mm Hg and / or diastolic blood pressure (DBP) ≥ 90 mm Hg; or who used 4 medications or more, with pressure control (SBP <140 mm Hg and DBP <90 mm Hg). Because this study assesses only the pressure criteria for the diagnosis of RH, individuals at the time of admission to the study were considered to have apparent RH.[9]

Those with uncontrolled blood pressure even when using 5 or more antihypertensive drugs were classified as having Refractory Arterial Hypertension.[9]

The Morisky Medication Adherence Scale of 8 items (MMAS-8) was used to assess adherence to the prescribed pharmacological treatment. Individuals with scores of 8, 7 - 6 and ≤ 5 were classified as having high, moderate, and low therapeutic adherence, respectively.

Statistical Analysis

Statistical analysis was performed using SPSS, version 23.0. Categorical variables were presented using absolute and relative frequencies, while continuous variables were presented using means and standard deviations. The investigation of associations was conducted using the calculation of chi-square (χ^2) and prevalence ratio (PR). The Kolmogorov-Smirnov test was used to certify the normality of the data distribution. The comparison of means was performed using Student's t test for independent samples. The mean blood pressure values obtained were compared with the target blood pressure levels of 140/90 mm Hg using the one sample t test. Similarly, the averages of the daily doses of the

302

Barletta et al.
Apparent Hypertension in African-Brazilians

Int J Cardiovasc Sci. 2021; 34(3):300-306
Original Article

antihypertensive drugs used were compared with the maximum doses of each drug, also using the one sample t rest. Significance was established at $p < 0.05$.

Results

A total of 120 individuals were included in the study, whose characterization was shown in Table 1. The mean SBP was higher than the target SBP of 140 mm Hg (t [119] = 5.603 and $p <0.05$), while there was no statistical difference between the mean DBP and the target DBP of 90 mm Hg (t [119] = 0.529 and $p = 0.598$) (Table 1).

Regarding the medication profile (Table 2), the mean amount of oral antihypertensive drugs used by each individual was 4.71 (SD, 1.08). In addition, 79.2% of the individuals used the ACEI / ARB + Diuretic + CCB therapeutic regimen. As shown in Table 2, there was a statistical difference between the average doses of the drugs used and the full doses of these drugs. Among these individuals, considering those who needed 4 drugs or more, 82.4% used some beta-blocker, and 49.5% used spironolactone (Figure 1). The mean of [K +] of those who did not use spironolactone was 4.32 (SD 0.72) mmol / L and of those who did, 4.49 (SD 0.54) mmol / L, with no statistical difference (t [91] = - 1.305, $p = 0.195$). The creatinine means among those who did not use spironolactone and those who did it were, respectively, 1.092 (SD 0.468) mg / dL and 1.095 (SD 0.276) mg / dL, with no statistical difference (t [93] = - 0.049, $p = 0.961$).

Table 1 – Characterization of the sample	
N	120
Sex	
Female	90 (75%)
Male	30 (25%)
Age (years)	63.07 ± 11.36
Race/color	
Black	72 (60%)
Brown	48 (40%)
Blood pressure	
Mean SBP (mm Hg)	153.09 ± 25.59
Mean DBP (mm Hg)	90.82 ± 16.91

SBP: Systolic blood pressure; DBP: diastolic blood pressure

A total of 34.2% of individuals met the criteria for Refractory Hypertension.[9] Of these, 34.1% did not use spironolactone, and 53.7% did not use the combination of chlorthalidone and spironolactone.

Regarding therapeutic adherence, the mean score on the MMAS-8 scale was 6.62 (SD 1.38) points, and the percentage of individuals with low therapeutic adherence was 19.2%; moderate adherence, 50.0%; and high adherence, 30.8% (Table 3). Comparing the groups of high and low therapeutic adherence, being a man was associated with better adherence (χ^2 (1) = 4.266 [p = 0.039] and PR = 1.524 [95% CI 1.055 - 2.200]). There was no statistically significant difference between the mean age and the quantity of drugs used in these groups (t (58) = - 1.330 [p = 0.189] and t (58) = - 0.372 [p = 0.711], respectively).

Although the mean pressure levels in the group with high therapeutic adherence were lower compared to the group with low adherence, there was no statistically significant difference (t (58) = 0.809 and p = 0.422 for mean SBP and for mean DBP, t (61) = 0.810; p = 0.421).

Discussion

Regarding the diagnosis of RH, it is imperative to rule out potential causes for the difficult control of blood pressure, highlighting the inappropriate choice of antihypertensives, poor therapeutic adherence, the effect of white coat hypertension, and secondary hypertension.[6–8]

For the treatment of RH, the recommended therapeutic regimen should include oral antihypertensive drugs with complementary pharmacodynamics. With this, as an ideal therapy, treatment with 3 drugs is recommended, including a thiazide or thiazide-type diuretic (preferably chlorthalidone), a blocker of the renin-angiotensin-aldosterone system (ARB or ACEI) and a dihydropyridine calcium channel blocker (CCB), in full tolerated doses and at appropriate intervals.[8,12,13] It was observed that 79.2% of the individuals used this triple therapy. Despite this, the mean SBP verified was greater than 140 mm Hg. This may have happened due to not using the full doses of ACEI / ARB and CCB in a statistically significant way.

Tu et al.,[14] demonstrated that blood pressure levels in black people would be more sensitive to the effects of aldosterone.[14] Other studies have shown higher plasma levels of aldosterone in black people.[15,16] Given these facts, knowing that primary hyperaldosteronism is imputed in the genesis of RH,[6,8] it is reasonable to understand the importance of using aldosterone antagonists in the

Table 2 – Antihypertensive drugs and percentage of use in the sample

Drug	Percentage of individuals using the drug	Average of daily doses compared to the maximum doses of each drug (mg)[1]
Diuretic		
Hydrochlorothiazide	48.3%	25.00 ± 0.00[2]
Spironolactone	47.5%	30.26 ± 10.28 ($p<0.05$)
Chlorthalidone	45%	24.54 ± 2.38 ($p=0.159$)
Furosemide	11.7%	42.86 ± 10.69 ($p<0.05$)
ACEI/ARB		
Losartan	65.8%	94.94 ± 17.16 ($p=0.011$)
Enalapril	25%	36.00 ± 8.14 ($p=0.012$)
Captopril	4.2%	90.00 ± 54.77 ($p=0.07$)
Beta-blocker		
Carvedilol	36.7%	45.17 ± 10.52 ($p=0.004$)
Atenolol	21.8%	70.19 ± 29.17 ($p<0.05$)
Propranolol	9.2%	90.91 ± 36.18 ($p<0.05$)
Nebivolol	7.2%	5.56 ± 1.67 ($p<0.05$)
Metoprolol	5%	100.00 ± 54.77 ($p=0.07$)
CCB		
Amlodipine	70.8%	8.56 ± 2.33 ($p<0.05$)
Nifedipine	12.5%	41.67 ± 15.08 ($p<0.05$)
Alpha-2-agonist		
Clonidine	36.3%	0.27 ± 0.16 ($p<0.05$)
Vasodilator		
Hydralazine	17.5%	147.62 ± 79.41 ($p=0.892$)

1 - The t test of a sample was used to compare the average dose of drugs with the full dose of each drug.
2 - All patients using hydrochlorothiazide used a daily dose of 25mg, so that the standard deviation was zero, thus making it impossible to apply the statistical test; ACEI: Angiotensin-converting enzyme inhibitor; ARB: Angiotensin II receptor blocker; CCB: calcium channel blocker

therapeutic regimen of black patients, as revealed by Saha et al.,[17] when demonstrating that treatment with amiloride or spironolactone may provide an additional reduction in blood pressure in blacks already receiving conventional antihypertensive therapy.[17] In the present study, considering those who needed 4 drugs or more, only 49.5% used spironolactone, even without plausible justification for not using it. This fact may have contributed to the high mean of SBP.

In fact, robust studies indicate that spironolactone is preferably the fourth drug to be added to the triple ARB / ACE + CCB + thiazide diuretic regimen in the treatment of RH.[12,13,18] It is noteworthy that the PATHWAY-2 study, which demonstrated the superiority of spironolactone as the fourth antihypertensive agent, compared to doxazosin and bisoprolol, based on the reduction of home SBP.[19] Based on this and the superiority of chlorthalidone over hydrochlorothiazide,[20] the most recent guidelines of the American Heart Association started to define Refractory Hypertension as the failure to control blood pressure, despite the use of at least 5 antihypertensive agents of different classes, including a long-acting thiazide-type diuretic, such as chlorthalidone, and a mineralocorticoid receptor antagonist, such as spironolactone. [12]

Figure 1 – Frequency of drugs added to the ACEI/ARB + CCB + DIU regimen
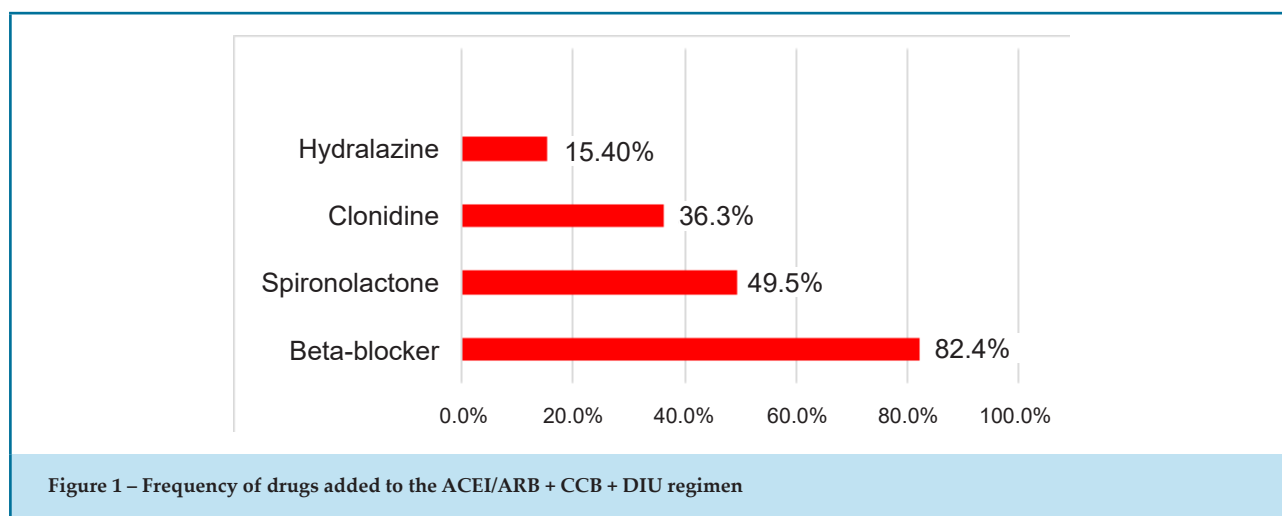
Table 3 – Characterization of groups according to therapeutic adherence

	Low adherence	Moderate Adherence	High adherence
Relative frequency	19.2%	50.0%	30.8%
Women	82.6%	83.3%	56.76%
Men	17.4%	16.7%	43.24%
Mean age (years)	65.74 ± 12.48	62.67 ± 12.23	62.05 ± 8.96
Mean quantity of OAH	4.78 ± 1.00	4.70 ± 1.02	4.68 ± 1.13
Mean SBP (mm Hg)	156.67 ± 28.40	152.98 ± 25.25	151.04 ± 24.80
Mean DBP (mm Hg)	91.87 ± 18.13	91.91 ± 17.73	88.39 ± 14.84

OAH: oral antihypertensive; SBP: systolic blood pressure; DBP: diastolic blood pressure

Considering this most current definition of refractory hypertension, in this study, 53.7% of the individuals who met the criteria of the 7th Brazilian Directive on Arterial Hypertension for Refractory Hypertension would not be seen as having pressure levels refractory to treatment. These data reveal, once again, the importance of ensuring that the medication regimen is the recommended regimen, before establishing the diagnosis of true RH.

On the other hand, chlorthalidone, an important medication for the control of RH, is not included in the list of Essential Medicines of the Brazilian public Unified Health System.[21] In a society where low-income individuals are mostly black and depend on the public Health System, [22,23] it is difficult to assess what is the real responsibility of the genetic background in the development of RH, given the socioeconomic issues involved.

Regarding therapeutic adherence, Rajpura et al.,[24] used the 4-item Morisky scale to assess how the perception of SAH and drug therapy influences therapeutic adherence, finding a 18.8% prevalence of high adherence, 47%, moderate adherence, and 34.2% low adherence.[24]

Morisky et al.,[25] In the MMAS-8 validation study, observed that 15.9% of the study sample had high adherence, 52.0% moderate adherence, and 32.1% low adherence.[25] In comparison with the studies cited, the present study revealed a lower prevalence of low therapeutic adherence (19.2%) and a higher prevalence of high adherence (30.8%). This may be due to the fact that the sample consisted of patients with apparent RH followed in a reference clinic, so that a stronger belief in the severity of the disease and need for medications may have contributed to better adherence.[24] Nevertheless, a considerable portion of the individuals did not have full

adherence to pharmacological treatment, which may also have influenced the high mean SBP.

In the present study, men showed higher adherence to drug treatment. This finding corroborates the systematic review conducted by Hope et al. with individuals using statins, in which being a man was a predictor of better therapeutic adherence.[26] However, the literature shows different results regarding the association between sex and adherence to pharmacological treatment: women showed greater adherence to the antihypertensive treatment regimen in a study conducted in Jordan,[27] while there was no statistical difference between the sexes in individuals from rural Vietnam.[28] These findings may be indicative that cultural and social factors have an important contribution to therapeutic adherence found in different countries.

De La Sierra et al.,[29] analyzed a large Spanish cohort of individuals treated for RH, finding a prevalence of 12.2% of RH; after investigating the data regarding ambulatory blood pressure measurement (ABPM) of these patients, it was found that in 37.5% of the cases, the ineffectiveness of the treatment was due to the white coat effect.[29] Considering the relevance of the white coat effect, the authors and the current guidelines for the management of SH point to ABPM as a valuable tool in the diagnosis of true RH, being the next propaedeutic step to be adopted in patients with apparent RH, as in the case of the present study.[8,12,13,30]

Because it is a cross-sectional study, there are inherent limitations to this type of research design. The number of individuals may not have been sufficient to demonstrate a statistically significant difference between the pressure levels of the groups of high and low therapeutic adherence and the performance of a multivariate analysis could reveal factors that better influence adherence. Adherence to non-drug therapy was not assessed. Furthermore, the use of indirect methods to assess medication adherence, such as MMAS-8, is vulnerable to memory bias, so that the answers given may not be reliable to the individual's real behavior.

Since no ABPM data were obtained, the study was not able to accurately distinguish between pseudoresistant patients and patients with actual RH. A comparison of the results of black patients with those of individuals who did not declare themselves as African-Brazilians could also have been considered.

It is evident that resistance to treatment with antihypertensive drugs is multifactorial. As evidenced in the literature, the appropriate choice of antihypertensive drugs, as well as the strengthening of the doctor-patient bond for better adherence to treatment, is essential for the management of RH. The importance of spironolactone in the treatment of RH, especially in black people, should be disseminated among physicians and reported in national guidelines. The white coat effect should not be underestimated either, so that the relevance of ABPM in the diagnosis of true RH should also be emphasized in future Brazilian guidelines.

Future studies that aim to assess the understanding of the mechanisms by which socio-environmental issues influence blood pressure levels in the black population are essential for the creation of public health policies and for the guarantee of equity.

Conclusion

The present study showed that two-thirds of the individuals did not have high therapeutic adherence and some of them did not use the ideal triple regimen for the management of RH, nor did they use full doses. These data culminated in the conclusion that most individuals included in the study were probably affected by pseudoresistance, which was initially diagnosed as apparent RH.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Sources of Funding

There were no external funding sources for this study.

Study Association

This study is not associated with any thesis or dissertation work.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of the *Hospital Ana Nery* under the protocol number 08501212800000045. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

Author Contributions

Conception and design of the research: Macedo CRB, Aras-Jr R. Acquisition of data: Barletta PHAAS, Machado MAB, Almeida BL, Moreira JL, Almeida VF, Santos TSS, Silva TA, Nascimento YM. Analysis and interpretation of the data: Barletta PHAAS, Machado MAB, Almeida BL, Moreira JL. Statistical analysis: Barletta PHAAS, Machado MAB. Writing of the manuscript: Barletta PHAAS, Moreira JL, Almeida VF, Machado MAB, Almeida BL. Critical revision of the manuscript for intellectual content: Santos TSS, Silva TA, Nascimento YM, Macedo CRB, Aras-Jr R.

References

1. Sarki AM, Nduka CU, Stranges S, Kandala N-B, Uthman OA. Prevalence of Hypertension in Low- and Middle-Income Countries. Medicine (Baltimore). 2015 Dec;94(50):e1959.

2. Go AS, Mozaffarian D, Roger VL, Benjamin EJ, Berry JD, Blaha MJ, et al. Heart Disease and Stroke Statistics—2014 Update. Circulation. 2014 Jan 21;129(3):e28–292.

3. Lolio CA de, Pereira JCR, Lotufo PA, Souza JMP de. Hipertensão arterial e possíveis fatores de risco. Rev Saude Publica. 1993 Oct;27(5):357–62.

4. Lessa Í, Magalhães L, Araújo MJ, Almeida Filho N de, Aquino E, Oliveira MMC. Hipertensão arterial na população adulta de Salvador (BA) - Brasil. Arq Bras Cardiol. 2006 Dec;87(6):747–56.

5. Noblat ACB, Lopes MB, Lopes AA. Raça e lesão de orgãos-alvo da hipertensão arterial em pacientes atendidos em um ambulatório universitário de referência na cidade de Salvador Raça e Lesão de Órgãos-Alvo da Hipertensão Arterial em Pacientes Atendidos em um Ambulatório Universitário de Referência na Cidade de Salvador. Arq Bras Cardiol.2004;82(2):116-20.

6. Doroszko A, Janus A, Szahidewicz-Krupska E, Mazur G, Derkacz A. Resistant Hypertension. Adv Clin Exp Med. 2016;25(1):173–83.

7. Braam B, Taler SJ, Rahman M, Fillaus JA, Greco BA, Forman JP, et al. Recognition and Management of Resistant Hypertension. Clin J Am Soc Nephrol. 2017 Mar 7;12(3):524–35.

8. Wei F-F, Zhang Z-Y, Huang Q-F, Yang W-Y, Staessen JA. Resistant hypertension. Kardiol Pol. 2018 Jul 6;76(7):1031–42.

9. Malachias MVB, Souza WKSB, Plavnik FL et al. 7ª Diretriz Brasileira de Hipertensão Arterial. Arq. Bras. Cardiol. 2016 Sep; 107(3 Suppl 3).

10. Howard G, Prineas R, Moy C, Cushman M, Kellum M, Temple E, et al. Racial and Geographic Differences in Awareness, Treatment, and Control of Hypertension. Stroke. 2006 May;37(5):1171–8.

11. Hyman DJ, Pavlik V. Medication adherence and resistant hypertension. J Hum Hypertens. 2015 Apr 11;29(4):213–8.

12. Whelton PK, Carey RM, Aronow WS, Casey DE, Collins KJ, Dennison Himmelfarb C, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Hypertension. 2018 Jun;71(6):1269–324.

13. Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension. Eur Heart J. 2018 Sep 1;39(33):3021–104.

14. Tu W, Eckert GJ, Hannon TS, Liu H, Pratt LM, Wagner MA, et al. Racial Differences in Sensitivity of Blood Pressure to Aldosterone. Hypertension. 2014 Jun;63(6):1212–8.

15. Kidambi S, Kotchen JM, Krishnaswami S, Grim CE, Kotchen TA. Aldosterone Contributes to Blood Pressure Variance and to Likelihood of Hypertension in Normal-Weight and Overweight African Americans. Am J Hypertens.2009;22:1303-8.

16. Ahmed KS, Bogdanet D, Abadi S, Dineen R, Boran G, Woods CP, et al. Rates of abnormal aldosterone/renin ratio in African-origin compared to European-origin patients: A retrospective study. Clin Endocrinol (Oxf). 2019 Apr;90(4):528–33.

17. Saha C, Eckert GJ, Ambrosius WT, Chun T-Y, Wagner MA, Zhao Q, et al. Improvement in Blood Pressure With Inhibition of the Epithelial Sodium Channel in Blacks With Hypertension. Hypertension. 2005 Sep;46(3):481–7.

18. Cai A, Calhoun DA. Resistant Hypertension: An Update of Experimental and Clinical Findings. Hypertens (Dallas, Tex 1979). 2017;70(1):5–9.

19. Williams B, MacDonald TM, Morant S, Webb DJ, Sever P, McInnes G, et al. Spironolactone versus placebo, bisoprolol, and doxazosin to determine the optimal treatment for drug-resistant hypertension (PATHWAY-2): a randomised, double-blind, crossover trial. Lancet (London, England). 2015 Nov 21;386(10008):2059–68.

20. Liang W, Ma H, Cao L, Yan W, Yang J. Comparison of thiazide-like diuretics versus thiazide-type diuretics: a meta-analysis. J Cell Mol Med. 2017 Nov;21(11):2634–42.

21. Brasil. Ministério da Saúde. Secretaria de Ciência, Tecnologia e Insumos Estratégicos. Departamento de Assistência Farmacêutica e Insumos Estratégicos. Relação Nacional de Medicamentos Essenciais: RENAME. Brasilia;2017. 210p.

22. Kilsztajn S, Toshiaki G, Sugahara L, De E, Lopes S, Santos Petrohilos S. Concentração e distribuição do rendimento por raça no brasil. R. Econ. Contemp. 2005 ago; 9(2): 367-84.

23. Campello T, Gentili P, Rodrigues M, Rizzo Hoewell G. Faces da desigualdade no Brasil: um olhar sobre os que ficam para trás Faces of inequality in Brazil: a look at those left behind. Saúde.Debate. 2018;3(num.espec):54-66.

24. Rajpura J, Nayak R. Medication Adherence in a Sample of Elderly Suffering from Hypertension: Evaluating the Influence of Illness Perceptions, Treatment Beliefs, and Illness Burden. J Manag Care Pharm. 2014 Jan;20(1):58–65.

25. Morisky DE, Ang A, Krousel-Wood M, Ward HJ. Predictive validity of a medication adherence measure in an outpatient setting. J Clin Hypertens (Greenwich). 2008 May;10(5):348–54.

26. Hope HF, Binkley GM, Fenton S, Kitas GD, Verstappen SMM, Symmons DPM. Systematic review of the predictors of statin adherence for the primary prevention of cardiovascular disease. Zeeb H, editor. PLoS One. 2019 Jan 17;14(1):e0201196.

27. Al-daken LI, Eshah NF. Self-reported adherence to therapeutic regimens among patients with hypertension. Clin Exp Hypertens. 2017 Apr 3;39(3):264–70.

28. Nguyen T-P-L, Schuiling-Veninga CCM, Nguyen TBY, Vu T-H, Wright EP, Postma MJ. Adherence to hypertension medication: Quantitative and qualitative investigations in a rural Northern Vietnamese community. Bishopric NH, editor. PLoS One. 2017 Feb 1;12(2):e0171203.

29. de la Sierra A, Segura J, Banegas JR, Gorostidi M, de la Cruz JJ, Armario P, et al. Clinical Features of 8295 Patients With Resistant Hypertension Classified on the Basis of Ambulatory Blood Pressure Monitoring. Hypertension. 2011 May;57(5):898–902.

30. Judd E, Calhoun DA. Apparent and true resistant hypertension: definition, prevalence and outcomes. J Hum Hypertens. 2014 Aug 16;28(8):463–8.

Reference Equation for the Six-Minute Walk Test in Brazilian Patients with Obesity

José Carlos do Vale Quaresma, João Regis Ivar Carneiro, Norma Ferreira Marschhausen, Gustavo Gavina da Cruz, José Fernandes Filho, Ronir Raggio Luiz
Universidade Federal do Rio de Janeiro, Rio de Janeiro, RJ – Brazil.

Abstract

Background: Obesity has repercussions on functional capacity (FC). The six-minute walk test (6MWT) is a useful tool for assessing submaximal FC, and the distance reached at 6 minutes of walking (D6MW) is a relevant prognostic marker.

Objective: This paper aims to establish a reference equation for the distance predicted in 6MWT in obese Brazilian subjects.

Methods: This study included 460 patients (306 women), with a body mass index (BMI) > 30 kg/m^2, 71% (328) of whom presented a grade III obesity (BMI ≥ 40 Kg/m^2) and were evaluated with 6MWT. Heart rate, blood pressure, oxygen saturation and Borg scale perception of effort were recorded before and after the 6MWT. For statistical analysis, Kolmogorov-Smirnov tests, an unpaired T-Test, Pearson's correlation, and multiple linear regression were used, together with a significance level set at $p < 0.05$.

Results: Gender, age, and BMI were significantly correlated with D6MW and were identified by multiple linear regression as the best predictors of the D6MW. Together, they explain 48.7% of the D6MW variance for obese Brazilian subjects. Based on these findings, an equation was proposed – D6MW = 930.138 + (27.130 x Genderfemales = 0; males = 1) - (5.550 x BMI kg/m^2) - (4.442 x Age years). When the average of the D6MW obtained with the above equation was compared to the average calculated with the equations described in medical literature for healthy and obese individuals, the latter tended to overestimate the D6MW.

Conclusion: The proposed reference equation exhibited better assessment of FC in obese Brazilian patients, providing proper subsidies for the follow up ofinterventions in this population.. (Int J Cardiovasc Sci. 2021; 34(3):307-314)

Keywords: 6-minute walk test, Obesity, Exercise tolerance.

Introduction

Obesity is a multifactorial condition that causes chronic deleterious implications on health and affects one's quality of life. It is recognized as an important cardiovascular risk factor which contributes to the reduction of cardiopulmonary functional capacity and exercise tolerance not only because of decreased skeletal muscle strength and elevated metabolic cost, but also because of progressive gait inefficiency.[1,2]

In Brazil, an increase in the prevalence of overweight and obese individuals has been observed in the last decade.[1,3] In a recent report published by the Ministry of Health, VIGITEL Brasil 2016,[4] it was stated that more than half of the population is overweight and that 18.9% of Brazilians are obese. These statistics show an increase of 60% in obesity taxes over the last 10 years, which contributes to a growth in hypertension (14.2%) and diabetes (61.8%) in the same period.

The six-minute walk test (6MWT) is a useful tool in the assessment of functional capacity and of the response to the demands required in daily life activities. In the last two decades, especially after the American Thoracic Society (ATS) published a guideline for the 6MWT, reference

308

Quaresma et al.
Reference Equation for the Six-Minute Walk Test

Int J Cardiovasc Sci. 2021; 34(3):307-314
Original Article

equations for the distance predicted in the test have been indicated for different populations, both for healthy individuals and for patients with several chronic diseases.[5-8]

In 2009, Iwama et al.,[9] proposed a reference equation for healthy Brazilian subjects. In 2011, Soares[10] also presented a reference equation for healthy adults in Brazil, taking into account the body mass index (BMI) in their composition. In 2013, based on a multicentric study, Britto et al.[11] published reference equations for the Brazilian population, which illustrates the growing interest in the 6MWT in our context.

The use of the 6MWT for the evaluation of obese patients has recently been observed, as shown in different already published studies.[12-15] Thus, this study aims to establish a reference equation for the distance predicted in 6MWT in obese Brazilian patients.

Methods

The sample size was defined by convenience, patients were recruited according to their admission to the Multidisciplinary Program for the Treatment of Obesity and Bariatric Surgery (PROCIBA) at the Clementino Fraga Filho University Hospital of the Federal University of Rio de Janeiro (HUCFF-UFRJ - Brazil) between August 2007 and August 2017. All patients had 6 or more years of schooling and signed a Free and Informed Consent Form. This study was approved by the UFRJ Research Ethics Committee (CEP-HUCFF-CAAE, logged under project number 1041.0.197.000-05).

Patients with unstable angina, myocardial infarction, cardiac arrhythmias, heart rate (HR) greater than 120 beats per minute at rest, blood presure (BP) ≥ 160/100 mmhg at rest, peripheral oxygen saturation lower than 95% at rest, neurological and /or orthopedic conditions capable of restricting gait were excluded.

Using a standardized technique,[16] the patients' weight (w) was obtained with a Filizola calibrated balance (0.1 kg of precision) when they were barefoot and wearing light clothes. The patients' height (h) was measured with a stadiometer (0.5 cm accuracy). Afterwards, their body mass index (BMI) was calculated using the following formula: $BMI = w (kg) / h (m^2)$.

The 6MWT was applied to all participants in accordance with the "ATS Statement: Guidelines for the Six-minute Walk Test".[16] Patients were advised to walk as fast as possible in a quiet and unobstructed hallway, 30 meters long, with each meter marked. Encouragement instructions were standardized and given every minute. The walk could be interrupted at any moment by the patient or the examiner in the presence of chest pain, intolerable dyspnea, dizziness, pallor, sweating, cramps, imbalance, and physical exhaustion. Before and after the test, the patients' HR and peripheral oxygen saturation were recorded with a pulse oximeter (Onix II, Nonin Medical Inc., Plymouth, Minnesota). Their BP was measured with a cuff diameter corresponding to the group of patients under study,[17] and their subjective perception of effort was graded according to the Borg scale.[18] The distance reached at 6 minutes of walking (D6MW) was recorded and compared to predicted values based on three reference equations employed in other populations.

Statistical Analysis

Statistical analysis was performed with the usage of the IBM-SPSS Statistic 22 program. Statistical significance was set at $p<0.05$. Data were presented as mean ± standard deviation. Categorical variables were described using absolute and percentage values. To compare the means, an unpaired T-Test was used. From an initial universe of 510 patients, the Kolmogorov-Smirnov test identified a distribution pattern with discrete asymmetry. To determine the explanatory variables (demographic and anthropometric attributes) that are significantly and independently best associated with the result variable (D6MC), Pearson's correlation was conducted.

The bivariate association between age and BMI with D6MC respectively, as well as the 95% confidence interval (CI) lines for individual predicted values, are shown in Figures 1 and 2. The participants selected for our sample were between the lines of 95% CI. Therefore, 460 obese patients (306 women) remained with a BMI ≥ 30 kg/m², the majority (71%) with grade III obesity (BMI> 40 kg/m²).[19]

Seeking to build a multiple linear regression model, and understanding the need to obey the assumptions for its use, it can be concluded that, despite the discreet asymmetry, the residues of our model have an approximately normal distribution, as the sample size is large enough to accept the premise of normality.[20]

Results

The general characteristics of the 460 obese patients, 306 women (67%), are presented in Table 1. A significant difference was observed between men and women for age and D6MC, with p<0.05, as well as for weight, height,
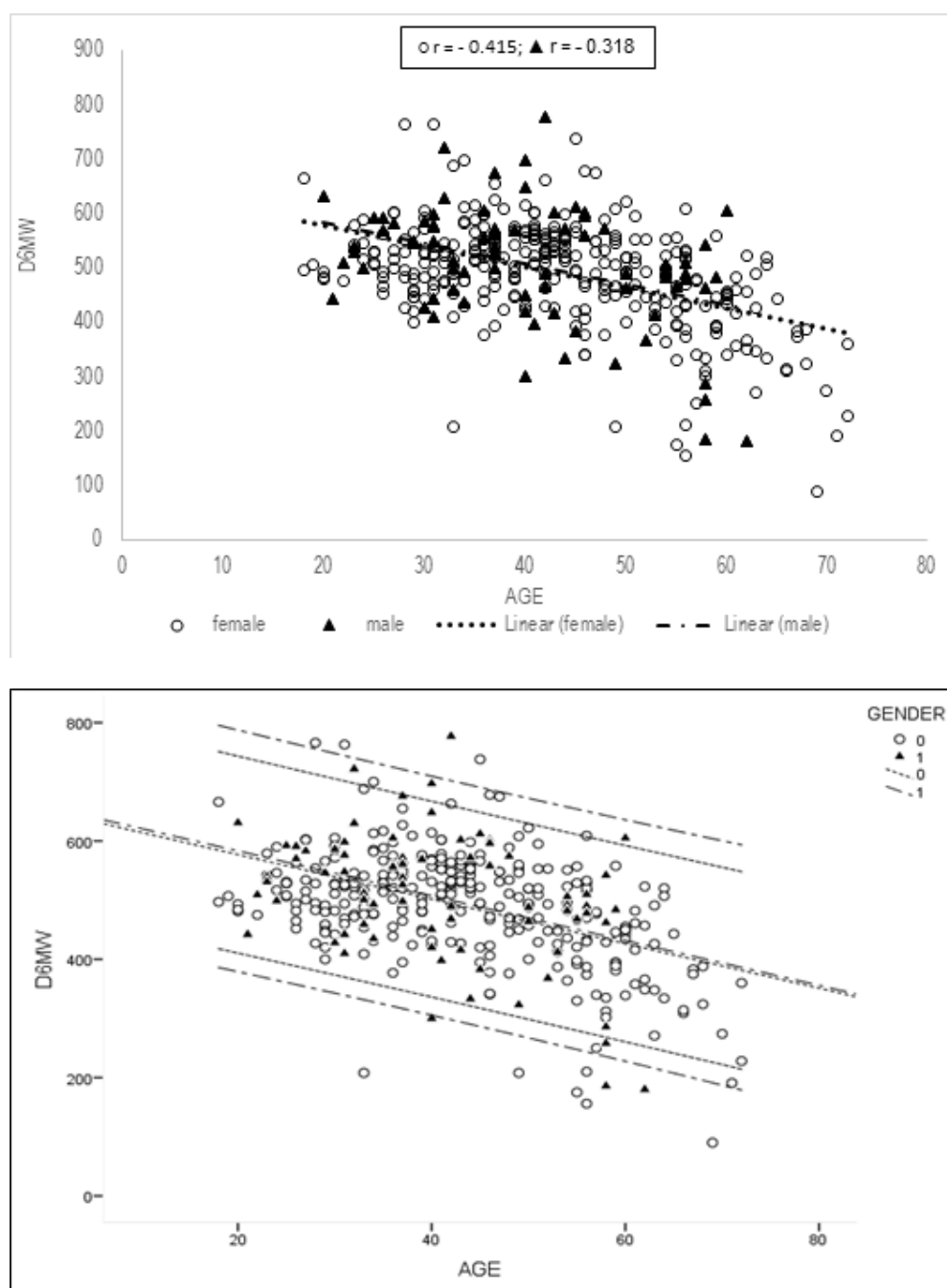
Figure 1 (A) – Correlation between distance reached at 6 minutes of walking (D6MW) and age. (B) Scattergram with lines of 95% CI for individual predictive value.

and BMI, with p <0.001. Taking the entire group into consideration, the D6MW had a significant correlation with sex (r = 0.102, p < 0.029), age (r = -0.387, p < 0.001), weight (r = -0.312, p < 0.001), height (r = 0.163, p < 0.001), and BMI (r = -0.464, p <0.001). Therefore, the D6MW is explained 1% due to sex, 14.9% to age, 9.7% to weight, 2.6% to height, and 21.5% to BMI.

For multiple linear regression, the best model adjusted for the D6MW predictor was that using the variables of gender, age, and BMI, which together explain 48.7% of the total D6MW variance (Table 2). The equation proposed as reference for Brazilian subjects with obesity is as follows: D6MW = 930.138 + (27.130 x Genderfemales = 0; males = 1) - (5.550 x BMI kg / m²) - (4.442 x Age years).

310

Quaresma et al.
Reference Equation for the Six-Minute Walk Test

Int J Cardiovasc Sci. 2021; 34(3):307-314
Original Article
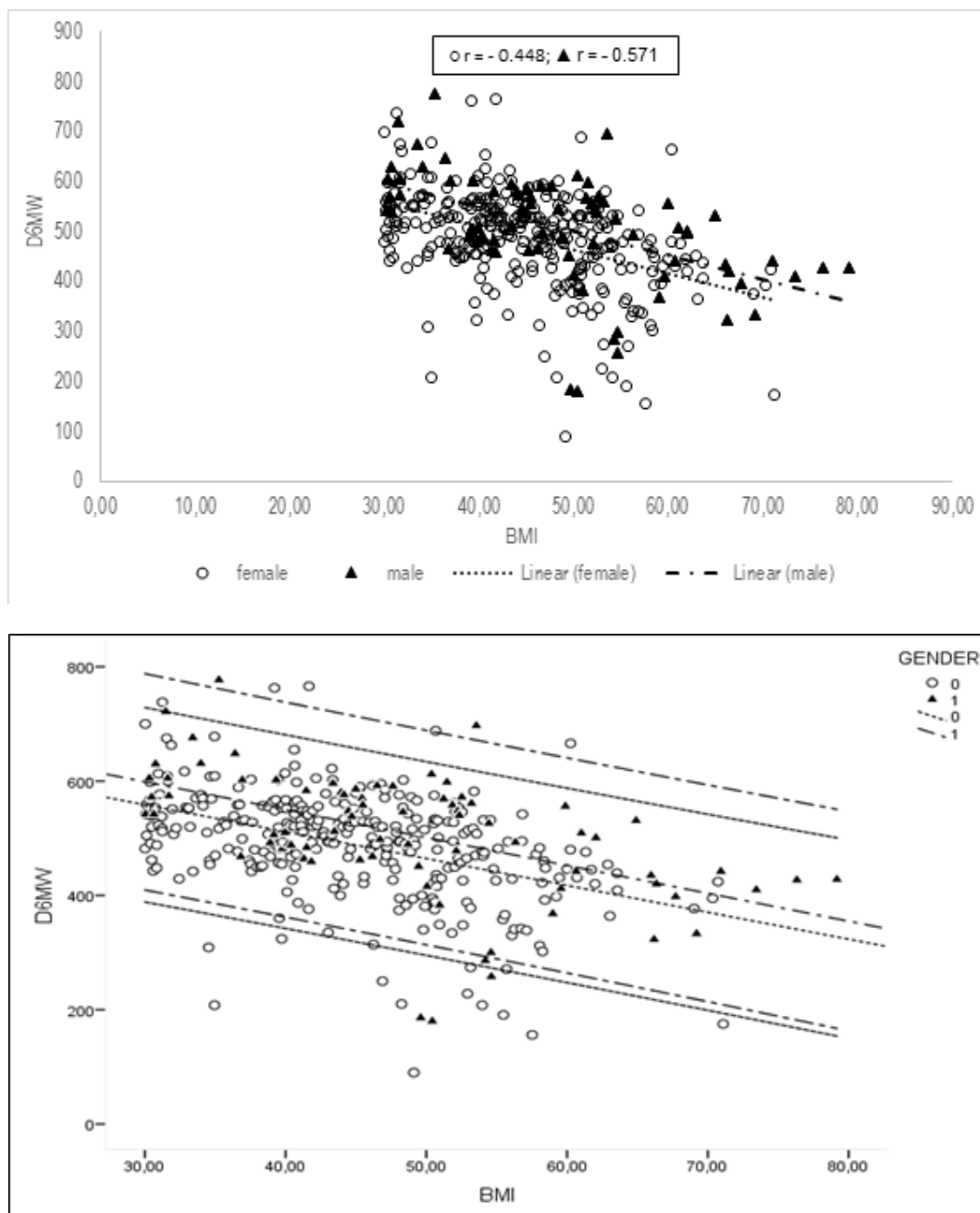
Figure 2 (A) – Correlation between distance reached at 6 minutes of walking (D6MW) and body mass index (BMI). (B) Scattergram with lines of 95% CI for individual predictive value.

When we compared the mean of the D6MW for the whole group, obtained with the above equation, to the mean calculated by the Enright [5] and Iwama [9] equations for healthy individuals, and to the mean calculated by the Capodaglio equation[13] for obese individuals, it was observed that these equations tend to overestimate the values for D6MW (Figure 3).

Discussion

Functional capacity to exercise is an important marker of mortality and morbidity. In obese patients, walking requires greater metabolic and cardiopulmonary demand. Moreover, the additional musculoskeletal dysfunction due to joint overload and osteoarthrosis

Table 1 – General characteristics		
Characteristics	**Male**	**Female**
	(n = 154)	**(n = 306)**
Obesity Grade I, n (%)	18 (12)	52 (17)
Obesity Grade II, n (%)	18 (12)	44 (14)
Obesity Grade III, n (%)	118 (76)	210 (69)
Age (years)		
Mean ± SD	40 ± 11.2	43 ± 12.1
Weight (kg)		
Mean ± SD	149.6 ± 37.8	116.7 ± 26.0
Height (m)		
Mean ± SD	1.75 ± 0.07	1.61 ± 0.07
BMI (kg / m²)		
Mean ± SD	48.99 ± 11.61	44.78 ± 8.88
D6MW (m)		
Mean ± SD	506 ± 110	489 ± 95.4

BMI: Body mass index; D6MW: distance reached at 6 minutes of walking;
Obesity Grade I: IMC ≥ 30 and ≤ 34.9; Obesity Grade II: IMC ≥ 35 and ≤ 39.9; Obesity Grade III: IMC ≥ 40

Table 2 – Predictive model for the distance reached in the 6-minute walk test in obese Brasilian subjects					
Variable	**Coefficient**	**SEM**	**p**	**95% CI**	
				Minimum	**Maximum**
Constant	930.138	21.641	< 0.001	887.609	972.667
Gender	27.130	7.301	< 0.001	12.782	41.479
AGE (years)	-4.442	0.289	< 0.001	-5.009	-3.874
BMI (kg / m²)	-5.550	0.345	< 0.001	-6.228	-4.872

The proposed reference equation is: $D6MC = 930.138 + (27.130 \times Gender_{females = 0; males = 1}) - (5.550 \times BMI_{kg/m^2}) - (4.442 \times Age_{years})$
Gender factor: female = 0; male = 1; D6MW: Distance reached at 6 minutes of walking; BMI: Body mass index

(knees, ankles and hip), associated with eventual loss of muscle mass, can be factors that contribute to a lower performance in walking.[2,6,21] As 6MWT is easy to apply, has a low cost, is safe, and is easily correlated with the activities of daily life, mostly at the submaximal level, it represents a relevant element in the evaluation of obese patients' functional capacity. Consequently, D6MW becomes a significant prognostic indicator.[6,22]

Previous studies have already described age, sex, weight, height, and BMI as variables capable of influencing D6MW.[5,9,12,13,23,24] For obese individuals, especially those with BMI ≥ 40 kg / m2, as already mentioned, musculoskeletal dysfunctions and loss of muscle mass are factors that have a considerable influence on D6MW, particularly with advancing age[2,25] (Figure 1).

312

Quaresma et al.
Reference Equation for the Six-Minute Walk Test

Int J Cardiovasc Sci. 2021; 34(3):307-314

Original Article
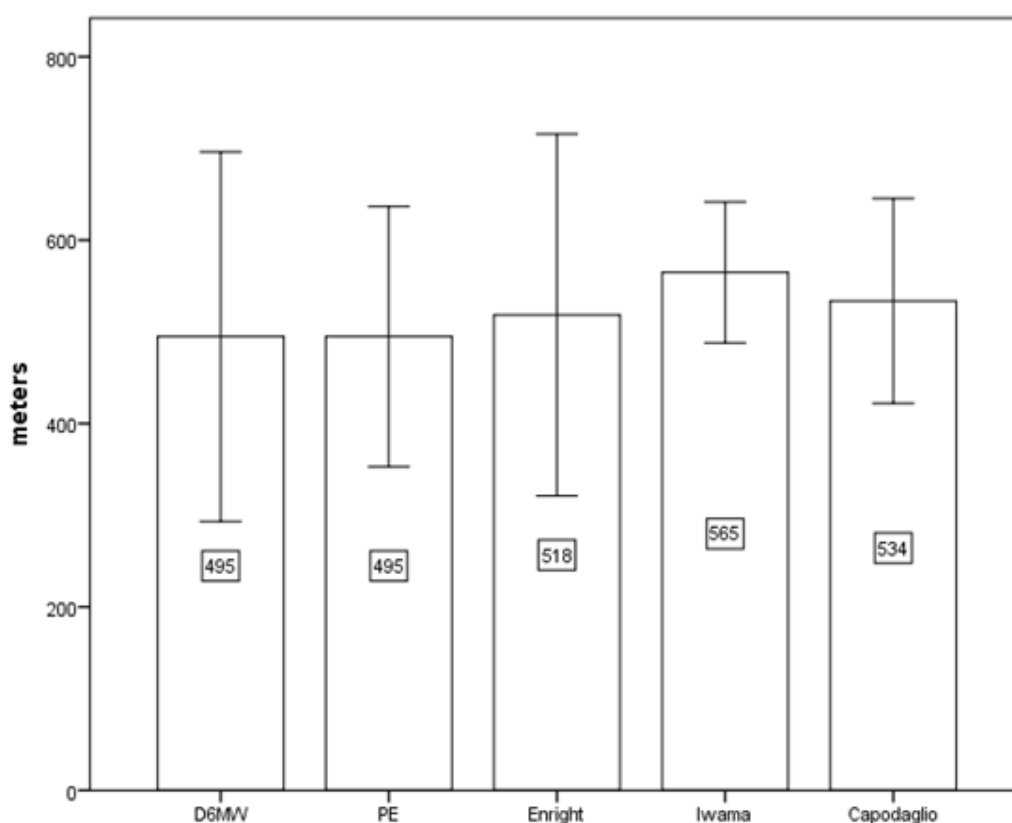
Figure 3 – Mean of the distance reached at 6 minutes of walking (D6MC), of the proposed equation (PE), and distances predicted by the equations present in the literature (see text).

The importance of BMI in the D6MW variance in a population of obese patients has been described in medical literature,[12,15,21,26] despite the significant difference in BMI between the genders (p <0.001) found in our patient group, where the BMI was able to explain 32.6% for men and 20% for women of the D6MW results . It was observed that, for a growing value of BMI, there is a reduction of D6MC in both sexes (Figure 2).

In our study, for the whole group, age was able to explain 14.9% and BMI 21.5% of the results. Data slightly different from those previously obtained by Capodaglio with obese patients,[13] where age explained 12.9% and BMI 24% of the D6MW results. This difference occurs because our population is older and with a smaller number of male subjects, who are proportionally heavier. However, our results were similar to Capodaglio's in relation to the total variance of the D6MW, explained by the three chosen variables (gender, age, and BMI), that is, 48% in Capodaglio`s study and 48.7% in our investigation.

A greater number of variables introduced in the equation, as already pointed out by other authors,[14, 20] could provide a better evaluation from a purely mathematical point of view. On the other hand, this study would lose in practicality, since a greater number of variables would lead to a greater complexity in the collection of data in an outpatient environment of basic health care.

Our study, does, however have some limitations. The sample was chosen for convenience, allowing for some selection bias. This study consists of patients with a predominance of grade III obesity, most of whom were female, who sought out bariatric surgery to treat their obesity. In addition, about 50% of the D6MC variance remains unexplained by our regression model. Caution should be taken when using the proposed equation for patients with different characteristics from our cohort. This study should also be repeated with a larger number of participants under the age of 40 and over 60, and with grade I and II obesity.

Conclusion

The reference equation proposed in this study shows a significant adjustment, when compared to the equations already described in the literature, and allows for a better estimate of the submaximal functional capacity of Brazilian patients with obesity, which provides better subsidies for monitoring the therapeutic interventions performed in this population.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Sources of Funding

There were no external funding sources for this study.

Study Association

This article is part of the thesis of Doctoral submitted by José Carlos do Vale Quaresma, from *Universidade Federal do Rio de Janeiro.*

Author Contributions

Conception and design of the research: JCV Quaresma. Acquisition of data: JCV Quaresma, NF Marschhausen, GG Cruz. Analysis and interpretation of the data: JCV Quaresma, NF Marschhausen, GG Cruz, JRI Carneiro, J Fernandes Filho, RR Luiz. Statistical analysis: JCV Quaresma, RR Luiz. Writing of the manuscript: JCV Quaresma, NF Marschhausen, GG Cruz, JRI Carneiro, J Fernandes Filho, RR Luiz. Critical revision of the manuscript for intellectual content: JCV Quaresma, GG Cruz, JRI Carneiro, J Fernandes Filho, RR Luiz.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of the CEP-HUCFF under the protocol number 1041.0.197.000-05. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

References

1. Simão AF, Precoma DB, Andrade JP, Correa Filho H, Saraiva JF, Oliveira GM, et al. I Diretriz Brasileira de Prevenção Cardiovascular. Arq Bras Cardiol. 2013;101(6 Suppl 2):1-63.

2. Donini LM, Poggiogalle E, Mosca V, Pinto A, Brunani A, Capodaglio P. Disability affects the 6-minute walking distance in obese subjects (BMI>40 kg/m(2)). PLoS One. 2013;8(10):e75491.

3. Herdy AH, Lopez-Jiménez F, Terzic CP, Milani M, Stein R, Carvalho T, et al. South American Guidelines for Cardiovascular Disease Prevention and Rehabilitation. Arq Bras Cardiol. 2014;103(2 Suppl 1):1-31.

4. MinistériodaSaúde. VIGITEL BRASIL In: http://portalarquivos.saude. gov.br/images/pdf/2017/abril/17/Vigitel.pdf, editor. Brasilia, Brasil: Ministério da Saúde; 2016.

5. Enright PL, Sherrill DL. Reference equations for the six-minute walk in healthy adults. Am J Respir Crit Care Med. 1998;158(5 Pt 1):1384-7.

6. ATS Statement: Guidelines for the Six-Minute Walk Test. Am J Respir Crit Care Med. 2002;166(1):111-7.

7. Casanova C, Celli BR, Barria P, Casas A, Cote C, de Torres JP, et al. The 6-min walk distance in healthy subjects: reference standards from seven countries. Eur Respir J. 2011;37(1):150-6.

8. Dourado VZ. Equações de referência para o teste de caminhada de seis minutos em indivíduos saudáveis. Arq Bras Cardiol. 2011;96(6):e128-e38.

9. Iwama AM, Andrade GN, Shima P, Tanni SE, Godoy I, Dourado VZ. The six-minute walk test and body weight-walk distance product in healthy Brazilian subjects. Braz J Med Biol Res. 2009;42(11):1080-5.

10. Soares MR, Pereira CA. Six-minute walk test: reference values for healthy adults in Brazil. J Bras Pneumol. 2011;37(5):576-83.

11. Britto RR, Probst VS, Andrade AF, Samora GA, Hernandes NA, Marinho PE, et al. Reference equations for the six-minute walk distance based on a Brazilian multicenter study. Braz J Phys Ther. 2013;17(6):556-63.

12. Larsson UE, Reynisdottir S. The six-minute walk test in outpatients with obesity: reproducibility and known group validity. Physiother Res Int. 2008;13(2):84-93.

13. Capodaglio P, De Souza SA, Parisio C, Precilios H, Vismara L, Cimolin V, et al. Reference values for the 6-Min Walking Test in obese subjects. Disabil Rehabil. 2012;35(14):1199-203.

14. Donini LM, Poggiogalle E, Mosca V, Pinto A, Migliaccio S, Brunani A, et al. Critical review of the equations predicting 6-minute walking distance in obese subjects. Monaldi Archives for Chest Disease. 2015;81(1-2):745-52.

15. Beriault K, Carpentier AC, Gagnon C, Menard J, Baillargeon JP, Ardilouze JL, et al. Reproducibility of the 6-minute walk test in obese adults. Int J Sports Med. 2009;30(10):725-7.

16. WHO. Physical status: the use and interpretation of anthropometry. Report of a WHO Expert Committee. World Health Organ Tech Rep Ser . 1995;854:1-452.

17. Malachias MV, Gomes MA, Nobre F, Alessi A, Feitosa AD, Coelho EB. 7th Brazilian Guideline of Arterial Hypertension. Arq Bras Cardiol . 2016 Sep;107(3 Suppl 3):7-13.

18. Borg GA. Psychophysical bases of perceived exertion. Med Sci Sports Exerc. 1982;14(5):377-81.

19. WHO. Obesity: Preventing and Managing the Global Epidemic. Report of a WHO Consultation. World Health Organ Tech Rep Ser . 2000;894:i-xii, 1-253.

20. Lumley T, Diehr P, Emerson S, Chen L. The Importance of the Normality Assumption in Large Public Health Data Sets. Annu Rev Public Health. 2002;23(1):151-69.

21. Hulens M, Vansant G, Claessens AL, Lysens R, Muls E. Predictors of 6-minute walk test results in lean, obese and morbidly obese women. Scand J Med Sci Sports. 2003;13(2):98-105.

22. Arena R, Myers J, Williams MA, Gulati M, Kligfield P, Balady GJ, et al. Assessment of Functional Capacity in Clinical and Research Settings. A Scientific Statement From the American Heart Association Committee on Exercise, Rehabilitation, and Prevention of the Council on Clinical Cardiology and the Council on Cardiovascular Nursing. Circulation. 2007;116(3):329-43.

23. Troosters T, Gosselink R, Decramer M. Six minute walking distance in healthy elderly subjects. Eur Respir J. 1999;14(2):270-4.

24. Chetta A, Zanini A, Pisi G, Aiello M, Tzani P, Neri M, et al. Reference values for the 6-min walk test in healthy subjects 20-50 years old. Respir Med. 2006;100(9):1573-8.

25. Donini LM, Poggiogalle E, Migliaccio S, Pinto A, Lubrano C, Lenzi A. Sarcopenic Obesity: Correlation with Clinical, Functional, and Psychological Status in a Rehabilitation Setting. Food and Nutrition Sciences. 2014;Vol.05No.20:12.

26. Maniscalco M, Zedda A, Giardiello C, Faraone S, Cerbone M, Cristiano S, et al. Effect of Bariatric Surgery on the Six-Minute Walk Test in Severe Uncomplicated Obesity. Obesity Surgery. 2006;16(7):836-41.

Cardiopulmonary Resuscitation in Prone Position

Leandro Menezes Alves da Costa,[1] Rafael Amorim Belo Nunes,[1,2] Thiago Luis Scudeler[3]

Hospital Alemão Oswaldo Cruz,[1] de São Paulo, SP - Brazil
Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo,[2] São Paulo, SP - Brazil
Instituto do Coração (InCor),[3] São Paulo, SP - Brazil

Abstract

Mechanical ventilation in prone position is an alternative strategy for patients with acute respiratory discomfort syndrome (ARDS) to improve oxygenation in situations when traditional ventilation modalities have failed. However, due to the significant increase in ARDS cases during the SARS-CoV-2 pandemic and the experimental therapeutic use of potentially arrhythmogenic drugs, cardiopulmonary resuscitation in this unusual position could be needed. Therefore, we will review the available scientific evidence of cardiopulmonary resuscitation in prone position.

Relevance

The current Coronavirus Disease 2019 (COVID-19) pandemic resulting from SARS-CoV-2 infection requires the highest level of medical response from health care services worldwide. Pneumonia is the most common comorbid condition, with acute respiratory discomfort syndrome (ARDS) as the main complication. Current studies have demonstrated that 20 to 41% of patients with COVID-19 develop ARDS, and 12.3% of these patients require mechanical ventilation.[1,2] For patients where predefined ventilation parameters are not met and patients with refractory hypoxemia, prone-position ventilation (PPV) has been suggested as a valuable alternative.[3,4]

PPV alters the mechanical and physiological structure of the gaseous exchange, creating a more homogenous ventilation system, decreasing ventral alveolar extension, and diminishing dorsal alveolar collapse.[5] This can effectively reduce the difference between transpulmonary dorsal and ventral pressures. In addition, PPV reduces pulmonary compression and improves corporeal perfusion.[6,7] Prone ventilation should be initiated in the first 36 hours of mechanical ventilation and ideally be maintained for 12 to 16 hours.[4]

During this period of treatment, the patient may become vulnerable to emergency situations, with cardiac arrest as the diagnosis with the worst prognosis. Moreover, the current use of experimental drugs may increase the occurrence of malignant arrhythmia. The combination of hydroxychloroquine and azithromycin predisposes to QT interval prolongation on electrocardiogram.[8] This could consequently increase the potential risk for dangerous ventricular arrhythmias, requiring specific technical knowledge in the performance of synchronized electric cardioversion or cardiac defibrillation while the patient is in prone position. Additionally, an assistance team with little experience in cardiopulmonary resuscitation while in prone position represents a particularly challenging complication, especially considering the adoption of respiratory isolation and use of personal protective equipment.

Objective

To review the scientific evidence related about prone cardiopulmonary resuscitation.

Background

First described by Dr. McNeil in 1989,[9] the first case of cardiopulmonary resuscitation (CPR) in prone position claimed success in practice by Dr. Sun and colleagues in 1992.[10] While still not adopted as a routine practice, this technique meets the prerequisite ideas of resuscitation, guaranteeing adequate ventilation associated with thoracic compressions, requiring only simple training.

Keywords

Mailing Address: Leandro Menezes Alves da Costa
Rua João Julião, 331. Postal Code: 01327-001, São Paulo, SP – Brazil.
E-mail: leandro1910@uol.com.br

316

Costa et al.
Cardiopulmonary resuscitation in prone position

Int J Cardiovasc Sci. 2021; 34(3):315-318
Review Article

Several small studies have shown that dorsal compressions cause an increase in arterial pressure in comparison to conventional compressions. A pilot study in which six patients received 15 minutes of CPR in conventional position, followed by 15 minutes of CPR in prone position, resulted in a systolic arterial pressure increase from 48 mmHg to 72 mmHg with prone-position CPR.[11] A separate study compared the levels of systolic and diastolic arterial pressure (SAP, DAP) with invasive monitoring in 11 cadavers and found higher levels of SAP and DAP in patients who received CPR in prone position (79±20 / 17±10 mmHg in the experimental prone group, compared to 55±20 / 13±7 mmHg in the conventional group, p = 0.028).[12]

Mazer et al.[11] suggested a possible explanation for the increased efficiency of prone-position CPR.[11] According to their study, external cardiac compressions in prone positions generate a greater force due to the costovertebral articulations and their increased rigidity. This allows greater variation in intra-thoracic pressure and more effective direct cardiac compression, providing better circulatory effects. Moreover, the prone position provides high level of patency in airways, and the increased intra-thoracic pressure variation favors lung ventilation.

The American Heart Association included CPR in prone position in their recommendations for advanced treatment in life support in 2010.[13] These recommendations are applied to patients unable to move spontaneously, making the shifting to the supine position impossible, especially patients who underwent dorsal surgical procedures with vascular resection, neurosurgeries, or treatments to the spinal vertebrae.[14-19] These recommendations have remained unchanged in modern revisions since 2015.[20]

Cardiac compressions

Prone-position CPR can be performed with one or two hands and with or without external counterpressure.[21-23] For thoracic compressions, place the hypothenar region of the hand above the patient's thoracic vertebrae, and the other hand over the first, lacing them together. A study by Kwon and colleagues used computerized tomographic images to demonstrate that the best position for thoracic compressions lies 0-2 vertebral segments below the inferior angle of the scapula (T8-T9). Typically, this region provides more direct access to the larger left ventricle in the transversal area (Figure 1).[24]

Prone-position CPR should be similar to conventional CPR with compressions between 5 and 6 cm, with frequency between 100 to 120 compressions per minute,
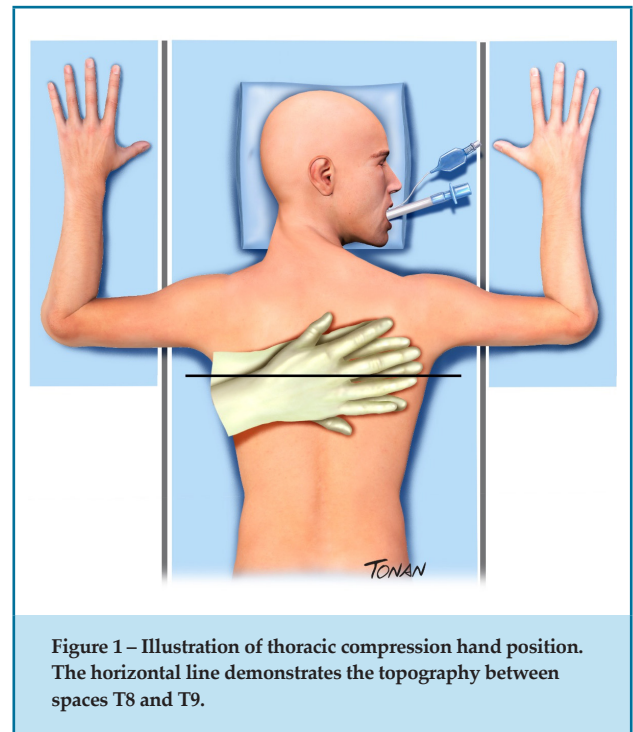
Figure 1 – Illustration of thoracic compression hand position. The horizontal line demonstrates the topography between spaces T8 and T9.

allowing the thorax to return to the original position. A capnography allows for an effective measurement of the exhaled CO_2 to evaluate the effectiveness of the treatment. In 2001, Brown et al.,[24] published the first systematic review article about prone-position CPR. The authors identified 22 intubated patients who received prone-position CPR, 10 of whom received hospital discharge following treatment.[25]

Defibrillation

Defibrillation in prone position is another important aspect in prone-position CPR. It can be performed in the posterolateral-prone-position (one of the blades is positioned in the middle axillary line on the left, at the fifth intercostal space and the other blade is positioned in the distal portion of the scapula on the right) or bilateral axillary.[26,27] (Figures 2 and 3)

Conclusion

Cardiopulmonary resuscitation in prone position proves to be a viable alternative in situations where it is not possible to return the patient to the traditional supine position, since it provides immediate initiation of chest compressions, reduces the risk of displacement of tubes and catheters, and contamination of the health professionals involved in patients' care.

Study Association

This study is not associated with any thesis or dissertation work.

Author Contributions

Conception and design of the research: Leandro MA Costa, Thiago L Scudeler. Acquisition of data: Leandro MA Costa, Thiago L Scudeler. Analysis and interpretation of the data: Leandro MA Costa, Thiago L Scudeler. Writing of the manuscript: Leandro MA Costa, Thiago L Scudeler. Critical revision of the manuscript for intellectual content: Leandro MA Costa, Thiago L Scudeler.
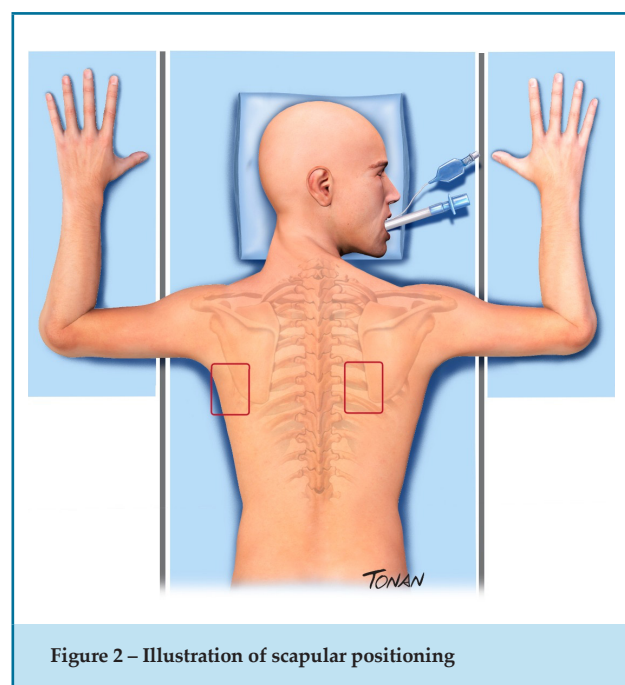
Figure 2 – Illustration of scapular positioning
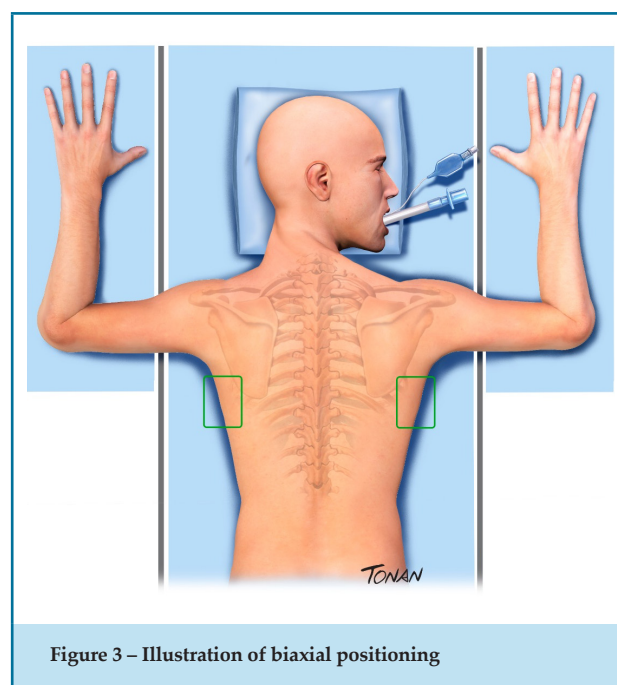
Figure 3 – Illustration of biaxial positioning

References

1. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA. 2020;323(11):1061-9.

2. Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. JAMA Intern Med. 2020;180(7):1-11.

3. Gattinoni L, Tognoni G, Pesenti A, Tacconi P, Mascheroni D, Labarta V, et al. Effect of prone positioning on the survival of patients with acute respiratory failure. N Engl J Med. 2001;345(8):568-73.

4. Alhazzani W, Møller MH, Arabi YM, Loeb M, Gong MN, Fan E, et al. Surviving sepsis campaign: guidelines on the management of critically ill adults with coronavirus disease 2019 (COVID-19). Crit Care Med. 2020;48(6):e440-69.

5. Cornejo RA, Diaz JC, Tobar EA, Bruhn AR, Ramos CA, González RA, et al. Effects of prone positioning on lung protection in patients with acute respiratory distress syndrome. Am J Respir Crit Care Med. 2013;188(4):440-8.

6. Albert RK, Hubmayr RD. The prone position eliminates compression of the lungs by the heart. Am J Respir Crit Care Med. 2000;161(5):1660-5.

7. Nyren S, Radell P, Lindahl SG, Mure M, Petersson J, Larsson SA, et al. Lung ventilation and perfusion in prone and supine postures with reference to anesthetized and mechanically ventilated healthy volunteers. Anesthesiology. 2010;112(3):682-7.

8. Simpson T, Salazar J, Vittinghoff E, Probert J, Iwahashi A, Olgin JE, et al. Association of QT prolonging medications with risk of autopsy causes of sudden death. JAMA Int Med. 2020;180(5):1-9.

9. McNeil EL. Prone CPR aboard aircraft (McNeil method) J Emerg Nurs. 1994;20:446.

10. Sun WZ, Huang FY, Kung KL, Fan SZ, Chen TL. Successful cardiopulmonary resuscitation of two patients in the prone position using reversed precordial compression. Anesthesiology. 1992;77(1):202-4.

11. Mazer SP, Weisfeldt M, Bai D, Cardinale C, Arora R, Ma C, et al. Reverse CPR: a pilot study of CPR in the prone position. Resuscitation. 2003;57(3):279-85.

12. Wei J, Tung D, Sue SH, Wu SV, Chuang YC, Chang CY. Cardiopulmonary resuscitation in prone position: a simplified method for outpatients. J Chin Med Assoc. 2006;69(5):202-6.

13. Lowenthal A, Lehmann-Meurice C, Otteni JC. Efficacy of external cardiac massage in a patient in the prone position. Ann Fr Anesth Reanim. 1993;12(6):587-9.

14. Tobias JD, Mencio GA, Atwood R, Gurwitz GS. Intra-operative cardiopulmonary resuscitation in the prone position. J Pediatr Surg. 1994;29(12):1537-8.

15. Kelleher A, Mackersie A. Cardiac arrest and resuscitation of a 6-month old achondroplastic baby undergoing neurosurgery in the prone position. Anaesthesia. 1995;50(4):348-50.

16. DeQuin PF, Hazouard E, Legras A, Lanotte R, Perrotin D. Cardiopulmonary resuscitation in the prone position: Kouwenhoven revisited. Intensive Care Med. 1996;22(11):1272-82.

17. Brown J, Rogers J, Soar J. Cardiac arrest during surgery and ventilation in the prone position: a case report and systematic review. Resuscitation. 2001;50(2):233-8.

18. Taylor JCL, Buchanan CCR, Rumball MJ. Cardiac arrest during craniotomy in prone position. Trends Anaesth Cri Care. 2013;3(4):224-6.

19. Brooks SC, Anderson ML, Bruder E, Daya MR, Gaffney A, Otto CW, et al. Part 6: Alternative techniques and ancillary devices for cardiopulmonary resuscitation: 2015 American Heart Association Guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation. 2015;132(18 Suppl 2):S436-43.

20. Sun W, Huang F, Kung K, Fan S, Chen T. Successful cardiopulmonary resuscitation of two patients in the prone position using reversed precordial compression. Anesthesiology. 1992;77(1):202-4.

21. Dequin P-F, Hazouard E, Legras A, Lanotte R, Perrotin D. Cardiopulmonary resuscitation in the prone position: kouwenhoven revisited. Intensive Care Med. 1996;22(11):1272.

22. Tobias JD, Mencio GA, Atwood R, Gurwitz GS. Intraoperative cardiopulmonary resuscitation in the prone position. J Paediatr Surg. 1994;29(12):1537-8.

23. Kwon MJ, Kim EH, Song IK, Lee JH, Kim HS, Kim JT. Optimizing prone cardiopulmonary resuscitation: identifying the vertebral level correlating with the largest left ventricle cross-sectional area via computed tomography scan. Anesth Analg. 2017;124(2):520-3.

24. Brown J, Roger J, Soar J. Cardiac arrest during surgery and ventilation in the prone position: a case report and systematic review. Resuscitation. 2001;50(2):233-8.

25. Miranda CC, Newton MC. Successful defibrillation in the prone position. Br J Anaesth. 2001;87(6):937-8.

26. Link MS, Atkins DL, Passman RS, Halperin HR, Samson RA, White RD, et al. Part 6: Electrical therapies: automated external defibrillators, defibrillation, cardioversion, and pacing.. Circulation. 2010;122(18 Suppl 3):S706-19.

27. Cave DM, Gazmuri RJ, Otto CW, Nadkarni VM, Cheng A, Brooks SC, et al. Part 7: CPR techniques and devices: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation. 2010;122(18 Suppl 3):S720-8.

Marginalization, Vulnerability and Economic Dynamics in COVID-19

Andres Felipe Valencia Rendon,[ID] Isabela Mendes Volschan,[ID] Manoella de Novais Pereira,[ID] Alessandra de Freitas Pimentel,[ID] Wagner Lima Monteiro,[ID] Gláucia Maria Moraes de Oliveira[ID]

Universidade Federal do Rio de Janeiro, Rio de Janeiro, RJ – Brazil.

Abstract

COVID-19, caused by the coronavirus family SARS-CoV-2 and declared a pandemic in March 2020, continues to spread. Its enormous and unprecedented impact on our society has evidenced the huge social inequity of our modern society, in which the most vulnerable individuals have been pushed into even worse socioeconomic situations, struggling to survive.

As the pandemic continues, we witness the huge suffering of the most marginalized populations around the globe, even in developed, high-income latitudes, such as North America and Europe. That is even worse in low-income regions, such as Brazil, where the public healthcare infrastructure had already been struggling before the pandemic.

Cities with even more evident social inequity have been impacted the most, leaving the most socioeconomically disadvantaged ones, such as slum residents and black people, continuously inflating the statistics of COVID-19 sufferers.

Poverty, marginalization, and inequity have been well-known risk factors for morbidity and mortality from other diseases. However, COVID-19 has deepened our society's wound. It is up to us to heal it up. If we really care for the others and want to survive as a species, we must fight social inequity.

Introduction

One of the most disastrous diseases in human history, COVID-19, caused by the coronavirus family SARS-CoV-2, continues to spread across the world, after being declared pandemic by the World Health Organization

on March 11, 2020, causing 2 486 405 deaths worldwide.[1] The rapid spread and high estimated infectivity of SARS-CoV-2 coupled with the illness severity have led to widespread shuttering of businesses and implementation of mandatory stay-at-home orders around the world, in addition to a global economic shutdown.[2]

The dynamics between health and inequity has been regularly present for marginalized populations worldwide. The desperate measures to stop the virus spread have had an economic impact on the most vulnerable countries and communities.[3]

Known before the current pandemic, a study extending from 1950 to 1991 and involving 20 developed, developing and underdeveloped countries, has revealed that the increasing prevalence of infectious diseases will not only increase human mortality and morbidity, but will result in the gradual erosion of the state capacity and increase poverty.[4] The disease-induced economic decline has been found to have a negative effect on the capacity to manage financial resources, resilience, the search for responses, autonomy and legitimacy.[5]

Even before the COVID-19 pandemic, the balance between inequity and health has been in turmoil, with the most marginalized populations around the world being the most impacted.[6] Currently, an important portion of those populations has been forced even deeper into poverty. Among other factors, this is the result of a historic confluence of social, structural, and economic inequity.[7] In this phenomenon, informal workers and unemployed ones are greatly affected, and this is compounded by their precarious backgrounds.[8,9]

The soaring unemployment rate seen in the pandemic and the reduced capacity to obtain goods, like food and basic resources, have pushed a large number of the global population into struggling conditions.[10]

The aggressiveness of the new virus took the international community by surprise and drove different healthcare systems in different latitudes to a nearly complete collapse.

Even highly developed countries, like the United States of America (USA), one of the biggest economies in the globe, has struggled to give its citizens the appropriate care they desperately need; and sadly, people affected by COVID-19 are counted by millions.[11]

The disease-related complications, rates of hospitalization and mortality are not homogeneous among the population, even within the same affected areas. New York City (NYC), with a population of 8 398 748 individuals and one of the most affected cities by the new disease, has evidenced a substantial variation in the rates of COVID-19 hospitalization and death across its boroughs. Bronx, which has the highest proportion of racial/ethnic minorities, most of them living in poverty, and the lowest levels of educational attainment, had higher rates of COVID-19-related hospitalization and death than the other four boroughs of NYC, including Manhattan, which has the highest population density but the lowest rates of hospitalization and death.[12] This phenomenon shows that not only the pathogen inner infective capability is important to its spread, but the social economical background of the community is of great importance for the viral spread dynamics. Early diagnosis and monitoring of patients with COVID-19 are critical to optimize individual outcomes and to prevent further community transmission.[11] In NYC, 34% and 28% of the deaths from COVID-19 occurred in Hispanic and black individuals, respectively, which represent only 29% and 22% of that city population; however, 27% of the deaths from COVID-19 occurred in white individuals, which represent 32% of the NYC population.

This phenomenon is more evident in African and Latin American latitudes, where many countries score poorly on the WASH Performance Index, which is a measure of access to abundant clean water and improved sanitation. If increased transmission due to fecal contamination is combined with climatically reduced contact transmission, the epidemiological dynamics of COVID-19 in Latin America may be fundamentally distinct from that currently observed in the Northern hemisphere.[13,14]

The stay-at-home policies implemented worldwide are harder to apply to underdeveloped countries like those in Latin America. Policies, such as lockdown, have a great economic impact on the general population. In Brazil, the concept of remote work is not feasible for the great majority of the population. A local survey shows that only 27.1% of the population can work remotely, and this percentage represents people of high educational level, which in Brazil is scarce, reflecting and confirming the country's known social inequity. This scenario is even worse in the southeastern region of the country, which accounts for 42% of the Brazilian population and comprises some of the federal units with the highest demographic densities, such as São Paulo (166.23 pop/km²) and Rio de Janeiro (365.23 pop/km²).

That population density and unique social dynamics have pushed the Brazilian Unified Public Health System (SUS) to its boundaries. The SUS, known as the world´s biggest social health care system with more than 200 million users, has almost faced a collapse with the current pandemic.[15,16] The city of Rio de Janeiro, known for its great social status breaches, has been one of the most affected. There, hospitals have been challenged to almost their healthcare limits because of the high number of patients in need for inpatient/intensive care.[17]

Some of the greatest threats faced by healthcare workers treating COVID-19 patients are the various difficulties of patients' access to medical institutions. In Rio de Janeiro, on average, those patients live in the city's periphery, have a low income, and, inside their own communities, deep in the slums, they have to cope with violence and segregation, in addition to a great limitation of public transportation. In our personal experience, we have seen that low baseline economic status is related to in-hospital complications and can influence in-hospital mortality.[18,19] These markers of marginalization, among others, are determinants of the individual outcomes related to different clinical and social scenarios.

Marginalized communities are those excluded from mainstream social, economic, educational, and/or cultural life. Examples of marginalized populations are groups excluded due to race, sexual orientation, age, language, physical ability, and/or immigration status. Marginalization occurs due to unequal power relationships between social groups.[9]

As portrayed by Rogers, "there is a distinction between inherent vulnerability, arising from one's corporeality; situational vulnerability stemming from one's personal, social, political, economic, or environmental situatedness as an individual or member of a group; and pathogenic vulnerability, emerging in sociopolitical contexts, where a pre-existing vulnerability is multiplied by oppression or injustice".[20,21]

Vulnerable groups of people are those disproportionally exposed to risk, but the composition of such groups change dynamically.[22] A person not considered vulnerable at the outset of the pandemic can become vulnerable depending on the policies adopted. The risks of sudden loss of income or of access to social support have consequences difficult to estimate; in addition, identifying all those who might become vulnerable is a challenge.[23]
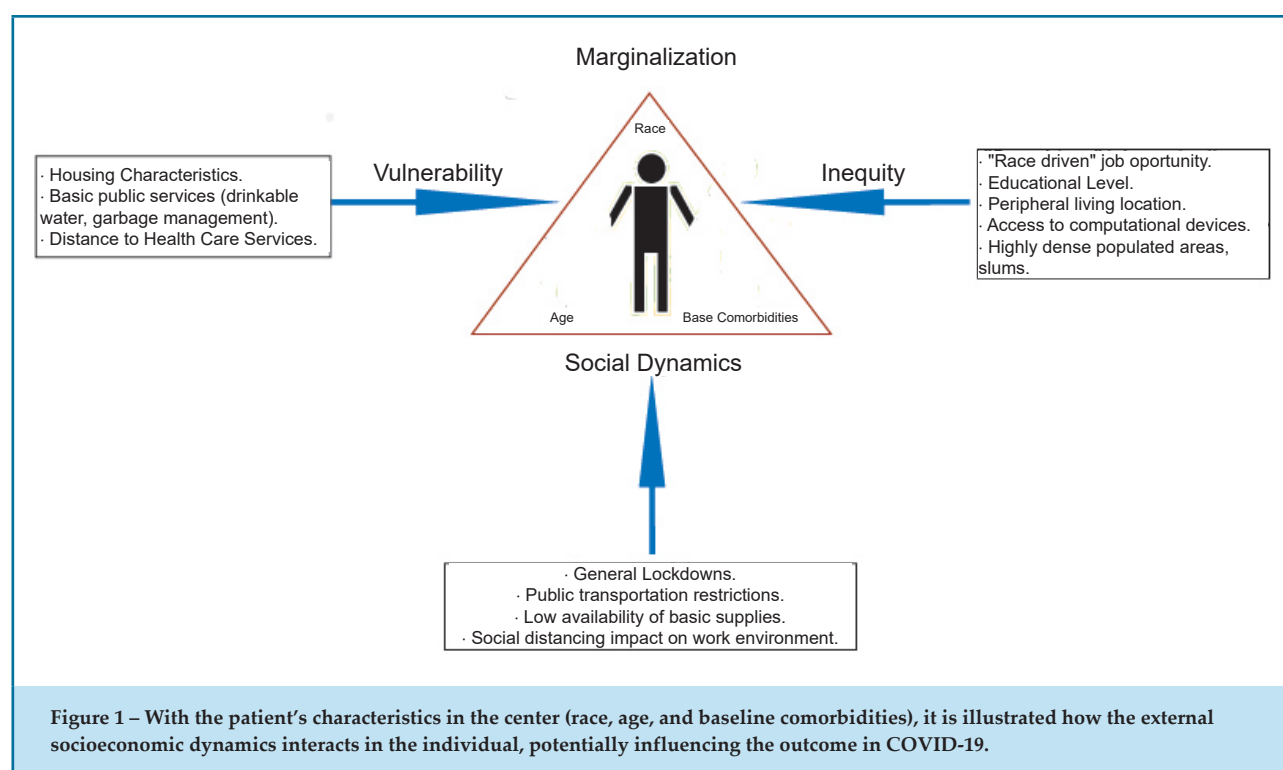
Populations are heterogeneous in composition (for example, those living with disability, people living in poverty, and racial, ethnic, sexual and gender minorities), and the intersection of those identities within an individual or group can further compound their baseline disadvantage.[24] When analyzing the environmental factors of those communities, African Americans are 75% more likely to reside in proximity to a polluting facility, like a factory or refinery, than other Americans, and, as compared to white individuals, they are exposed to a 38% more polluted air.[25]

Even biological risk factors for COVID-19, such as hypertension, diabetes, asthma, and obesity, can reflect environmental and sociological precipitating and contributing factors, as much as racial differences in biology.[26] Cardiovascular diseases (CVD), such as hypertension and myocardial infarction, are well known to be related to COVID-19 mortality and its complications. In addition to those comorbidities, the outcome is compounded by one's socioeconomic status and even local community.[27] Among the various minority population groups, black men have the highest overall death rate from CVD, which extends to black women, whose death rates from CVD are higher than those of white women.[28] In addition, individuals of Hispanic or Latino ancestry in the USA have the highest incidence of nonalcoholic fatty liver disease.[29]

International evidence has shown that marginalized groups are much more likely to be infected and subsequently die from COVID-19.[30] Three groups have disproportionately suffered the health burden: ethnic minorities; the socioeconomically disadvantaged; and the elderly.[31] The first two groups are highly prevalent in Brazil, inflating the socioeconomic challenge in our country, making it even more vulnerable to the current phenomenon.[32,33]

The COVID-19 pandemic has evidenced a well spread phenomenon. Social inequity is a fact of the modern world, a consequence of wealth imbalance, and has recently become even deeper in our society. The current pandemic has only shown its already multifactorial disastrous effects on humankind. (Figure 1)

Figure 1 – With the patient's characteristics in the center (race, age, and baseline comorbidities), it is illustrated how the external socioeconomic dynamics interacts in the individual, potentially influencing the outcome in COVID-19.

As with every crisis, we have the opportunity to learn. The world's biggest challenge today is not only to fight back the virus, but to better understand our particular conditions as humans. We have to fight as one, and we must recognize that social inequity not only destroys the most vulnerable members of our society but helps make our society more primitive.

The COVID-19 has managed to threaten the very existence of our society as we know it today, but the real risk behind the pandemic is the social illness. Marginalization, inequity, and racism are the real threats, and they require immediate attention and solutions. To have better results, let us not wait the next pandemic to start tackling the real issues affecting us globally. It is time to lose our chains!

Author Contributions

Conception and design of the research: Rendon AFV, Volschan IM, Oliveira GMM. Acquisition of data: Rendon AFV, Volschan IM, Pereira MN, Pimentel AF, Monteiro WL, Oliveira GMM. Analysis and interpretation of the data: Rendon AFV, Volschan IM, Pereira MN, Pimentel AF, Monteiro WL, Oliveira GMM. Writing of the manuscript: Rendon AFV, Volschan IM, Pereira MN, Pimentel AF, Monteiro WL, Oliveira GMM. Critical revision of the manuscript for intellectual content: Rendon AFV, Volschan IM, Pereira MN, Pimentel AF, Monteiro WL, Oliveira GMM.

Study Association

This article is part of the thesis of Cardiology master in Science submitted by Andres Felipe Valencia Rendon, from *Universidade Federal do Rio de Janeiro*.

References

1. COVID-19 Dashboard by the Centre for Systems cience and Engineering (CSSE)Johns Hopkins University [Internet]. Coronavirus Resource Center. [citado 30 dez 2020]. Disponível em: h https://Coronavirus.Jhu.edu/map.Html

2. Berwick DM. Choices for the "New Normal." JAMA. 2020;323(21):2125-6. DOI:10.1001/jama.2020.6949

3. Jones J, Sullivan PS, Sanchez TH, Guest JL, Hall EW, Luisi N, et al. Similarities and differences in COVID-19 awareness, concern, and symptoms by race and ethnicity in the United States: cross-sectional survey. J Med Internet Res. 2020;22(7):e20001. DOI:10.2196/20001

4. The World Bank. People, pathogens and our planet. Report number 69145-GLB; 2012. (The Economics of One Health; 2).

5. Tandon P. COVID-19: impact on health of people & wealth of nations. Indian J Med Res. 2020;151(2-3):121-3. DOI:10.4103/ijmr.IJMR_664_20

6. Hebert PL, Sisk JE, Howell EA. When does a difference become a disparity? conceptualizing racial and ethnic disparities in health. Health Aff (Millwood). 2008;27(2):374-82. doi:10.1377/hlthaff.27.2.374

7. Nunes J. The COVID-19 pandemic: securitization, neoliberal crisis, and global vulnerabilization. Cad Saude Publica. 2020;36(5):e00063120. DOI:10.1590/0102-311x00063120

8. Pereira M, Oliveira AM. Poverty and food insecurity may increase as the threat of COVID-19 spreads. Public Health Nutr. 2020;23(17):3236-40. DOI:10.1017/S1368980020003493

9. Hendl T, Chung R, Wild V. Pandemic surveillance and racialized subpopulations: mitigating vulnerabilities in COVID-19 Apps. J Bioethical Inq. 2020;17(4):829-34. DOI:10.1007/s11673-020-10034-7

10. Mahler, DG, Lakner C, Aguilar AC, Wu H. The World Bank: The impact of COVID-19 (Coronavirus) on global poverty: Why Sub-Saharan Africa might be the region hardest hit. [citado 30 dez 2020]. Disponível em: https://blogs.worldbank.org/opendata/impact-covid-19-coronavirus-global-poverty-why-sub-saharan-africa-might-be-region-hardest

11. Clark E, Fredricks K, Woc-Colburn L, Bottazzi ME, Weatherhead J. Disproportionate impact of the COVID-19 pandemic on immigrant communities in the United States. PLoS Negl Trop Dis. 2020;14(7):e0008484. DOI:10.1371/journal.pntd.0008484

12. Wadhera RK, Wadhera P, Gaba P, Figueroa JF, Maddox KEJ, Yeh RW, et al. Variation in COVID-19 hospitalizations and deaths across New York City Boroughs. JAMA. 2020;323(21):2192-5. DOI:10.1001/jama.2020.7197

13. Miller MJ, Loaiza JR, Takyar A, Gilman RH. COVID-19 in Latin America: novel transmission dynamics for a global pandemic? PLoS Negl Trop Dis. 2020;14(5):e0008265. DOI:10.1371/journal.pntd.0008265

14. Abrams EM, Szefler SJ. COVID-19 and the impact of social determinants of health. Lancet Respir Med. 2020;8(7):659-61. DOI:10.1016/S2213-2600(20)30234-4

15. Chaves M, Silva CL. Uma avaliaçao do sistema único de saude nas capitais brasileiras: sugestoes para a criaçao de politicas publicas. JGCG. 2018;12(3):49-63.

16. Pêgo B, Moura R, Nunes M,Krüger C, Moreira P, Ferreira G, et al. Pandemia e fronteiras brasileiras: análise da evoluçao da Covid-19 e proposições. Dirur, Diretoria de Estudos e Politicas Regionais, Urbabas e Ambientais. 2020(16):68.

17. Ponce D. The impact of coronavirus in Brazil: politics and the pandemic. Nat Rev Nephrol. 2020;16(9):483. DOI:10.1038/s41581-020-0327-0

18. Candido DS, Claro IM, Jesus JG, Souza WM, Moreira FRR, Dellicour S, et al. Evolution and epidemic spread of SARS-CoV-2 in Brazil. Science. 2020;369(6508):1255-60. DOI: 10.1126/science.abd2161

19. Brant LCC, Nascimento BR, Teixeira RA, Lopes MACQ, Malta DC, Oliveira GMM, et al. Excess of cardiovascular deaths during the COVID-19 pandemic in Brazilian capital cities. Heart. 2020;106(24):1898-905. DOI:10.1136/heartjnl-2020-317663

20. Susan Dodds WR. Why bioethics needs a concept of vulnerability. Int J Fem Approaches Bioeth. 2012;5(2):11. DOI:10.3138/ijfab.5.2.11

21. Rogers W, Ballantyne A. Special populations: vulnerability and protection. R Eletr Com Inf Inov Saúde. 2008;2(Suppl 1):31-41. DOI:10.3395/reciis.v2.Sup1.207en

22. Acharya R, Porwal A. A vulnerability index for the management of and response to the COVID-19 epidemic in India: an ecological study. Lancet Glob Health. 2020;8(9):e1142-51. DOI:10.1016/S2214-109X(20)30300-4

23. The Lancet. Redefining vulnerability in the era of COVID-19. Lancet. 2020;395(10230):1089. DOI:10.1016/S0140-6736(20)30757-1

24. Gray DM, Anyane-Yeboa A, Balzora S, Issaka RB, May FP. COVID-19 and the other pandemic: populations made vulnerable by systemic inequity. Nat Rev Gastroenterol Hepatol. 2020;17(9):520-2. doi:10.1038/s41575-020-0330-8

25. Ahmed F, Ahmed N, Pissarides C, Stiglitz J. Why inequality could spread COVID-19. Lancet Public Health. 2020;5(5):e240. DOI:10.1016/S2468-2667(20)30085-2

26. American College of Physicians. Racial and Ethnic Disparities in Health Care, Updated 2010. Philadelphia: American College of Physicians; 2010.

27. Graham G. Disparities in cardiovascular disease risk in the United States. Curr Cardiol Rev. 2015;11(3):238-45. DOI:10.2174/1573403X11666141122220003

28. Mensah GA, Mokdad AH, Ford ES, Greenlund KJ, Croft JB. State of disparities in cardiovascular health in the United States. Circulation. 2005;111(10):1233-41. DOI:10.1161/01.CIR.0000158136.76824.04

29. Khazanchi R, Evans CT, Marcelin JR. Racism, not race, drives inequity across the COVID-19 continuum. JAMA Netw Open. 2020;3(9):e2019933. DOI:10.1001/jamanetworkopen.2020.19933

30. Adhikari S, Pantaleo NP, Feldman JM, Ogedegbe O, Thorpe L, Troxel AB. Assessment of community-level disparities in coronavirus disease 2019 (COVID-19) infections and deaths in large US metropolitan areas. JAMA Netw Open. 2020;3(7):e2016938. DOI:10.1001/jamanetworkopen.2020.16938

31. Ali S, Asaria M, Stranges S. COVID-19 and inequality: are we all in this together? Can J Public Health. 2020;111(3):415-6. DOI:10.17269/s41997-020-00351-0

32. Williams DR, Cooper LA. COVID-19 and health equity-a new kind of "herd immunity". JAMA. 2020;323(24):2478-80. DOI:10.1001/jama.2020.8051

33. Swift R. COVID-19 & Minority Health Access. Infec Dis Insights. 2020 Mar;8:1-7.

LETTER TO THE EDITOR

The Big Mistake of not Considering Physical Activity an Essential Element of Care During the Covid-19 Pandemic

Francisco José Gondim Pitanga,[1] Carmem Cristina Beck,[2] Cristiano Penas Seara Pitanga[3]

Universidade Federal da Bahia,[1] Salvador, BA – Brazil.
Instituto Federal de Santa Catarina,[2] Florianópolis, SC – Brazil.
Universidade Católica do Salvador,[3] Salvador, BA – Brazil.

Reply

Dear Editor,

In response to the letter to the editor entitled "Declaring physical activity as 'essential' during the Covid-19 pandemic may not be a good measure"[1] that presented contributions to our point of view entitled "Should physical activity be considered essential activity during the Covid-19 pandemic?"[2] we thank you for the suggestions and we present a reply letter with our arguments:

Although the benefits of physical activity for the cardiovascular, metabolic, immune systems, as well as for mental health are very well documented in the literature,[3,4,5] the discussion about physical activity is considered essential during the new coronavirus pandemic remains with different positions on the part of the researchers.

The main source of disagreement seems to be about the greater probability of infection when practicing physical activity in open environments or in fitness centers, a fact that lacks scientific proof. The study cited by the authors of the letter to the editor, about contamination by the new coranavirus in dance studios, was carried out

at the beginning of the pandemic, when the biosafety protocols currently adopted did not exist, both for outdoor activities and for fitness centers.[6]

From a political point of view, which seems to be the main source of argument for the authors of the letter to the editor, we clarify that since February 2020, the Federal Government of Brazil published law nº 13,979, of February 6, 2020, which provides for measures to facing the public health emergency of international importance resulting from the coronavirus responsible for the 2019 outbreak, a fact that leads us to believe that all necessary measures have been taken to face the pandemic.

Specifically with regard to physical activity, both the Federal Government of Brazil and the Legislative Assembly of the State of Santa Catarina, Brail, published documents regarding physical activity as essential during the pandemic. In the case of the state of Santa Catarina, law nº 17941 of 05/08/2020 was published and the Federal Government, Decree nº 10,344, of May 11, 2020 was published.

It is important to note that in the case of the state of Santa Catarina, despite the law that considered physical activity as essential, having been published in the beginning of May 2020, its capital Florianópolis, it remains among the Brazilian capitals that it presents in relation to too, small number of deaths, as well as low lethality of the disease. It is noteworthy that in this capital, since the enactment of the state law, public spaces were released for physical activity and the fitness centers were opened so that people could attend them, obviously following strict biosafety protocols.

On the other hand, as we have a recent disease, specific

Keywords

COVID-19, Betacoronavirus, Exercise; Pandemics; Hospitalization; Physical Activity; Quality of Life; Epidemiology.

Mailing Address: Francisco José Gondim Pitanga
Av. Reitor Miguel Calmon, s/n. Postal Code: 40110-060, Vale do Canela , Salvador, BA – Brazil.
E-mail: pitanga@lognet.com.br

studies on physical activity as a protective factor for mortality due to Covid-19, as well as on the worsening of the clinical picture are still scarce, despite the fact that the first published recently of them when it was demonstrated that physical activity was a protective factor for hospitalizations due to the new coronavirus, despite the information on lifestyle having been collected in 2010.[7]

Another more recent study carried out in 45 African countries demonstrated an association between physical inactivity and mortality due to Covid-19. It is noteworthy that the association was observed only in accumulated deaths, not remaining statistically significant when deaths were adjusted per million inhabitants[8].

It is important to note that despite the scarcity of studies on physical activity and Covid-19, there are several studies that demonstrate that physical activity can influence the reduction of the worsening of the clinical picture and mortality, as well as positively, in the effects of vaccination in relation to influenza/H1N1, with different authors suggesting that these results can be transported to Covid-19, since these are pandemics with similar viral characteristics.[9,10]

Thus, in our view, physical activity should be considered essential during the pandemic of the new coronavirus. We go even further, suggesting that the increase in the practice of physical activity by the population may make us better prepared not only for the current pandemic, but also for future ones that may come to affect us. Therefore, we insist on suggesting to our government officials that they consider physical activity as an essential activity in any legal determination that may be published.

References

1. Almeida RT, Queiroz CO, Aquino EML. Declaring Physical Activity as 'Essential' During the COVID-19 Pandemic May not be a Good Measure. Int. J. Cardiovasc. Sci. 2020; 33(5): 589-590.

2. Pitanga FJG, Beck CC, Pitanga CPS. Should Physical Activity Be Considered Essential During the COVID-19 Pandemic?. Int. J. Cardiovasc. Sci. 2020; 33(4): 401-403.

3. Lin X, Alvim SM, Simoes EJ, Bensenor IM, Barreto SM, Schmidt MI, et al. Leisure time physical activity and cardio-metabolic health: results from the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil). J Am Heart Assoc. 2016;5(6):pii003337.

4. Krinski K, Elsangedy HM, Colombo H, Buzzachera CF, Soares IA, Campos W, Silva SG. Physical exercise effects in the immunological system. Rev Bras Med. 2010;67(7):227-8.

5. Mammen G, Faulkner G. Physical activity and the prevention of depression: a systematic review of prospective studies. Am J Prev Med. 2013;45(5):649-57.

6. Cortez, ACL, Pitanga FJG, Santos MAA, Nunes RAM, Rosas DAB, Dantas EHM, Centers of physical activities and health promotion during the covid-19 pandemic Rev. Assoc. Med. Bras. 2020; 66(10): 1328-1334.

7. Hamer M, Kivimäki M, Gale CR, Batty GD. Lifestyle risk factors, inflammatory mechanisms, and COVID-19 hospitalization: A community-based cohort study of 387,109 adults in UK. Brain Behav Immun. 2020; 87: 184-187. doi:10.1016/j.bbi.2020.05.059.

8. Okeahalam C, Williams V, Otwombe K. Factors associated with COVID-19 infections and mortality in Africa: a cross-sectional study using publicly available data. BMJ Open. 2020;10(11):e042750. doi: 10.1136/bmjopen-2020-042750.

9. Wong CM, Lai HK, Ou CQ, et al. Is exercise protective against influenza-associated mortality?. PLoS One. 2008;3(5):e2108. doi:10.1371/journal.pone.0002108.

10. Woods JA, Keylock KT, Lowder T, et al. Cardiovascular exercise training extends influenza vaccine seroprotection in sedentary older adults: the immune function intervention trial. J Am Geriatr Soc. 2009;57(12):2183-2191. doi:10.1111/j.1532-5415.2009.02563.

CASE REPORT

Acute Coronary Syndrome in a Patient With Single-Vessel Coronary Artery: Case Report

Bruno Dala Vedova Gomes Beato, Carolina de Souza Galvão, Eduardo Belisário Falchetto, Eduardo Kei Marquesini Washizu, Fábio Ávila Tofani, Juliano Moreira Reis Filho

Hospital Felício Rocho, Belo Horizonte, MG – Brazil.

Introduction

Anomalies of coronary arteries affect 1-2% of the population.[1,2] They are associated with increased risk of sudden death and coronary artery injury during surgical procedures.[1,2] Among the coronary artery anomalies, the single-vessel coronary artery disease subtype has a low incidence – 0.03-0.04% in patients without other heart diseases and 0.024% in patients with other heart diseases.[2] Concomitant presence of acute coronary syndrome in these patients may have an impact on their prognosis and survival.[3]

Here we report a rare and challenging case of an 81-year-old woman with high-risk unstable angina undergoing emergency catheterization which indicated the presence of single-vessel coronary artery disease with lesions in multiple segments.

Clinical case

Eighty-one year-old female, with hypertension, diabetes, and non-dialysis chronic kidney disease, hospitalized due to a crushing retrosternal pain, initially occurring after physical exertion, that progressed to pain even at rest, and radiated to the shoulders and was accompanied by sweating. The electrocardiography showed sinus bradycardia, low voltage QRS in the frontal and horizontal planes, with end conduction delay in the right bundle branch, with no changes in the ST-segment and normal troponin. On physical examination the blood pressure was 220 x 110mmHg, with no other abnormal findings.

Keywords

The patient had unstable angina with a TIMI risk score of 4 and Grace score of 104, and the treatment protocol for acute coronary syndrome without ST elevation, with aspirin, ticagrelor and enoxaparin. The patient had recurrence of pain, and urgent coronary angiography was performed, which revealed left coronary artery bifurcation atherosclerosis with severe lumen occlusion (80%) and calcification in the distal third. Type 3 anterior descending artery with severe lumen occlusion (70%) in the middle third and moderate occlusion in the distal third (40%). First diagonal branch with good diameter and atherosclerosis, with severe occlusion in the proximal-mid segment (80%). Circumflex artery with good diameter and atherosclerosis, with severe occlusion in the middle third (90%). Anomalous origin of the right coronary artery from the middle third of the anterior descending artery, with minimal wall irregularities (Figures 1 and 2). No evidence of cardiovascular abnormalities was found in the transthoracic echocardiography (left atrium 42 mm, left ventricle ejection fraction 74%.

The case was discussed by the Heart Team (interventional, surgery and clinical cardiologists). The patient had a Syntax Score I 21, Euroscore II 2.13% and STS score 5.16%. According to the Syntax Score II, predicted four-year mortality was higher with percutaneous revascularization (25.9% vs. 16.4%). In addition, the interventional cardiology team found the percutaneous approach risky to perform, since it consists of implantation of multiple stents within one coronary artery.

Then, the surgical procedure consisted of arterial mammary grafting to the left anterior descending artery, and coronary artery bypass to first marginal branch, second marginal branch and diagonal branch. The surgery was successfully performed, without
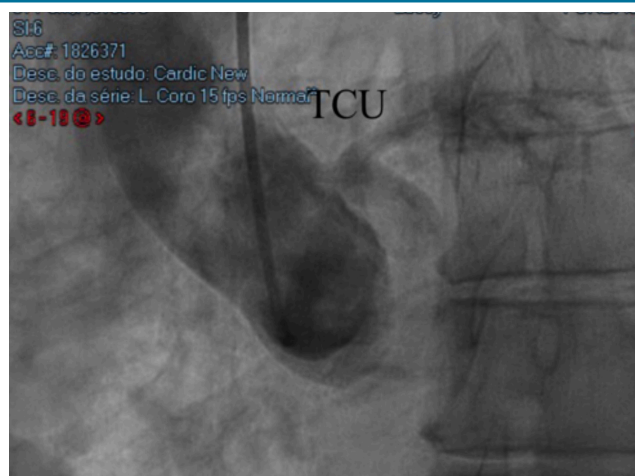
Figure 1 – Aortography showing single-vessel coronary artery arising from the left coronary sinus of Valsalva

Figure 2 – Cranial-right anterior oblique view (B) and caudal-right anterior oblique view (C) showing severe obstruction in the proximal and middle third of the left coronary trunk, severe obstruction in the middle third of descending artery, anomalous origin of the right coronary artery from the middle third of descending artery and severe obstruction in the middle third of the circumflex artery

complications; the patient stayed at the intensive care unit for seven days, with good clinical course, until discharge. Pre-discharge transthoracic echocardiography showed preserved systolic function.

Discussion

Nearly 85% of patients with single-vessel coronary artery disease are asymptomatic, and the diagnosis of the disease is made by imaging tests during investigation of other cardiovascular diseases. Few cases (about 15%) are symptomatic, with chest pain, syncope, and arrhythmia.

In these patients, ischemic symptoms may occur in the absence of obstructive coronary artery disease because of unfavorable anatomy or structure of anomalous vessels.

The present case illustrates a rare presentation of acute coronary syndrome caused by the anterior descending artery occlusion. Until 2005, only seven cases had been reported in the literature.[2]

Single-vessel coronary artery anomaly can be classified by the angiographic model developed by Lipton et al (1979) and adapted by Yamanaka et al. in 1990 (Figure 3).[1] This classification is based on the location of the coronary artery ostium (right or left) and its direction, and its
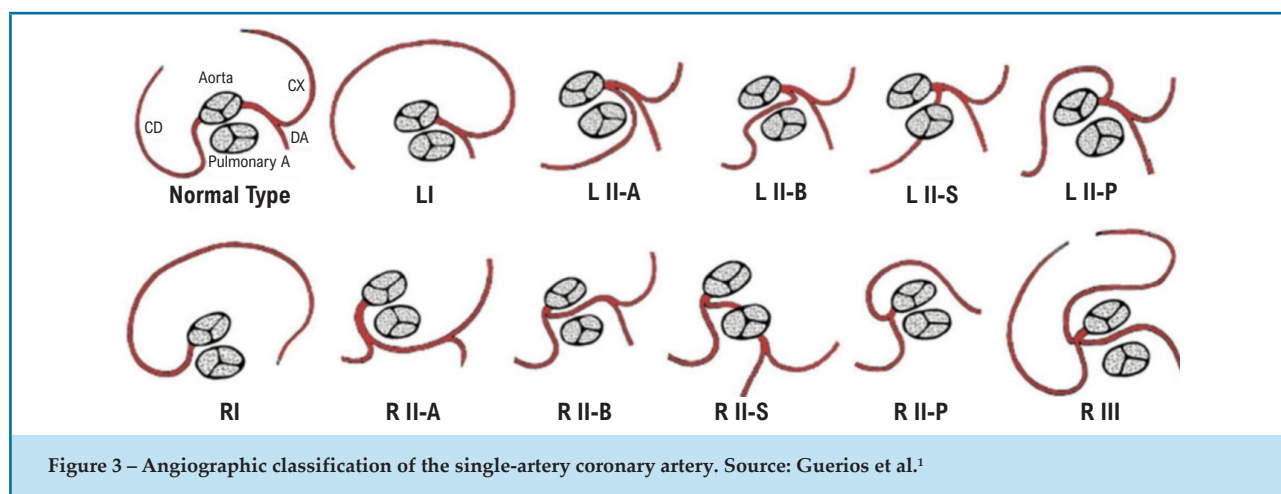
Figure 3 – Angiographic classification of the single-artery coronary artery. Source: Guerios et al.[1]

relationship with other vessels. In single-vessel coronary artery type I, the single artery has a normal course, and collateral vessels compensate for the absent coronary artery. In type II, the anomalous coronary artery arises near the opposite coronary artery, passes through the heart base and its relation to large vessels may vary: anterior course in relation to pulmonary and aortic arteries (subtype A), between large vessels of the base (subtype B), posterior to the large vessels of the base (subtype P) and combinations of these (C). In type III, the proximal segment of the right coronary artery originates the anterior descending artery and the circumflex branch, separately.[1,4,5] The present case is classified as type II A, since the anomalous coronary artery arises from the contralateral coronary artery, and the anterior artery flows the large vessels of the base.

Single coronary artery anomaly seems to be associated with higher incidence of atherosclerotic disease as compared with normal coronary artery, according to studies by Sharbaught et al.,[6] Lipton et al.,[4] and Fernandes et al..[7] When intervention is indicated, surgical therapy is the approach of choice, with endovascular approach and stent implantation (after a careful analysis of anatomical conditions – courses of the vessels, tortuosity, acute angles, among others). Angioplasty is a challenging approach even for experienced interventional cardiologists.[8,9] In the present case, the presence of single coronary artery and severe lesions in multiple segments made the endovascular approach difficult, and the patient underwent myocardial revascularization successfully.

Conclusion

It is important to recognize anatomical variations of the coronary arteries and their implications to the best clinical decisions and planning of technical strategies when intervention is indicated. In the case of our patient, the presence of acute ischemia and severe lesions of multiple vessels at angiography, including single ostium (absence of collateral circulation), the discussion by the Heart Team and the experience of the cardiovascular surgery team were decisive in the decision of the best intervention approach to this patient, who had an excellent clinical outcome.

Author contributions

Conception and design of the research: Beato BDVG, Galvão CSS, Reis Filho JM. Acquisition of data: Galvão CSS, Reis Filho JM. Writing of the manuscript: Beato BDVG, Galvão CSS, Falchetto EB, Marquesini EK, Toffani FA. Critical revision of the manuscript for intellectual content: Beato BDVG, Falchetto EB, Marquesini EK, Toffani FA.

References

1. Guerios EE, Andrade PMP, Melnick G, Barbosa Neto D S. Artéria coronária única. Rev Bras Cardiol Invasiva [online]. 2010. 18(2):226-30.

2. Teixeira ICD, Brant AX, Ares A, Sarbi B, Moscoso I, Salman AA. et al . Artéria coronária única submetida a angioplastia com implante de Stent. Arq Bras Cardiol.2005;84(1):55-8.

3. Kamana VK, Ramachandran P, Krishnan AM, Chowdary RK, Malpe UP. Anomalous Single Coronary Artery Presenting with Acute Myocardial Infarction. J Clin Diagn Res. 2016;10(12):OD01–OD02.

4. Lipton MJ, Barry WH, Obrez I, Silverman JF, Wexler L. Isolated single coronary artery: Diagnosis, angiographic classification, and clinical significance. Radiology. 1979;130(1):39-47.

5. Yamanaka O, Hobbs RE. Coronary artery anomalies in 126,595 patients undergoing coronary angiography. Cathet Cardiovasc Diagn. 1990;21(1):28-40.

6. Sharbaugh MJAH, White RS. Single coronary artery: analysis of the anatomic variation, clinical importance, and report of five cases. JAMA. 1974;230(2):243-6.

7. Fernandes ED, Kadivar H, Hallman GL, Reul GJ, Ott DA, Cooley DA. Congenital malformations of the coronary arteries: the Texas Heart Institute Experience. Ann Thorac Surg.1992;54(4):732-40.

8. Rigatelli G1, Cardaioli P. Endovascular therapy for congenital coronary artery anomalies in adults. J Cardiovasc Med (Hagerstown). 2008 Feb;9(2):113-21.

9. Elbadawi A, Baig B, Elgendy IY, Alotaki E, Mohamed AH, Barssoum K, et al. Single Coronary Artery Anomaly: A Case Report and Review of Literature. Cardiol Ther. 2018;7(1):119–23.

330

Reactive Pericarditis post Meningococcal Vaccine: First Case Report in the Literature

Ebrahim Khalid Al-Ebrahim, Alaa Algazzar, Mohammed Qutub
King Abdulaziz University, Jeddah - Saudi Arabia

Introduction

Autoimmune allergic reaction causing myopericarditis following vaccination is extremely rare and, in this regard, much attention has been paid to smallpox vaccine.[1] Halsell et al.,[2] reported 18 cases of probable myopericarditis in 230,734 primary vaccines after smallpox vaccination (an incidence of 7.8 per 100,000 over 30 days). No cases of myopericarditis following *smallpox* vaccination were reported among 95,622 vaccines who were previously vaccinated. A causal relationship was supported by the close temporal clustering (7-19 days; mean, 10.5 days following vaccination) and wide temporal distribution, occurrence in only primary vaccinees, and lack of evidence for alternative etiologies associated with myopericarditis.[2]

The meningococci causing primary meningococcal pericarditis (PMP) are usually of serotype C (88% of cases in one series) or, less commonly, serotypes B or W135.[3] PMP is a purulent pericarditis caused by N. meningitidis, with no evidence of previous meningococcemia or meningitis, with development of cardiac tamponade in many cases. Evaluation of PMP versus viral pericarditis is important since the former usually requires pericardial drainage in addition to antibiotics.

Case presentation

Chief complaints

A 22-year-old Saudi male presented to the hospital emergency department with retrosternal chest pain,

Keywords

Meningococcal Vaccines/adverse effects; Pericarditis/complications; Reaction.

stiff neck, fatigue, and sudden fever. The patient had taken ibuprofen for symptomatic relief, and had no significant medical history.

History of present illness

The patient reported meningococcal vaccination (Meningococcal groups A, C, W-135 and Y conjugate vaccine) 5 days before admission.

History of past illness

No history of smoking, hypertension, diabetes, dyslipidemia or family history of premature coronary artery disease. Review of systems was unremarkable. The patient had no history of medication use or recreational drugs, or any medical preparations prior to admission. The patient was born in Saudi Arabia and his immunization status was up to date.

Physical examination

On physical examination, blood pressure was 130/70 mm Hg, heart rate was 95 beats/min, oral temperature 37.5 °C and the oxygen saturation 100% on room air. There was diffuse redness and tenderness over the vaccination site. Cardiac examination revealed normal jugular venous pressure (JVP), normal apical beat, normal S1 and S2 with no extra heart sounds, murmurs, or rubs.

Laboratory tests

Extensive evaluation of laboratory results found normal levels of lymphocytes, monocytes, and eosinophils. Other laboratory results showed elevated troponin, aspartate aminotransferase (AST), lactate dehydrogenase (LDH), brain natriuretic peptide (BNP), erythrocyte sedimentation rate (ESR) and C-reactive

Mailing Address: Ebrahim Khalid Al-Ebrahim
King Abdul Aziz University - Al Ehtifalat St. Postal Code: 21589, Jeddah - Saudi Arabia
E-mail: E.alebrahim97@gmail.com

protein (CRP). Results of five consecutive days are described in Table 1.

The results of virus studies investigating other possible causes of myopericarditis were negative for HIV and hepatitis virus. Blood and urine cultures were negative Stool cultures were negative for enteroviruses. Serum electrolyte levels and chest radiography findings were normal.

Imaging tests

An initial electrocardiogram (ECG) showed diffuse concave upward ST-segment elevation on limb leads II, III, aVF, and chest leads V3, V4, V5, V6 (Figure 1), with PR segment elevation in lead aVR. An echocardiogram performed on admission revealed normal biventricular systolic function without regional wall motion abnormalities and trivial pericardial effusion and CT coronary angiography revealed normal coronaries.

Final diagnosis

The diagnosis of pericarditis was made based on the presence of fever, recent immunization and absence of risk factors for coronary artery disease with positive ECG changes and elevated cardiac markers.

Treatment and hospital course

The patient was admitted to the cardiac intensive care unit for observation and monitoring. A regimen of acetylsalicylic acid, 600 mg orally every 6 h, colchicine 0.5 mg twice daily was started, and pantoprazole 40 mg once daily was administered for gastric protection. The patient showed a dramatic clinical improvement after four days of therapy, with normalization of inflammatory and cardiac markers. The findings of an echocardiogram performed one week after discharge were normal.

Outcome and follow-up

After five days of treatment and at follow-up visits, for one month, the patient was asymptomatic, and has an uneventful clinical course.

Discussion

Perimyocarditis is an acute inflammation of the pericardium and the underlying myocardium resulting in myocellular damage. It can be considered an acute pericarditis with elevated cardiac biomarkers. Although cardiac biomarkers were elevated in our patient, the echocardiography showed normal myocardium and normal wall motion.

PMP is a rare form, usually presented as acute purulent pericarditis, that is complicated by cardiac tamponade and requires pericardial drainage. PMP is typically caused by Neisseria meningitidis of serotype C, or, less commonly, B or W135. In general, meningococcal myopericarditis is categorized into three etiologies;

Table 1 – Circulating biomarkers of the patient in five consecutive days					
Cardiac markers	**1st day**	**2nd day**	**3rd day**	**4th day**	**5th day**
Troponin-I (ug/L) *	16	9.90	6.46	4.16	0.02
Mass CK-MB (ug/L)	30	25	16	2.5	1.3
NT-pro BNP (pig/ml)	-	2107	1576	364	100
CRP (mg/L)	90	135	103	55	13
ESR (mm/h)	34	74	80	44	7
AST (U/L)	100	-	44	25	-
LDH (U/L)	387	414	356	324	200

- **NT-pro BNP:** N-terminal prohormone of brain natriuretic peptide.
- **CRP:** C reactive protein
- **ESR:** Erythrocyte sedimentation rate
- **AST:** Aspartate amino transferase.
- **LDH:** Lactate dehydrogenase.
- **Normal Troponin level up to** 0.04 ug/l
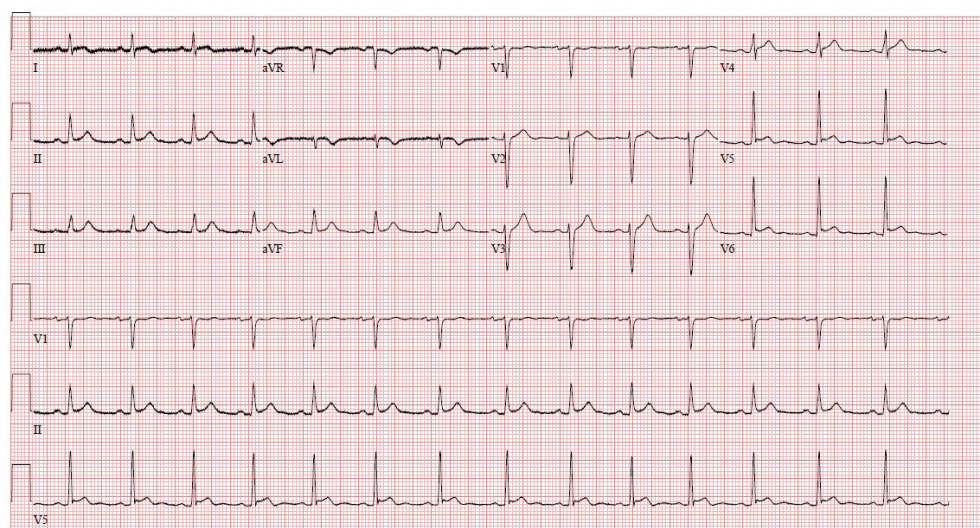
Figure 1 – Echocardiogram showing diffuse concave upward ST-segment elevation on limb leads II, III, aVF, and chest leads V3,V4, V5, V6 (Figure 1), with PR segment elevation in lead aVR

primary meningococcal disease, secondary disease due to disseminated meningococcemia, and reactive meningococcal pericarditis (RMP), an immunologic complication.[4] Because of the negative history of infection, the exposure to meningococcal conjugate vaccine (groups A, C, W-135 and Y) five days prior to the onset of symptoms, and negative serology for infectious and autoimmune diseases, we concluded that pericarditis was reactive rather than a result of direct infection of the myocardium, and a combination of acetylsalicylic acid and colchicine was initiated.

Many case reports of RMP following meningococcal infection have been reported, but no case report of RMP following meningococcal vaccination has been published. RMP is a rare condition and may be more severe than purulent pericarditis; cardiac tamponade is relatively common, requiring high doses of steroids and/or pericardiocentesis. RMP is usually seen 6-15 days after the onset of illness and is characterized by a type III hypersensitivity reaction, either against the specific serotype of the N. meningitidis or against a newly antigenic, damaged pericardial tissue because of molecular mimicry with microbial antigens. Contrary to purulent pericarditis, RMP represents a late complication and there have been many reported cases of RMP post-meningococcal infection in global literature since 1969 (Table 2).[5-10] Severe disease, age (adults and young teenagers), and serogroup C seem to predispose to post-infectious, immune-related

complications including arthritis, vasculitis, pleuritis, and pericarditis.[7-9] Recently, much attention has been given to smallpox vaccine due to its association with myocarditis.[1] There is one reported case of myocarditis that developed hours after diphtheria, tetanus, and acellular pertussis *(DTaP)* vaccination in a 3-month-old infant,[11] and another case of myocarditis after tetanus vaccination in a 14-year-old child.[12] In line with these observations, our patient was a young adult, presenting in poor clinical condition, elevated inflammatory markers suggestive of severe disease, and responsive to anti-inflammatory drugs without antibiotics. We considered the diagnosis of reactive pericarditis rather than myopericarditis due to normal echocardiography and a conservative course of management. The clinical data presented in the case report support the etiologic relationship between meningococcal vaccination and pericarditis. It may be an association, or even a causative relationship. Taking the risk of myocardial biopsy in consideration, histopathological diagnosis of the myocardial biopsy will show diffuse inflammation and will not specify the exact meningococcal etiology.

Conclusion

Further observations and studies are needed to support this case report to prove a causative role of meningococcal vaccine in pericarditis.

Table 2 – Previous case reports of reactive meningococcal pericarditis in the literature

Reference	Patient age/y	Time of pericarditis diagnosis	*Neisseria meningitidis* serogroup	Clinical presentation	Therapy
Chiappini [5]	10	7 d	C	Meningitis	Prednisone + Aspirin
El Bashir [6]	13	7 d	C	Meningitis	Dexamethasone + Ibuprofen, later diclofenac sodium
Dupont[7]	14	3 d	C	Meningitis	ASA
Stephani [8]	14	9 d	C	Meningitis, endophthalmitis	Prednisone + Antibiotics
Fuglsang Hansen [9]	N/A	11 d	N/A	Meningitis	Steroid + Pericardiocentesis
Akinosoglou K [10]	28	N/A	B	Meningococcemia and acute abdominal pain	Steroid + Antibiotics

y: years; d: days; CSF, cerebrospinal fluid; ASA, acetylsalicylic acid; NSAID, non-steroid anti-inflammatory drug; N/A: not available; Limited data due to language constrains (Danish, German).

Patients who have chest complaints after vaccination should be evaluated for post-vaccine pericarditis and myocarditis. High clinical suspicion, careful examination and close observation may be required so that atypical presentation and manifestations are not overlooked. Endomyocardial biopsy specimens might help to determine the relative causative role of vaccine in the development of myocarditis. In our case, the mild illness, uncomplicated course, and good response to treatment deferred the need for biopsy. To our knowledge, there is no case report of reactive pericarditis following meningococcal vaccination.

Author contributions

Conception and design of the research: Al-Ebrahim EK, Qutub M. Analysis and interpretation of the data: Algazzar A. Writing of the manuscript: Al-Ebrahim EK. Critical revision of the manuscript for intellectual content: Algazzar A, Qutub M.

Limitation of the report

In these cases, in order to find the cause/effect relationship (or the association), large epidemiological studies are needed.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Sources of Funding

There were no external funding sources for this study.

Study Association

This study is not associated with any thesis or dissertation work.

Ethics approval and consent to participate

This article does not contain any studies with human participants or animals performed by any of the authors.

References

1. Arness MK, Eckart RE, Love SS, Atwood JE, Wells TS, Engler RJ, Collins LC, Ludwig SL, Riddle JR, Grabenstein JD, Tornberg DN. Myopericarditis following smallpox vaccination. Am J Epidemiol 2004;160(7):642–51.

2. Halsell JS, Riddle JR, Atwood JE, Gardner P, Shope R, Poland GA, Gray GC, Ostroff S, Eckart RE, Hospenthal DR, Gibson RL, Grabenstein JD, Arness MK, Tornberg DN; Department of Defense Smallpox Vaccination Clinical Evaluation Team. Myopericarditis following smallpox vaccination among vacciniaive US military personnel. JAMA 2003;289(24):3283-9.

3. Hardy DJ, Bartholomew WR, Amsterdam D. Pathophysiology of primary meningococcal pericarditis associated with neisseria meningitidis group C. A case report and review of the literature. Diagn Microbiol Infect Dis. 1986;4(3):259–65.

4. Finkelstein YY, Adler Y, Nussinovitch M. A new classification for pericarditis associated with meningococcal infection. Eur J Pediatr. 1997;156:585–8.

5. Chiappini E, Galli L, de Martino M, De Simone L. Recurrent pericarditis after meningococcal infection. Pediatr Infect Dis J 2004;23(7):692-3.

6. El Bashir H, Klaber R, Mukasa T, Booy R. Pericarditis after meningococcal infection: case report of a child with two distinct episodes. Pediatr Infect Dis J. 2004; 23(3)23: 279-81.

7. Dupont M, du Haut Cilly FB, Arvieux C, Tattevin P, Almange C, Michelet C. Recurrent pericarditis during meningococcal meningitis. 2 case reports. Presse Med 2004;33(8):533-4

8. Stephani U., and Bleckmann H.: Rare complications in a case of generalized meningococcal disease: immunologic reaction versus bacterial metastasis. Infection 1982;10(1):23-7.

9. Fuglsang Hansen J., Johansen I.S.: Immune-mediated pericarditis in a patient with meningococcal meningitis. Ugeskr Laeger. 2013;175(14):967-8.

10. Akinosoglou K, Alexopoulos A, Koutsogiannis N, Gogos C, Lekkou A.Neisseria meningitidis presenting as acute abdomen and recurrent reactive pericarditis. Braz J Infect Dis 2016;20(6):641-4.

11. Cassimatis DC, Atwood JE, Engler RM, Linz PE, Grabenstein JD, Vernalis MN. Smallpox vaccination and myopericarditis: a clinical review. J Am Coll Cardiol. 2004;43(9):1503–10.

12. Dilber E, Karagoz T, Aytemir K,Ozer S, Alehan D, Oto A. Acute myocarditis associated with tetanus vaccination. Mayo Clin Proc. 2003;78(11):1431–3.

Vol. 34, Nº 4, July and August 2021

Embolic Stroke of Undetermined Source (ESUS) and Stroke in Atrial Fibrillation Patients: not so Different after all?

Valeria Cristina Scavasine, Gustavo da Cunha Ribas, Rebeca Teixeira Costa, Guilherme Henrique Weiler Ceccato, Viviane de Hiroki Flumignan Zétola, Marcos Christiano Lange

Transfusion of Blood Products in the Postoperative of Cardiac Surgery

Antonieta Moraes , Juliana Neves Giordani , Cristiane Tavares Borges , Pauline Eloise Mariani , Laura Maggi da Costa, Leonardo Hennig Bridi , Ari Tadeu Lirio dos Santos , Renato Kalil

Echocardiographic and Ultrasonographic Parameters Associated with Protein-losing Enteropathy in Patients with Fontan Physiology: a Systematic Review with Meta-analysis

Marianna Freitas Mourato, Felipe Alves Mourato, Sandra da Silva Mattos, Juliana Rodrigues Neves

Effects of Low-to-Moderate Doses of Anabolic Steroids on Lipid Profile and Muscle Hypertrophy in Resistance Training Practitioners: A Systematic Review with Meta-Analysis

Mário César Carvalho Tenório, Cláudio Luiz Paz, Flávia Valladares, Marcelo Guimarães Junior, Cloud Kennedy Couto de Sá, Luis Correia

Continuous Aerobic Training and High Intensity Interval Training Increase Exercise Tolerance in Heart Failure Patients: A Retrospective Study

Diego Busin, Alexandre M. Lehnen, Olga S. Tairova, Eduardo P. Comparsi, Daniela Carneiro, Micael Potter, Luís F. Deresz, Pedro Dal Lago, Ramiro B. Nunes

Does Hypertension Knowledge Influence Levels of Physical Activity in Hypertensive Patients From a Southern Brazilian Community?

Rafaella Zulianello dos Santos, Andrea Schaefer Korbes, Eliara Ten Caten Martins, Mateus De Lucca, Leonardo De Lucca, Marlus Karsten, Magnus Benetti

Relationship between Discordance of Low-Density Lipoprotein and Non-High-Density Lipoprotein Cholesterol and Risk Stratification in Acute Myocardial Infarction

Murat Eren, Ozge Kurmus, Turgay Aslan, Kursat Akbuga, Hatice Tolunay

How much do the Patients with Acute Myocardial Infarction Know about Chest Pain, Thrombolytic Therapy, and Other Factors Affecting the Treatment Time in the Emergency Room?

Banu Ozmen, Cenk Conkbayir, Refika Hural, Didem Melis Oztas, Murat Ugurlucan, Barış Okcun, Zerrin Yiğit

QTc, Tp-e Interval and Tp-e/QTc Ratio in Patients with Hypocalcemia-case Control Study

Begum Seyda Avci, Akkan Avci, Arif Aksu, Muge Gulen, Onder Yesiloglu, Hasan Koca, Salim Satar

Cardiovascular Risk Assessment after COVID-19 Infection before Resuming Sports Activities - Practical Flowchart and Meta-Analysis

Luís Puga, Paulo Dinis, Rogério Teixeira, Joana Maria Ribeiro, Hélder Dores, Lino Gonçalves