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EDITORIAL

Psoriatic March, Skin Inflammation and Cardiovascular Events – Two Plaques for one Syndrome

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Traditionally, psoriasis has been regarded as a disease affecting only the skin and joints. Unfortunately, this is still the view among many doctors.

In this issue, Campos et al.,[1] published an interesting observational study on cardiovascular (CV) risk factors and risk measurement in patients with psoriatic arthritis, which allow us, in this editorial, to put the spotlight on some points of great interest in this area.

As the understanding of psoriasis has evolved, the perception of the disease pathophysiology changed from an organ-specific hyperkeratotic disorder of keratinocytes to an underlying dysregulation of the immune system mediated by cytokines. These concepts led to a further shift in its classification from a skin disease to a T-cell mediated disease.[2]

In the last years, a number of studies have demonstrated that psoriasis, mainly with systemic involvement (psoriatic arthritis), is associated with a higher prevalence of CV and metabolic diseases, and the prevalence of CV risk factors are increased in patients with psoriatic arthritis, including hypertension, diabetes, obesity, dyslipidemia and metabolic syndrome.[3] The results of the cross-sectional study by Campos et al.,[1] support these associations.

The close association of skin inflammation with CV disease and metabolic syndrome is a relative new topic in medicine. Inflammatory skin diseases, such as atopic dermatitis and psoriasis, produce a wide range of proinflammatory cytokines and chemokines not only in the lesional skin, but also in the circulation, causing systemic inflammation, insulin resistance and endothelial dysfunction, which may lead to atherosclerosis, myocardial infarction and CV comorbidities – the so called *psoriatic march*[4] or *inflammatory skin march*[5] (Figure 1).

The chronic state of inflammation appears to be a central mechanism underlying the pathophysiology of insulin resistance, visceral adiposity, hypertension and dyslipidemia.[6] But, what are the molecular mechanisms responsible for the association between psoriasis and cardiovascular comorbidities?

In 2012, Flammer and Ruschitzka[7] proposed the theory of *two plaques for one syndrome*. The cytokine profiles of
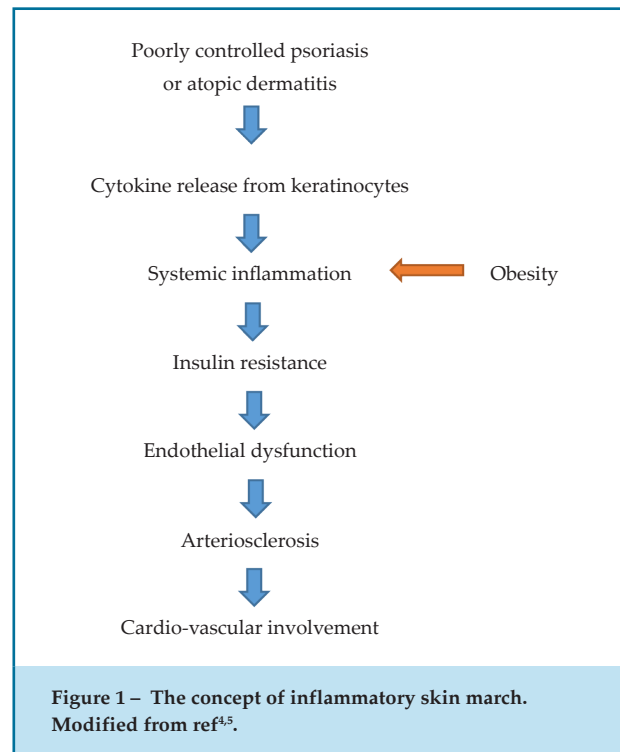
Keywords

Psoriasis; Dermatitis, Atopic; Risk Factors; Systemic Inflammatory Response Syndrome; Arthritis, Psoriatic; Inflammation; Comorbidity.

Figure 1 – **The concept of inflammatory skin march. Modified from ref[4,5].**

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psoriasis skin lesions and atherosclerosis vascular lesions are very similar, showing increased number of Th1 and Th17 lymphocytes. The Th1 and Th17 cytokine pathways have been shown to be involved in the pathogenesis of both psoriasis and atherosclerosis. The overexpression of Th17 cytokines in patients with psoriasis may mediate vascular inflammation and the development of atherosclerosis and CV comorbidities. Other mechanisms proposed are shared genetic factors, secretion of adipokines, lipoprotein composition and function, angiogenesis, oxidative stress, microparticles and hypercoagulability.[8]

While metabolic comorbidities are still underdiagnosed and undertreated in patients with long-standing psoriasis, the question arises whether earlier and more stringent control of the disease-driving inflammatory processes could potentially prevent the development and worsening of comorbidities. In this context, can we consider psoriasis as an independent risk factor for CV disease?

Several factors are associated with a higher risk of developing CV disease, including age, high blood pressure, obesity, smoking, stress and family history. Many (if not all) of these risk factors are also present in psoriatic patients.[9] Metabolic syndrome is more frequent in patients with psoriasis than in general population. Campos *et al.*[1] found dyslipidemia in 93%, hypertension in 46%, obesity in 40% and diabetes in 33% of the sample studied (psoriatic arthritis patients aged between 30 to 74 years, without other chronic inflammatory diseases, seen at the rheumatology outpatient clinic of a referral hospital in João Pessoa / Paraiba).

Su *et al.*,[10] found that the risk of developing severe vascular events is higher when psoriasis acts as a disease amplifier (i.e., when metabolic disorder precedes psoriasis), compared to when it acts as the disease initiator. Reich[2] proposed a simplified model, based on the excellent paper by Davidovici *et* al.,[11] that illustrates many potential functional interplays between shared genetic risk factors that drive both psoriasis and obesity, and may promote the development of CV comorbidities (Figure 2).

There are, however, opposing arguments to this model, and the debate so far has been whether there is a causal relationship between psoriasis and CV diseases.[9] Campos *et al.*,[1] found a high prevalence of cardiovascular risk factors in psoriatic arthritis patients, and the majority of

SHARED GENETIC RISK FACTORS

OBESITY

PSORIASIS

Cardiovascular disease

Figure 2 – Model of interplay between metabolic co-morbidities and psoriasis. Modified from ref[2,11].
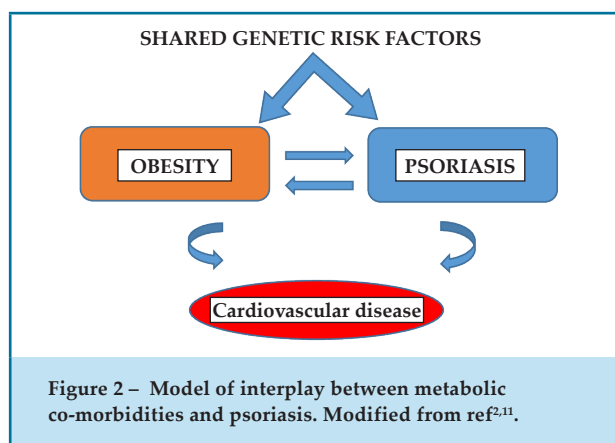
the sample was stratified into high or intermediate CV risk. This raises important issues regarding this association, including determining the minimum degree of psoriasis severity required to significantly increase the CV risk.

So, despite not being a (yet) consensual topic, there is strong evidence to suggest that psoriasis is an independent risk factor for the development of metabolic and CV comorbidities. In this regard, treatment of psoriasis might be expected to reduce the risk of developing these diseases.[2,9] Although inflammation suppression, mainly by immunomodulatory agents, has been suggested as a promising target for the management of CV diseases, Campos *et al.*,[1] found no significant difference in CV parameters with the different drugs used by the study population. Nevertheless, other studies have shown positive effects with the new cytokine-targeted therapies, mainly anti-TNFα.[8] A limitation of the study by Campos *et al.*[1] is, in fact, its cross-sectional nature and absence of a control group.

In conclusion, since optimal treatment of psoriasis is the one that not only ameliorates skin condition but also decreases the risk for CV and metabolic disorders, an early diagnosis and appropriate intervention made by internal medicine physicians, dermatologists and immunologists, are mandatory.[9] Campos *et al.*,[1] highlight the importance of assessing CV risk in psoriasis patients (mainly, but not exclusively with the severe forms of the disease), reinforcing this new perspective for inflammatory skin conditions.

References

1. Campos BPS, Gomes GDS, Braz AS, Vilela AT. Cardiovascular Risk Factors and Risk Measurement in Patients with Psoriatic Arthritis in a University Hospital. Int J Cardiovasc Sci. 2020; 33(2):112-118.

2. Reich K. The concept of psoriasis as a systemic inflammation: implications for disease management. J Eur Acad Dermatl Venereol. 2012;26(Suppl 2):3-11

3. Haroon M, Gallagher, P.; Heffernan, E.; FitzGerald, O. High prevalence of metabolic syndrome and of insulin resistance in psoriatic arthritis is associated with the severity of underlying disease. J. Rheumatol. 2014;41(4):1357-65.

4. Boehncke WH, Boehncke S, Tobin AM, Kirby B. The 'psoriatic march': a econcept of how severe psoriasis may drive cardiovascular comorbidity. Exp Dermatol. 2011;20:303–7.

5. Yamanaka K, Mizutani H. "Inflammatory skin march": IL-1 mediated skin inflammation, atopic dermatitis, and psoriasis to cardiovascular diseases. J Allergy Clin Immunol. 2015;136(3):823-4

6. Fumian MM, de Motta NA, Maia R, Fraga CA, Barreiro EJ, de Brito FC. LASSBio-1425, an analog of thalidomide, decreases triglyceride and increases HDL cholesterol levels by inhibition of TNF-a production. Int J Cardiol. 2016 Jan 1;202:497-9.

7. Flammer AJ, Ruschitzka F. Psoriasis and atherosclerosis: two plaques, one syndrome? Eur Heart J. 2012;33:1989-91.

8. Furue, M.; Kadono, T. "Inflammatory skin march" in atopic dermatitis and psoriasis. Inflamm Res. 2017;66(10):833-42.

9. Hu SC, Lan CE. Psoriasis and cardiovascular comorbidities: focusing in severe vascular events, cardiovascular risk factors and implications for treatment. Int J Mol Sci 2017;18(10):2211.

10. Su YS, Yu HS, Li WC, Ko YC, Chen GS, Wu CS, et al. Psoriasis as initiator or amplifier of the systemic inflammatory march: impact on development of severe vascular events and implications for treatment strategy. J Eur Acad Dermatol Venereol. 2013;27(7):876-83.

11. Davidovici BB, Sattar N, Prinz JC, Puiz L, Emery P, Barker JN, et al. Psoriasis and systemic inflammatory diseases: potential mechanistic links between skin disease and co-morbid conditions. J Invest Dermatol. 2010;130(7):1785-96.

Cardiovascular Risk Factors and Risk Measurement in Patients with Psoriatic Arthritis in a University Hospital

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Abstract

Background: Psoriatic Arthritis is the spondyloarthritis associated with psoriasis, which is often related to high mortality due to cardiovascular causes.

Objectives: To quantify cardiovascular risk factors (hypertension, diabetes, dyslipidemia, obesity and smoking) and to measure risk by the Global Cardiovascular Risk Score in patients with psoriatic arthritis.

Methods: Patients with psoriatic arthritis according to the Classification Criteria for Psoriatic Arthritis, aged between 30 and 74 years and without any other clinically manifest chronic inflammatory disease, atherosclerotic disease or heart failure were included. After an interview, clinical examination and data extraction from medical records, risk stratification was performed using a calculator available on the online platform of the Framingham Heart Study. We considered p < 0.05 as significant. Chi-square test and Fisher's exact test were used to compare frequencies, as well as correlation measurements.

Results: 45 patients were included, 68,9% of which were women and the mean age was 53,94 years. Dyslipidemia was confirmed in approximately 93%, hypertension in 46%, obesity in 40%, 33.3% were diabetics and, 13.3%, smokers; 95% had increased abdominal circumference. It was observed that 53% had high cardiovascular risk, 29% had intermediate risk and 18% had low risk. Individuals with altered C-reactive protein and erythrocyte sedimentation rate presented, respectively, higher levels of LDL-C and total cholesterol.

Conclusions: There was a high occurrence of risk factors and the majority of the sample was stratified into high or intermediate cardiovascular risk. (Int J Cardiovasc Sci. 2020; 33(2):112-118)

Keywords: Cardiovascular Diseases; Risk Factors; Obesity; Dyslipidemias; Inflammation; Arthritis, Psoriatic.

Introduction

Psoriasis is a chronic immune-mediated inflammatory disease, which classically involves the skin and affects 1.3% of the Brazilian population.[1-3] Psoriatic arthritis (PsA) is an inflammatory joint pathology that occurs in association with psoriasis, present in 10 to 30% of those with cutaneous manifestations.[4,5] The course of PsA ranges from mild manifestations to a debilitating picture. Skin injuries usually precede arthropathy and severity of cutaneous disease is unrelated to joint disease activity.[6] Its pathogenesis is not well established,

but genetic, immunological, environmental factors — infections and traumas — obesity and smoking are likely to be involved.[7-14]

The CASPAR (Classification Criteria for Psoriatic Arthritis) criteria are those recommended by the Brazilian Society of Rheumatology for PsA classification and diagnosis. It takes into account the presence of inflammatory joint disease associated with some of the following: current psoriasis, personal or family history of psoriasis, dactylitis, juxta-articular bone formation (in hands or feet), negative rheumatoid factor and psoriasis

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onychodystrophy. Sensitivity and specificity of this method are 99.7% and 99.1%, respectively.[15]

Inflammatory rheumatologic diseases are associated with high mortality, largely due to cardiovascular causes. It may be justified by an increase in inflammatory cytokines, atherosclerosis, endothelial dysfunction, individual genetics, use of medications with a negative effect on the cardiovascular system, in addition to traditional risk factors.[16] Psoriasis is related to increased risk of acute myocardial infarction (AMI), especially in severe cases.[17-20]

However, unlike other inflammatory diseases, these patients are more often obese. The pathophysiology of psoriasis and obesity involves many common cytokines that contribute to the components of metabolic syndrome: hypertension, dyslipidemia and insulin resistance.[14,18] In addition to the presence of comorbidities that act as a cardiovascular risk (CVR) factor, many studies detected increased rates of cardiovascular disease in this group.[19,21,22] Only one in every seven patients with psoriasis is aware of the atherosclerotic disease and metabolic syndrome risk they present.[23] Characterization of an association between PsA and increased CVR would justify automatic reclassification of patients with this condition in high CVR, without the need for scores that could attribute different risk.

Objectives

To quantify cardiovascular risk factors (hypertension, diabetes, dyslipidemia, obesity and smoking) and to measure risk by the Global Cardiovascular Risk Score in patients with psoriatic arthritis.

Methods

Cross-sectional study carried out between September 2016 and June 2017 at the Rheumatology outpatient clinic of *Hospital Universitário Lauro Wanderley* (HULW), João Pessoa - PB.

Population and sample

Study population consisted of all PsA patients followed at the rheumatology outpatient clinic of a reference hospital. Sample was chosen for convenience and a non-probabilistic stratified sample was adopted, due to the low prevalence of the disease.

Inclusion criteria

The study included patients classified according to the CASPAR criteria[24] (evaluated by a rheumatologist); aged between 30 and 74 years, since the Global Cardiovascular Risk Score (GCRS) used is restricted to individuals of this age group.[25] After adequate information, the patients signed the informed consent form (ICF).

Exclusion criteria

Patients with clinically manifest heart failure or atherosclerotic cardiovascular disease (coronary, cerebrovascular or peripheral occlusive disease) were excluded, until assessment, since the score used estimates the risk of onset and does not apply to patients with manifested cardiovascular disease.[25] Individuals diagnosed with another chronic inflammatory disease, other than PsA, were also eliminated.

Instruments for data collection

The CASPAR[24] criteria were used to confirm PsA classification/diagnosis; sociodemographic and clinical questionnaire based on the Framingham score[25] was used for global CVR; and a specific calculator was used for risk assessment, available on the online platform of the Framingham Heart Study; in addition to medical records data.

Procedures for data collection

This study was approved by the Research Ethics Committee of HULW - João Pessoa, PB - under protocol number 56336216.1.0000.5183.

Psoriatic arthritis patients underwent an interview and clinical examination for data collection and risk stratification according to the Framingham score[25] for global CVR. The most recent data of laboratory results were used with a maximum delay of six months between testing and evaluation.

This score considers the following: age, High Density Lipoprotein Cholesterol (HDL-C), total cholesterol, untreated systolic blood pressure (SBP) or treated SBP, smoking and diabetes. Age, condition of hypertension, smoking and diabetes are self-reported by the research participant, while HDL-C, total cholesterol, triglycerides, C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were obtained from the medical record.

The SBP used to calculate the CVR was measured by the researchers during the interview, as well as height and weight — for calculation of body mass index (BMI) — and abdominal circumference.

This score quantifies the percentage risk of developing the main cardiovascular events — coronary artery disease (CAD), stroke, peripheral arterial disease or heart failure — in the next 10 years. Patients with less than 5% probability of presenting any of the aforementioned outcomes were considered at low risk. Patients at intermediate risk were males with calculated risk between 5% and 20% or females with risk between 5% and 10%. High-risk individuals were men with calculated risk greater than 20% and women whose risk is greater than 10%.[26]

Data analysis

The sociodemographic and clinical characteristics were analyzed through descriptive statistics using frequencies for categorical variables, and mean and standard deviation (SD) for parametric scalar variables with a 95% confidence interval (95% CI), or median and interquartile range (IQR) for non-parametric variables. Shapiro-Wilk test was used to evaluate normality.

In inferential analysis, Chi-square and Fisher's exact test were used to compare frequencies between independent groups. To evaluate the correlation between two scalar variables, the Spearman method was used. Mann-Whitney test was used for independent samples. We considered $p < 0.05$ as significant. Statistical analysis was performed using the SPSS for MAC program (23.0 version).

Results

Among the 45 study participants, most were female (68.90%) and the mean age was 53.94 years (standard deviation 9.8). The sociodemographic data are shown in Table 1. The distribution of cutaneous psoriasis and AP forms is shown in Table 2.

Most of the sample had plaque psoriasis alone (32 individuals) and the most prevalent type of arthritis in this study was symmetrical polyarthritis (41 individuals), of which five also presented spondylitis. Most of the patients were diagnosed with cutaneous psoriasis prior to the diagnosis of PsA (66.67%), 24.44% had both diagnoses on the same occasion, and 8.89% had PsA before cutaneous manifestations. There was no difference in the

types of psoriasis or the time of diagnosis of psoriasis or PsA between the different groups of CVR.

Regarding the frequency of CVR factors among the patients in this study, dyslipidemia was present in 93% of the sample, 46% were hypertensive, 40% were obese (BMI ≥ 30 kg/m²), 33.3% had type 2 diabetes mellitus, 13.3% self-reported smoking, and 95% presented increased abdominal circumference.

Among the 45 participants, 43 had increased waist circumference, that is, women with a circumference greater than or equal to 80 cm and men with an abdominal

Table 1 - Socio-demographic data

Variables	N	%
Sex		
Female	31	68.89
Male	14	31.11
Ethnicity		
White	08	17.78
Non-white	37	82.22

Table 2 - Absolute frequency and percentage of each type of psoriasis and PsA

Variables	N	%
Type of psoriasis		
Plaque	32	71.11
Palmoplantar	07	15.56
Plaque + Palmoplantar	03	6.67
Guttate	02	4.44
Generalized Pustular	01	2.22
Arthritis type		
Symmetrical polyarthritis	36	80.00
Symmetric polyarthritis + spondylitis	05	11.12
Spondylitis	01	2.22
Asymmetric oligoarthritis	01	2.22
Distal arthritis	01	2.22
Mutilating Arthritis	01	2.22

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waist greater than or equal to 90 cm.[27] Patients who presented at least one of the following were considered dyslipidemic: LDL-C > 130 mg/dL or triglycerides > 150 mg/dl, values adopted by the 2017 Brazilian Dyslipidemia and Atherosclerosis Prevention Guideline.[26]

Individuals with altered serum CRP and ESR levels presented, respectively, higher levels of LDL-C (p = 0.02) and total cholesterol (p = 0.04). There was no significant difference between serum levels of CRP or ESR according to the different categories of CVR — low, intermediate or high risk.

Participants in this study had a median CVR of 13.70% (IQR 5.6-25.3). Patients at high risk for cardiovascular outcomes in the next 10 years accounted for 53% of the sample, 29% had intermediate risk and 18% were low risk.

Psoriatic arthritis medications used by the participants in this research data collection period are listed in Table 3. No association was found between the medication used and the calculated CVR compared by Fisher's exact test. Analyzing the presence of CVR factors and the type of medication used, it was evidenced that patients using leflunomide had significantly higher BMI (t = 2.41, p = 0.03)

Discussion

This study was performed to quantify risk factors and to assess the CVR of PsA patients followed at a tertiary referral hospital in northeastern Brazil. Corroborating with the high CVR found in the sample, in 2013, a systematic review evidenced increased risk of AMI, cardiovascular

Table 3 - Absolute frequency and percentage of each type of medication used for PsA

Medication	N	%
Metotrexate	26	57.78
Leflunomide	10	22.22
Adalimumab	08	17.78
Infliximab	07	15.56
Corticoid	03	6.67
Ustekinumab	02	4.44
Etanercept	02	4.44
Naproxen	01	2.22
None	04	8.89

mortality and stroke in patients with aggressive psoriasis — those who, by definition, require hospital admission or systemic therapy which includes carriers of PsA. Other manifestations of atherosclerotic disease also have increased frequency in patients with psoriasis, such as stroke and peripheral arterial disease.[27] Although notorious, the high occurrence of CVR factors, as well as the risk estimated by GCRS[25] in patients with PsA, do not provide enough evidence to use a multiplier factor for the usual scores, as in rheumatoid arthritis, for example, in which the calculated risk is multiplied by 1.5.[28]

Prevalence of hypertension, obesity, hyperlipidemia, type 2 diabetes and the occurrence of at least one cardiovascular event were 37.1%, 30%, 20.7%, 12% and 8.2%, respectively, resulting in a 4.9% increase in the risk of cardiovascular disease, 17.5% in hypertension, 6.2% in hyperlipidemia, 5.3% in type 2 diabetes and 3.5% in obesity compared with patients with psoriasis without arthritis.[29] A 2013 systematic review found a higher prevalence of hypertension in psoriasis patients than in the control group.[30] The same occurred with diabetes in another systematic review of the same year.[31] A population study from the UK found an increased smoking frequency, and all previously mentioned risk factors in psoriasis patients compared to the control group.[32] The sample of this study also revealed a high occurrence of the main predictors of CVR, especially dyslipidemia. The prevalence of hyperlipidemia found in the Canadian study is considerably lower, which may be justified by the non-contribution of low HDL-C patients in the Canadian research statistics, in addition to the current cut-off points being more stringent.

Similar to this study, in which the majority of individuals was diagnosed with psoriasis before articular manifestations, skin disease precedes arthritis in approximately 75% of the cases, is simultaneous in 10% of the diagnoses and occurs afterwards in 15%.[33]

Studies reveal a large range of variation in the incidence of each type of joint involvement: 15%–78% of the polyarticular form, 16%–70% of asymmetric oligoarthritis, 1%–17% of the form affecting the distal interphalangeal, 2%–16% of the mutilating form and 2%–27% of spondylitis. The overlap between the several subgroups of PsA is frequent and the joint involvement can change, so that patients starting symptomatology with asymmetric oligoarthritis can develop symmetrical polyarthritis over time, for example. Thus, the current trend is to classify PsA in three main clinical presentations: polyarticular, oligoarticular and axial; it is estimated that

they correspond to 41%, 31% and 28% of the patients, respectively.[33] In this study, the polyarticular form was also the most prevalent, followed by the overlap of this form with spondylitis.

A 2009 retrospective cohort study using a UK database, estimated to represent 5% of the population in this region, found an increased risk of stroke in PsA, which was higher according to the severity of the disease.[34] The presence of high levels of inflammatory biomarkers —— suggestive of increased disease activity — were predictors of clinical cardiovascular events in the study by Husted J.A. et al.[29] In our study, individuals with serum alterations of CRP and ESR presented, respectively, higher levels of LDL-C and total cholesterol, factors known to be related to the development of atherosclerosis and its consequences. However, there was no significant difference between serum levels of CRP or ESR according to the different categories of CVR — low, intermediate or high risk.

Psoriatic arthritis drug therapy includes non-steroidal anti-inflammatory drugs (NSAIDs), glucocorticoids and disease-modifying drugs (DMDs) — sulfasalazine, methotrexate, leflunomide and biological agents. DMDs are defined as drugs capable of preventing disease progression.[35] NSAIDs and glucocorticoids, used to alleviate PsA symptoms, are associated with an increase in unfavorable cardiovascular outcomes, such as AMI, which, in a way, may also eventually contribute to the increase of CVR.[36,37] On the other hand, in several studies, DMDs are related to reduced CVR. Risk was reduced in patients using these medications compared to those who used other systemic therapies, probably because of the greater effectiveness in reducing the disease activity, reducing inflammation and its propensity to the formation of atherosclerosis. Inflammation suppression by immunomodulatory agents represents a promising new target for the management of cardiovascular diseases both in the general population and among patients with chronic inflammatory conditions.[27,38] Methotrexate is the first-line DMD in PsA, due to its effectiveness in the treatment of cutaneous and joint involvement combined with its low cost. Its anti-inflammatory effect is mediated by adenosine and can neutralize neutrophils, T-cells and macrophages — the main agents in the pathogenesis of psoriasis and PsA.[33,39] Currently, the most widely used biological DMDs for PsA treatment, and approved by the Brazilian National Agency of Sanitary Surveillance (ANVISA), are the TNF-α inhibitors: etanercept, adalimumab, golimumab, infliximab, and certolizumab pegol.[40] However, in this study, there was no significant difference in cardiovascular parameters according to the different medications in use.

This research presented some limitations, because, although performed in a specialized outpatient clinic, the sample obtained was small and there was no comparison with the control group, thus no inferences could be made. Since it was an observational study, it was subject to memory bias. In addition, it was hampered by the lack of data in the medical records.

Conclusions

Most of the patients in the sample were stratified as high or intermediate CVR. Despite the high incidence of CVR factors, there was no parallel between them and the time of PsA diagnosis. It is recommended to use traditional CVR scores since there is not enough evidence to use a multiplier factor in this estimation, or to use a different calculator.

Authors' contributions

Research creation and design: Campos B, Gomes G, Telis A. Data acquisition: Campos B. Data analysis and interpretation: Campos B, Telis A. Statistical analysis: Telis A. Writing: Campos B, Gomes G, Braz A, Telis A. Critical revision of the manuscript for intellectual content: Braz A, Telis A. Supervision/major investigator: Telis A.

Potential Conflict of Interest

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

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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 *Universidade Federal da Paraíba* under protocol number CAAE: 56336216.1.0000.5183. 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. Gelfand JM, Weinstein R, Porter SB, Neimann AL, Berlin JA, Margolis DJ. Prevalence and treatment of psoriasis in the United Kingdom: a population-based study. Arch Dermatol. 2005;141(12):1537-41.

2. Sociedade Brasileira de Dermatologia. Consenso Brasileiro de Psoríase 2012 - Guias de avaliação e tratamento. 2a ed. Rio de Janeiro; 2012.

3. World Health Organization.(WHO). Global report on psoriasis.2016. [Cited in 2018 23 dez] [Available in: http://www.who.int/iris/handle/10665/204417]

4. Mease PJ, Gladman DD, Papp KA, Khraishi MM, Thaci D, Behrens F, et al. Prevalence of rheumatologist-diagnosed psoriatic arthritis in patients with psoriasis in European/North American dermatology clinics. J Am Acad Dermatol. 2013;69(5):729-35.

5. Farley E, Menter A. Psoriasis: comorbidities and associations. G Ital Dermatol Venereol. 2011;146(1):9-15.

6. Gottlieb AB, Kircik L, Eisen D, Jackson JM, Boh EE, Strober BE, et al. Use of etanercept for psoriatic arthritis in the dermatology clinic: the Experience Diagnosing, Understanding Care, and Treatment with Etanercept (EDUCATE) study. J Dermatolog Treat. 2006;17(6):343-52.

7. Ritchlin CT. Pathogenesis of psoriatic arthritis. Curr Opin Rheumatol. 2005;17(4):406-12.

8. Prinz JC. Psoriasis vulgaris--a sterile antibacterial skin reaction mediated by cross-reactive T cells? An immunological view of the pathophysiology of psoriasis. Clin Exp Dermatol. 2001;26(4):326-32.

9. Pattison E, Harrison BJ, Griffiths CE, Silman AJ, Bruce IN. Environmental risk factors for the development of psoriatic arthritis: results from a case-control study. Ann Rheum Dis. 2008;67(5):672-6.

10. Ko HC, Jwa SW, Song M, Kim MB, Kwon KS. Clinical course of guttate psoriasis: long-term follow-up study. J Dermatol. 2010;37(10):894-9.

11. Armstrong AW, Harskamp CT, Dhillon JS, Armstrong EJ. Psoriasis and smoking: a systematic review and meta-analysis. Br J Dermatol. 2014;170(2):304-14.

12. Bremmer S, Van Voorhees AS, Hsu S, Korman NJ, Lebwohl MG, Young M, et al. Obesity and psoriasis: from the Medical Board of the National Psoriasis Foundation. J Am Acad Dermatol. 2010;63(6):1058-69.

13. Cullen G, Kroshinsky D, Cheifetz AS, Korzenik JR. Psoriasis associated with anti-tumour necrosis factor therapy in inflammatory bowel disease: a new series and a review of 120 cases from the literature. Aliment Pharmacol Ther. 2011;34(11-12):1318-27.

14. Vlam K, Gottlieb AB, Mease PJ. Current concepts in psoriatic arthritis: pathogenesis and management. Acta Derm Venereol. 2014;94(6):627-34.

15. Carneiro S, Azevedo VF, Bonfiglioli R, Ranza R, Goncalves CR, Keiserman M, et al. Recommendations for the management and treatment of psoriatic arthritis. Rev Bras Reumatol. 2013;53(3):227-41.

16. Mota LM, Brenol CV, Pollak DF, Pinheiro GR, Laurindo IM, Pereira IA, et al. Safe use of biological therapies for the treatment of rheumatoid arthritis and spondyloarthritides. Rev Bras Reumatol. 2015; 55(3):281-309.

17. Samarasekera EJ, Neilson JM, Warren RB, Parnham J, Smith CH. Incidence of cardiovascular disease in individuals with psoriasis: a systematic review and meta-analysis. J Invest Dermatol. 2013;133(10):2340-6.

18. Sterry W, Strober BE, Menter A, International Psoriasis C. Obesity in psoriasis: the metabolic, clinical and therapeutic implications. Report of an interdisciplinary conference and review. Br J Dermatol. 2007;157(4):649-55.

19. Horreau C, Pouplard C, Brenaut E, Barnetche T, Misery L, Cribier B, et al. Cardiovascular morbidity and mortality in psoriasis and psoriatic arthritis: a systematic literature review. J Eur Acad Dermatol Venereol. 2013; 27(Suppl 3):12–29.

20. Ogdie A, Yu Y, Haynes K, Love TJ, Maliha S, Jiang Y, et al. Risk of major cardiovascular events in patients with psoriatic arthritis, psoriasis and

21. Samarasekera EJ, Neilson JM, Warren RB, Parnham J, Smith CH. Incidence of cardiovascular disease in individuals with psoriasis: a systematic review and meta-analysis. J Invest Dermatol. 2013;133(10):2340-6.

22. Gelfand JM, Neimann AL, Shin DB, Wang X, Margolis DJ, Troxel AB. Risk of myocardial infarction in patients with psoriasis. JAMA. 2006;296(14):1735-41.

23. Skiveren J, Philipsen P, Therming G. Patients with psoriasis have insufficient knowledge of their risk of atherothrombotic disease and metabolic syndrome. Clin Exp Dermatol. 2015;40(6):600-4.

24. Taylor W, Gladman D, Helliwell P, Marchesoni A, Mease P, Mielants H, et al. Classification criteria for psoriatic arthritis: development of new criteria from a large international study. Arthritis Rheum. 2006;54(8):2665-73.

25. D'Agostino RB, Vasan RS, Pencina MJ, Wolf PA, Cobain M, Massaro JM, et al. General cardiovascular risk profile for use in primary care: the Framingham Heart Study. Circulation. 2008;117(6):743-53.

26. Faludi AA, Izar MC, Saraiva JF, Chacra AP, Bianco HT, Afiune Neto A, et al. Atualização da Diretriz Brasileira de Dislipidemias e Prevenção da Aterosclerose – 2017. Arq Bras Cardiol. 2017;109(2 Suppl 1):1-76.

27. Associação Brasileira para o Estudo da Obesidade e da Síndrome Metabólica. Diretrizes brasileiras de obesidade 4a ed . São Paulo;2016. p.1-186.

28. Agca R, Heslinga SC, Rollefstad S, Heslinga M, McInnes IB, Peters MJ, et al. EULAR recommendations for cardiovascular disease risk management in patients with rheumatoid arthritis and other forms of inflammatory joint disorders: 2015/2016 update. Ann Rheum Dis. 2017;76(1):17-28.

29. Husted JA, Thavaneswaran A, Chandran V, Eder L, Rosen CF, Cook RJ, et al. Cardiovascular and other comorbidities in patients with psoriatic arthritis: a comparison with patients with psoriasis. Arthritis Care Res (Hoboken). 2011;63(12):1729-35.

30. Armstrong AW, Harskamp CT, Armstrong EJ. The association between psoriasis and hypertension: a systematic review and meta-analysis of observational studies. J Hypertens. 2013;31(3):433-42; discussion 42-3.

31. Armstrong AW, Harskamp CT, Armstrong EJ. Psoriasis and the risk of diabetes mellitus: a systematic review and meta-analysis. JAMA Dermatol. 2013;149(1):84-91.

32. Neimann AL, Shin DB, Wang X, Margolis DJ, Troxel AB, Gelfand JM. Prevalence of cardiovascular risk factors in patients with psoriasis. J Am Acad Dermatol. 2006;55(5):829-35.

33. Goldenstein-Schainberg C, Favarato MH, Ranza R. Conceitos atuais e relevantes sobre artrite psoriásica. Rev Bras Reumatol. 2012;52(1): 98-106.

34. Gelfand JM, Dommasch ED, Shin DB, Azfar RS, Kurd SK, Wang X, et al. The risk of stroke in patients with psoriasis. J Invest Dermatol. 2009;129(10):2411-8.

35. Ash Z, Gaujoux-Viala C, Gossec L, Hensor EM, FitzGerald O, Winthrop K, et al. A systematic literature review of drug therapies for the treatment of psoriatic arthritis: current evidence and meta-analysis informing the EULAR recommendations for the management of psoriatic arthritis. Ann Rheum Dis. 2012;71(3):319-26.

36. Johnsen SP, Larsson H, Tarone RE, McLaughlin JK, Norgard B, Friis S, et al. Risk of hospitalization for myocardial infarction among users of rofecoxib, celecoxib, and other NSAIDs: a population-based case-control study. Arch Intern Med. 2005;165(9):978–84.

37. Maxwell SR, Moots RJ, Kendall MJ. Corticosteroids: do they damage the cardiovascular system? Postgrad Med J. 1994;70(830):863-70.

38. Eder L, Gladman DD. Atherosclerosis in psoriatic disease: latest evidence and clinical implications. Ther Adv Musculoskelet Dis. 2015;7(5):187-95.

39. Carneiro S, Azevedo VF, Bonfiglioli R, Ranza R, Gonçalves CR, Keiserman M, et al. Recomendações sobre diagnóstico e tratamento da artrite psoriásica. Rev Bras Reumatol. 2013;53(3):227-41.

40. Acosta Felquer ML, Coates LC, Soriano ER, Ranza R, Espinoza LR, Helliwell PS, et al. Drug therapies for peripheral joint disease in psoriatic arthritis: a systematic review. J Rheumatol. 2014;41(11):2277-85.

The Challenge of Controlling Resistant Hypertension

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Hypertension is the main risk factor for cardiovascular disease, stroke, disability and death.[1] Despite the accumulated knowledge about hypertension and many treatment options, some hypertensive patients do not achieve the recommended blood pressure goals even receiving non-pharmacological treatment and three antihypertensive drugs. These individuals have the so-called "resistant hypertension" and are at increased risk of involvement of target organs, higher morbidity and mortality.

Several international scientific societies, including the Brazilian Society of Cardiology,[1] have dedicated to publishing evidence-based guidelines for the management of arterial hypertension,[2,3] and specific position statements on resistant hypertension have also been produced.[4,5] The Department of Hypertension of the Brazilian Society of Cardiology is about to issue an updated statement on the subject.

This issue of the International Journal of Cardiovascular Sciences presents the results of the study entitled "Association between Therapeutic Adherence and the Profile of Patients with Resistant Hypertension", by Araújo and Aras Junior.[6] The study was conducted with hypertensive patients seen in an outpatient clinic of a university hospital in Brazil and adds to the knowledge about the management of resistant hypertension in our country.[6] The study brings encouraging results, showing that 83% of patients had good adherence to treatment, maybe because they were seen in a tertiary health care institution. Twenty percent of patients had pseudoresistant hypertension and 17% refractory hypertension (patients with uncontrolled hypertension

Keywords

Hypertension/prevention and control; Blood Pressure; Drug Resistance; Medication Adherence; Morbidity.

even taking five or more antihypertensive drugs). However, even with good adherence to treatment, only 38% of the individuals had controlled blood pressure.[6]

In view of the high risk of resistant hypertension, blood pressure control of patients with this condition is imperative. However, for different reasons, control has been shown to be less than desirable, at least in our country. In the Brazilian study ReHOT (Resistant Hypertension Optimal Treatment), blood pressure control during office (<140/90 mm Hg) and 24-hour ambulatory blood pressure monitoring (<130/80 mm Hg) was achieved in only 21% of patients, while when ambulatory blood pressure monitoring (ABPM) control was considered alone, 44% and 46.2% control were observed in the groups that received spironolactone and clonidine, respectively.[7] In the PATHWAY-2 (Prevention and treatment of hypertension with therapy based on algorithm number 2) study, carried out in the United Kingdom, the target for systolic blood pressure below 135 mmHg was achieved in 69% of patients.[8]

It is important to remember that resistant hypertension is a relatively common condition. In the ReHOT study, resistant hypertension was observed in 12% of the Brazilian hypertensive population,[7] which is comparable with the rates reported in population studies, such as National Health and Nutrition Examination Survey (12%)[9] and the Brazilian Longitudinal Study of Adult Health (11 %).[10] A recent survey conducted in the United States revealed that 20% of North American hypertensive patients are apparently resistant to treatment, corresponding to 3% of the adult population.[11]

Patients with resistant hypertension, in general, have a higher frequency of comorbidities, such as obesity, diabetes mellitus, obstructive sleep apnea, history of cardiac, cerebrovascular and renal diseases.[7]

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It is essential that patients with resistant hypertension and possible associated clinical conditions be properly identified. For an effective treatment, there must be awareness and interaction of patients with the health team, selection of pharmacological and nonpharmacological treatment, and good treatment adherence, aiming at blood pressure control and reduction of morbidity and mortality of these high-risk patients.

References

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

2. 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):e13-e115.

3. Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi 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 and the European Society of Hypertension: The Task Force for the management of arterial hypertension of the European Society of Cardiology and the European Society of Hypertension. J Hypertens. 2018 ;36(10):1953-2041.

4. Carey RM, Calhoun DA, Bakris GL, Brook RD, Daugherty SL, Dennison-Himmelfarb CR, et al. Resistant Hypertension: Detection, Evaluation, and Management: A Scientific Statement From the American Heart Association. Hypertension. 2018 Nov;72(5):e53-e90.

5. Alessi A, Brandão AA, Coca A, Cordeiro AC, Nogueira AR, Magalhães DF, et al. First Brazilian position on resistant hypertension. Arq Bras Cardiol. 2012;99(1):576-85.

6. Araújo LBS, Aras-Junior R. Association between Therapeutic Adherence and the Profile of Patients with Resistant Hypertension. Int J Cardiovasc Sci. 2020; 33(2):121-130.

7. Krieger EM, Drager LF, Giorgi DMA, Pereira AC, Barreto-Filho JAS, Nogueira AR, et al. Spironolactone Versus Clonidine as a Fourth-Drug Therapy for Resistant Hypertension: The ReHOT Randomized Study (Resistant Hypertension Optimal Treatment). Hypertension. 2018 Apr;71(4):681-90.

8. 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. 2015;386(10008):2059-68.

9. Egan BM, Zhao Y, Axon RN, Brzezinski WA, Ferdinand KC. Uncontrolled and apparent treatment resistant hypertension in the United States, 1988 to 2008.Circulation. 2011; 124:1046–1058. doi: 10.1161/CIRCULATIONAHA.111.030189.

10. Lotufo PA, Pereira AC, Vasconcellos PS, Santos IS, Mill JG, Bensenor IM. Resistant hypertension: risk factors, subclinical atherosclerosis, and comorbidities among adults-the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil). J Clin Hypertens (Greenwich). 2015;17(9):74-80.

11. Carey RM, Sakhuja S, Calhoun DA, Whelton PK, Muntner P. Prevalence of Apparent Treatment-Resistant Hypertension in the United States. Hypertension. 2019 Feb;73(2):424-31.

ORIGINAL ARTICLE

Association between Therapeutic Adherence and the Profile of Patients with Resistant Hypertension

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Abstract

Background: Resistant hypertension (RH) consists of increased blood pressure (BP) despite the use of 3 or more antihypertensives or BP control only when is use of 4 or more antihypertensives. It is fundamental to exclude pseudoresistance, which can be attributed to poor therapeutic adherence. Adherence evaluation, generally by the Morisky-Grenn test, is important because, when appropriate, it is associated with fewer cardiovascular complications and better BP control.

Objectives: To evaluate the adherence of patients with RH and to investigate its relation with epidemiological, anthropometric and clinical characteristics, as well as to estimate the prevalence of pseudoresistance and to outline strategies to improve adherence.

Methods: Retrospective observational cohort from an interview with patients followed at an outpatient clinic for RH. Therapeutic adherence, demographic, anthropometric data, cardiovascular risk factors, comorbidities, complementary exams and BP level were collected. One-way ANOVA and Student's t-tests were used for normal variables, and the Kruskal-Wallis and Mann-Whitney tests were used for non-normal tests. Categorical variables were compared using the Chi-Square test. We considered a 5% significance level in all tests.

Results: 217 individuals were included. Of these, 17% had poor adherence. Epidemiological and clinical characteristics, complications, comorbidities, BP level or drugs used were statistically insignificant between groups. The poor adherence group used significantly more drugs ($p = 0.0313$) and 28% of pseudoresistance was estimated.

Conclusions: Most of the individuals presented good therapeutic adherence by the Morisky test. Only the number of antihypertensive drugs had a statistically significant influence on adherence, while the epidemiological, anthropometric and clinical characteristics were statistically insignificant. (Int J Cardiovasc Sci. 2020; 33(2):121-130)

Keywords: Hypertension; Antihypertensive Agents/pharmacology; Antihypertensive Agents/therapeutic use; Blood Pressure Determination; Drug Resistance; Life Style; Prognosis.

Introduction

Resistant hypertension (RH) is defined as uncontrolled blood pressure (BP) despite the use of three or more antihypertensives at the maximum tolerated doses (including, preferably, thiazide diuretics) or as BP control only when in use of four or more drugs.[1-3]

In the investigation of RH, it is always necessary to exclude the possibility of pseudoresistance, since the differentiation between true and apparent RH determines specific therapeutic measures.[1,3] Factors related to pseudoresistance include white coat hypertension, poor BP measurement technique, inadequate therapeutic regimen and/or poor therapeutic adherence,[1-3] which

is an important and challenging cause, since studies indicate that 50-80% of patients with systemic arterial hypertension (SAH) do not adhere to the medications.[1]

The RH treatment — as well as that of non-resistant hypertension — is based on non-medication and medication measures. Drug therapy consists of the association of antihypertensives with action on the main pathophysiological mechanisms of BP elevation. Thus, a diuretic, renin-angiotensin-aldosterone system inhibitor – ACE inhibitor (ACEI) or angiotensin receptor blocker (ARB) – and a calcium channel blocker (CCB) should be initially prescribed at full tolerated doses and adequate intervals.[1,3]

Studies indicate that, with good adherence to treatment, there is better clinical evolution regarding minimizing and/or postponing cardiovascular complications, in addition to more effective control of BP.[1,3] Therefore, failure to adhere to the proposed therapy, being one of the main obstacles to the control of BP,[3,4] contributes to higher morbidity and mortality.

There are several strategies for the detection and evaluation of therapeutic adherence, but without any consensus.[5] Questionnaires based on patient reports, despite low sensitivity and accuracy, are the most commonly used method due to simplicity and low cost.[4,5] Of these, the most used in Brazil[4] is the Morisky-Grenn test (TMG),[6] composed of questions that can easily be inserted in the medical interview.[5,7] In addition, it has been shown to be useful for identifying patients that either adhere or not to the treatment,[5] with sensitivity of 43.6% and specificity of 81%.[4]

In view of the high prevalence of poor adherence to antihypertensive treatment and considering the impact on morbidity and mortality due to impaired BP control, it is important to analyze this aspect in the follow-up of patients with SAH. Special attention is paid to individuals with RH, since they require more antihypertensive agents, which may contribute to poor adherence to treatment.

Therefore, the main objective of the study is to determine the degree of therapeutic adherence of patients with RH followed in a referral clinic through the Morisky scale and to evaluate its relationship with the epidemiological, anthropometric and clinical profile of these patients, as well as with the cardiovascular outcomes, complications and comorbidities associated with SAH. Secondary objectives are to estimate the prevalence of pseudoresistance and to devise strategies to improve therapeutic adherence.

Methods

Study design and sample

The study was an observational retrospective cohort based on interview with patients. The convenience sample included individuals aged 18 years and older, followed between 2012 and 2017, at the service of Severe Hypertensive Cardiovascular Disease of Ambulatório José Maria de Magalhães Neto Ambulatory, belonging to *Complexo Hospitalar Universitário Professor Edgard Santos* (Complexo-HUPES), *Universidade Federal da Bahia* (UFBA), who accepted to participate in the study by providing written Informed Consent. There were no exclusion criteria.

Analyzed variables

For all patients included in the study, a standardized questionnaire was used to collect data on therapeutic adherence through the Morisky-Grenn test, as well as epidemiological data (sex, age, education and ethnicity), anthropometric data (body mass index [BMI], systolic BP and diastolic BP) and clinical data (time of diagnosis of hypertension, time of follow-up in the outpatient clinic, alcoholism, current and previous smoking, antihypertensive drugs in use, comorbidities and complications — prior acute myocardial infarction [AMI], prior stroke, diabetes mellitus [DM], dyslipidemia and metabolic syndrome). In addition, data from routine laboratory exams and 24-hour ambulatory blood pressure monitoring (ABPM) were evaluated. BP measurement was performed according to the recommendations of the Brazilian Society of Cardiology.[1]

Patients were stratified according to the Morisky-Grenn test in having good therapeutic adherence (6 to 8 points) or poor therapeutic adherence (5 points or less). In both subgroups, the epidemiological, anthropometric and clinical profiles, presence of comorbidities and complications, blood pressure levels and antihypertensive medications in use were analyzed.

Statistical analysis

The parameters studied were evaluated in terms of the type of distribution using the D'Agostino-Pearson statistical test. The data collected are presented as mean and standard deviation (mean ± SD) for continuous variables with normal distribution and as median and interquartile range for non-normal continuous variables.

Categorical variables are presented by absolute numbers and percentages.

The patients were compared according to the degree of therapeutic adherence by the one-way ANOVA test for variables with normal distribution, and Kruskal-Wallis, followed by Dunn's post-test, when the variables were not normally distributed. Categorical variables were also compared by the distribution of events using Fisher's or Chi-Square test. Comparison between two groups was done with unpaired Student's t-test (with Welch's correction when necessary) when they presented normal distribution, or with the nonparametric Mann-Whitney test for variables without normal distribution. A significant value of $p < 0.05$ was considered. Prism software version 7.04 (GraphPad Software, Inc., San Diego, CA, USA) was used.

Ethical considerations

This project is an addendum to the project "Clinical and Metabolic Evaluation in Resistant Systemic Arterial Hypertension", inserting itself in its specific objectives. The project was approved by the Ethics and Research Committee of Hospital Ana Nery, protocol number 138371, on 11/05/2012. All patients enrolled in the study signed an Informed Consent.

Results

The study included 216 individuals, who were classified according to the Morisky Therapeutic Adherence Scale. Of these, 136 (83%) had good therapeutic adherence and 28 (17%) had poor adherence. The percentage of each test response can be seen in figure 1.

The epidemiological, anthropometric and clinical characteristics of these individuals can be seen in table 1, while the prevalence of comorbidities and complications can be seen in table 2.

By comparing the epidemiological and clinical characteristics between the groups divided according to the degree of therapeutic adherence, there is no statistical significance for the variables considered (table 1), similarly for complications and comorbidities (table 2).

In the group with good therapeutic adherence, 37.83% of the individuals had controlled BP (normal or prehypertension), whereas of the individuals with poor adherence, 26.92% had controlled BP. Despite the differences between the groups, there was no statistical significance ($p = 0.2921$) (table 3).

The antihypertensive drugs most commonly used by the individuals in the sample were amlodipine (68.91%) [CCB], losartan (66.37%) [ARB], hydrochlorothiazide (47.7%), chlorthalidone (44.34%) [thiazide diuretics] and
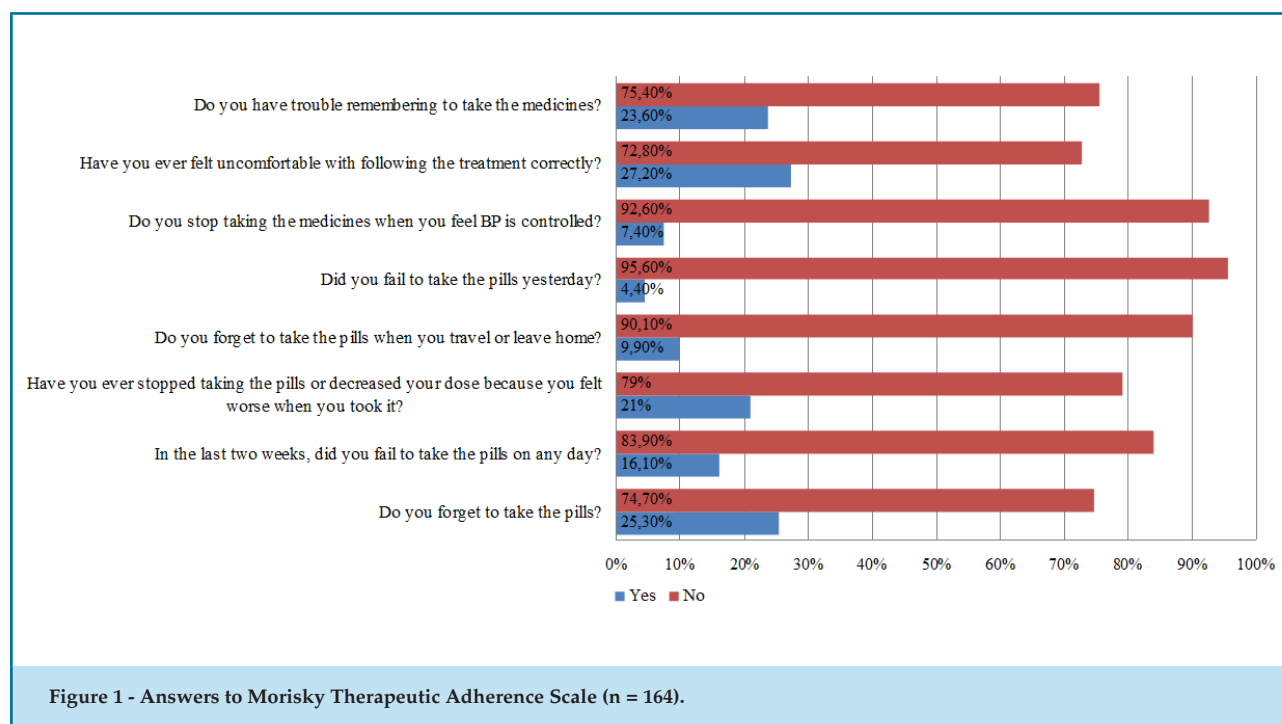
Figure 1 - Answers to Morisky Therapeutic Adherence Scale (n = 164).

Table 1 - Epidemiological, anthropometric and clinical profile

Variables	Frequency (%)/ mean (SD)			
	General	Good adherence	Poor adherence	p value (< 0.05)
Gender	(n = 216)	(n = 135)	(n = 28)	
Female	73.14%	75.5%	71.42%	0.6494
Male	26.85%	24.4%	28.58%	
Age (years)	(n = 212) 63.49 (11.57)	(n = 127) 63.91 (11.44)	(n = 25) 62 (55 -69.5)	0.4292
Education	(n = 212)	(n = 134)	(n = 28)	
Illiterate	11.3%	11.19%	14.28%	
Incomplete primary school	13.6%	13.43%	17.85%	
Complete primary school	8.9%	8.95%	10.71%	
Incomplete middle school	30.6%	28.35%	17.85%	
Complete middle school	5.1%	5.22%	3.57%	0.6077
Incomplete high school	7.5%	6.71%	17.85%	
Complete high school	18.8%	23.88%	10.71%	
Vocational training	1.4%	0%	7.14%	
Incomplete higher education	0.4%	0%	0%	
Graduated	1.8%	2.23%	0%	
Ethnicity	(n = 215)	(n = 134)	(n = 28)	
White	8.37%	7.46%	14.28%	
Black	53.48%	55.22%	50%	0.4479
Brown	38.13%	36.56%	35.71%	
BMI (kg/m²)	(n = 165)	(n = 118)	(n = 26)	
Low weight (< 18,5)	2%	1.69%	0%	
Ideal (18,5 – 24,9)	13%	12.71%	15.38%	
Overweight (25 – 29.9)	35%	34.74%	23.07%	0.3403
Obesity I (30 – 34,5)	34%	34.74%	34.61%	
Obesity II (35 – 39,9)	12%	10.16%	19.23%	
Obesity III (> 40)	5%	5.93%	7.69%	
Abdominal circumference (cm)	(n = 136)	(n = 96)	(n = 23)	
Normal (♂ ≤ 102; ♀ ≤ 88)	22%	21.87%	21.73%	0.9888
Increased (♂ > 102; ♀ > 88)	77%	78.12%	78.26%	
Systolic blood pressure (mmHg)	(n = 160) 149.5 (133 – 166.8)	(n = 111) 149.5 (130 – 166)	(n = 26) 152.7 (26.91)	0.6893
Diastolic blood pressure (mmHg)	(n = 160) 88 (77 – 100.4)	(n = 111) 87 (77 – 98.88)	(n = 26) 90 (16.99)	0.6673

Cont. Table 1 - Epidemiological, anthropometric and clinical profile

Variables	Frequency (%)/ mean (SD)			
	General	**Good adherence**	**Poor adherence**	**p value (< 0.05)**
Mean blood pressure (mmHg)	(n = 158) 107.5 (98 – 120)	(n = 111) 107 (98 – 120)	(n = 26) 110.9 (18.82)	0.7299
Time of diagnosis of SAH (years)	(n = 178) 20 (14.75 – 30)	(n = 124) 20 (14.25 – 27.75)	(n = 26) 22.73 (12.19)	0.3648
Follow-up time at the outpatient clinic (years)	(n = 176) 15 (8 – 20.75)	(n = 122) 15 (7.75 – 25.75)	(n = 26) 17.23 (12.12)	0.6630
Alcoholism	(n = 215) 14.41%	(n = 135) 15.5%	(n = 28) 10.71%	0.4017
Current smoking	(n = 215) 1.64%	(n = 128) 1.56%	(n = 27) 3.7%	0.7544
Previous smoking	(n = 182) 35.16%	(n = 128) 32.81%	(n = 27) 29.62%	0.5673

* Data analysis was performed using the Kruskal-Wallis test, followed by the Dunn post-test, and the comparison between the groups was done by the Mann-Whitney test (except for the variable 'age', for which it was used the one-way ANOVA test, and the comparison between the groups was done by Student's t-test).

Table 2 - Comorbidities and complications

Variables	Frequency (%)			
	General	**Good adherence**	**Poor adherence**	**p value (< 0.05)**
Previous AMI	18.5% (n = 178)	17.74% (n = 124)	19.23% (n = 26)	0.8586
Previous stroke	21.6% (n = 180)	19.53% (n = 128)	36% (n = 25)	0.6016
DM	43.95% (n = 182)	40.62% (n = 128)	44.44% (n = 27)	0.8587
Dyslipidemia	95.6% (n = 162)	93.04% (n = 115)	100% (n = 22)	0.2052
Metabolic syndrome	57.4% (n = 162)	53.04% (n = 115)	66.6% (n = 24)	0.2249

* Data analysis was done using Fisher's test.

spironolactone (42.86%) [potassium sparing diuretic]. The distribution of the use of these drugs according to each group can be seen in figure 2, which shows that there was no statistical difference between the groups concerning the drugs used. Regarding the use of the thiazide diuretic + ACE/ARB + CCB combination, recommended as initial therapy for patients with RH, it was found to be used by 68.8% of individuals with good adherence and 72% of those with poor adherence, with no difference between groups (p = 0.7534). Most of the individuals in both groups used 4 or 5 medications (figure 3). However, the group that had poor therapeutic

Table 3 - Classification of blood pressure

Classification of BP (mmHg)	Frequency (%)		p value (< 0.05)
	Good adherence (n = 111)	Poor adherence (n = 26)	
Normal (SBP ≤ 120; DBP ≤ 80)	10.81%	7.69%	
Pre-hypertension (SBP 121 – 139; DBP 81 – 89)	27.02%	19.23%	
SAH stage 1 (SBP 140 – 159; DBP 90 – 99)	23.42%	34.61%	0.2921
SAH stage 2 (SBP 160 - 179; DBP 100 – 109)	24.32%	19.23%	
SAH stage 3 (SBP ≥ 180; DBP ≥ 110)	14.41%	19.23%	

* Data analysis was performed using the Chi-Square test.
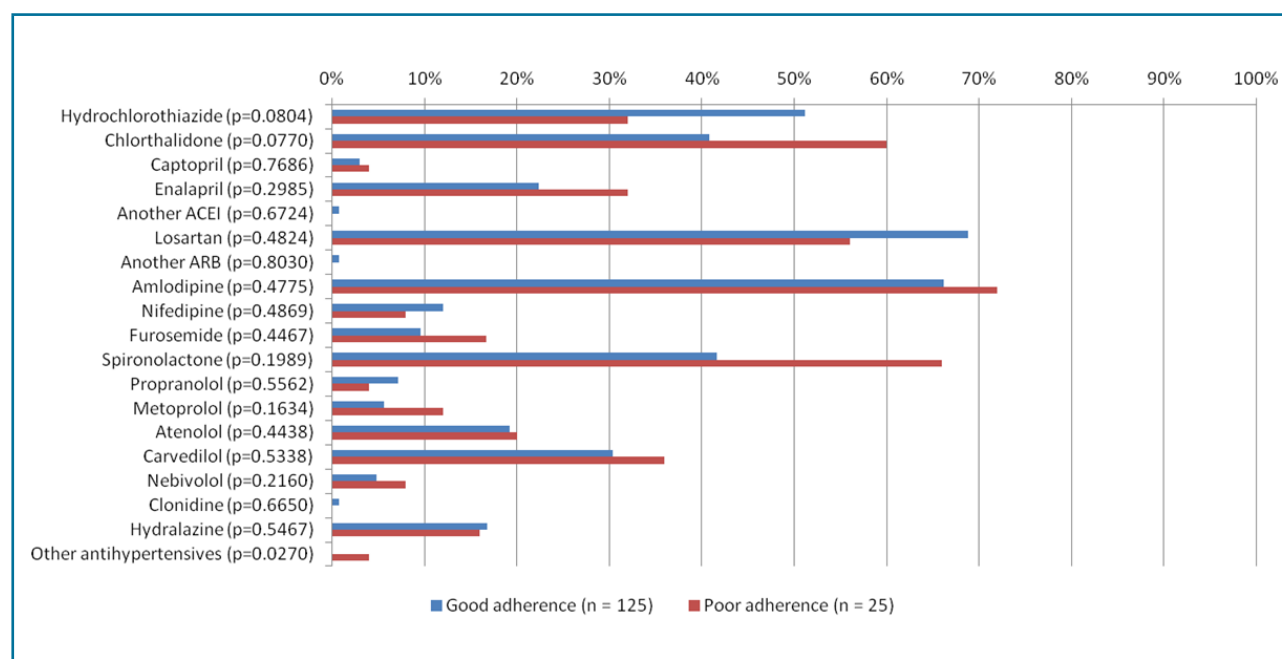
Figure 2 - Antihypertensive drugs in use according to degree of therapeutic adherence.
* Hydrochlorothiazide is used by 51.2% of individuals with good adherence and 32% of individuals with poor adherence (p = 0.0804); chlorthalidone is used by 40.8% of the individuals with good adherence and 60% of the individuals with poor adherence (p = 0.0770); captopril is used by 3.2% of the individuals with good adherence and 4% of the individuals with poor adherence (p = 0.7686); enalapril is used by 22.4% of individuals with good adherence and 32% of individuals with poor adherence (p = 0.2985); another ACEI is used by 0.8% of the individuals with good adherence and 0% of the individuals with poor adherence (p = 0.6724); losartan is used by 68.8% of individuals with good adherence and 56% of individuals with poor adherence (p = 0.4824); another ARB is used by 0.8% of individuals with good adherence and 0% of individuals with poor adherence (p = 0.8030); amlodipine is used by 66.2% of the individuals with good adherence and 72% of the individuals with poor adherence (p = 0.4775); nifedipine is used by 12% of individuals with good adherence and 8% of individuals with poor adherence (p = 0.4869); furosemide is used by 9.6% of individuals with good adherence and 16.7% of individuals with poor adherence (p = 0.4467); spironolactone is used by 41.6% of individuals with good adherence and 66% of individuals with poor adherence (p = 0.1989); propranolol is used by 7.2% of the individuals with good adherence and 4% of the individuals with poor adherence (p = 0.5562); metoprolol is used by 5.6% of individuals with good adherence and 12% of individuals with poor adherence (p = 0.1634); atenolol is used by 19.2% of the individuals with good adherence and 20% of the individuals with poor adherence (p = 0.4438); carvedilol is used by 30.4% of the individuals with good adherence and 36% of the individuals with poor adherence (p = 0.5338); nebivolol is used by 4.8% of individuals with good adherence and 8% of individuals with poor adherence (p = 0.2160); clonidine is used by 0.8% of individuals with good adherence and 0% of the individuals with poor adherence (p = 0.6650); hydralazine is used by 16.8% of the individuals with good adherence and 16% of the individuals with poor adherence (p = 0.5467); other antihypertensives are used by 0% of the individuals with good adherence and 4% of the individuals with poor adherence (p = 0.0270). The combination ACEI/ARB + thiazide diuretic + CCB is used by 68.8% of the individuals with good adherence and 72% of the individuals with poor adherence (p = 0.7534).

adherence used, on average, a larger number, with statistical significance (p = 0.0313).

Considering the need to exclude pseudoresistance for the diagnosis of true RH, it is estimated that 43 (19.9%) of the patients attending the outpatient clinic presented pseudoresistance, reported through the Morisky test (low adherence), inadequate therapeutic regimen (no inclusion of thiazide diuretic in the scheme) and ABPM (white coat hypertension). Thus, excluding pseudoresistance and considering the criteria for the definition of RH (uncontrolled BP despite the use of 3 or more antihypertensives – one of them being a thiazide diuretic – or BP control only when in use of 4 or more antihypertensives), 108 (50%) individuals attending the outpatient clinic presented true RH. In addition, 36 (16.6%) individuals at the outpatient clinic (33% of patients with true RH) had refractory arterial hypertension (BP uncontrolled despite the use of 5 or more antihypertensives, including a thiazide diuretic).

Discussion

The prevalence of good therapeutic adherence found in this study (83%) was similar to that found in the ReHOT study,[8] which was approximately 80%, and that found by Garg et al.,[9] where it was 84%. However, other studies show lower rates of good adherence, such as 31.3% found by Jesus et al.,[10] 51.0% found by Bloch et al.,[11] and 31.2% found by Prado-Jr , et al.[12] The relatively

high rate of good therapeutic adherence in this study can be explained by the fact that patients are followed up at a reference outpatient clinic for Resistant Arterial Hypertension, so more attention is possibly given to the issue of adherence.

An analysis of the answers given by the patients in the Morisky test reveals that the main affirmative answer was about the discomfort of correctly following the proposed therapy (27.2%). This provides evidence of the need to ensure that the patient has understood the importance of using medications to control BP. The second and third most prevalent responses were, respectively, about forgetting to take the medications (25.3%) and having difficulty remembering to take the medications (23.6%). Faced with this reality, it is fundamental to draw together patient and family strategies to help patients remember to take their medications. Another response with considerable prevalence was about discontinuing the use or reducing the dose of medications because of feeling worse (21%). At all appointments, it is the physician's responsibility to ask patients about any adverse effects and discomfort with the use of the medications in order to, if necessary, change or make dose adjustments, thus avoiding that the patient does so improperly.

Literature shows that different factors may contribute to poor therapeutic adherence of hypertensive patients, such as gender, age, education, ethnicity, smoking, alcohol consumption, comorbidities and duration of
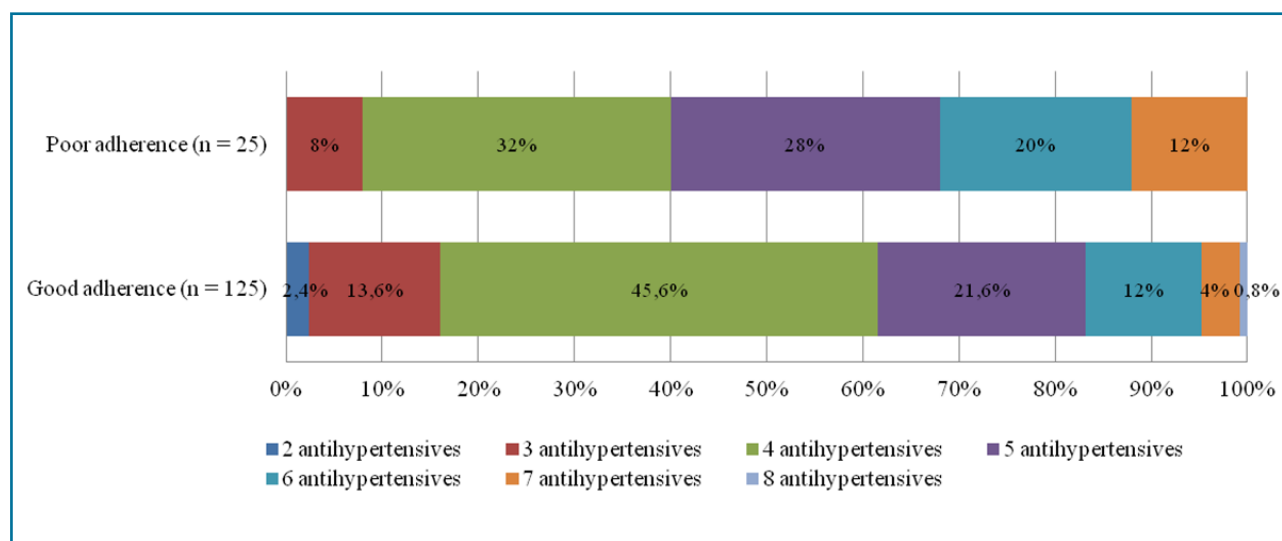
Figure 3 - Number of antihypertensive drugs according to degree of therapeutic adherence.
* In the group with good adherence, the median number of antihypertensive drugs used is 4 (4 - 5), while in the group with poor adherence the mean of antihypertensive drugs is 4,96 (1,17), with p value 0.0313. † The comparison between groups was done by the Mann-Whitney test.

follow-up.[5,10] All of these variables were analyzed. However, there was no statistical significance for any of them as contributors to poor adherence, possibly because it is a cohort population with high cardiovascular risk and poorly diversified ethnic profile.

The number of medications used may also have an impact on the degree of therapeutic adherence,[5,10] which was confirmed in this study, since the group with poor adherence used a significantly higher number of antihypertensive drugs. It is important to consider this finding when making prescriptions, as the use of tablets with drug combinations may be an effective strategy to improve adherence. In addition, emphasizing the need to change lifestyle, consider switching the drug class or increasing the dose of some drug already used — always considering the risk of developing adverse effects when increasing the dose — may be better for therapeutic adherence than just adding more drugs to the patient's prescription.

There is evidence that poor therapeutic adherence is one of the main obstacles to pressure control.[3,4,10,12] Therefore, patients with greater adherence tend to have lower pressure levels and greater BP reductions.[11,12] In this sample, it was found that, regardless of the degree of adherence, most individuals did not have good BP control, with no statistical difference between the groups. Even so, an expected trend can be identified in the groups: of the individuals with controlled BP, most are part of the group that has good adherence, whereas of the individuals with uncontrolled BP, most are part of the group with poor adherence.

The absence of BP control in a large part of the population with poor adherence is expected.[3,4,10] However, in the group with good adherence, poor BP control was not expected. This can be explained by the low sensitivity of the Morisky test — only 43.6% — which, despite being the most used method in Brazil to quantify adherence to antihypertensive therapy, facilitating the comparison between studies, may not be the ideal one.[4,10] Thus, considering that patients with poor BP control have lower chances of having good therapeutic adherence,[12] patients classified by Morisky test as having good adherence could possibly have poor adherence. Therefore, Morisky test cannot be considered efficient to relate BP control to the patients' posture as for taking their medications.[12] In addition, the high rate of poor BP control in the group with good adherence can also be explained by the fact that it is a group of individuals already very severe, so the pathophysiology

of the disease itself makes it difficult to control BP levels even in those patients who follow the therapeutic scheme appropriately. Thus, it remains controversial in this population whether the adequate use of medications is as determining for the control of BP in severe patients as it would be for patients with nonresistant SAH.

Not only is adherence important for controlling BP levels, but also the use of appropriate therapy – to the extent that, when inappropriate, it is indicative of pseudoresistance. In this sample, most of the patients used the combination of thiazide diuretic + ACE/ARB + CCB, but a considerable percentage did not use this combination, which is worrying, as they are patients with severe SAH seen at a reference clinic.

Correct diagnosis of RH requires verification of adherence to treatment,[11] since poor adherence with uncontrolled BP will lead to unnecessary tests and modifications of prescription.[10] Despite the difficulty of controlling all causes of pseudoresistance to exclude cases of apparent RH[2], the presence of pseudoresistance can be estimated. In this sample, patients with pseudoresistant SAH were identified from the evaluation of therapeutic adherence by the Morisky test, the therapeutic regimen used and ABPM. An estimated 28% of pseudoresistance in an outpatient clinic specialized in severe hypertension raises some questions about the way these patients are being monitored and the criteria for staying in a tertiary care service.

Therefore, considering the results found, adherence to antihypertensive therapy can be increased by instructing patients on the importance of taking medications — ensuring that they have understood it — and by drawing strategies with the patients and their family to help them remember to take the medications properly. In addition, investigating possible adverse effects and discomfort with the use of medications is critical in order to, if necessary, change the drug or make dose adjustments to prevent the patient from discontinuing the medication on their own. Prescription of combined drugs in a single tablet also appears to be an effective strategy to improve adherence, as well as the judgment of the need to introduce another drug into the prescription, as this may compromise adherence to the entire prescription.

The lack of data on pill counts or evaluation of serum levels of drugs brings a limitation to data analysis, especially considering that the Morisky test presents a sensitivity of only 40.3% for the evaluation of therapeutic adherence. Within the sample, no cases

of secondary hypertension were investigated, which is also a limitation of the study.

Comparison of studies of patients with RH is difficult due to the small number of studies that consider only this subgroup of hypertensive patients, as well as those that consider therapeutic adherence to evaluate the diagnosis of RH and its differentiation from pseudoresistance.[10,11] Considering adherence to the diagnosis of RH is fundamental, since poor adherence to therapy and RH do not coexist, because it must have good adherence to define SAH as resistant.[10] Thus, further studies focusing on this specific group of patients with RH are needed to improve therapeutic management, blood pressure control and clinical outcomes.

Conclusion

The majority of patients included in the study showed good therapeutic adherence according to the Morisky scale. An analysis of the factors that could influence adherence, only the number of antihypertensive drugs had a statistically significant influence, while the epidemiological, anthropometric and clinical characteristics were statistically insignificant. The estimated prevalence of pseudoresistance was approximately 20%, considering the Morisky test, the therapeutic regimen used and ABPM.

Authors' contributions

Research creation and design: Araújo LBS. Data acquisition: Araújo LBS. Data analysis and interpretation: Araújo LBS. Statistical analysis: Araújo LBS. Manuscript writing: Araújo LBS. Critical revision of the manuscript for intellectual content: Araújo LBS and Aras Junior R. Supervision/as the major investigator: Araújo LBS. and Aras Junior R.

References

1. 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(3Suppl):1-83.

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

3. Calhoun DA, Jones D, Textor S, Goff DC, Murphy TP, Toto RD, et al. Resistant Hypertension: Diagnosis, Evaluation, and Treatment. Circulation. 2008;117(25):510-26.

4. Ben AJ, Neumann CR, Mengue SS. Teste de Morisky-Green e Brief Medication Questionnaire para avaliar adesão a medicamentos. Rev Saúde Pública. 2012;46(2):279-89.

5. Gusmão JL, Ginani FG, Silva GV, Ortega KC, Mion Jr D. Adesão ao tratamento em hipertensão arterial sistólica isolada. Rev Bras Hipertens. 2009;16(1):38-43.

6. Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. Med Care. 1986;24(1):67-74.

7. Ulbrich EM, Mantovani MF. Fatores preditivos para complicações em pessoas com hipertensão arterial sistêmica e ações para o gerenciamento de cuidados da enfermagem na atenção primária. [tese]. Curitiba: Universidade Federal do Paraná; 2015.

8. Krieger EM, Drager LF, Giorgi DM, Pereira AC, Barreto Filho JA, Nogueira AR, et al. Spironolactone Versus Clonidine as a Fourth-Drug Therapy for Resistant Hypertension: The ReHOT Randomized Study (Resistant Hypertension Optimal Treatment). Hypertension. 2018;71(4):681-90.

9. Garg JP, Elliott WJ, Folker A, Izhar M, Black HR. Resistant Hypertension Revisited: A Comparison of Two University-Based Cohorts. Am J Hypertens. 2005;18(5Pt 1):619-26.

10. Jesus NS, Nogueira AR, Pachu CO, Luiz RR, Oliveira GMM. Blood Pressure Treatment Adherence and Control after Participation in the ReHOT. Arq Bras Cardiol. 2016;107(5):437-45.

11. Bloch KV, Melo AN, Nogueira AR. Prevalência da adesão ao tratamento anti-hipertensivo em hipertensos resistentes e validação de três métodos indiretos de avaliação da adesão. Cad Saúde Pública. Dez 2008;24(12):2979-84.

12 Prado JC Jr, Kupek E, Mion D Jr. Validity of four indirect methods to measure adherence in primary care hypertensives. J Hum Hypertens. 2007;21(7):579-84.

Factors Associated With Quality of Life in Patients with Systemic Arterial Hypertension

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In 1966, Avedis Donabedian published a seminal article[1] showing the importance of measuring health care quality. Donabedian also defined that it should be done in the dimensions of structure, process or results.[2] The author showed that the "results" dimension is not necessarily related to the other two. While the measurement of some results, such as mortality, is easy to be carried out, other results are difficult to be measured, such as quality of life and patients' satisfaction.

In the early 80's, I became interested in the subject of health care quality. My thesis to obtain the master's degree in Internal Medicine from the Federal University of Rio de Janeiro Medical School was entitled "Hypertension: health care quality at the HU-UFRJ".

Therefore, it was a pleasant surprise when I was invited to write an editorial of an article about quality of life of patients with systemic arterial hypertension on this issue of International Journal of Cardiovascular Sciences.

Based on the hypothesis that "physical conditioning is the main component of quality of life of hypertensive subjects", in a cross-sectional study, the authors evaluated the effects of isometric handgrip training on blood pressure of hypertensive individuals to assess the factors associated with the quality of life of these patients.

For this purpose, the authors used the SF-36 questionnaire, developed by the Rand Corporation,[4] which is a generic measure of quality life that has been translated and validated in Portuguese.[5] The instrument allows the determination of descriptive information and comparisons of populations, and assessment of health perception and quality of life of patients over time.

Keywords

Blood Pressure, Cardiovascular Diseases/prevention and control; Antihypertensive Agents/therapeutic use; Hypertension/ therapy; Exercise; Quality of Life.

This is then the first limitation of the study to be discussed. The authors did not present the calculation of the sample size required to describe the characteristics of the study population with respect to the eight domains of the questionnaire. In addition, according to the abstract of the study, 45 hypertensive patients participated in the study, but Table 1 in the article: "Factors Associated with Quality of Life in Patients with Systemic Arterial Hypertension"[3] describes 80 participants (n = 80).

Participants that met the eligibility criteria, which were probably developed for the intervention study, were hypertensive, and overweight or obese (probably mostly obese class I, since the mean BMI was 30.7 kg/m²). Obesity is associated with hypertension, and to analyze the effect of each condition using the quality of life questionnaire, the authors should have performed a multiple-variable analysis, which, in turn, would be impossible considering the relatively small sample size. The lack of a multiple-variable analysis also hinders the assessment of the effect of medication use on patients' quality of life,[6] especially knowing that the more severe the disease, the more drugs (and at higher doses) a patient receives.[7]

Analysis of the statistically significant variables showed known and expected data, such as: the positive relationships between functional capacity and higher education level, and functional capacity and muscle strength, and a negative relationship between functional capacity and higher BMI. However, how are these data related to hypertension?

The only result related with arterial hypertension does not make sense – the positive relationship between physical aspects and systolic blood pressure – which may have resulted from contamination by any other variable. This result deserves criticism, as it may lead the readers to understand that an elevated systolic blood pressure is beneficial, while it has already been shown that an

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intensive blood pressure control improves patients' survival and quality of life. In fact, with the recent publications by the Sprint Research Group[8] and the Sprint Mind Investigators,[9] the control of blood pressure to lower levels became a target in all guidelines.

Despite these problems in this study, I congratulate the authors for the decision to walk this important and hard path of study. A good quality of life guarantees treatment compliance of chronic diseases and must be investigated in hypertension.

References

1. Donabedian A. The quality of medical care. The Milbank Quartely. 2005;83($):691-729.

2. Donabedian A. Criteria and Standards for quality assessments and monitoring. QRB. Qual Rev Bull. 1986;12(3) 99-108.

3. Silva GO, Andrade-Lima A, Germano-Soares AH,Lima Jr D, Rodrigues SLC, Ritti-Dias R, et al. Factors Associated with Quality of Life in Patients with Systemic Arterial Hypertension.Int J Cardiovasc Sci. 2020; 33(2):133-142.

4. Kimmel PL. Just whose quality of life isit anyway? Controversies and consistencies in measurements of quality of life. Kidney Int. 2000; 57(Suppl 74):S113-S120.

5. Ciconelli RM, Ferraz MB, Santos W, Meinão I, Quaresma MR. Tradução para a língua portuguesa e validação do questionário genérico de avaliação de qualidade de vida SF-36 (Brasil SF-36). Rev Bras Reumatol. 1999; 39(3): 143-50.

6. Guyatt GH. Measuring health-related quality of life: General issues. Can Respir J. 1997; 4(3):123-30.

7. Croog SH, Levine S, Testa MA, Brown B, Bulpitt CJ, Jenkins CD, et al. The effects of antihypertensive therapy on the quality of life. N Engl J Med. 1986; 314(26): 1656-64.

8. The Sprint Research Group. Wright JT Jr, Williamson JD, Whelton PK, Snyder JK, Sink KM, Rocco DM, et al. A randomized trial of intensive versus standard blood-pressure control. N Engl J Med. 2015; 373(22): 2103-16.

9. The Sprint Mind Investigators. Williamson JD, Pajews Ki NM, Auchus AP, Bryan RN, Chelune G, et al. Effect of intensive vs standard blood pressure control on probabel dementia. JAMA. 2019; 321(6): 553-61.

ORIGINAL ARTICLE

Factors Associated with Quality of Life in Patients with Systemic Arterial Hypertension

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Abstract

Background: Hypertensive patients present, in addition to worse cardiovascular health, lower health-related quality of life compared to normotensive subjects. Factors such as functional capacity, functional status, pain, participation in social activities, mental and emotional health, fatigue and energy level, along with perception of general health, seem to be relevant for evaluation in this population. However, evidence is unclear in hypertensive patients.

Objective: To analyze the factors associated with quality of life in hypertensive patients.

Methods: Forty-five patients were recruited. The dependent variables of the present study are the quality of life domains. Demographic data and clinical conditions were considered independent variables. The Medical Outcomes Short-Form Health Survey (SF-36) questionnaire was used to measure quality of life. Handgrip strength, blood pressure and anthropometric indicators were evaluated. Crude and adjusted linear regression analysis was used.

Results: It was verified that education level, body mass index and muscle strength were associated with the functional capacity domain (p < 0,05), whereas systolic blood pressure was associated with the physical domain (p < 0,05). Women presented lower quality of life on the pain domain compared to men and educational level was associated with the social domain (p < 0,05).

Conclusion: Hypertensive patients with lower levels of body mass index, higher levels of education and muscle strength presented a better quality of life on the physical domain, while the social aspects presented a positive relationship with education level. Women presented a worse quality of life on the pain domain compared to men. (Int J Cardiovasc Sci. 2020; 33(2):133-142)

Keywords: Cardiovascular Diseases/physiopathology; Hypertension; Vital capacity; Exercise; Quality of Life; Risk Factors.

Introduction

It is estimated that cardiovascular diseases are responsible for approximately 30% of worldwide deaths.[1] In Brazil, the mortality rate reached at least 20% of individuals older than 30, which corresponded to 962,931 deaths, in 2009 alone, according to the Ministry of Health.[2] Thereby, the costs associated with cardiovascular diseases were around 30.8 billion, burdening the Health System. One of the main risk factors for cardiovascular and cerebrovascular diseases is systemic arterial hypertension,[3] which affects around 25% of the general population and 65% of the elderly population.[4]

Besides the cardiovascular problems, a recent meta-analysis[5] demonstrated that hypertensive patients present worse quality-of-life indicators compared to

normotensives, mainly in the parameters related to the physical domain. However, the quality-of-life concept is extended, once it refers to personal satisfaction, defined in relation to the daily life, which is influenced by individual evaluation of physical, psychological, social and spiritual well-being.[6,7] The World Health Organization defines quality of life as "an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns."

In this context, different parameters can directly affect the quality of life of these patients. Among these parameters, the physical aspect, for example, evaluated through the physical limitations in daily activities, dissatisfaction with functional capacity and mobility, can negatively reflect the quality of life.[8] Additionally, the frequency with which an hypertensive patient feels body pain or discomforts can interfere with the execution of daily living activities.[9] Thus, these limitations, caused by health, physical or emotional problems related to hypertension, must be better understood for a greater understanding of the quality of life of these individuals.[10]

Beyond the physical aspects, deterioration of an individual's mental health, as a reflection of hypertension, can lead to reduced frequency of participation in relevant social activities for the individual's personal life, for example.[11] In fact, the emotional aspects can be related to damages to one of the four main dimensions of mental health (anxiety, depression, loss of behavioral or emotional control and physiological well-being).[12] Another aspect that deserves attention is related to vitality as energy level and fatigue, which can support the evaluation of the subjective well-being of hypertensive individuals.[13] Lastly, evaluating the individual's general health perception can be interesting, considering the impact of the presence of diseases and its complications in the individual's health.[10]

Therefore, questionnaires that aim to analyze quality of life are necessary, such as the 36-item Short Form Health Survey (SF-36),[14] which consists of 36 items, one of which measures the health transition, and the other 35 are grouped into scales and divided into eight domains: functional capacity, physical aspects, pain, general health, vitality, social aspects, emotional aspects and mental health. These eight domains can also be aggregated in summary: measurements of physical and emotional factors.[15]

In this context, some studies have investigated the factors associated with quality of life in hypertensive individuals, given its relevance to the health of those patients. Indeed, the influence of the factors associated with quality of life can predict long-term functional independence, adherence to anti-hypertensive therapy and incidence of survival in hypertensives.[16-18] Previous studies have suggested that clinical aspects directly affect the quality of life in hypertensive individuals,[19] such as comorbidities (heart failure, acute myocardial infarction and angina pectoris),[20] medication,[21,22] disease knowledge level and blood pressure values.[22]

On the other hand, it is unknown whether physical fitness and demographic characteristics are related to quality of life in hypertensive individuals. Studies with other population subgroups have demonstrated that increases in muscle strength and body weight reduction, for example, have been constantly related to an improvement in daily activities in healthy elderly individuals,[23,24] leading to greater functional independence and physical fitness, which lead to better quality of life. Indeed, it is known that older individuals, consequently with worse physical fitness, present reduced quality-of-life indicators — due to decreased mass — of strength and muscle resistance, leading to increased fatigue during the performance of daily activities.[25]

Therefore, identifying factors related to quality of life, such as physical fitness, may help health professionals to propose interventions. Thus, the aim of the present study was to analyze the factors associated with quality of life in hypertensive individuals. Our hypothesis is that physical fitness is the main component associated with quality of life in hypertensive individuals.

Methods

This is a correlational cross-sectional study that analyzed the initial data of an interventional study that analyzed the effects of isometric handgrip training in the blood pressure of hypertensive individuals.[26]

All individuals were recruited by flyers in *Universidade de Pernambuco* in the Santo Amaro Campus, public hospitals, or through media advertisements (online journals and social media) in the city of Recife and metropolitan region. The project was approved by the Research Ethics committee of *Universidade de Pernambuco* and all patients signed an informed consent form.

Subjects

The inclusion criteria of the study were: a) use of anti-hypertensive medication; b) age above 18 years;

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c) absence of any other chronic disease; d) not having performed physical exercise in the last six months. Subjects that did not adequately answer the quality-of-life questionnaire were excluded from the study.

Data collection

The data collection occurred between August 2015 and August 2016. The dependent variables of the study are the quality-of-life domains. Demographic data and clinical conditions were considered as independent variables.

We evaluated the patients' sex, age and educational level, as well as health history (time of hypertension and medications). Before all cardiovascular evaluations, the patients were instructed to a) have a light meal before arriving at the laboratory; b) avoid physical activities of moderate to vigorous intensity for at least 24h before the laboratory visit; and c) avoid smoking, caffeine and alcohol consumption for at least 12h. In the laboratory, the subjects initially remained in the supine position for a period of rest of 10 min to perform the measurements with a controlled temperature between 22 and 24ºC.

Quality of life

Quality of life was measured through the SF-36 questionnaire[27] after an individual interview with the hypertensive subjects by a trained researcher. For each of the SF-36 domains (functional capacity, physical aspects, pain, general health, vitality, social aspects, emotional aspects and mental health), the respective scores were calculated, which varied from 0 to 100, where 0 corresponds to the worst health status and 100 to the best health status.

Anthropometric measurements

Body mass, height and waist circumference were obtained. Body mass was measured in a digital scale, Filizola brand, with 0,1 kg precision and height was determined in a stadiometer coupled to the scale with 0,1 cm precision. Waist circumference was obtained using the umbilical scar as reference.[28] The body mass index was calculated by dividing body mass by square height in meters.

Muscle strength

Muscle strength was measured through a digital hand dynamometer (CAMRY, United States) adjustable and calibrated with a 0 to 100 kg/f scale. The test was performed three times, for each arm, with a 1-minute interval between each try and the highest value found was considered the result. This procedure showed an intraclass correlation coefficient (test and retest with a 1-week interval) from 0,986 to 0,989.[29]

Clinical blood pressure

Clinical blood pressure was obtained in an Omron HEM 742 device. All the procedures followed the recommendations of the 7th Brazilian Guidelines of Hypertension[30] and showed good reproducibility indicators.[31] The intraclass correlation coefficient for systolic blood pressure was 0,85 and, for diastolic blood pressure, 0,92.[31]

Statistical analysis

To analyze the factors associated with quality of life, we performed the crude and adjusted linear regression analysis. Initially, the crude analysis was performed to establish the variables included in the multiple models. Therefore, only the variables that showed $p \leq 0.30$ were included. The significance level adopted and the criteria for the variable to remain in the model was $p < 0.05$. Multicollinearity analysis was performed to identify the existence of a strong correlation between two (or more) independent variables, which could affect the relationship with the dependent variable. Thus, Variance Inflation Factors (VIF) lower than five were assumed with tolerance lower than 0.20. All analyses were performed in the Statistical Package for the Social Sciences (SPSS), version 20, and the data are presented as mean±standard deviation and relative frequency.

Results

Table 1 shows the general characteristics of the hypertensive patients included in the study.

Tables 2 and 3 show the relationship between the demographic, clinical and physical fitness variables with the quality of life of hypertensives in the physical and emotional domains.

Figure 1 shows the variables that presented a statistically significant relationship. It was found that individuals with lower educational level, higher body mass index and lower muscle strength showed the worse quality of life in the functional capacity domain ($p < 0.05$ for all). Higher systolic blood pressure was related to higher values in the physical aspects domain ($p < 0.05$). Women presented

Table 1 - General characteristics of the hypertensive individuals from this study (n = 80)

Variables	Values
Demographic	
Sex (% women)	70,5
Age (years)	57,7 ± 9,7
Educational level (years of study)	9,5 ± 3,1
Clinical parameters	
Hypertension time (months)	12,4 ± 9,3
Medications (units)	1,8 ± 0,7
SBP (mmHg)	132,0 ± 16,3
DBP (mmHg)	74,4 ± 9,6
Health-related physical fitness	
Muscle strength (kgf)	31,7 ± 10,5
Body mass index (kg/m²)	30,7 ± 5,3
Quality of life	
Functional capacity (score)	75,9 ± 21,6
Physical aspects (score)	70,1 ± 38,2
Pain (score)	29,4 ± 21,3
General health (score)	56,3 ± 10,6
Vitality (score)	54,4 ± 12,3
Social aspects (score)	48,2 ± 11,2
Emotional aspects (score)	77,3 ± 38,5
Mental health (score)	57,1 ± 10,3

SBP: systolic blood pressure; DBP: diastolic blood pressure. Values presented in frequency or mean and standard deviation.

worse quality of life in the pain domain compared to men and educational level was directly related to social aspects (p < 0.05). The other factors did not present statistically significant relationships with the quality-of-life domains (p > 0.05 for all).

Discussion

The main findings of the present study were a) educational level and muscle strength were positively related to functional capacity, while body mass index showed a negative correlation; b) patients with higher educational level presented higher scores in the social aspects domain; c) systolic blood pressure levels showed a positive relationship with the physical aspects domain; and, d) female patients presented worse scores in the pain domain.

The quality of life evaluation is an important outcome in different populations, mainly because of its prognostic value. For example, an improvement in this indicator is associated with greater survival rate in hypertensive patients, while a worse quality of life predicts lower survival rates.[16] In the conceptual model proposed by Wilson and Cleary,[32] several factors influence an individual's quality of life, including physical and social functioning, mental health and general health perception. In this context, the SF-36, which is an instrument that evaluates quality of life, includes eight domains (functional capacity, physical aspects, pain, general health, vitality, social aspects, emotional aspects and mental health) that detail these factors.[14] These domains measure the capacity of performing tasks and daily activities in addition to subjective measures of well-being, including how the individuals feel physically and emotionally regarding their health.[33]

Considering functional capacity and social aspects, the present study observed that educational level is associated with these indicators in hypertensive individuals. This data is in accordance with a previous study[34] that evaluated 1,124 hypertensive individuals and identified that patients with lower educational level reported worse scores in the functional capacity domain. A possible explanation for those results is that individuals with higher educational levels have a better perception about healthy habits such as exercising and weight reduction along with the importance of social interaction,[35-37] which are directly related to physical function and social aspects of the quality of life of hypertensive individuals. Additionally, patients with higher educational levels may have better access to good quality medical care, along with better knowledge of health and habits that can influence longevity, increasing life expectancy,[38,39] and positively changing the quality of life of these patients.

Muscle strength levels were also associated with higher scores in the functional capacity domain in hypertensive individuals, corroborating with other studies.[40,41] Indeed, a previous study[40] with healthy elderly individuals observed that men and women with lower grip strength were more likely to report deteriorations in general health. Both findings are relevant since they suggest that healthy or hypertensive individuals with lower grip strength have a lower quality of life. In this context, these

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Table 2 - Factors associated with quality of life in the physical domain in hypertensive individuals

Variables	Functional Capacity				Physical Aspects				Pain				General Health			
	Crude		Adjusted[1]		Crude		Adjusted[2]		Crude		Adjusted[3]		Crude		Adjusted	
	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p
Demographic																
Sex (% women)	0.229	0.047	ns	ns	0.208	0.072	ns	ns	-0.233	0.043	-0.243	0.043	-0.169	0.149	ns	ns
Age (years)	-0.040	0.732	-	-	0.008	0.944			0.043	0.717			-0.126	0.291	ns	ns
Educational level (years)	0.183	0.135	0.231	0.044	0.011	0.932			-0.107	0.387			0.101	0.417		
Clinical parameters and physical fitness																
Hypertension time (years)	-0.071	0.549	-	-	0.056	0.638			-0.164	0.165	ns	ns	0.003	0.980		
Medications (units)	-0.016	0.890	-	-	-0.191	0.105	ns	ns	-0.019	0.875			-0.080	0.509		
SBP (mmHg)	-0.074	0.539	-	-	0.282	0.017	0.282	0.017	-0.146	0.226	ns	ns	0.025	0.838		
DBP (mmHg)	0.093	0.440	-	-	0.137	0.254	ns	ns	-0.157	0.191	ns	ns	-0.003	0.981		
Muscle strength (kgf)	0.236	0.042	0.290	0.011	0.184	0.114	ns	ns	-0.189	0.104	ns	ns	-0.202	0.085	ns	ns
Body mass index (kg/m²)	-0.302	0.007	-0.390	0.001	-0.134	0.243	ns	ns	0.175	0.126	ns	ns	0.193	0.095	ns	ns

B: pattern regression coefficient; SBP: systolic blood pressure; DBP: diastolic blood pressure; Ns: non significant; $1r = 0.486$; $r^2 = 0.236$, $F = 6.583$, $p = 0.001$. $2r = 0.486$; $r^2 = 0.236$, $p = 0.001$; $3r = 0.243$; $r^2 = 0.059$, $F = 4.254$, $p = 0.001$.

individuals may present benefits from interventions to increase muscle mass and strength, and consequently, quality of life. Additionally, it is noteworthy that Trosclair et al.,[42] demonstrated the relationship between grip strength and global strength, which reinforces the grip strength test measurement, mainly due to its ease of application and reproducibility.[29] Also, the relationship between muscle strength and the functional capacity domain may be explained by greater efficiency in the performance of moderate and vigorous daily activities. Thereby, climbing stairs, carrying groceries, walking long distances and performing domestic activities more easily and vigorously can positively influence the quality of life of those patients.[43]

In the present study, hypertensive individuals with lower body mass index showed lower scores in the functional capacity domain; in other words, overweight and obesity impair daily activities, reducing the quality

of life of hypertensive individuals. Similarly, Awotidebe et al.,[44] observed that all quality-of-life domains were worse in hypertensive individuals with higher body mass. Psychological and psychosocial problems related to higher body mass index are probably factors associated with a decrease in the quality of life of those individuals.[45,46] Indeed, obesity has been widely related to anxiety and depression, which increases dissatisfaction levels, causes loss of interest and lack of enjoyment, negatively affecting quality of life. Besides, higher body mass can also lead to negative consequences related to general mobility, mortality and health costs, which can also directly affect the perception of quality of life.[47]

Contrary to expectations, systolic blood pressure showed a positive association with the physical aspects of quality of life, disagreeing with other results found in the literature.[22,48,49] Indeed, a previous study[50] observed that patients with higher blood pressure have a lower

Table 3 - Factors associated with quality of life in the emotional domain in hypertensive individuals

Variables	Vitality				Social aspects				Emotional aspects				Mental Health			
	Crude		Adjusted		Crude		Adjusted[1]		Crude		Adjusted		Crude		Adjusted	
	b	p	b	p	b	p	b	P	b	p	b	p	b	p	b	P
Demographic																
Sex (% women)	0.121	0.300	ns	ns	0.093	0.426			0.034	0.773			-0.073	0.535		
Age (years)	0.017	0.885			-0.013	0.916			0.120	0.308			0.174	0.141	ns	ns
Educational level (years)	0.150	0.227	ns	ns	0.344	0.004	0.332	0.006	0.036	0.770			-0.027	0.829		
Clinical parameter and physical fitness																
Hypertension time (years)	-0.079	0.507			0.153	0.196	ns	ns	-0.076	0.253	ns	ns	0.023	0.848		
Medications (units)	-0.107	0.371			-0.121	0.306			-0.179	0.130	ns	ns	-0.115	0.335		
SBP (mmHg)	0.030	0.807			-0.030	0.805			0.136	0.259	ns	ns	0.061	0.617		
DBP (mmHg)	-0.041	0.735			-0.042	0.730			-0.082	0.497			-0.035	0.771		
Muscle strength (kgf)	0.073	0.537			0.053	0.649	ns	ns	0.017	0.886			-0.162	0.167	ns	ns
Body mass index (kg/m²)	0.067	0.565			0.131	0.253			-0.067	0.559			-0.208	0.069	ns	ns

B: pattern regression coefficient. SBP: systolic blood pressure; DBP: diastolic blood pressure, ns: non significant. $^1 r = 0.344$; $r^2 = 0.118$, $F = 8.832$, $p = 0.004$.

quality of life, which is a reflection of greater impairments in the physical aspects of these individuals, due to the disease.[51,52] A possible explanation for the association found in the present study is the fact that patients with higher blood pressure may be aware of their status and look for alternatives besides medication or exercise in order to improve their blood pressure levels, such as nutritional interventions, smoking cessation, improvements in sleep quality and stress control. This behavior could have affected the relationships due to the fact that they are strategies recommended in literature,[53] which could improve their physical aspect without improving blood pressure levels initially. Interestingly, when hypertensive individuals were submitted to exercise training programs, aspects related to the quality of life improved in 6 to 10 weeks after the beginning of the program,[54] while modifications in biological variables,

such as blood pressure, occurred later (over 12 weeks from the intervention).[55]

Women showed worse quality of life in the pain domain compared to men. These results are similar to a previous epidemiological study with 4,506 adults that observed that muscle pain, headache and pain perception in the SF-36 were worse in women than in men.[56] To explain this relationship, the literature indicates that the pain perception is influenced by complex interactions between biological variables (sexual hormones, genetics, pain pathways and variations in the central nervous system) and psychosocial variables (depression, anxiety, depreciation on the job market, gender role expectations, social learning factors and importance given to pain), where women are more susceptible to the symptoms, especially in advanced age due to menopause and hormonal dysfunctions.[56,57]

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Factors associated with quality of life

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Original Article

Figure 1 - Relationship between statistically significant variables.
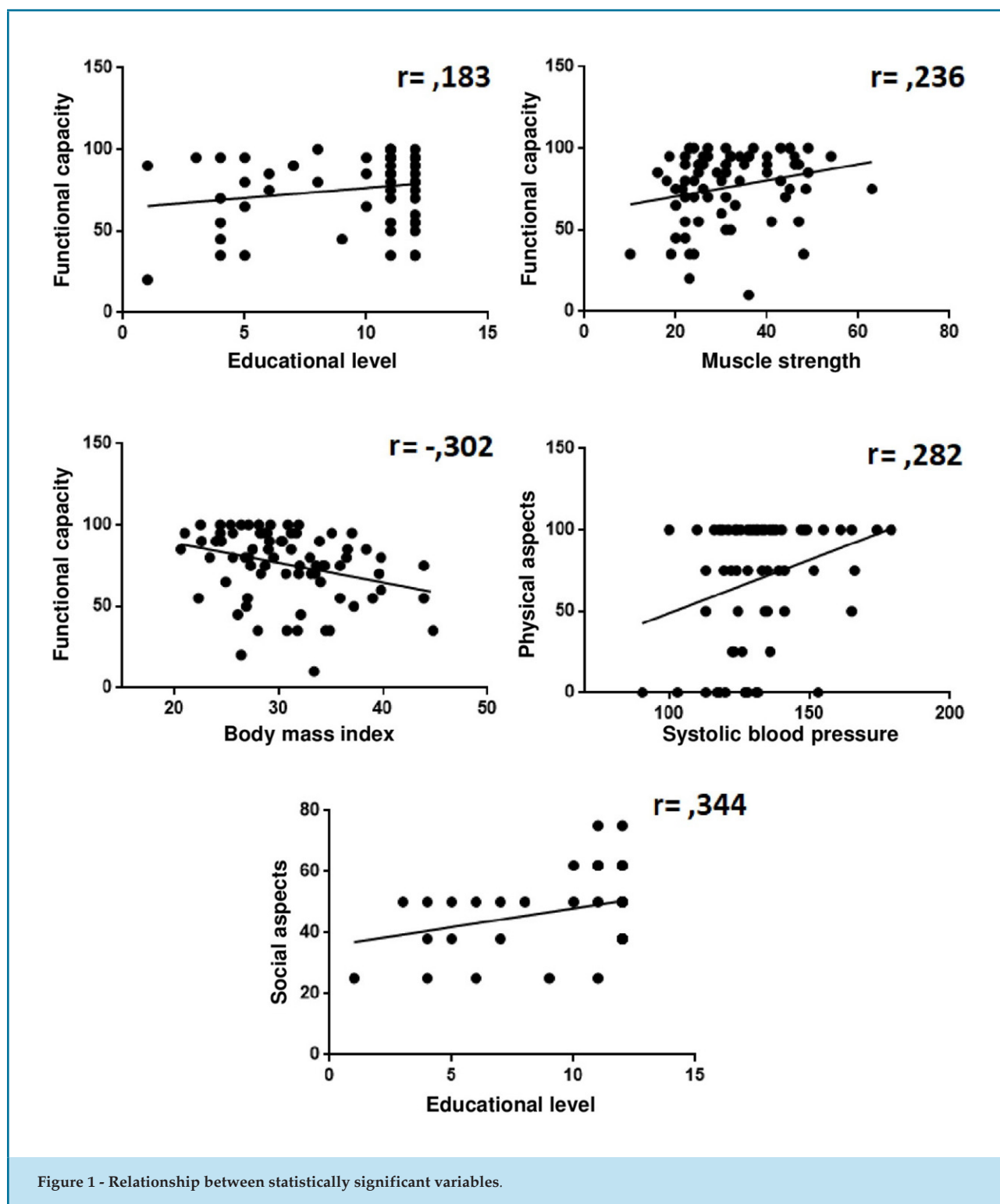
This study presents some limitations that must be considered. The sample of the present study was composed of medicated hypertensive individuals that enrolled in an exercise intervention aiming to reduce their cardiovascular risk, then the specific sample characteristics limit the generalizability of the findings to other hypertensive individuals, especially those with other associated pathologies (cardiac or cerebrovascular diseases, diabetes) or even to resistant hypertensive individuals, since only one patient presented this characteristic. The sample

size did not allow us to perform stratified analysis by medication class. Lastly, the fact that this study presents an associative nature makes it impossible to inflict causality to the observed associations.

Perspectives

The perception of quality of life has been established as an efficient form of predicting cardiovascular events and survival rate in hypertensive patients.[16] The results of the present study showed that some modifiable factors, such as muscle strength, body mass index, educational level and blood pressure influence the quality of life of these patients, and that has not been sufficiently investigated in the literature. Thus, in practical terms, interventions such as physical exercise and nutritional monitoring that promote previous control of these variables may positively affect the quality of life of hypertensive individuals. Additionally, it is suggested to carry out further studies to evaluate a broader sample of hypertensive patients, including individuals with other morbidities such as diabetes and dyslipidemia, and longitudinal studies evaluating quality of life, as well as its influence, for longer periods.

Conclusion

In conclusion, it was verified that hypertensive individuals with lower body mass index, higher educational level and muscle strength presented a better quality of life in the physical domain, while the social aspects have a positive relationship with educational level. Women report worse quality of life in the pain domain compared to men.

Author contributions

Conception and design of the research: Andrade-Lima A, Germano-Soares AH, Lima-Junior D, Rodrigues SLC, Ritti-Dias RM, Farah BQ. Acquisition of data: Silva GO, Rodrigues SLC, Farah BQ. Analysis and interpretation of the data: Silva GO, Andrade-Lima A, Germano-Soares AH, Lima-Junior D, Rodrigues SLC, Ritti-Dias RM, Farah BQ. Statistical analysis: Silva GO, Andrade-Lima A, Germano-Soares AH, Ritti-Dias RM, Farah BQ. Obtaining financing: Rodrigues SLC, Ritti-Dias RM, Farah BQ. Writing of the manuscript: Silva GO, Andrade-Lima A, Germano-Soares AH, Lima-Junior D, Rodrigues SLC, Ritti-Dias RM, Farah BQ. Critical revision of the manuscript for intellectual content: Silva GO, Andrade-Lima A, Germano-Soares AH, Lima-Junior D, Rodrigues SLC, Ritti-Dias RM, Farah BQ.

Potential Conflict of Interest

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

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 de Pernambuco* (CEP-UPE) under the protocol number 30806014.0.0000.5207. 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. Gaui EN, Oliveira GMMd, Klein CH. Mortality by Heart Failure and Ischemic Heart Disease in Brazil from 1996 to 2011. Arq Bras Cardiol. 2014;102(6):557-65.

2. Mansur AP, Favarato D. Mortality due to cardiovascular diseases in Brazil and in the metropolitan region of Sao Paulo: a 2011 update. Arq Bras Cardiol. 2012;99(2):755-61.

3. Lewington S, Clarke R, Qizilbash N, Peto R, Collins R. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. Lancet. 2002;360(9349):1903-13.

4. Picon RV, Fuchs FD, Moreira LB, Fuchs SC. Prevalence of hypertension among elderly persons in urban Brazil: a systematic review with meta-analysis. Am J Hypertens. 2013;26(4):541-8.

5. Ye R, Liu K, Zhang Z, Gong S, Chen X. Health-related quality of life of hypertension in China: a systematic review and meta-analysis. J Cardiovasc Med (Hagerstown). 2018;19(8):430-8.

6. Kimmel PL. Just whose quality of life is it anyway? Controversies and consistencies in measurements of quality of life. Kidney International. 2000;57:113-20.

7. Development of the World Health Organization WHOQOL-BREF quality of life assessment. The WHOQOL Group. Psychol Med. 1998;28(3):551-8.

8. Hays RD, Liu H, Spritzer K, Cella D. Item Response Theory Analyses of Physical Functioning Items in the Medical Outcomes Study. Med Care. 2007;45(5):S32-S8.

9. McHorney CA, Ware JE, Jr., Rogers W, Raczek AE, Lu JF. The validity and relative precision of MOS short- and long-form health status scales and Dartmouth COOP charts. Results from the Medical Outcomes Study. Med Care. 1992;30(5 Suppl):Ms253-65.

10. Stewart AL, Ware JE (editors). Measuring functioning and well-being: The medical outcomes study approach. London: Duke University Press: 1992.

11. Stewart AL, Hays RD, Ware JE Jr. The MOS short-form general health survey. Reliability and validity in a patient population. Med Care. 1988;26(7):724-35.

12. Veit CT, Ware JE Jr. The structure of psychological distress and well-being in general populations. J Consult Clin Psychol. 1983;51(5):730-42.

13. Croog SH, Levine S, Testa MA, Brown B, Bulpitt CJ, Jenkins CD, et al. The effects of antihypertensive therapy on the quality of life. N Engl J Med. 1986;314(26):1657-64.

14. Cote I, Grégoire J-P, Moisan J. Health-related quality-of-life measurement in hypertension. Pharmacoeconomics. 2000;18(5):435-50.

15. Ware J, Jr., Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. Med Care. 1996;34(3):220-33.

16. Liang JW, Cheung YK, Willey JZ, Moon YP, Sacco RL, Elkind MSV, et al. Quality of life independently predicts long-term mortality but not vascular events: the Northern Manhattan Study. Qual Life Res. 2017;26(8):2219-28.

17. Nunes MI. The relationship between quality of life and adherence to treatment. Curr Hypertens Rep. 2001;3(6):462-5.

18. Souza ACCd, Borges JWP, Moreira TMM. Quality of life and treatment adherence in hypertensive patients: systematic review with meta-analysis. Rev Saúde Pública. 2016 Dec 22;50:71.

19. Soutello ALS, Rodrigues RCM, Jannuzzi FF, São-João TM, Martinix GG, Nadruz Jr W, et al. Quality of life on arterial hypertension: Validity of Known Groups of MINICHAL. Arq Bras Cardiol. 2015;10(4):299-307.

20. Aydemir O, Ozdemir C, Koroglu E. The impact of co-morbid conditions on the SF-36: a primary-care-based study among hypertensives. Arch Med Res. 2005;36(2):136-41.

21. Trevisol DJ, Moreira LB, Fuchs FD, Fuchs SC. Health-related quality of life is worse in individuals with hypertension under drug treatment: results of population-based study. J Hum Hypertens. 2012;26(6):374-80.

22. Mena-Martin FJ, Martin-Escudero JC, Simal-Blanco F, Carretero-Ares JL, Arzua-Mouronte D, Herreros-Fernandez V. Health-related quality of life of subjects with known and unknown hypertension: results from the population-based Hortega study. J Hypertens. 2003;21(7):1283-9.

23. Gopinath B, Kifley A, Liew G, Mitchell P. Handgrip strength and its association with functional independence, depressive symptoms and quality of life in older adults. Maturitas. 2017;106:92-4.

24. Assimakopoulos K, Karaivazoglou K, Tsermpini EE, Diamantopoulou G, Triantos C. Quality of life in patients with nonalcoholic fatty liver disease: A systematic review. J Psychosom Res. 2018 Sep;112:73-80.

25. Gobbens RJ, Luijkx KG, van Assen MA. Explaining quality of life of older people in the Netherlands using a multidimensional assessment of frailty. Qual Life Res. 2013;22(8):2051-61.

26. Farah BQ, Rodrigues SLC, Silva GO, Pedrosa RP, Correia MA, Barros MVG, et al. Supervised, but Not Home-Based, Isometric Training Improves Brachial and Central Blood Pressure in Medicated Hypertensive Patients: A Randomized Controlled Trial. Front Physiol. 2018 Jul 23;9: 961-70.

27. Ciconelli RM, Ferraz MB, Santos W, Meinão I, Quaresma MR. Brazilian-Portuguese version of the SF-36. A reliable and valid quality of life outcome measure. Rev bras reumatol. 1999;39(3):143-50.

28. Lohman T, Roche A, Martorell R. Anthropometric standardization reference manual: Champaign: Human Kinetics Books; 1991.

29. Farah BQ, Correia MdA, Rodrigues SLC, Cavalcante BR, Ritti-Dias RM. Reliability of handgrip maximal voluntary contraction in hypertensive adults. Rev Bras Ativ Fís Saúde. 2014;19(5):590-6.

30. Malachias M, Souza W, Plavnik FL, Rodrigues C, Brandao AA, Neves M, et al. 7th Brazilian Guideline of Arterial Hypertension. Arq Bras Cardiol. 2016;107(3 Suppl 3):79-83.

31. Gerage AM, Benedetti TR, Farah BQ, Santana F da S, Ohara D, Andersen LB, et al. Sedentary behavior and light physical activity are associated with brachial and central blood pressure in Hypertensive patients. PLoS One. 2015;10(12):e0146078.

32. Wilson IB, Cleary PD. Linking clinical variables with health-related quality of life. A conceptual model of patient outcomes. JAMA. 1995;273(1):59-65.

33. Stewart AL, Hays RD, Wells KB, Rogers WH, Spritzer KL, Greenfield S. Long-term functioning and well-being outcomes associated with physical activity and exercise in patients with chronic conditions in the Medical Outcomes Study. J Clin Epidemiol. 1994;47(7):719-30.

34. Xu X, Rao Y, Shi Z, Liu L, Chen C, Zhao Y. Hypertension Impact on Health-Related Quality of Life: A Cross-Sectional Survey among Middle-Aged Adults in Chongqing, China. Int J Hypertens. 2016;2016:7404957.

35. Brennan SL, Turrell G. Neighborhood disadvantage, individual-level socioeconomic position, and self-reported chronic arthritis: a cross-sectional multilevel study. Arthritis Care Res (Hoboken). 2012;64(5):721-8.

36. Appel LJ, Champagne CM, Harsha DW, Cooper LS, Obarzanek E, Elmer PJ, et al. Effects of comprehensive lifestyle modification on blood pressure control: main results of the PREMIER clinical trial. JAMA. 2003;289(16):2083-93.

37. Ho AK, Thorpe CT, Pandhi N, Palta M, Smith MA, Johnson HM. Association of anxiety and depression with hypertension control: a US multidisciplinary group practice observational study. J Hypertens. 2015;33(11):2215-22.

38. Jasilionis D, Shkolnikov VM. Longevity and Education: A Demographic Perspective. Gerontology. 2016;62(3):253-62.

39. Bardage C, Isacson DG. Hypertension and health-related quality of life. an epidemiological study in Sweden. J Clin Epidemiol. 2001;54(2):172-81.

40. Sayer AA, Syddall HE, Martin HJ, Dennison EM, Roberts HC, Cooper C. Is grip strength associated with health-related quality of life? Findings from the Hertfordshire Cohort Study. Age Ageing. 2006;35(4):409-15.

41. Jakobsen LH, Rask IK, Kondrup J. Validation of handgrip strength and endurance as a measure of physical function and quality of life in healthy subjects and patients. Nutrition. 2010;26(5):542-50.

42. Trosclair D, Bellar D, Judge LW, Smith J, Mazerat N, Brignac A. Hand-Grip Strength as a Predictor of Muscular Strength and Endurance. The Journal of Strength & Conditioning Research. 2011;25(Suppl 1):S99.

43. Garcia PA, Dias JMD, Dias RC, Santos P, Zampa CC. Estudo da relação entre função muscular, mobilidade funcional e nível de atividade física em idosos comunitários. Rev Bras Fisioter. 2011;15(1):15-22.

44. Awotidebe TO, Adeyeye VO, Ogunyemi SA, Bisiriyu LA, Adedoyin RA, Balogun MO, et al. Joint predictability of physical activity and body weight status on health-related quality of life of patients with hypertension. J Exerc Rehabil. 2017;13(5):588-98.

45. Ogunlana MO, Adedokun B, Dairo MD, Odunaiya NA. Profile and predictor of health-related quality of life among hypertensive patients in south-western Nigeria. BMC Cardiovasc Disord. 2009 Jun 17;9:25.

46. Pan HJ, Cole BM, Geliebter A. The benefits of body weight loss on health-related quality of life. J Chin Med Assoc. 2011;74(4):169-75.

47. Seidell JC. Obesity, insulin resistance and diabetes--a worldwide epidemic. Br J Nutr. 2000;83(Suppl 1):S5-S8.

48. Erickson SR, Williams BC, Gruppen LD. Perceived symptoms and health-related quality of life reported by uncomplicated hypertensive patients compared to normal controls. J Hum Hypertens. 2001;15(8):539-48.

49. Erickson SR, Williams BC, Gruppen LD. Relationship between symptoms and health-related quality of life in patients treated forhypertension. Pharmacotherapy. 2004;24(3):344-50.

50. Erickson SR, Williams BC, Gruppen LD. Relationship between symptoms and health-related quality of life in patients treated for hypertension. Pharmacotherapy. 2004;24(3):344-50.

51. Dimenas ES, Wiklund IK, Dahlof CG, Lindvall KG, Olofsson BK, De Faire UH. Differences in the subjective well-being and symptoms of normotensives, borderline hypertensives and hypertensives. J Hypertens. 1989;7(11):885-90.

52. Cuffee Y, Ogedegbe C, Williams NJ, Ogedegbe G, Schoenthaler A. Psychosocial risk factors for hypertension: an update of the literature. Curr Hypertens Rep. 2014;16(10):483.

53. Malachias M, Póvoa R, Nogueira A, Souza D, Costa L, Magalhães M. 7th Brazilian Guideline of Arterial Hypertension: Chapter 3 - Clinical and Complementary Assessment. Arq Bras Cardiol. 2016;107(3 Suppl 3):14-7.

54. Tsai JC, Yang HY, Wang WH, Hsieh MH, Chen PT, Kao CC, et al. The beneficial effect of regular endurance exercise training on blood pressure and quality of life in patients with hypertension. Clin Exp Hypertens. 2004;26(3):255-65.

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

56. Bingefors K, Isacson D. Epidemiology, co-morbidity, and impact on health-related quality of life of self-reported headache and musculoskeletal pain--a gender perspective. Eur J Pain. 2004;8(5):435-50.

57. Palmeira CCdA, Ashmawi HA, Posso IdP. Sexo e percepção da dor e analgesia. Rev Bras Anestesiol. 2011;61(6):820-8.

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EDITORIAL

Arterial Stiffness: The New Frontier in Hypertension and Cardiovascular Disease

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Vascular age is a reflection of cardiovascular and non-cardiovascular factors that contribute to accelerated vascular aging (AVA) and stiffness of large elastic arteries, leading to increased cardiovascular morbidity and mortality.[1] Arterial stiffness has been regarded as an important biomarker in the assessment of subclinical atherosclerosis and cardiovascular risk.[1-4] The addition of pulse wave velocity (PWV) measurements to traditional risk factors has improved the prediction of the ten-year risk of cardiovascular diseases in 13% of individuals at intermediate risk.[5]

In addition, the altered behavior of central hemodynamic parameters, such as central systolic blood pressure (cSBP) and the (heart rate-corrected) augmentation index (AI), is influenced by arterial stiffness and plays a crucial role in the interface between the traditional cardiovascular continuum vascular aging continuum, which represents the current view of the pathophysiology of cardiovascular diseases.[6-8] (Figure 1)

Part of the residual cardiovascular risk in hypertensive patients, a concept that has gained much attention in recent years, has been related to the AVA process. An early detection of this condition allows a more effective cardiovascular protection. In the pathophysiology of the residual risk and development of cardiovascular disease, there is a bidirectional interaction of AVA and hypertension. The accumulation of risk factors contributes to changes in the vessel wall that lead to vascular aging and stiffening of elastic arteries, and consequent elevation of blood pressure levels. In the opposite direction, increased blood pressure promotes arterial stiffening, providing a feedback to the AVA process.[2-4]

The CAFE study[9] has presented the first evidence of the clinical impact of central hemodynamic parameters and arterial stiffness on the reduction of cardiovascular events. The therapeutic strategy of amlodipine plus perindopril promoted greater reductions in cSBP and cardiovascular events compared with atenolol plus thiazide (control intervention).

Vlachopoulos et al.,[10] produced one of the most striking evidences of the clinical application of arterial stiffness in predicting the risk for cardiovascular events. In a meta-analysis, the authors showed that an increase in aortic PWV by 1 m/s was associated with an increase of 15% in cardiovascular mortality and 15% in all-cause mortality.

Thus, the main guidelines on cardiovascular disease prevention have incorporated the assessment of arterial stiffness and central hemodynamics for risk stratification, aiming at early recognition of subclinical target organ lesions in patients' follow-up.[2-4]

In the article published in this issue, Barroso et al.,[11] present the results of the comparison of two methods of central pressure and arterial stiffness evaluation – applanation tonometry, considered the gold standard, and the oscillometric method that has been recently validated for clinical use. Twenty-seven patients were assessed using both methods. There was no difference in mean cSBP between the methods, but PWV and pulse pressure were underestimated by the oscillometric method. These results validate the oscillometric method for clinical application in the Brazilian population and suggest that patients with elevated PWV detected by the oscillometric method are at elevated cardiovascular risk, expressed by a more aggressive AVA process.

The incorporation of arterial stiffness measures to traditional risk scores and its recognition as a biomarker

Keywords

Vascular Stiffness; Hypertension; Blood Pressure; Indicators of Morbidity and Mortality; Target Organs, Risk Factors.

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Figure 1 – Interaction between the traditional cardiovascular continuum and the vascular aging continuum (Adapted from Mikael et al.;[6] and Dzau et al.[8])

LVH: left ventricular hypertrophy; CHD: coronary heart disease; AMI: acute myocardial infarction; AVA: accelerated vascular aging; isolated systolic hypertension
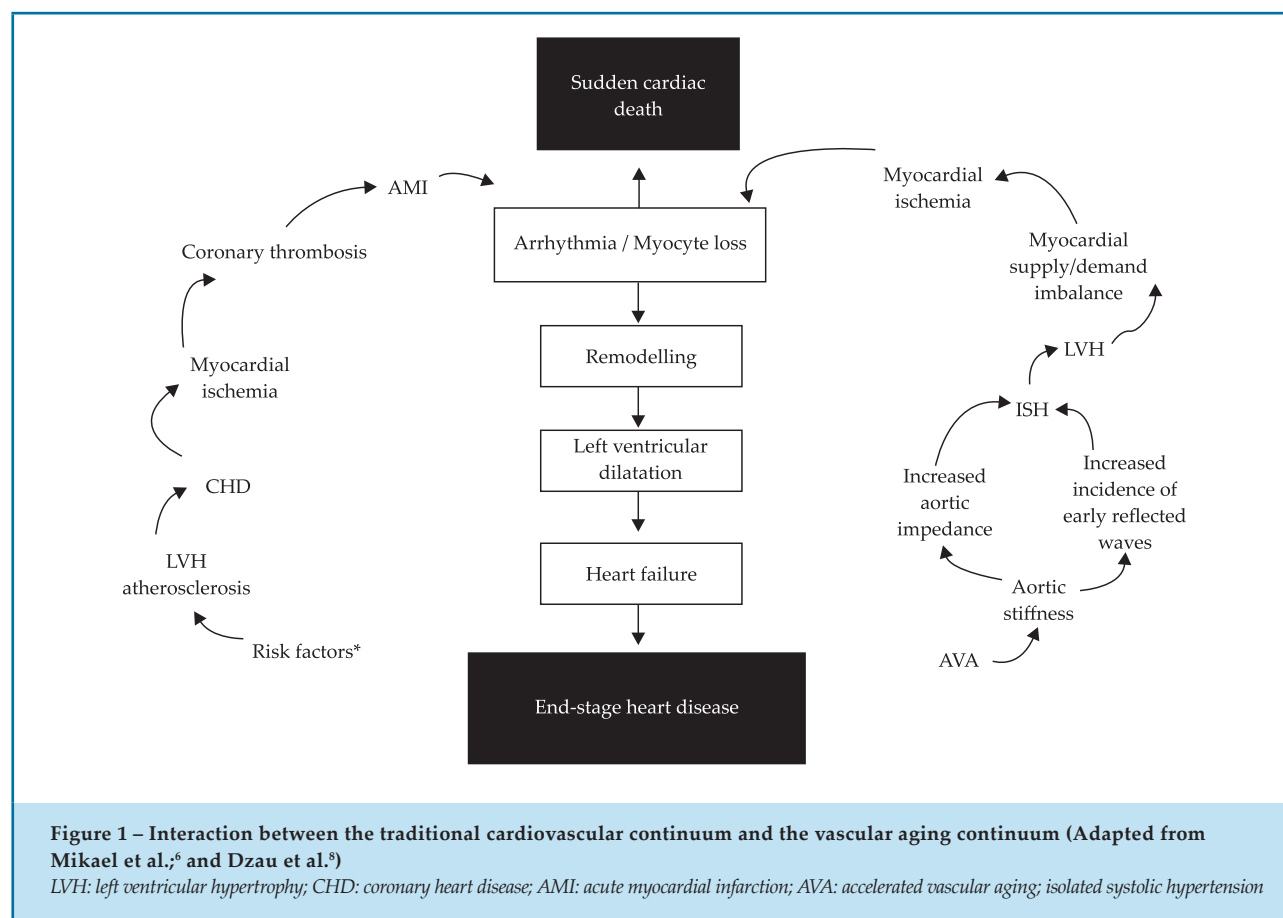
of subclinical target organ lesion, significantly improves the capacity to predict cardiovascular events. This concept adds to the knowledge about the AVA in guiding the diagnosis, risk stratification and treatment of hypertensive patients, allowing a personalization of therapeutic strategies and reduction of hypertension-related risk.

References

1. Nilsson PM, Boutouyrie P, Laurent S. Vascular aging: A tale of Eva and Adam in cardiovascular risk assessment and prevention. Hypertension. 2009;54(1):3-10.

2. Sociedade Brasileira de Cardiologia. VII Diretriz Brasileira de Hipertensão. 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: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Hypertension. 2018;71(6):1269-324.

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

5. Ben-Shlomo Y, Spears M, Boustred C, May M, Anderson SG, Benjamin EJ, et al. Aortic pulse wave velocity improves cardiovascular event prediction: an individual participant meta-analysis of prospective observational data from 17,635 subjects. J Am Coll Cardiol. 2014;63(7):636-46.

6. Mikael LR, Paiva AMG, Gomes MM, Sousa ALL, Jardim PC, Vitorino PVO, et al. Vascular Aging and Arterial Stiffness. Arq Bras Cardiol. 2017;109(3):253-8.

7. Roman MJ, Devereux RB, Kizer JR, Lee E, Galloway JM, Ali T, et al. Central pressure more strongly relates to vascular disease and outcome than does brachial pressure: the Strong Heart study. Hypertension. 2007; 50(1):197-203.

8. Dzau VJ, Antman EM, Black HR, Hayes DL, Manson JE, Plutzky J, et al. The cardiovascular disease continuum validated: clinical evidence of improved patient outcomes: part I: Pathophysiology and clinical trial evidence (risk factors through stable coronary artery disease). Circulation. 2006;114(25):2850-70.

9. Williams B, Lacy PS, Thom SM, Cruickshank K, Stanton A, Collier D, et al . for the CAFE Steering Committee and Writing Committee. Differential impact of blood pressure-lowering drugs on central aortic pressure and clinical outcomes: principal results of the Conduit Artery Function Evaluation (CAFE) study. Circulation. 2006;113(9):1213-25.

10. Vlachopoulos C, Aznaouridis K, Stefanadis C. Prediction of cardiovascular events and all-cause mortality with arterial stiffness: a systematic review and meta-analysis. J Am Coll Cardiol. 2010; 55(13):1318-27.

11. Barroso WKS, Gonçalves CF, Berigó JAC, Melo MA, Arantes AC, Lelis ES, et al. Tonometric and Oscillometric Methods for Measurement of Central Blood Pressure Parameters: a Comparison in Patients with Borderline Hypertension or Stage 1 Hypertension. International J Cardiovasc Sc. 2020; 33(2):145-150.

Tonometric and Oscillometric Methods for Measurement of Central Blood Pressure Parameters: a Comparison in Patients with Borderline Hypertension or Stage 1 Hypertension

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Abstract

Background: Changes in arterial compliance are among the first changes detectable in hypertensive syndrome. Methods with good reproducibility as compared with the gold standard for identifying such changes are desirable in clinical practice.

Objectives: To compare central pressure measurements and arterial stiffness obtained by two non-invasive methods (tonometry and oscillometry).

Methods: This was a descriptive, cross-sectional study with a convenience sample of patients with borderline hypertension or stage 1 hypertension. Peripheral and central blood pressure measurements were obtained by tonometry (SphygmoCor®), considered the gold standard, and oscillometry (Mobil O´graph®). Comparisons of results were made by unpaired t-test, and p values < 0.05 were considered statistically significant.

Results: No difference was found in central pressure measurements obtained by SphygmoCor® (117 x 80.1 mmHg) compared with Mobil O´graph (112 x 81.4 mmHg). Mean augmentation index (AIx) was 26.1% and 21.3%, and mean pulse pressure (PP) amplification 10.7 mmHg and 10.0 mmHg by Sphygmocor® and Mobil O´graph®, respectively (p > 0.05). Mean pressure wave velocity (PWV), 8.4 m/s vs. 7.4 m/s (p = 0.013) and mean central pulse pressure, 37.7 mmmHg and 30.9 mmHg (p = 0.013) were significantly higher by SphygmoCor® than Mobil O´graph®.

Conclusion: Values of central systolic blood pressure, AIx and pulse pressure amplification obtained by oscillometry were not statistically different compared with tonometry; values of PWV and cPP, however, were underestimated by oscillometry. (Int J Cardiovasc Sci. 2020; 33(2):145-150)

Keywords: Hypertension; Risk Factors; Blood Pressure; Vascular Stiffness.

Introduction

Guidelines for the management of hypertension have recommended an early diagnosis and treatment of arterial hypertension as a fundamental strategy to reduce the occurrence of cardiovascular events.[1-3] In this regard, the use of biomarkers can increase the accuracy of the diagnosis, especially in patients with borderline hypertension and in patients with stage 1

hypertension. In these patients, in up to 18% of the cases, cardiovascular risk is underestimated by the conventional risk stratification model.[4,5]

The best biomarkers for risk stratification in hypertensive patients are intima–media thickness (IMT) of common carotid artery and pulse-wave velocity (PWV).[1,2,6,7] There is strong evidence that PWV is a method capable of identifying subclinical lesions and accurately determining the risk stratification for

occurrence of cardiovascular events. For hypertensive patients, this biomarker is mainly indicated at initial stages of blood pressure (BP) elevation and in those at low or moderate cardiovascular risk.[8-10]

Several non-invasive devices have been developed aiming at estimating central blood pressure and other parameters of arterial stiffness from measurements of peripheral arteries (radial, brachial and carotid arteries), using mathematical algorithms and methods of calibration or estimation. These devices have allowed the determination of several parameters that until then were obtained only by invasive methods.[11]

Among the non-invasive methods, arterial tonometry for measurement of PWV is considered the gold-standard method and is validated for intra-arterial pressure measurements. However, electronic tonometers are expensive and technically more difficult to be use. In contrast, oscillometric methods are validated, and faster and easier to perform, providing a better cost-benefit relationship.[12-15]

Our objective was to statistically compare results obtained by two non-invasive methods – tonometry and oscillometry – in patients with stage 1 hypertension and patients with borderline hypertension in Brazil.

Methods

This was a descriptive, cross-sectional study, conducted in patients attending the *Liga de Hipertensão Arterial da Universidade Federal de Goiás* (LHA/UFG), a program aiming at providing a comprehensive, multidisciplinary care to patients with cardiovascular diseases. The study was approved by the ethics committee of the General Hospital of the Federal University of Goias (approval number 000985/2016) This is one of the sub-studies of the original project entitled "*Correlação entre Valores Obtidos na Medida Central da Pressão Arterial com a Espessura das Camadas Íntima e Média das Artérias Carótidas em Pacientes com Pressão Arterial Sistêmica Limítrofe ou Hipertensos Estágio 1*" (Correlation of Central Blood Pressure with intima–media thickness of common carotid artery in patients with borderline hypertension or stage 1 hypertension".

Between March 2016 and July 2016, a total of 1,500 medical records of adult patients attending the LHA/UFG were reviewed, and 240 were selected. The selection was based on the data registered during this period, including BP values measured at the last visit. BP was considered as borderline or stage 1 hypertension according to the

Brazilian guidelines of arterial hypertension.[1] Patients participating in other research protocols for less than one year and patients with comorbidities – diabetes mellitus, end-stage chronic diseases (chronic renal failure and congestive heart failure), cardiovascular diseases (including coronary artery disease and stroke) were excluded. We intended to select patients at low cardiovascular risk (Figure 1).

At a second stage, telephone contact attempts to the patients were made, using the telephone numbers registered on the medical records. When patients could not be contacted, new attempts were made by the Medical Registry. Three telephone calls were made in different days and times. When telephone contact was successful, patients were invited to participate in the study, and a visit was scheduled at the LHS for those who accepted to participate.

Two-hundred forty medical records were first selected. After screening for the criteria described above and after the telephone contacts were made, the final sample consisted of 31 patients who agreed to participate in the study. Two of these were excluded for the presence of previous cardiovascular event (ischemic stroke) after the review of the medical records, and two were excluded for technical difficulties in obtaining central BP measurements (one using the SphygmoCor® and the other using the Mobil O'Graph®), because of the presence of cardiac arrhythmia. Thus, the convenience sample was composed of 27 patients.

All patients signed the informed consent form, and then completed a form on anthropometry, life habits, and history of past diseases. Measurements of peripheral and central BP were then taken, registered on the study form and then filed in an electronic database.

Peripheral BP (PBP) was measured at the office following the Brazilian Guidelines of Hypertension recommendations.[1] Measurements were taken using semiautomated devices (OMRON®, modelHEM-705CP, validated by international institutions and recommended for epidemiological applications.[16] Central blood pressure was measured by trained observers, using different methods. The first method consisted of applanation tonometry (portable pressure transducer or sensor), attached to a dedicated software for collection and analysis of the data. The results obtained, as well as the last PBP (measured at the physician's office) were inserted into the database. For PBP readings, the transducer was placed on the radial artery of patients in

Figure 1 - Flowchart of patients' selection.
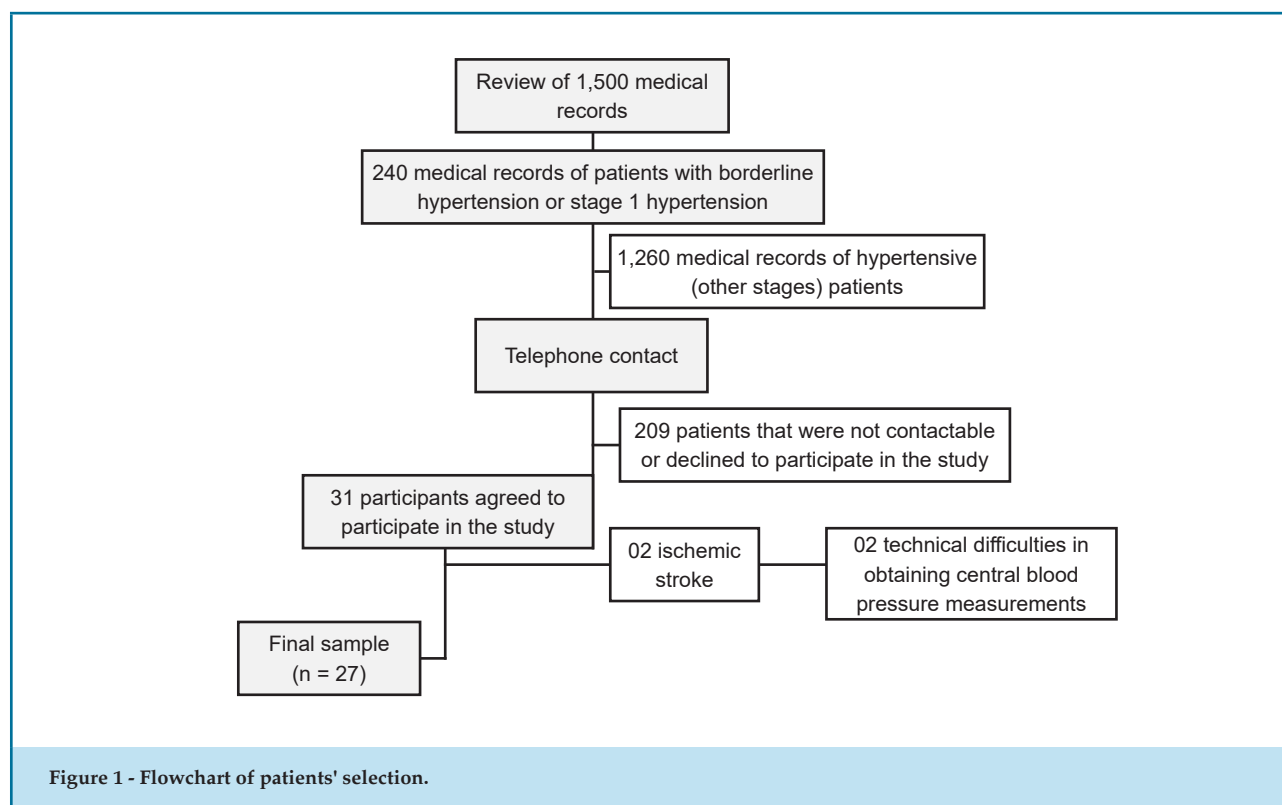
supine position. Data were obtained by transfer function for central systolic blood pressure (cSBP) central diastolic blood pressure (cDBP), central pulse pressure (cPP), pulse pressure (PP) amplification and augmentation index (AIx). For measurement of pulse wave velocity (PWV), the transducer was placed on femoral and carotid arteries, and the velocity at which pressure moved down this distance was determined in centimeters and multiplied by a correction factor of 0.8.[2,17]

The second method was a validated oscillometric method using the Mobil O'Graph® BP monitor. In this method, central BP is estimated by a mathematical algorithm derived from PWV of the brachial artery. This method also allowed the estimation of cSBP, CDBP, cPP, PP amplification, AIx and PWV. Central BP measurements were made with patients in siting position; data were analyzed with the Mobil O'Graph monitor analysis software.[14]

Statistical analysis

Statistical analysis of the data was made using the Stata software, version 14.0. First, a descriptive analysis was performed; qualitative variables were expressed as absolute and relative frequencies, and quantitative variables as mean, standard deviation and confidence interval. The Shapiro-Wil test was used to test normality of data distribution. Comparisons of peripheral and central measures obtained by the two different methods were made by unpaired t-test. Statistical significance was set at $p < 0.05$.

Results

Twenty-seven patients aged 50.8 ± 15 years participated in the study, most of them (63%) were women. Most patients (59.3%) were physically inactive, with mean body mass index (BMI) of 27.3 ± 4.8 Kg/m² (95%CI 25.4 - 29.3) (Table 1).

Regarding pBP measurements, four patients were classified as borderline hypertensive and 23 as hypertensive; 81.5% of them used at least one anti-hypertensive agent.

Central SBP (128 mmHg) was significantly lower than pSBP, both by tonometric (117.7 mgHg) and oscillometric (112 mmhg) methods ($p < 0.006$ and $p < 0.001$ respectively). No statistically significant difference was observed for the diastolic component of BP (Table 2).

Comparisons between Shpygmocor® and Mobil O'Graph®, the methods used for determination of cBP parameters, revealed no statistical difference for PASc, AIx and PP amplification, but statistical difference was observed for PWV and cPP (Table 3).

Table 1 - Lifestyle characteristics of the study group (n = 27)

Variable	n	%
Physical exercise (frequency)		
Regular	11	40.7
Irregular	01	3.7
None	15	55.6
Alcohol consumption (frequency)		
Never	17	63.0
Rarely	03	11.1
< 4x/week	05	18.5
> 4x/week	02	7.4
Smoking load (pack-years)		
None	25	92.6
< 5	01	3.7
> 20	01	3.7

Table 2 - Comparison of peripheral blood pressure measurements obtained by OMRON 705CP with the same measurements obtained by SphygmoCor® and Mobil O'Graph® (n = 27)

Variable	Mean	SD	95%CI	p
pSBP	128.4	13.4	123.0-133.7	
cSBP (SphygmoCor®)	117.7	14.0	112.1-123.2	0.006*
cSBP (Mobil O'Graph®)	112,0	10,1	108.0-116.0	0.001*
pDBP	76.1	10.5	71.9-80.2	
cDBP (Shpygmocor®)	80.1	10.6	75.9-84.3	0,172*
cDBP (Mobil O'Graph®)	81,4	10,5	77.2-85.5	0,070*

*SD: standard deviation; CI: confidence interval; pSBP: peripheral systolic blood pressure; cSBP: central systolic blood pressure; pDBP: peripheral diastolic blood pressure; cDBP: central diastolic blood pressure. * Compared with OMRON 705CP.*

Discussion

Arterial stiffness and cBP are better predictors of cardiovascular events compared with peripheral parameters of BP, especially in the initial stages of hypertensive disease and in hypertensive patients at low and moderate risk,[5,9,18,19,20] and considered as important tools in restratification of these patients.[1,2]

The values of peripheral BP (128.4 s 76.1 mmHg) found in our sample are consistent with those of patients in the initial stages of hypertensive disease.

Analysis of BP in large arteries (rather than peripheral values) showed that, corroborating previous studies, an amplification of systolic pressure occurs, from central to peripheral arteries, and diastolic pressure tended to remain unchanged.[21] Central SBP determined by tonometry was 10.7 mmHg lower than pSBP (p = 0.006), whereas by oscillometry, this difference was

Table 3 - Comparison of central blood pressure measurements obtained by SphygmoCor® with the same measurements obtained by Mobil O'Graph® (n = 27)

Variable	Mean	SD	95%CI	p
cSBP (SphygmoCor®)	117.7	14.0	112.1-123.2	0.09
cSBP (Mobil O'Graph®)	112.0	10.1	108.0-116.0	
cDBP (SphygmoCor®)	80.1	10.6	75.9-84.3	0.654
cDBP (Mobil O'Graph®)	81.4	10.5	77.2-85.5	
cPP (Shpygmocor®)	37.7	12.6	32.7-42.7	0.013
cPP (Mobil O'Graph®)	30.9	5.4	28.7-33.0	
PPA (Shpygmocor®)	10.7	5.7	8.4-12.9	0.619
PPA (Mobil O'Graph®)	10.0	3.8	8.5-11.5	
AIx (Shpygmocor®)	26.1	18.3	18.9-33.4	0.244
AIx (Mobil O'Graph®)	21.3	11.2	16.9-25.7	
PWV (Shpygmocor®)	8.4	1.6	7.8-9.1	0.013
PWV (Mobil O'Graph®)	7.4	1.4	6.8-7.9	

SD: standard deviation; CI: confidence interval; cSBP: central systolic blood pressure; cDBP: central diastolic blood pressure; cPP: central pulse pressure; PPA: pulse pressure amplification; AIx: augmentation index; PWV: pulse wave velocity

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16.4 mmHg (0.001). No statistical difference was found for the diastolic component of BP (Table 2).

It is of note that, compared with peripheral pressures, central BP shows a better correlation with clinical outcomes. This is probably explained by the fact that central pressures have lower variability, and from the pathophysiological point of view, central pressure reflects the levels of tension on target organs.[22-26] In the comparison between central BP values obtained by tonometry and by oscillometry, no difference was found for cSBP, cDBP, PP amplification, and AIx, but differences were found for cPP (37.7 mmHg and 30.9 mmHg, p = 0.013) and PWV (8.4 m/s and 7.4 m/s, p = 0.013). These findings also corroborate previous findings showing a tendency of the oscillometric method in underestimating parameters of cBP.[12,14,15]

A study with 320 patients comparing an oscillometric (ARCSolver - Mobil O Graph®) method with the tonometric (SphygmoCor®) method, the results of most parameters agreed with those obtained by tonometric method.[27] In another study with 89 patients, the authors also reported good reproducibility between the methodsand suggested that oscillometry should be considered in everyday clinical practice, as it is an easy-to-perform test, with good cost-benefit relationship.[28]

A guideline on protocols, equipment and non-invasive methods for estimation of central BP, published by the Artery Society in 2017, showed that, compared with intra-arterial BP measurement and the non-invasive tonometry method, the oscillometric method tend to underestimate PWV measurements, which should be considered in the use of this method.[29]

More recently, a risk score (SAGE score) has been validated, using clinical criteria to identify hypertensive patients at higher risk for developing elevated arterial spiffiness. In this patients, analysis of central BP would be indicated,[30] i.e., there is a current thinking of the scientific community that the method should be incorporated in cardiovascular risk stratification as an effective tool to early detect patients at higher risk.

Despite the small sample size, we believe that our main objective in this study, to compare central hemodynamics indices obtained by different methods in patients at low cardiovascular risk, was achieved.

To our knowledge, this is the first nation-wide study to evaluate the reproducibility of the oscillometric method in comparison with tonometric method in patients with borderline BP or patients with stage 1

hypertension, that may contribute to the advance, debate and implementation of this tool into clinical practice.

Conclusion

The parameters of central BP and those that reflect arterial compliance, particularly PWV, show better correlation with cardiovascular outcomes in hypertensive patients than peripheral BP measurements.

The use of non-invasive methods (tonometry and oscillometry) were validated for intra-arterial BP measurements of these parameters. Although tonometry is considered the gold standard among non-invasive methods, oscillometry has good reproducibility and may be considered a promising instrument to be used in clinical practice.

Author contributions

Conception and design of the research: Barroso WKS, Vitorino PVO. Acquisition of data: Barroso WKS, Gonçalves CF, Berigo JAC, Melo MA, Oliveira ACA, Vitorino PVO. Analysis and interpretation of the data: Barroso WKS, Gonçalves CF, Berigo JAC, Vitorino PVO. Statistical analysis: Vitorino PVO. Writing of the manuscript: Barroso WKS, Gonçalves CF, Berigo JAC, Melo MA, Vitorino PVO. Critical revision of the manuscript for intellectual content: Barroso WKS, Gonçalves CF, Berigo JAC, Melo MA, Oliveira ACA, Lelis ES, Sousa WM, Rezende JM, Jardim TV, Sousa ALL, Jardim PCBV, Vitorino PVO.

Potential Conflict of Interest

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

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Study Association

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Ethics approval and consent to participate

This study was approved by the Ethics Committee of the *Hospital das Clínicas da Universidade Federal de*

Goiás under the protocol number 000985/2016. 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. 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(3 Supl.3):1-83 .

2. 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 ;39(33):3021-104.

3. Salinas AM, Coca A, Olsen MH, Sánchez R, Barroso WKS, Kones R, et al. Clinical perspective on antihypertensive drug treatment in adults with grade 1 hypertension and low problems in cardiology. Curr Probl Cardiol; 2017;42(7):196-225.

4. Sociedade Brasileira de Cardiologia. Departamento de Hipertensão Arterial. Posicionamento brasileiro sobre pré-hipertensão, hipertensão do avental branco e hipertensão mascarada: diagnóstico e conduta. Arq Bras Cardiol. 2014;102(2):110-9.

5. Vlachopoulos C, Aznaouridis K, O´Rourke MFea. Prediction of Cardiovascular Events and All-Cause Mortality with Central Hemodynamics: A Sistematic Review and Meta-Analysis. Eur Heart J. 2010;31(15):1865-71.

6. Vlachopoulos C, Xaplanteris P, Aboyans V, Brodmann M, Cifkova R, Cosentino F, et al. The role of vascular biomarkers for primary and secondary prevention. A position statement from the European Society of Cardiology Working group on peripheral circulation. Atherosclerosis. 2015;241(2):507-32.

7. Van Bortel LM, Laurent S, Boutouyrie P, Chowienczyk P, Cruickshank JK, De Backer T, et al. Expert consensus document on the measurement of aortic stiffness in daily practice using carotid-femoral pulse wave velocity. J Hypertens. 2012;30(3):445-8.

8. Cunha PG, Cotter J, Oliveira P, Vila I, Boutouyrie P, Laurent S, et al. Pulse wave velocity distribution in a cohort study: from arterial stiffness to early vascular aging. J Hypertens. 2015;33(7):1438-45.

9. Sociedade Brasileira de Cardiologia.Departamento de Hipertensão Arterial. Posicionamento luso brasileiro de pressão arterial central. Arq Bras Cardiol. 2017;108(2):100-8.

10. Mikael LM, Paiva AMG, Gomes MM, Sousa ALL, Jardim PCBV, Vitorino PVO, et al. Vascular aging and arterial stiffness. Arq Bras Cardiol.2017;109(3):253-8.

11. Mceniery CM, Cockroft JR, Roman MJ, Franklin SS, Wilkinson LB. Central blood pressure: Current evidence and clinical importance. European heart journal. 2014;35(26):1719-25.

12. Ding FH, Fan WX, Zhang RY, Zhang Q, Wang JG. Validation of the noninvasive assessment of central blood pressure by the SphygmoCor and Omron Devices Against the Invasive Catheter Measurement. Am J Hypertens. 2011;24(12):1306-11.

13. Townsend RR, Wilkinson IB, Schiffrin EL, Avolio AP, Chirinos JA, Cockcroft J Rea. Recommendations for Improving and Standardizing Vascular Research on Arterial Stiffness: A Scientific Statement From the American Heart Association. Hypertension. 2015;66(3):698-722.

14. Hametner B, Wassertheurera W, Kropfa J, Mayera C, Eberc B, Weber T. Oscillometric estimation of aortic pulse wave velocity: comparison with intra-aortic catheter measurements Blood Press Monit. 2013;18(3):173-6.

15. Papaioannou TG, Protogerou A, Stefanadis C. Comparison between Mobil-O-Graph and the SphygmoCor device for central systolic blood pressure estimation: consensus is required for validation protocol. Blood Press Monit. 2012;17(6):259-60.

16. Bonilla PI, Sánchez EM, Peralta JL, Oquendo MI. Validación de dos sistemas de automedida de presión arterial, modelos OMRON HEM-705 CP y OMRON M1 (HEM 422C2-E). Aten Primaria 2002;30(1):22-8.

17. Laurent S, Cockroft J, Bortel LV, Boutouyrie P, Giannattasio C, Hayoz D,et al. Expert consensus document on arterial stiffness: methodological issues and clinical applications. Eur Heart J. 2006;27(21):2588-605.

18. Sabovic M, Safar M, Blacker J. Is there any Additional Prognostic Value of Central Blood Pressure Wave Forms Beyond Peripheral Blood Pressure. Curr Pharm Des. 2009;15(3):254-66.

19. Koivistoinen T, Lyytikäinen LP, Aatola H, Luukkaala T, Viikari MJ, Lehtimäki T, et al. Pulse Wave Velocity Predicts the Progression of Blood Pressure and Development of Hypertension in Young Adults. Hypertension. 2018;71(3):451-6.

20. Laurent S, Briet M, Boutouyrie P. Arterial Stiffness as Surrogate End Point Needed Clinical Trials. Hypertension. 2012;60(2):518-22.

21. Camacho F,Avolio A, Lovel 1 N H. Estimation of pressure pulse amplification between aorta and brachial artery using stepwise multiple regression models. Physiol Measurement. 2004; 25(4):879-89.

22. McEniery C M, Yasmin, Hall I R, Qasem A,Wilkinson I B, Cockcroft J R. Normal vascular aging: differential effects on wave reflection and aortic pulse wave velocity: the Anglo-Cardiff Collaborative Trial (ACCT). J Am Coll Cardiol. 2005;46(9):1753-60.

23. McEniery C M, Yasmin, Mc Donnell B, Munnery M, Wallace S M, Rowe C V, et al. Central pressure: variability and impact of cardiovascular risk factors: the Anglo-Cardiff Collaborative Trial II. Hypertension. 2008;51(6):1476-82.

24. Roman M, Devereux R, Kizer Jea. Central pressure more strongly relates to vascular disease and outcome than does brachial pressure: The Strong Heart Study. Hypertension. 2007;50(1):197-203.

25. Roman M J, OkinP M, Kizer J R, Lee E T, Howard B V, Devereux R B. Relations of central and brachial blood pressure to left ventricular hypertrophy and geometry: the Strong Heart Study. J Hypertens. 2010;28(2):384-8.

26. Huang Cm, Wang K L, Cheng Hm, Chuang S Y, Sung S H, Yu Wc, Et Al. Central Versus Ambulatory Blood Pressure In The Prediction Of All-Cause And Cardiovascular Mortalities . J Hypertens. 2011 March ; 29(3): 454–9.

27. Wassertheurer S, Kropf J, Weber T. A new oscillometric method for pulse wave analysis: comparison with a common tonometric method. J Hum Hypertens 2010;24(8):498-504.

28. Reshetnik A, Gohlisch C, Tölle M, Zidek W, Van Der Giet M. Oscillometric assessment of arterial stiffness in everyday clinical practice. Hypertens Res. 2016;40(2):1-6.

29. Sharman J E, Avolio A P, Baulmann J, Benetos A, Blacher J, Blizzard C L, et al. Validation of non-invasive central blood pressure devices: ARTERY Society task force consensus statement on protocol standardization. Eur Heart J.2017;38(37):2805-12.

30. Xaplanteris P, Vlachopoulos C, Protogerou A, Aznaouridis K, Terentes-Printzios D, Argyris AA, et al. A clinical score for prediction of elevated aortic stiffness: derivation and validation in 3943 hypertensive patients. J Hypertens. 2019;37(2):339-46.

ORIGINAL ARTICLE

Medical Behavior in Cardiorespiratory Arrest before and After Simulation Based on Advanced Cardiac Life Support (ACLS) Course

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Abstract

Background: The Advanced Cardiac Life Support (ACLS) course is designed to teach cardiovascular emergency, aiming to promote a harmonious and synchronized work of the entire hospital team, making the multidisciplinary job more effective in the execution of cardiopulmonary resuscitation (CPR).

Objective: To compare the effectiveness of CPR performed between physicians trained on ACLS and non-trained physicians.

Methods: A questionnaire was applied to physicians working at the emergency room of hospitals in Curitiba, state of Paraná, whose resolution required theoretical and practical knowledge about CPR. For analysis, descriptive statistics and Fisher's association analysis were used, and the medians of the groups were evaluated by Mann-Whitney/Kruskal-Wallis with significance of 5%.

Results: Thirty-four physicians were volunteers, of whom 20 had taken the ACLS course (Group A) and 14 had not (Group B). The trained physicians obtained the highest median (4.00 vs. 3.00, p = 0.06) of correct answers. Group A scored at least 3 of the 5 questions in the questionnaire, showing better performance than Group B (OR = 6.75, 95% CI, 1.1 < OR < 41.0, p = 0.04). The year of the course did not significantly change the performance in the questionnaire.

Conclusion: It is suggested that the ACLS course was effective in qualifying physicians to handle situations of cardiorespiratory arrest properly, which was reproduced by the better performance in the resolution of the questionnaire. It is believed that when the sample of volunteers is increased, the trends found materialize the other hypotheses proposed. (Int J Cardiovasc Sci. 2020; 33(2):151-157)

Keywords: Cardiopulmonary, Resuscitation; Advanced Cardiac Life Support/training; Heart Arrest.

Introduction

Advanced Cardiac Life Support (ACLS) is a course that has occurred in Brazil since 1996 and is designed to teach cardiovascular emergency. It starts with the simulation of real-life situations through a standard way of teaching an ideal clinical management professional in the medical field. The course structure is periodically reviewed according to new versions provided by the American Heart Association (AHA) guidelines.[1] In recent years, cardiovascular emergency courses have been applied to a larger number of physicians working in emergency rooms or elsewhere.[2] It is known that since its introduction, ACLS has undergone a series of conceptual and structural changes. The course has turned its focus on solving cases with defined objectives, and practical activities were emphasized. Modifications included theoretical updates according to evidence-based medicine and guidelines applied to the new teaching approach.[1]

Doctors' updating is crucial for adequate management of cardiorespiratory arrest. Training and continued education on cardiopulmonary resuscitation (CPR),[3,4] since success in cardiac arrest management requires technical and scientific efficiency, as well as adequate team training.[5] Cardiorespiratory arrest care should be considered mandatory and priority knowledge for all health professionals, regardless of their specialty. It requires adequate infrastructure with frequent updates to basic life support conduct for an effective, harmonious and synchronized work of the multidisciplinary team.[6,7]

This work aims to identify the effectiveness of ACLS course in enabling physicians to handle cardiovascular emergency situations. It was based on the assumption that ACLS essentially seeks to standardize the actions in a cardiorespiratory arrest situation, so the patients may receive the best treatment.[1]

The importance of this study is remarkable because if the alleged increase in effectiveness after ACLS training is confirmed, more hospitals or educational institutions would appreciate the application of the course and invest in the training of their professionals and students. This investment would be reflected in the patients with cardiorespiratory arrest, who would most likely be assisted by successful resuscitation teams.

Methods

Data collection

The ACLS efficacy analysis was performed by distributing a questionnaire to physicians working at the emergency room of hospitals in the city of Curitiba, state of Paraná. The questionnaire was to be answered on a volunteering basis and included 5 multiple choice questions. It contained an approach involving theoretical and practical knowledge about cardiopulmonary resuscitation (Supplementary 1). In addition to the questions, additional data were collected such as the physician's year of training, age, institution of graduation, medical specialty, employing hospital and participation in the ACLS course, as well as the year in which such training took place. Volunteering physicians answered the survey in front of a researcher in the emergency room. This was to avoid any potential consultation or communication among the volunteers, which could add bias to the results. In total, 34 physicians participated in the study. There was no specific criterion for determining the sample size. The number of volunteers was exclusively due to the number of physicians willing to participate in the study that met the inclusion criteria during the data collection period.

Once the data were collected, the main focus of the discussion was the comparison between the performance of volunteers who had attended the ACLS course versus the performance of those who did not, seeking to analyze the effectiveness of the course. Also, the retention of knowledge in the short and long term was examined by contrasting the results of the volunteers participating in the course to the year in which such training occurred.

Statistical analysis

The epidemiological data collected in the questionnaire was evaluated by descriptive statistics, and normality check was performed using the Kolmogorov-Smirnov test. The variables were represented by medians and values of the first and third quartiles. For the association analysis, independence tests were performed between the groups using Fisher's test with odds ratio calculation, and 95% confidence interval using the SISA program package. The analysis between the groups and the median number of correct questions were performed using the Mann-Whitney/Kruskal-Wallis tests with odds ratio calculation, in the GraphPad Prism program. P values lower than 0.05 were considered significant.

Results

The questionnaire was distributed to 34 volunteer physicians working at the emergency room of hospitals in Curitiba. Of this total, 20 had attended an ACLS course, while 14 had not. In order to facilitate exposure, the group of physicians who attended the ACLS course (n = 20) was named "Group A" and the group of physicians who had never attended an ACLS course (n = 14) was called "Group B". Since the data followed a non-normal distribution pattern, nonparametric statistical tests were performed.

Regarding the number of correct answers in the questionnaire, it could be observed that the groups (physicians who have attended an ACLS course versus physicians who have never attended such course) tend to be different, with p value of 0.06 (Figure 1). Group A obtained a median score greater than Group B (4.00 vs. 3.00). However, this difference was not statistically validated (p = 0.06). In addition, it was observed that Group A scored at least 3 of the 5 questions in the questionnaire, while Group B showed inferior

performance (OR = 6.75, 95% CI, 1.1 < OR < 41.0, p = 0.04) (Table 1). Of the 20 physicians who were part of Group A, only 2 scored less than 3 questions, so 90.00% of the sample answered correctly the majority of the questionnaire. In comparison, of the 14 professionals from Group B, 6 (42.86%) scored less than half of the test, while only 57.14% made 3 or more questions.

To investigate whether the time since the ACLS course to the date of the questionnaire could affect the performance of the volunteers, Group A was subdivided into two parts, according to the year of the course: (i) volunteers who took the ACLS course in the year of 2016; (ii) volunteers who took the ACLS course prior to the year of 2016 (Figure 2). None of the volunteers took the course during the year of 2017. No significant difference was noticed between the groups (p = 0.52). In each group, only 1 individual who took the course scored less than 3 questions. Thus, it could be observed that even physicians who were trained with outdated guidelines were able to achieve similar performance to that of recently trained professionals, and better than group B (p = 0.04).

Discussion

A questionnaire was distributed to physicians on duty at emergency units of hospitals in Curitiba, where 34 professionals were volunteers. Of these, 20 physicians had taken an ACLS course (group A), and 14 had not (group B).

Regarding the number of correct answers in the questionnaire, it was observed that group A obtained median score greater than Group B. However, this difference was not significant (p = 0.06). It is believed that this tendency would be confirmed by an increase in the sample number, which was not possible in this study, since it was difficult to recruit volunteers who fulfilled the inclusion criteria (physicians on duty in emergency departments of hospitals in the city of Curitiba during the data collection period). The researchers chose to look for volunteer physicians working at emergency care units to participate in the study because they believed that in that environment, cardiac arrest situations were found more frequently than in other medical settings, such as outpatient clinics, for example. Therefore, it would be indispensable for the professional to be knowledgeable about the management of CPR for quality emergency care. However, one limitation to sample size was the typical agitation of emergency room units, as well as physicians' allegations of insufficient time to answer the questionnaire questions with the utmost attention. Still, to avoid consultation or communication between professionals, they were required to answer the questionnaire in the presence of a researcher in charge, which also reduced the sample.
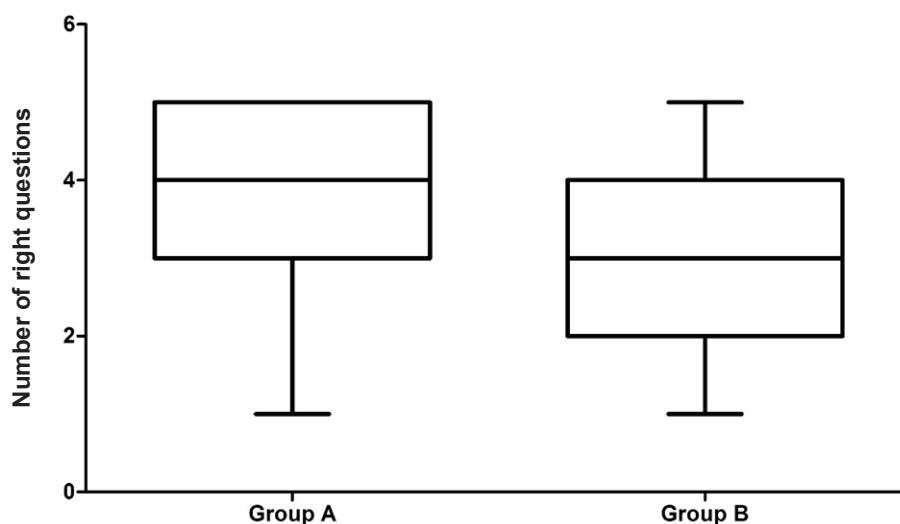
Figure 1 - Performance of the groups evaluated for the median number of correct answers in the questionnaire. Group A corresponds to the doctors who had taken an ACLS course; Group B corresponds to those who had not (p = 0.06).
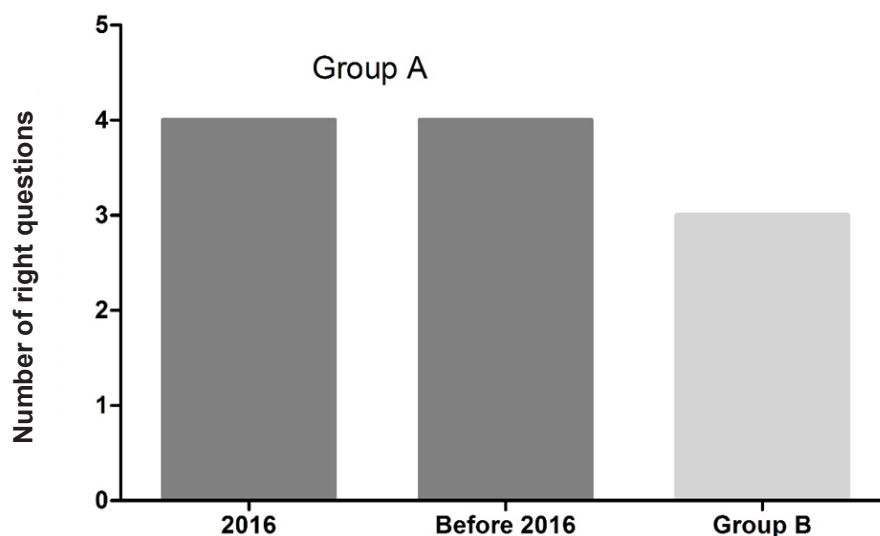
Figure 2 - Median number of correct answers in the questionnaire of groups A and B. Group A was subdivided into two according to the year of the course: (i) volunteers who took ACLS training in 2016; (ii) volunteers who took ACLS training before 2016. No significant difference was found in the number of correct answers in the subgroups, both of which reached a median higher than group B.

It was observed that group A scored at least 3 of the 5 questions of the questionnaire, whereas group B showed inferior performance, which suggests that physicians who took the course have a chance to show better performance in the questionnaire than those who never did.

The aim of this study was also to investigate whether the time since the ACLS course to the date of the questionnaire could affect the performance of volunteers. For this purpose, Group A was subdivided into two parts: volunteers who took ACLS training in 2016 and volunteers who had taken training previously. It was decided to organize the volunteers in this manner because the last modification of the guidelines was published in 2015 by the American Heart Association (AHA). No significant difference was observed between the groups, so the ACLS course allowed a large number of correct answers regardless of the year of training (p = 0.52). Even physicians who were trained with outdated guidelines were able to achieve performance similar to that of newly trained practitioners — still better than the group that never trained (p = 0.04). It is suggested that physicians trained under old protocols were able to update CPR concepts. Besides that, regardless of the year of training, knowledge retention was reflected by the better performance in the questionnaire.

It is assumed that the effectiveness of the course was able to promote significant changes in the approach of professionals trained on CPR, resulting in better medical care and longer survival of patients under CRP. It is hoped that this analysis may foster the importance of training and prior experience with real situations regarding the effectiveness in resuscitation of patients in cardiorespiratory arrest.

Thus, it is possible to recognize the effectiveness of the ACLS course in promoting better performance of the

Table 1 - Number of correct answers of different groups evaluated

Scores	Group A n = 20	Group B n = 14	p value **
25% quartile	3.00	2.00	NA
Median	4.00	3.00	0.06
75% quartile	5.00	4.00	NA
≥ 3/5*	18.00	8.00	0.04

(*) At least three scores on five questions answered in the questionnaire; (**) The difference between medians was evaluated by Mann-Whitney test, and the difference between the number of correct answers using Fisher's test. In bold, statistically significant (< 0.05). NA: not applicable.

professionals who answered the questionnaire, which reflects greater acquisition of knowledge and skills developed with the training.

Discussion

Considering the results obtained, it is proposed that the ACLS course was effective in qualifying physicians to deal more adequately with cardiorespiratory arrest situations — which was reproduced by better performance in the questionnaire — fulfilling the objective of this study. The year of course completion did not significantly change the volunteers' performance in solving the questions, pointing out adequate retention of knowledge and probable professional update of those physicians trained on non-recent protocols.

Although the reduced sample of professionals who volunteered to participate in the study had limited a better statistical result of some variables, it is believed that once the sample is increased, the trends found would support the hypotheses proposed.

Acknowledgments

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Author contributions

Conception and design of the research: Catolino DM, Knofholz J. Acquisition of data: Catolino DM. Analysis and interpretation of the data: Catolino DM. Statistical analysis: Catolino DM. Writing of the manuscript: Catolino DM. Critical revision of the manuscript for intellectual content: Knofholz J.

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 PUC-PR under the protocol number 1709.529. 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. Garrido FD, Romano MMD, Schmidt A, Pazin-Filho A. Can course formatinfluence the performance of students in an advanced cardiac life support(ACLS) program? Braz J Med Biol Res. 2011;44(1):23-8.

2. Lima E Jr, Knopfholz J, Menini CM. Stress during ACLS courses: is it important for learning skills? Arq Bras Cardiol. 2002;79(6):589-92.

3. Knopfholz J, Lima Jr E, Ribeiro APF, Boros GAB, Claviço J, Teider LD, et al. Management of cardiologic emergencies in general hospitals in the state of Paraná. Rev Bras Clin Med. 2012;10(6):499–502.

4. Duarte RN, Fonseca AJ Da. Diagnóstico e tratamento de parada cardiorrespiratória : avaliação do conhecimento teórico de médicos em hospital geral. Rev Bras Ter Intensiva. 2010;22(4):153–8.

5. Gomes AG, Garcia AM, Schmidt A, Mansur AP, Vianna CB, Ferreira D, et al. Diretriz de Apoio ao Suporte Avançado de Vida em Cardiologia– Código Azul–Registro de Ressuscitação Normatização do Carro de Emergência. Arq Bras Cardiol. 2003;81(SuplIV):1-14.

6. Feitosa-Filho GS, Feitosa GF, Guimarães HP, Lopes RD, Moraes Júnior R, Souto FA, et al. Update on cardiopulmonary resuscitation: what changed with the new guidelines.. Rev Bras Ter Intensiva. 2006;18(2):177–85.

7. Timerman A, Sauaia N, Piegas LS, Ramos RF, Gun C, Santos ES, et al. Fatores Prognósticos dos Resultados de Ressuscitação Cardiopulmonar em um Hospital de Cardiologia. Arq Bras Cardiol. 2001;77(2):142–51.

Supplementary File. Questionnaire about cardiopulmonary resuscitation.

Age: _____ University: _____ Year of graduation: _____

Medical Specialty: _____

Employing Hospital: _____

Have you ever attended an ACLS course? Yes __ No__ If yes, year of participation: _____

1. In a cardiorespiratory arrest in an adult patient not in a hospital environment, according to the current guidelines, what is the correct sequence that must be followed by a health professional after local safety?

A. Check responsiveness, contact the emergency service/get an Automated External Defibrillator (AED), check breathing and pulse sequentially, ventilate, start chest compressions.

B. Check responsiveness, start chest compressions, contact the emergency service/get an Automated External Defibrillator (AED), check breathing and pulse simultaneously.

C. Check responsiveness, contact the emergency service/get an Automated External Defibrillator (AED), check breathing and pulse simultaneously, start chest compressions.

D. Contact the emergency service/get an Automated External Defibrillator (AED), check responsiveness, check breathing and pulse sequentially, start chest compressions.

E. Contact the emergency service/get an Automated External Defibrillator (AED), check responsiveness, start chest compressions, check breathing and pulse simultaneously.

2. About the Cardiopulmonary Resuscitation (CPR) technique, mark the INCORRECT statement:

A. In 2015, the frequency of compressions was modified to the range of 100 to 120/min.

B. In 2015, the depth of adult compression was modified to at least 2 inches (5 cm), not to exceed 2.4 inches (6 cm).

C. Adequate ventilation would be 2 ventilations for every 30 compressions regardless of the number of professionals involved in CRP care, with each breath administered in one second in order to induce chest elevation.

D. After advanced airway management, ventilation should be performed at a frequency of 1 time every 3 seconds.

E. Cricoid compression should not be routinely used in orotracheal intubation during CPR.

3. About the Cardiopulmonary Resuscitation (CPR) technique, mark the INCORRECT statement:

A. Hyperkaliemia, acidosis and tricyclic intoxication are treated with sodium bicarbonate in the course of a CPR.

B. The defibrillator should be used as soon as it is available.

C. When the defibrillator arrives, if the pace is shocking, after 1 shock, do CPR immediately for about 5 minutes.

D. Vasopressin in CPR can be used in combination with epinephrine or alone.

E. Epinephrine should be given as soon as possible after initiation of CPR due to an initial non-shockable rhythm.

4. Determine the following assertions as true (T) or false (F) and choose the right answer:

i. Synchronized shock (360 J) every 2 min is the best course for ventricular fibrillation/pulseless ventricular tachycardia.

ii. The recommended dose of epinephrine is 1 mg every 3 to 5 minutes, while amiodarone is 300 mg in the first dose and 150 mg in the second dose.

iii. Immediately after the shock, if the patient returns to sinus rhythm, it is not necessary to apply compressions, being able to leave for post-CPR care

iv. Ventricular fibrillation is the main cause of CPR, while asystole represents the worse prognosis.

v. If in capnography PETCO$_2$ is < 10 mmHg, it means that CPR is good quality.

    a. F, F, F, T, T.

    b. F, T, F, F, F.

    c. T, T, F, F, F.

    d. F, T, F, T, F.

    e. T, F, F, T, T.

5. Male, 59 years old, diabetic, smoker, had cardiopulmonary resuscitation stopped in a non-hospital setting. After compression starts and the Automated External Defibrillator (AED) arrives, there is no pulse, and the following ECG rhythm occurs:

The conduct for this case, according to current guidelines of the American Heart Association regarding ACLS (Advanced Cardiac Life Support), would be:

A. Apply a shock and restart CPR immediately for about 2 minutes. If the rhythm changes to non-shockable, administer amiodarone 300 mg IV/10.

B. Apply a shock and restart CPR immediately for about 2 minutes. If the rhythm remains, apply a second shock, then epinephrine 1 mg IV/10.

C. Apply a shock and restart CPR immediately for about 2 minutes. If the rhythm remains, apply a second shock, then epinephrine 1 mg and amiodarone 300 mg IV/10.

D. Restart CPR immediately for about 2 minutes, then apply epinephrine 1 mg IV/10.

E. Restart CPR immediately for about 2 minutes, then apply epinephrine 1 mg and amiodarone 300 mg IV/10.

Internal Validation of a Risk Score for Prediction of Postoperative Atrial Fibrillation after Cardiac Surgery

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Abstract

Background: Postoperative atrial fibrillation (POAF) after cardiac surgery has great clinical and economic implications. Many attempts have been made to identify risk factors aiming at a better evaluation of prophylactic treatment strategies.

Objective: To perform an internal validation of a risk score for POAF.

Methods: A prospective cohort of 1,054 patients who underwent myocardial revascularization and/or valve surgery was included. The risk score model was developed in 448 patients, and its performance was tested in the remaining 606 patients. Variables with a significance level of 5% in the cohort were included and subjected to a multiple logistic regression model with backward selection. Performance statistics was performed using the c-statistic, the chi-square and the Hosmer-Lemeshow (HL) goodness-of-fit, Pearson's correlation coefficient.

Results: Four variables were considered predictors of outcome: age (≥ 70 years), mitral valve disease, the non-use or discontinuation of beta-blockers and a positive water balance ($> 1,500$ mL). The ROC curve was 0.76 (95% confidence interval [CI]: 0.72-0.79). The risk model showed a good ability according to the performance statistics – HL test $x^2 = 0.93$; $p = 0.983$ and $r = 0.99$ (Pearson's coefficient). There was an increase in the frequency of POAF with the increase of the score: very low risk = 0.0%; low risk = 3.9%; intermediate risk = 10.9%; and high risk = 60.0%; $p < 0.0001$.

Conclusion: The predictive variables of POAF allowed us to construct a simplified risk score. This scoring system showed good accuracy and can be used in routine clinical practice. (Int J Cardiovasc Sci. 2020; 33(2):158-166)

Keywords: Atrial Fibrillation; Myocardial Revascularization; Heart Valves/surgery; Perioperative Care; Risk Score; Prevention and Control.

Introduction

Atrial fibrillation (AF) remains the most prevalent event in perioperative period of cardiac surgery, with an incidence varying from 20 to 50%, according to the electrocardiographic or cardiac monitoring method used.[1-4] Its incidence has continuously increased over recent decades despite advances of surgical and anesthetic techniques.[3] Postoperative AF (POAF) is associated with worse clinical outcomes, with great impact on health care costs.[1,4-10]

Given the repercussions of AF, many investigations have been conducted to identify factors associated with the pathophysiology of AF, and thereby enable the development of preventive measures, guide the treatment of patients at greater risk, minimize the side effects of antiarrhythmic drugs and maximize the cost-benefit of the therapy.[6,11-13]

Our group has previously published a study on risk factors for the development of POAF, including age over 70 years, mitral disease, non-use of beta-blocker therapy

in the perioperative period and a positive water balance greater than 1,500 mL in the 48 after surgery.[14]

To this end, we sought to create and validate a risk stratification score of POAF, using preoperative and early postoperative indicators in patients undergoing cardiac surgery.

Material And Methods

Population and sample

The present study consists of a prospective analysis of 1,054 patients at the Institute of Cardiology of Rio Grande do Sul/University Foundation of Cardiology (*Instituto de Cardiologia do Rio Grande do Sul/Fundação Universitária de Cardiologia* - lClFUC). Study sample consisted of patients who underwent valve surgery and/or myocardial revascularization at the ICIFUC, and was collected during two periods, between 2002 and 2005 (n = 448 patients) and between 2010 and 2011 (n = 606 patients).

Study design

This was an observational prospective cohort study.

Inclusion criteria

Patients aged 18 years or older who underwent valve surgery (mitral and/or aortic valve replacement) and/or myocardial revascularization surgery were included. Patients who underwent additional procedure associated with any of these surgeries were also included.

Exclusion criteria

Patients who underwent emergency procedures, and patients with AF (detected by standard electrocardiography and 24-h ambulatory electrocardiographic monitoring) were excluded.

Study variables

The following variables were evaluated in the validation cohort: gender, age, presence of mitral valve disease (severe regurgitation and/or severe stenosis), use of beta-blockers in the preoperative period, discontinuation of beta-blocker therapy in the postoperative period, presence of a positive water balance greater than 1,500 mL within 48 hours after surgery, duration of hospitalization and in-hospital mortality.

Outcome

The diagnosis of POAF was considered an outcome in the perioperative period. POAF was desfined as an episode of arrhythmia, with electrocardiographic tracing with an irregular baseline secondary to disorganized atrial activity, which is referred to as the so-called "f" waves generating variable RR cycles. Episodes of POAF lasting longer than 15 minutes or requiring medical intervention were considered in the study due to the symptomatology or hemodynamic instability. Patients were monitored continuously for 72 hours, and daily electrocardiograms were obtained during hospitalization. In case of cardiovascular symptoms, additional monitoring was performed.

Procedures

Anesthesia and cardiopulmonary bypass (CPB) were performed according to local standard protocols. After cardiac surgery (immediate postoperative period), the patient remaining for 48 hours or longer in the intensive care unit.

Statistical analysis

Continuous variables with normal distribution were described as means and standard deviations. The hypothesis of normality was verified by the Kolmogorov-Smirnov test. Categorical (or categorized continuous) variables were described as counts and percentages and compared using the chi-square test or Fisher's exact test, when necessary. For construction of the risk score, a derivation cohort was collected between 2002 and 2005, and a validation cohort was collected during 2010-2011. Multivariate analysis with backward selection was applied. Statistical significance was set at $p < 0.05$.

Preliminary model of the risk score

Variables used for analysis were selected based on biological plausibility (association with POAF) and data from literature on POAF. A total of 67 variables were studied in the derivation cohort[14] of 448 patients included between 2002 and 2005.

Variables associated with POAF were selected in a multiple logistic regression model with backward selection, and those with p-values close to 0.05 in the model were maintained. Then, b coefficient of the logistic

equation was used for construction of a weighted risk score; when transformed into odds ratios, the values were rounded to compose the score.

Validation

The preliminary risk score (obtained in the derivation cohort) was applied in the validation cohort, and the following performance statistics were applied: C statistics (area under the receiver operating characteristic [ROC] curve), the chi-square of goodness-of-fit of Hosmer-Lemeshow (HL) and consequently Pearson›s correlation coefficient between the observed events and those predicted by the model.

Values for the area under the ROC curve greater than 0.70 indicate that the model has good discriminatory power. A chi-square of HL with p > 0.05 indicates good calibration of the model. A Pearson correlation coefficient r ≥ 0.7 indicates a strong association between observed and predicted values.

Obtaining the final risk score

After obtaining adequate performance in the validation, both databases (derivation and validation) were combined for the formulation of the final score. The variables were the same as those previously studied to achieve more accurate statistics for the coefficients. Performance statistics were obtained as described above.

In addition to the final score, a logistic model (formula below) was generated, which allows direct estimates of the probability of outcome occurrence. The use of a mathematical model is considered by some authors to be more appropriate for obtaining event estimates since a complex formula would limit the use among physicians. In individuals considered to be at high risk in the additive model, the use of the logistic model is the most adequate in determining the individual occurrence of the clinical outcome.[15]

P (event) = 1 {1 + exp (- ([30 + (31x1 +... + kak))

Data were processed and analyzed using the Statistical Package for the Social Sciences (SPSS), version 22.0.

Ethical considerations

This research project was submitted to the Research Ethics Committee of the ICIFUC (registration number 2345902).

Results

Characteristics

In the total sample (n = 1,054), 272 patients had POAF (25.7%). When considering only myocardial revascularization surgeries (63.8%), the POAF rate was 20.3%. In cases of valve intervention alone (23.9%), the frequency of POAF was 34.3% and, in combined surgeries (7.3%), the highest prevalence was observed – 36.6%.

Mean age of the patients was 60.1 ± 12.1 years old, and 26.6% of the patients were 70 years old or older. Most of the patients (65.2%) were men (Table 1).

POAF was associated with longer hospital stay compoared with patients without POAF (median of 10 days vs. 7 days, respectively, p < 0.05) and increased in-hospital mortality (5.5% vs. 1.0%, respectively; p < 0.001). In addition, with a mean follow-up of five years, we observed higher late mortality rate for patients with POAF compared with those without POAF (6.5% vs 1.4%, respectively, p = 0.002).

Development of the risk model (derivation cohort)

The multivariate analysis of the predictors in the derivation cohort (n = 448) is described in Table 2. Based on their statistical significance, the predictors selected for the construction of the score included age (≥ 70 years), mitral valve disease, the non-use or discontinuation of beta-blocker therapy and a positive water balance greater than 1500 mL.

Points were assigned to each variable according to the odds ratio obtained (Table 2).

The area under the ROC curve of the obtained model was 0.77 (95% confidence interval [CI] 0.73 to 0.81).

Validation of the risk model

External validation was performed in 606 patients of the validation cohort. The risk model had an accuracy of 0.78 (95% CI 0.73 to 0.82) measured by the area under the ROC curve, thus exhibiting a good discriminatory ability. Good correlation was noted between expected and observed POAF: r = 0.99, with chi-square = 1.73 (p = 0.94) (Hosmer-Lemeshow test).

Risk model in the total sample (n = 1,054)

The model was then edited using a combination of the developed score and data from the derivation

Table 1 - Characteristics of the sample and univariate analysis

Variable	Total (n = 1054)	POAF (n = 272)	Non-POAF (n = 782)	RR	95% CI	p
Age ≥ 70 years	281 (26.8%)	141 (41.9%)	167 (21.2%)	2.67	1.99-3.59	< 0.0001
Mean age ± SD	60.1 ± 12.1					
Male	690 (65.2%)	182 (66.9%)	508 (64.6%)	1.1	0.82-1.48	0.507
Type of surgery						
Revascularization	675 (63.8%)	141 (51.8%)	534 (67.9%)	1		
Valve surgery	306 (28.9%)	105 (38.6%)	201 (25.6%)	1.98	1.45-2.70	< 0.001
Combined	77 (7.3%)	26 (9.6%)	51 (6.5%)	1.93	1.11-3.28	0.14
Mitral valve disease	109 (10.3%)	46 (16.9%)	63 (8%)	2.33	1.55-3.51	< 0.001
Absence of beta-blocker	454 (42.9%)	197 (72.4%)	257 (32.7%)	5.40	3.98-7.33	< 0.001
Water balance > 1,500 mL	685 (64.7%)	203 (74.6%)	482 (61.3%)	1.85	1.36-2.52	< 0.001

p-values: Fisher's exact test; POAF: postoperative atrial fibrillation; CI: confidence interval.

Table 2 - Logistic regression and multivariate risk score (derivation – n = 448)

Variable	B	p	RR	95% CI	Points
Age ≥ 70 years	0.96	< 0.001	2.67	1.59-4.48	2
Mitral valve disease	0.77	0.03	2.18	1.08-4.35	1
Absence of beta-blocker	0.91	< 0.001	2.49	1.53-4.03	1.5
Water balance > 1,500 ml	0.5	0.06	1.65	0.96-2.83	0.5
Constant	-2.471	< 0.001	0.08		

and validation cohorts. Using the variables described, multiple logistic regression was performed, resulting in a recalibrated risk score based on the importance of the coefficient β of the logistic equation (Table 3). Variables related to the development of POAF included age (≥ 70 years), mitral valve disease, the non-use or discontinuation of beta-blockers and a positive water balance greater than 1500 mL.

The area under the ROC curve of the obtained model was 0.76 (95% Cl 0.72- 0.79) (Figure 1).

Table 4 and Figure 2 present the risk of POAF according to the score and the classification of this risk (additive score). There was a progressive increase in the proportion of the event, exhibited by an increase in the score: very low risk (score 0) = 0.0%; low risk (score 1 and 2) = 3.9%; intermediate risk (score 3 to 5) = 10.9%; and high risk (score 6 to 8) = 60.0%; p < 0.0001. The logistic equation should be used for risk assessment in the development of POAF individually (Table 3).

In the total sample, 46.8% of the operated patients had low and medium risk. The score predicted POAF in 7.4% of individuals at low risk and 11.7% of those at medium risk; 17% of the total sample was classified as very high risk. To test the calibration of the final score, the observed POAF was compared with that predicted in each of the four classification intervals of the score, resulting in a predicted/observed correlation coefficient of 0.99 with $x^2 = 0.98$ (p = 0.98) (Hosmer-Lemeshow test) (Figure 3).

Table 3 - Logistic regression and multivariable risk scores of the total sample (n = 1,054)					
Variable	B	P	RR	95% CI	Points
Age ≥ 70 years	0.93	< 0.001	2.55	1.84-3.53	2
Mitral valve disease	0.53	0.01	1.70	1.09-2.65	1
Absence of beta-blocker	1.61	< 0.001	5.04	3.67-6.90	4
Water balance > 1,500 ml	0.43	0.01	1.53	1.1-2.15	1
Constant	-2.56	< 0.001	0.07		

*Logistic equation: Prob(POAF) = 1 / (1 + exp (- (-2.56 + [0.93 * age ≥ 70] + [0.53 * mitral valve disease] + [1.61 * non-use and/or discontinuation of beta-blockers] + [0.43 * Water balance > 1500 mL]))).*
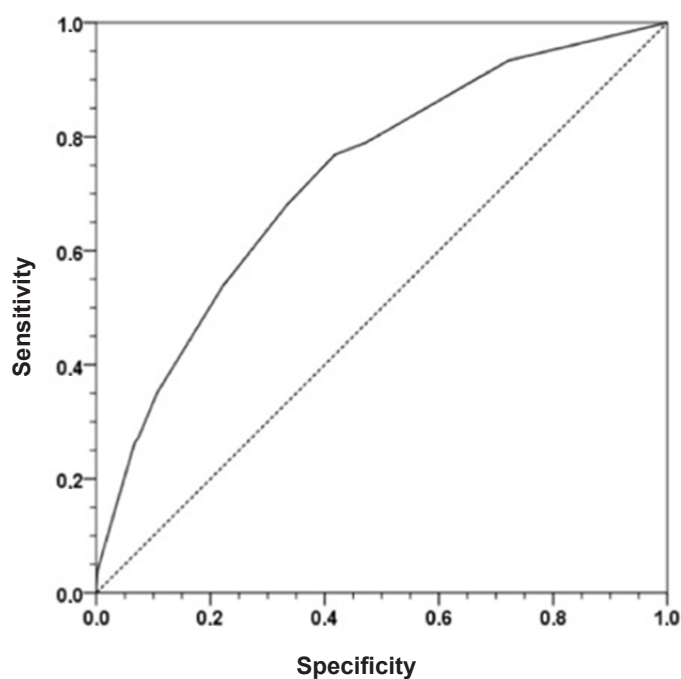
Figure 1 - Area under the ROC curve for the occurrence of postoperative atrial fibrillation: c = 0.76 (95% confidence interval 0.72 - 0.79) in the final model (n = 1,054).

Discussion

Despite advances in surgical techniques and postoperative management, POAF continues to be a very frequent complication. Alhough many factors associated with the occurrence of POAF have been reported, there are few prediction models available.[16-19]

Our study identified four predictors for POAF that comprised: age ≥ 70 years, mitral valve disease, the non-use of beta-blockers in the preoperative period or their discontinuation in the postoperative period and a positive water balance greater than 1,500 mL within 48 hours after the surgery. Thus, an easy-to-apply and clinically useful tool was used to calculate the POAF risk. The selection of the variables was made based on the experience of the department of cardiac surgery of the ICIFUC and available literature.[14,20] When using predictive risk models, we evaluate the possibility of

the risk of occurrence of POAF in a sample rather than individually.[21]

The incidence of POAF in this study was 25.7%, and when only valve surgeries combined with revascularization were considered, this number was 34.3%. This incidence is similar to the means reported in the literature.[3,22,23] It is worth mentioning that we used continuous monitoring only in the period of intensive therapy and after intermittent electrocardiography, which may have underestimated the cases of asymptomatic POAF. Few studies[24,25] used continuous monitoring and reported prevalence rates

of 44% to 64%. Therefore, the literature demonstrates a high prevalence of asymptomatic POAF that is generally greater than 25%, underscoring the need for indetifying factors that contribute to POAF, which was the main objective of this study.

The findings of longer hospitalization and increased early and late mortality associated with the occurrence of postoperative arrhythmia are consistent with the findings reported in the literature that strongly suggest that the prognosis of POAF patients is compromised in the long term.[7,25-27]

Age greater than 70 years was an important predictor of POAF in this study, adding two points to the score. Age as a predictor of POAF was reported to stratify the risk factors associated with arrhythmia.[16,28] Mathew et al.[26] demonstrated that a one-decade increase in age leads to a 75% increase in the risk of developing POAF; the authors also reported that patients older than 70 years were at high risk regardless of other clinical characteristics. Zaman et al.[28] showed that patients over 60 years of age have a 3.8-fold increased risk for development of AF compared with the population under 60 years, and such risk is likely related to atrial dysfunction and fibrosis. These factors are linearly

Table 4 - Risk scores and frequency of postoperative atrial fibrillation (n = 1,054)

Score	Sample (n = 1058)	POAF (n)	POAF (%)	Risk category
0	189	14	7.4	Low
1 and 2	307	36	11.7	Medium
3 to 5	382	181	30.9	High
6 to 8	180	104	57.8	Very high
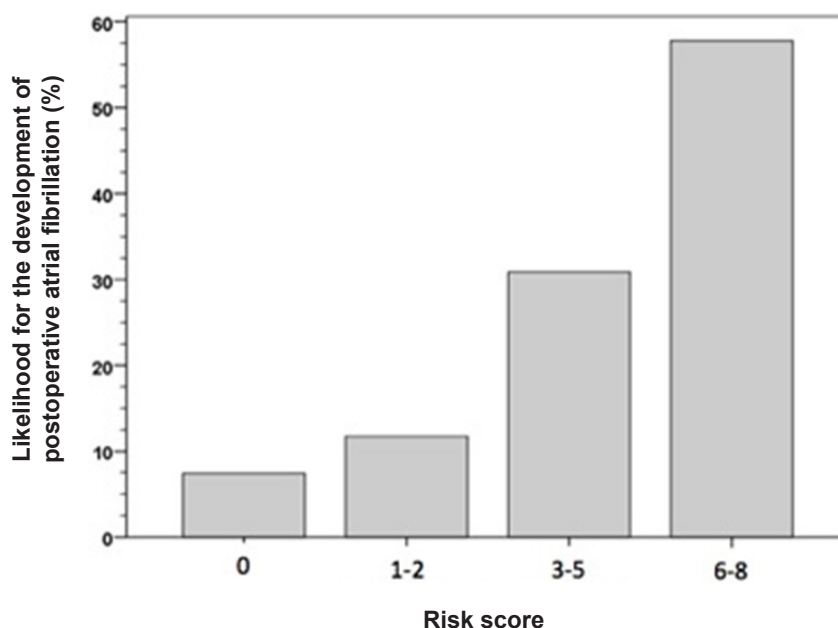
Figure 2 - Increase in the risk (expressed in %) for development of postoperative atrial fibrillation according to the score.
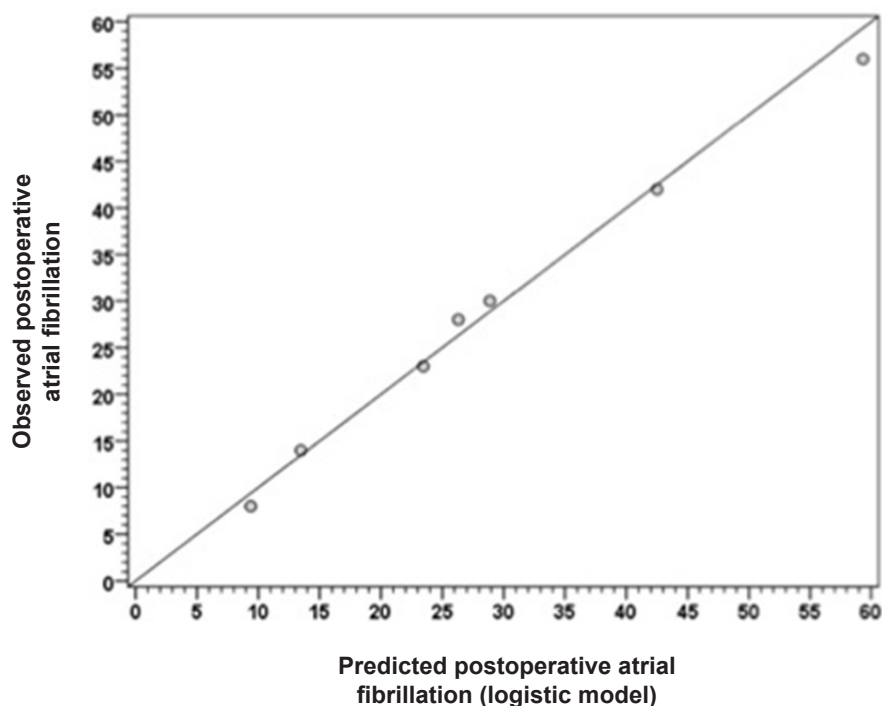
Figure 3 - Dispersion of points representing predicted postoperative atrial fibrillation (POAF) (by logistic model) and observed POAF among the patients (n = 1,054, events = 272 POAF). The Pearson coefficient was r = 0.99 m with x^2 (Hosmer-Lemeshow) = 0.98 (p = 0.986), indicating good performance of the final risk score model.

associated with age and consequently associated with a reduction of atrial electric conduction velocity, generating an arrhythmogenic substrate.[28]

The presence of mitral valve disease was a predictor of POAF in our sample, adding one point to the score, and increasing by 2.3-fold the risk for POAF. This factor alone had not been described by other authors in studies on POAF and differs from the classic association with AF. As a pathophysiological mechanism, stenosis and mitral insufficiency cause atrial dysfunction due to left atrial pressure and volume overload with consequent atrial dysfunction and arrhythmic substrate. We emphasize that pathophysiological changes at the cellular level in valve disease have been poorly described in the literature. In addition, surgical manipulation of the atria may be associated with the development of POAF. The diameter of the left atrium alone was not a predictor of POAF.[14,29]

The absence of beta blockers or their discontinuation in the postoperative period had an important contribution (possibly four points) to the score developed in our study. Previous studies, including meta-analyses, have

described this strong association. In a meta-analysis including 28 studies and 4,074 patients, Crystal et al.,[30] reported an OR of 0.35 (95% CI 0.26-0.49) associated with this finding. Andrews et al.,[31] analyzing 24 studies, reported that patients with ejection fractions greater than 30% were associated with an OR of 0.28 (95% CI 0.21-0.36). The worst clinical scenario would be the non-use of beta-blokers during the pre- and postoperative periods.

The only postoperative factor per se, namely, the presence of a positive water balance greater 1,500 mL in 48 hours after surgery, was a predictor of POAF in our cohort, contributing one point to the score. The mechanism was likely related to atrial dilatation during this critical inflammatory period, which has been described by Kalus et al.[32] High risk scores for the other variables in the preoperative period could guide a restrictive strategy in the management of postoperative hydration if there is no clinical contraindication.

The area under the ROC curve was 0.76 (95% CI 0.72 - 0.79), reflecting the discriminating power of the model. Regarding the calibration, an HL test of r = 0.99, x^2 = 0.98

(p = 0.986) was obtained, indicating good performance of the model. The only POAF prediction score that had a similar discrimination was reported by Mathew et al.,[26] in which an area under the ROC curve of 0.77 was obtained after the definition of 10 pre-, intra- and postoperative predictor variables.[26] Previously reported prediction scores had lower discrimination values compared with our risk score.[11,12,26,33-35] The absence of a perfect discrimination can be explained by the multifactorial origin of the POAF, pathophysiological mechanisms that have not been fully characterized to date, and heterogeneity of heart diseases.

Our risk model was developed and validated in one center, and several studies have suggested that the scores have a lower efficacy when applied in different patients from those used to construct the model. Therefore, external validation is fundamental to determine the clinical relevance of this risk model. However, as with any risk stratification score, this tool should be reassessed in the long term regarding existing variables and incorporation of new variables.

It is important to highlight that, since these results were obtained from a clinical database, caution is needed when extrapolating them to the general population. This is the first clinical predictive score for POAF developed in a Brazilian population.

Conclusion

In summary, we detected four risk variables for the development of POAF during the postoperative period of heart valve surgery and/or revascularization in a Brazilian sample. Using these risk variables, it was possible to construct a score that had a good predictive ability for the outcome occurrence. In addition, this model enables the appropriate classification of patients with a low, medium, high or very high risk of developing POAF.

Author contributions

Conception and design of the research: Ronsoni RM, Leiria TLL, Pires LM, Kruse ML, Pereira E, Silva RG, Lima GG. Acquisition of data: Ronsoni RM, Leiria TLL, Pires LM, Kruse ML, Pereira E, Silva RG, Lima GG. Analysis and interpretation of the data: Ronsoni RM, Leiria TLL, Pires LM, Kruse ML, Pereira E, Silva RG, Lima GG. Statistical analysis: Ronsoni RM, Leiria TLL, Pires LM, Kruse ML, Pereira E, Silva RG, Lima GG. Obtaining financing: Ronsoni RM, Leiria TLL, Pires LM, Kruse ML, Pereira E, Silva RG, Lima GG. Writing of the manuscript: Ronsoni RM, Leiria TLL, Pires LM, Kruse ML, Pereira E, Silva RG, Lima GG. Critical revision of the manuscript for intellectual content: Ronsoni RM, Leiria TLL, Pires LM, Kruse ML, Pereira E, Silva RG, Lima GG.

References

1. Villareal RP, Hariharan R, Liu BC, Kar B, Lee VV, Elayda M, et al. Postoperative atrial fibrillation and mortality after coronary artery bypass surgery. J Am Coll Cardiol. 2004;43(5):742–8.

2. Mariscalco G, Engström KG. Atrial fibrillation after cardiac surgery: Risk factors and their temporal relationship in prophylactic drug strategy decision. Int J Cardiol. 2008;129(3):354–62.

3. Echahidi N, Pibarot P, O'Hara G, Mathieu P. Mechanisms, Prevention, and Treatment of Atrial Fibrillation After Cardiac Surgery. J Am Coll Cardiol. 2008;51(8):793-801.

4. Aranki SF, Shaw DP, Adams DH, Rizzo RJ, Couper GS, VanderVliet M, et al. Predictors of Atrial Fibrillation After Coronary Artery Surgery. Circulation. 1996;94(3):39-46.

5. Creswell LL, Schuessler RB, Rosenbloom M, Cox JL. Hazards of postoperative atrial arrhythmias. Ann Thorac Surg. 1993;56(3):539–49.

6. Hogue CW, Creswell LL, Gutterman DD, Fleisher LA. American College of Chest Physicians. Epidemiology, mechanisms, and risks: American College of Chest Physicians guidelines for the prevention and management of postoperative atrial fibrillation after cardiac surgery. Chest. 2005;128(2):9S–16S.

7. Almassi GH, Schowalter T, Nicolosi AC, Aggarwal A, Moritz TE, Henderson WG, et al. Atrial fibrillation after cardiac surgery: a major morbid event? Ann Surg. 1997;226(4):501-11.

8. Wann LS, Curtis AB, January CT, Ellenbogen KA, Lowe JE, Estes NA. 2011 ACCF/AHA/HRS Focused Update on the Management of Patients With Atrial Fibrillation (Updating the 2006 Guideline) A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation. 2011;123(1):104–23.

9. Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B, et al. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Eur Heart J. 2016;37(38):2893-962.

10. Macle L, Cairns J, Leblanc K, Tsang T, Skanes A, Cox JL, et al. 2016 Focused Update of the Canadian Cardiovascular Society Guidelines for the Management of Atrial Fibrillation. Can J Cardiol. 2016;32(10):1170–85.

11. Amar D, Shi W, Hogue CW, Zhang H, Passman RS, Thomas B, et al. Clinical prediction rule for atrial fibrillation after coronary artery bypass grafting. J Am Coll Cardiol. 2004;44(6):1248–53.

12. Magee MJ, Herbert MA, Dewey TM, Edgerton JR, Ryan WH, Prince S, et al. Atrial fibrillation after coronary artery bypass grafting surgery: development of a predictive risk algorithm. Ann Thorac Surg. 2007;83(5):1707–12.

13. Gillinov AM, Bagiella E, Moskowitz AJ, Raiten JM, Groh MA, Bowdish ME, et al. Rate Control versus Rhythm Control for Atrial Fibrillation after Cardiac Surgery. N Engl J Med. 2016;374(20):1911–21.

14. Silva RG da, Lima GG de, Guerra N, Bigolin AV, Petersen LC. Risk index proposal to predict atrial fibrillation after cardiac surgery. Rev Bras Cir Cardiovasc. 2010;25(2):183–9.

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

16. Mathew JP, Parks R, Savino JS, Friedman AS, Koch C, Mangano DT, et al. Atrial fibrillation following coronary artery bypass graft surgery: predictors, outcomes, and resource utilization. MultiCenter Study of Perioperative Ischemia Research Group. JAMA. 1996;276(4):300–6.

17. Echahidi N, Mohty D, Pibarot P, Després J-P, O'Hara G, Champagne J, et al. Obesity and metabolic syndrome are independent risk factors for atrial fibrillation after coronary artery bypass graft surgery. Circulation. 2007;116(11):I213-9.

18. Osranek M, Fatema K, Qaddoura F, Al-Saileek A, Barnes ME, Bailey KR, et al. Left atrial volume predicts the risk of atrial fibrillation after cardiac surgery: a prospective study. J Am Coll Cardiol. 2006;48(4):779–86.

19. Sabzi F, Zokaei AH, Moloudi AR. Predictors of atrial fibrillation following coronary artery bypass grafting. Clin Med Insights Cardiol. 2011 Jul;5:67–75.

20. Silva RG Da, Lima GG De, Laranjeira A, Costa AR Da, Pereira E, Rodrigues R. Fatores de risco e morbimortalidade associados à fibrilação atrial no pós-operatório de cirurgia cardíaca. Arq Bras Cardiol. 2004;83(2):99-104.

21. Shahian DM, Blackstone EH, Edwards FH, Grover FL, Grunkemeier GL, Naftel DC, et al. Cardiac surgery risk models: a position article. Ann Thorac Surg. 2004;78(5):1868–77.

22. Maisel WH, Rawn JD, Stevenson WG. Atrial Fibrillation after Cardiac Surgery. Ann Intern Med. 2001;135(12):1061-73

23. Nazeri A, Razavi M, Elayda MA, Lee V-V, Massumi A, Wilson JM, et al. Race/ethnicity and the incidence of new-onset atrial fibrillation after isolated coronary artery bypass surgery. Hear Rhythm. 2010;7(10):1458–63.

24. Siebert J. Atrial fibrillation after coronary artery bypass grafting without cardiopulmonary bypass. Eur J Cardio-Thoracic Surg. 2000;17(5):520–3.

25. Helgadottir S, Sigurdsson MI, Ingvarsdottir IL, Amar DO, Gudbjartsson T. Atrial fibrillation following cardiac surgery: risk analysis and long-term survival. J Cardiothorac Surg. 2012;7(1):87–93.

26. Mathew JP, Fontes ML, Tudor IC, Ramsay J, Duke P, Mazer CD, et al. A multicenter risk index for atrial fibrillation after cardiac surgery. JAMA. 2004;291(14):1720–9.

27. El-Chami MF, Kilgo P, Thourani V, Lattouf OM, Delurgio DB, Guyton RA, et al. New-Onset Atrial Fibrillation Predicts Long-Term Mortality After Coronary Artery Bypass Graft. J Am Coll Cardiol. 2010;55(13):1370–6.

28. Zaman AG, Archbold RA, Helft G, Paul EA, Curzen NP, Mills PG. Atrial fibrillation after coronary artery bypass surgery: a model for preoperative risk stratification. Circulation. 2000;101(12):1403–8.

29. Magalhães L, Figueiredo M, Cintra F, Saad E, Kuniyoshi R, Teixeira R, et al. II Diretrizes Brasileiras de Fibrilação Atrial. Arq Bras Cardiol. 2016;106(4):1-16

30. Crystal E, Garfinkle MS, Connolly SS, Ginger TT, Sleik K, Yusuf SS. Interventions for preventing post-operative atrial fibrillation in patients undergoing heart surgery. Crystal E. Cochrane Database Syst Rev. 2013 Jan;(1):CD003611.

31. Andrews TC, Reimold SC, Berlin JA, Antman EM. Prevention of supraventricular arrhythmias after coronary artery bypass surgery. A meta-analysis of randomized control trials. Circulation. 1991;84(5):III236-44.

32. Kalus JS, Caron MF, White CM, Mather JF, Gallagher R, Boden WE, et al. Impact of fluid balance on incidence of atrial fibrillation after cardiothoracic surgery. Am J Cardiol. 2004;94(11):1423–5.

33. Thorén E, Hellgren L, Jidéus L, Ståhle E. Prediction of postoperative atrial fibrillation in a large coronary artery bypass grafting cohort. Interact Cardiovasc Thorac Surg. 2012;14(5):588–93.

34. Mariscalco G, Biancari F, Zanobini M, Cottini M, Piffaretti G, Saccocci M, et al. Bedside tool for predicting the risk of postoperative atrial fibrillation after cardiac surgery: the POAF score. J Am Heart Assoc. 2014;3(2):1–9.

35. Tran D, Perry J, Jean D, Elmestekawy E, Wells GA. Predicting New-Onset Postoperative Atrial Fibrillation in Cardiac Surgery Patients. J Cardiothorac Vasc Anesth. 2015;29(5):1117–26.

ORIGINAL ARTICLE

Factors Associated to the Knowledge of Cardiac Arrest by Health Professionals

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Abstract

Background: Knowledge of cardiac arrest by health professionals is associated with sociodemographic, occupational and training characteristics.

Objectives: To evaluate the factors associated with the knowledge of health professionals on Cardiac Arrest.

Methods: A cross-sectional study conducted in a large public hospital in the countryside of Bahia - Brazil. The sample consisted of 18 doctors, 32 nurses and 50 nursing technicians. To evaluate the knowledge of the professionals, a questionnaire was constructed according to the current guidelines for resuscitation of the American Heart Association of 2015, and after that, it was submitted to three judges with expertise in PCR to verify content validity. Data were analyzed through descriptive statistics with univariate, bivariate and multivariate analyses using the logistic regression model. A value of p < 0.05 was adopted as level of significance.

Results: The prevalence of insufficient knowledge of cardiac arrest among health professionals was 78%. After logistic regression, belonging to the professional category of nursing technician (p = 0.003) and nurse (p = 0.001) and working in the form of on-call duty for 24h (p = 0.005) was associated to insufficient knowledge.

Conclusions: Insufficient knowledge of cardiac arrest among health professionals is high, which is a problem that requires urgent interventions in order to guarantee the quality of care. These actions should be based on realistic scenarios involving theoretical and practical activities. The periodicity of training should be short, given the deterioration of knowledge. The creation and validation of the data collection instrument allows for its applicability in other studies. (Int J Cardiovasc Sci. 2020; 33(2):167-174)

Keywords: Heart Failure; Heart Arrest; Cardiopulmonary Ressuscitation; Health Personnel; Mortality & Morbidity; Nurses.

Introduction

Cardiac arrest (CA) is a serious life-threatening emergency situation. Among all life-threatening emergencies, this is considered the most fearsome, since the chance of the victim surviving is directly related to fast, safe and effective care.[1]

According to the Brazilian Society of Cardiology, 200,000 cardiac arrests occur annually in Brazil, and approximately half of these occur in a hospital environment.[2]

CA is a situation that requires immediate and rapid action by health professionals, since it involves risk to the patient, given that the chance of survival after the event ranges from 2% to 49%, depending on the initial heart rate and early initiation of resuscitation.[3] However, survival may double or triple when cardiopulmonary resuscitation (CPR) is performed with high quality.[4]

The high morbidity and mortality rate caused by CPR, as well as the risk of imminent death and the high chances of disability that this event can cause, support the conduction of a survey of the knowledge among health professionals on this topic, since this knowledge can be related to several characteristics, such as sociodemographic, occupational and professional training, even with the presence of guidelines and protocols for CPR.

The aim of this study is to evaluate the factors associated with the knowledge of Cardiac Arrest by health professionals in a general hospital in the countryside of Bahia - Brazil, as well as to estimate the prevalence of health professionals' knowledge of CPR.

Methods

This is a cross-sectional study performed in a large public hospital with a partnership with the Unified Health System, located in the municipality of Feira de Santana, in the countryside of Bahia.

The sample of this study consisted of 100 participants, of which 18 were doctors, 32 nurses and 50 nursing technicians who worked in the Medical Clinic, Surgical Clinic, Orthopedic Clinic, Semi-Intensive Care, Adult Intensive Care Units, and Units constituting the Emergency section.

Sampling was conducted by accessibility considering the following inclusion criteria: having worked as a physician, nurse or nursing technician of the aforementioned units; having been involved in the procedures related to cardiac arrest in the last 12 months. Exclusion criteria were: doctors, nurses or nursing technicians who were on medical leave, vacation or certified by the time of data collection.

The data collection instrument was divided into four blocks: sociodemographic, occupational, training characteristics and the specific block to evaluate knowledge of CA/CPR, named *Questionário de Conhecimento sobre Parada Cardiorrespiratória e Ressuscitação Cardiopulmonar* (Knowledge of Cardiac Arrest and Cardiopulmonary Ressucitation Questionnaire – KCACPRQ). It was created according to a literature review and the American Heart Association guidelines of 2015.[5] In order to evaluate the content validity of the first version, the KCACPRQ was subjected to evaluation by three judges, a nurse, a doctor and a nursing technician, with expertise in Cardiac Arrest and Cardiopulmonary Resuscitation as instructors of Advanced Cardiovascular Life Support (ACLS). These experts assessed the criteria clarity, relevance, content and feedback for each of the CA/CPR questions, and also provided comments and suggestions that qualified the instrument. The judges were allowed, at the time of assessment, to consult the new AHA –2015 guidelines in order to clarify any doubts.

After the assessment, approval and meeting the modifications suggested by the group of judges, the final version of the questionnaire with 20 items was elaborated, with five response options, with only one of these being considered correct.

Before the actual collection, a pre-test was carried out with a professional from each category in order to detect a potential need for modifications of the questionnaire, and data collection then began. Data collection took place between January and February 2018, after approval by the Research Ethics Committee.

In order to verify the ease with which participants responded to the KCACPRQ, the feasibility of the questionnaire was assessed.[6] For this purpose, at the end of each application respondents positioned themselves in an instrument that used as parameters: the level of easiness to understand the instructions of the questionnaire, to understand the questions/items and to indicate the answers.

Participants were approached in the workplace and when they accepted to participate, they answered individually to the questionnaire, without the aid of electronic devices or consultation material.

To estimate the professionals' knowledge of CA and CPR, the KCACPRQ generated a percentage from 0 to 100%, since each correctly answered question corresponds to a 5% success rate. The AHA conducts ACLS courses in which the student, in addition to performing well in the practical test, must obtain a minimum score in the written test. In order for the student to obtain a certificate at the end of the test, the AHA establishes a minimum criterion of correctness of 84% in theoretical test.[5] In this study, 85% was adopted as the cut-off point, so the participant who scored 85% or better was classified as having sufficient knowledge. For those who scored below 85%, these were classified as having insufficient knowledge.

The research protocol was evaluated and approved by the Research Ethics Committee of the *Universidade Estadual de Feira de Santana* (CAAE: 78645817.2.0000.0053). The participants of the study had autonomy to agree to participate or not, after signing the Term of Free and Informed Consent, which clarified their rights. In addition, the ethical standards of the Declaration of Helsinki of 1975, revised in 2008, were followed, as well as those of Resolution 466/2012.

Statistical analysis

The data were analyzed through univariate, bivariate and multivariate analyses. In the univariate analysis, the absolute and relative frequencies of each categorical variable were estimated. For the quantitative variables,

the descriptive measures of centrality and dispersion were calculated.

In bivariate analysis, the prevalence ratios with their respective confidence intervals, at the 95% level, were estimated for the crossing between level of knowledge and the other variables related to sociodemographic characteristics, occupational characteristics and health professional's training characteristics on CA. To perform these two analyses, the application software Statistical Package for the Social Sciences version 22.0 was used.

Pearson's Chi-square test (X^2) or Fisher's exact test was used in the selection of variables for this multivariate analysis. The level of significance for entry in the multivariate model was $p \leq 0.10$.

To verify the factors associated with health professionals' knowledge, the multivariate logistic regression model was used, one of the most important tools in the statistical analysis of data when one intends to predict the occurrence of a given event as a function of a set of variables. Applying the logistic regression model is a form of statistical modeling suitable for categorical and usually dichotomous response variables.[7]

The dependent or response variable was the knowledge of professionals and the independent variables were sociodemographic, occupational and training variables that were included in the model. For purposes of analysis, the continuous variables that entered the model were recategorized based on the theoretical framework.

After defining the final multivariate model, the results obtained in Odds Ratio were converted to Prevalence Ratio using Poisson's Regression. After adjustment of the model with the "maximum likelihood" estimator, the significance of the model variables was evaluated through Wald's Test. In order to evaluate the accuracy and goodness-of-fit of the logistic model, the Hosmer-Lemeshow[7] test was used. The level of statistical significance adopted was 5%. For this analysis, the application software Data Analysis and Statistical Software version 12.0 was used.

Results

Construction and evaluation of content validity of the KCACPRQ

The questionnaire submitted for evaluation of the judges presented 22 questions on Cardiac Arrest and Cardiopulmonary Resuscitation. The judges pointed out that eight of these questions lacked clarity, which required changes to achieve comprehensibility. The content was considered adequate in 21 questions, and only one item was considered inadequate. The pertinence of the items in their respective categories was considered adequate by the judges. The analysis of the feedback of the questions resulted in seven items with divergent templates, and changes were made to meet this criterion.

The judges pointed out two items with confusing formulations and with content contemplated in other items, and as such, they were withdrawn from the instrument in order not to harm the knowledge determination of the participating professionals. Ten items had changed the wording of the statement and the organization of the alternatives. Thus, the final version of the questionnaire has 20 questions about cardiac arrest and cardiopulmonary resuscitation (Chart 1).

The pre-test showed that the professionals answered the instrument without difficulties and considered the instrument adequate. Regarding the practicality of the instrument, Table 1 presents its main results.

Profile of health professionals

The study included 100 health professionals, of whom 50% were nursing technicians, 32% as nurses and 18% as doctors. Among the professionals, it was observed that 78% were women. Approximately half, 50.5%, were over 35 years of age. The most prevalent self-reported skin color was black or brown (72%). With regard to schooling, 34% had a graduate degree. The most mentioned marital status was not having a partner (52%). More than half (57%) reported having children.

Regarding occupational characteristics, the majority (83%) of professionals worked in closed units. The most prevalent work time was over 05 years (76.8%). A large proportion (61.6%) of the professionals worked full time. About 56.6% of the participants reported a different employment relationship. The most prevalent work shift was the on-call duty (68%). With regard to the working day, 37.9% worked with a weekly workload between 30 and 40 hours.

Regarding training characteristics, the majority (59%) of professionals had up to 10 years of training. Regarding training in CA/CPR, 80.8% of the professionals reported having received it. Training in CA/CPR at work was reported by 57.6% of participants. The time interval that received training in the most frequent CA/PCR was 06 months ago (44.9%). Regarding the time of contact with CA/CPR, the majority (69.2%) reported it as being

Chart 1 - Items of the *Questionário de conhecimento sobre parada cardiorrespiratória e ressuscitação cardiopulmonar* categorized by area of knowledge	
Category	**Question**
CA diagnosis 02 items	1. Which pulse should be checked for the initial evaluation of the patient? 2. How much time should be used to check pulse and breath at the same time?
Ventilation 04 items	4. What is the compression-ventilation relationship with the patient that has CA but has not yet been intubated? 5. What is the compression-ventilation relationship with the CA patient who was intubated? 12. How should the patient be ventilated in CA if it is connected to the mechanical ventilator? 13. What is the oxygen flow for patient ventilation when in CA?
External thoracic compression 05 items	6. With which frequency are External Thoracic Compressions done after intubation? 7. What should be the depth of the External Cardiac Compressions? 16. It is a characteristic of the quality of External Thoracic Compression: 17. Regarding the return of the chest after the External Thoracic Compression: 18. How and what should be the support site for the health professional's hands on the patient's chest in order to perform External Thoracic Compressions?
Defibrillation 05 items	3. What is the recommended course of initial care in the case of CA for Non-Pulse Ventricular Tachycardia? 8. What are CA rhythms that should be treated with defibrillation? 9. What are CA rhythms that should NOT be treated with defibrillation? 10. What is the maximum energy load used in the Single Phase and Biphasic Defibrillator for "shockable" CA rates, respectively? 15. After defibrillation, what should be the next step?
Medications 04 items	11. What is the dose and frequency of Adrenalin administration in CA? 14. How should medications be prepared and administered during CA? 19. Which drug is used at all CA rates? 20. When indicated, which doses of Amiodarone for the first and second administrations, respectively?

between 0 and 30 days. The most reported mean CA/PCR service was between 0 and 2 CA/PCR per month (44.7%). Regarding the perception of personal security when assisting, 79.8% reported feeling safe to perform care in CA/CPR.

Prevalence of knowledge of Cardiac Arrest and Cardiopulmonary Resuscitation among health professionals

Table 2 presents the prevalence of this study's outcome, considering an 85% criterion, according to the American Heart Association.

A total of 78% of health professionals presented insufficient knowledge about Cardiac Arrest and Cardiopulmonary Resuscitation. Only 22% of the participants presented sufficient knowledge.

Factors associated with the knowledge of cardiac arrest and cardiopulmonary resuscitation by health professionals

After analyzing the level of knowledge and other variables, the following ten variables were added to the final model for multivariate analysis[7]: female sex (p = 0.015), technical level of education (p = 0.045), professional category as nurse (p = 0.000) and nursing technician (p = 0.000), had another job (p = 0.083), worked under on-call duty (p = 0.009), weekly workload above 40 hours (p = 0.003), receiving CA/CPR training for over 12 months (p = 0.048), time of contact with CA/CPR over 30 days (p = 0.046) and not having personal safety in performing CA/CPR (p = 0.037). The results of the logistic regression are shown in Table 3.

Diagnostic analysis of the final model was performed using the Hosmer-Lemeshow test, which revealed

Table 1 - Practicability assessment - Knowledge questionnaire on cardiac arrest and cardiopulmonary resuscitation

Practicability assessment	n	%
I found it easy to understand the instructions of the questionnaire (n = 100)		
Strongly agree	50	50.0
Slightly agree	33	33.0
I have no opinion about it	4	4.0
Slightly disagree	11	11.0
Strongly disagree	2	2.0
I found it easy to understand the questions in the questionnaire (n = 99)		
Strongly agree	49	49.5
Slightly agree	34	34.3
I have no opinion about it	3	3.0
Slightly disagree	11	11.1
Strongly disagree	2	2.0
I found it easy to mark the answers of the questionnaire (n = 99)		
Strongly agree	55	55.6
Slightly agree	29	29.3
I have no opinion about it	0	0.0
Slightly disagree	12	12.1
Strongly disagree	3	3.0

Table 2 - Prevalence of knowledge of Cardiac Arrest and Cardiopulmonary Resuscitation among health professionals

Knowledge of Cardiopulmonary Arrest and Cardiopulmonary Resuscitation by Health Professionals (n = 100)	n	%
Sufficient	22	22
Insufficient	78	78

Table 3 - Multivariate analysis of logistic regression type for Insufficient Knowledge of Cardiac Arrest[7]

Variable	Prevalence ratio	CI (95%)	p-value
Professional category (n = 100)			
Doctor	*		
Nurse	3.21	1.591 – 6.847	0.001
Nursing technician	2.98	1.470 – 6.426	0.003
Work shift (n = 100)			
Day and night service	*		
On-call duty	3.05	0.630 – 0.904	0.005

p = 0.73, demonstrating the goodness-of-fit of the final model.

Discussion

Developing and validating a data collection instrument based on the methodological aspects that guide this elaboration[8] constituted a primordial phase to ensure the correct measurement of the outcome variable. The development of the questionnaire focused on central issues related to the topic and, above all, it was focused on the main changes of the 2015 AHA guidelines. By validating the content of the instrument with judges and the participants themselves, while taking into account the indicators of clarity and pertinence, it was possible to achieve the necessary adequacy of the instrument in capturing what it proposes to measure,[8] in this case the knowledge of professionals on a specific topic. In addition, considering the dimensionality of the instrument, it can help professionals to identify the knowledge gaps, providing support for actions directed to fragility points that can be developed.

The evaluation of knowledge about CA/CPR among medical, nursing, and life sciences undergraduate students, among others, has been the subject of scientific publications and, at the same time, reveals the insufficiency of knowledge in this area, corroborating with the results found in this study.[9–13]

This is an important finding, since knowledge is considered the triggering factor for decision-making and behavior, essential to guarantee the subsidies of the conducted procedures in order to maintain the victim's life.[14–15] Thus, the knowledge the professional possesses is a determinant factor in the survival of patients who are afflicted by CA.[10,16]

The high prevalence of insufficient knowledge about cardiac arrest can be explained by several factors. The actions of permanent education in health in these services, and even the search for qualification courses can be considered as part of the process of training these professionals in their respective studies. A study among undergraduates in health sciences showed that 99.9% of the participants did not reach the 84% minimum score recommended by the American Heart Association, characterizing insufficient knowledge about the subject of Basic Life Support.[13]

During the training of nurses, the theoretical and practical contents on CA/CPR have been worked in a very limited and superficial way, and in most cases do not meet the needs of students.[16] Nursing professionals are often subjected to grueling workloads, as well as low salaries and double work hours. These facts contribute to the reduction of time dedicated to improvement and search for knowledge. Organizational aspects of the work may influence the participation of nurses in training, drawing attention to the absence of time allocated for this purpose, little financial resources, and shiftwork.[17]

One study showed that only 6% of nursing undergraduate students in a pre-test achieved at least the minimum score for resuscitation. However, after the training course, the percentage of approvals increased to 72%.[18] Another study conducted among nursing undergraduate students in Brazil also presented similar results, in which approximately 20% of the students knew the correct conduct after the detection of CA.[19] This fact brings important information: even during undergraduate studies, the students have low knowledge on this topic, evidencing the fragility of their education. However, it demonstrates the effectiveness of the training program.

In an international context, a recent study carried out in a tertiary hospital in Tanzania showed poor performance of health professionals in theoretical and practical tests (only 4% scored higher than 75% in the theoretical test).[20] The multiprofessional team is responsible for the first service in CA cases, hence why in many cases, training for the recognition and initial care of this situation is necessary. As a potential strategy, the deployment of Rapid Response Teams to act in emergencies and actions of permanent education can be effective.[21]

A study carried out in a hospital with 750 beds in India showed the impact of training in CPR with respect to the return to spontaneous circulation and living hospital discharge among the studied patients. The study showed that return to spontaneous circulation increased from 19.7% to 30.1% after the team training, and hospital discharge alive rates rose from 27.5% up to 52.9%.[22]

Poor knowledge of professionals requires constant updating of CA protocols. Although there is interest on the part of professionals to undertake improvement courses in this area, some barriers are still found, such as the lack of initiative of managers or employers in order to guarantee resources, spaces and incentive.[23]

This study presents some limitations that should be considered. Among them, we highlight a convenience sample, not allowing the generalization of the results found. Selection bias may have occurred, since the participation of the professionals happened through their availability for acceptance, in addition to the TCLE signature having a certain identification, making professionals feel less comfortable to respond, leading to refusal to participate in this study. Moreover, it was not possible to evaluate the practical ability of professionals in this stage of the study.

Conclusions

The current prevalence of insufficient knowledge about cardiorespiratory arrest among the health professionals studied is high, a serious problem that requires urgent interventions in order to guarantee the quality of care during cardiopulmonary resuscitation. These actions should be based on realistic scenarios, involving theoretical and practical activities, using active teaching methodology in order to obtain a good result in the teaching-learning process. The periodicity of training should be short, given the deterioration of knowledge and new evidence that may arise with respect to actions related to cardiopulmonary resuscitation.

These results can subsidize permanent health education teams of hospitals and non-hospital institutions, as well as technical training schools and universities, especially in nursing degrees and technical nursing courses.

The creation and validation of the data collection instrument allows for its applicability in other studies, in addition to being able to be used in non-hospital units that attend severe patients with imminent cardiac arrest, and educational institutions could similarly evaluate the students' knowledge about the subject.

Author contributions

Conception and design of the research: Novaes Neto EM, Freitas KS. Acquisition of data: Novaes Neto EM. Analysis and interpretation of the data: Novaes Neto EM, Freitas KS. Statistical analysis: Novaes Neto EM, Freitas KS. Writing of the manuscript: Novaes Neto EM, Freitas KS. Critical revision of the manuscript for intellectual content: Novaes Neto EM, Freitas KS.

Potential Conflict of Interest

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

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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 Estadual de Feira de Santana* under the protocol number 7864.5817.2.0000.0053. 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. Alves CA, Barbosa CNS, Faria HTG. Parada Cardiorrespiratória e Enfermagem: o conhecimento acerca do suporte básico de vida. Cogitare Enferm. [Internet] 2013; 18(2): 296-301 [acesso em 02 fev 2018]. Disponível: http://revistas.ufpr.br/cogitare/article/view/32579/20693

2. Gonzalez MM, Timerman S, Gianotto-Oliveira R, Polastri TF, Canesin MF, Schimidt A, et al. I diretriz de ressuscitação cardiopulmonar e cuidados cardiovasculares de emergência da Sociedade Brasileira de Cardiologia: resumo executivo. Arq. Bras. Cardiol. [Internet] 2013; 100(2): 105-113 [acesso em 27 dez 2017]. Disponível: http://publicacoes.cardiol.br/consenso/2013/Diretriz_Emergencia.pdf

3. Horsted T, Rasmussen LS, Meyhoff CS, Nielsen SL. Long-term prognosis after out-of hospital cardiacarrest. J. Resuscitation. [Internet] 2007; 72(2) [acesso em 20 jan 2018]. Disponível: http://www.resuscitationjournal.com/article/S0300-9572(06)00344-3/pdf

4. Dalri MCB, Araújo IEM, Silveira RCCP, Canini SRMS, Cyrillo RMZ. Novas diretrizes da ressuscitação cardiopulmonar. Rev. Latino-Am. Enfermagem. [Internet] 2008; 16(6) [acesso em 15 fev 2018]. Disponível: http://dx.doi.org/10.1590/S0104- 11692008000600020.

5. AMERICAN HEART ASSOCIATION (AHA). Destaques das Diretrizes da American Heart Association 2015: Atualização da Diretrizes de RCP e ACE. Guidelines 2015/ CPR & ECC. 2015. 36p.

6. Coluci MZO, Alexandre NMC. Development of a questionnaire to evaluate the usability of assessment instruments. Rev Enf UERJ. 2009;17(3):378-82.

7. Corrar LJ, Paulo E, Dias J M. Análise multivariada. 6a.ed. São Paulo: Atlas; 2007.

8. Alexandre NMC, Colluci MZO. Construção de instrumentos de medidas na área de saúde. Ciência Saúde Coletiva. 2015;20(3):925-36.

9. Guedes RSML. Avaliação do conhecimento de residentes em enfermagem e medicina acerca da parada e reanimação cardiorrespiratória [dissertação]. Pernambuco: Universidade Federal de Pernambuco; 2014.

10. Lima SG, Macedo LA, Vidal ML, Sá MPBO. Educação permanente em SBV e SAV: impacto no conhecimento dos profissionais de enfermagem. Arq. Bras. Cardiol. [Internet] 2009; 93(6) [acesso em 05 jan 2018]. Disponível: http://dx.doi.org/10.1590/S0066- 782X2009001200012.

11. Almeida AO, Araújo IE, Dalri MCB, Araujo S. Conhecimento teórico dos enfermeiros sobre parada e ressuscitação cardiopulmonar, em unidades não hospitalares de atendimento à urgência e emergência. Rev. Latino-Am. Enfermagem. [Internet] 2011; 19(2) [acesso em 18 jun 2012]. Disponível: http://www.scielo.br/pdf/rlae/v19n2/pt_06.pdf

12. Filgueiras Filho NM, Bandeira AC, Delmondes T, Oliveira A, Lima Jr AS, Cruz V, et al. Avaliação do conhecimento geral de médicos emergencistas de hospitais de Salvador – Bahia sobre o atendimento de vítimas com parada cardiorrespiratória. Arq Bras Cardiol. 2006;87(5):634-40.

13. Tavares LFB, Bezerra IMP, Oliveira RF, Sousa LVA, Raimundo RD, Sousa EC, et al. Conhecimento de estudantes de graduação em ciências da saúde em testes objetivos sobre suporte básico de vida. J Human Growth Develop. 2015; 25(3): 297-306.

14. Vieira LJES, Carneiro RCMM, Frota MA, Gomes ALA, XimenesLB. Actions and possibilities of accidents prevention with children in daycare at Fortaleza, Ceara State. CiencSaude Coletiva. [Internet] 2009; 14(5): 1687-1697 [acesso em 30 jan 2018]. Disponível em: http://dx.doi.org/10.1590/S1413-81232009000500010

15. Vieira JE, Tamousauskas MRG. Avaliação das resistências de docentes a propostas de renovações em currículos de graduação em medicina. Rev Bras Educ Med. 2013; 37(1):32-8.

16. Bellan MC, Araújo IEM, Araújo S. Capacitação teórica do enfermeiro para o atendimento da parada cardiorrespiratória. Rev. Bras. Enferm. [Internet] 2010; 63(6) [acesso em 10 jun 2012]. Disponível: http:// dx.doi.org/10.1590/S0034-71672010000600023

17. Santana N, Fernandes JD. O processo de capacitação profissional do enfermeiro intensivista. Rev Bras Enferm. 2008; 61(6): 809-15.

18. Madden C. Undergraduate nursing students' acquisition and retention of CPR knowledge and skills. Nurse Educ Today. 2006; 26(3): 218-27.

19. Oliveira SS, Santos JO, Zeitoun SS. Suporte Básico de Vida: avaliação do conhecimento dos graduandos de enfermagem. J Health Sci Inst. 2014; 32(1): 53-8.

20. Kaihula WT, Sawe HR, Runyon MS, Murray BL. Assessment of cardiopulmonary resuscitation knowledge and skills among healthcare providers at an urban tertiary referral hospital in Tanzania. BMC Health Serv Res. 2018; 18:935.

21. Veiga VC, Carvalho JC, Amaya LEC, Gentile JKA, Rojas SSO. Atuação do Time de Resposta Rápida no processo educativo de atendimento da parada cardiorrespiratória. Rev Bras Clin Med. 2013; 11(3): 258-62.

22. Pareek M, Parmar V, Badheka J, Lodh N. Study of the impact of training of registered nurses in cardiopulmonary resuscitation in a tertiary care centre on patient mortality. Indian J Anaesth. 2018;62(5):381-4.

23. Torquato IM, Menezes ABR, Nogueira MF, Trigueiro JVS, Albuquerque AM, Ferreira JA. Conhecimento da equipe de enfermagem acerca da assistência em reanimação cardiopulmonar. J Nurs UFPE on line. [Internet] 2012; 6(12): 2874-2883 [acesso em 28 jan 2018] Disponível em: http://10.5205/reuol.2265-25464-1-LE.0612201202 ISSN: 1981-8963

ORIGINAL ARTICLE

Predictors of Post-Discharge 30-Day Hospital Readmission in Decompensated Heart Failure Patients

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Abstract

Background: Heart failure (HF) is worldwide known as a public health issue with high morbimortality. One of the issues related to the evolution of HF is the high rate of hospital readmission caused by decompensation of the clinical condition, with high costs and worsening of ventricular function.

Objective: To quantify the readmission rate and identify the predictors of rehospitalization in patients with acute decompensated heart failure.

Methods: Hospital-based historic cohort of patients admitted with acute decompensated HF in a private hospital from Recife/PE, from January 2008 to February 2016, followed-up for at least 30 days after discharge. Demographic and clinical data of admission, hospitalization, and clinical and late outcomes were analyzed. Logistic regression was used as a strategy to identify the predictors of independent risks.

Results: 312 followed-up patients, average age 73 (± 14), 61% males, 51% NYHA Class III, and 58% ischemic etiology. Thirty-day readmission rate was 23%. Multivariate analysis identified the independent predictors ejection fraction < 40% (OR = 2.1; p = 0.009), hyponatremia (OR = 2.9; p = 0.022) and acute coronary syndrome (ACS) as the cause of decompensation (OR = 1.1; p = 0,026). The final model using those three variables presented reasonable discriminatory power (C-Statistics = 0.655 – HF 95%: 0.582 – 0.728) and good calibration (Hosmer-Lemeshow p = 0.925).

Conclusions: Among hospitalized patients with acute decompensated heart failure, the rate of readmission was high. Hyponatremia, reduced ejection fraction and ACS as causes of decompensation were robust markers for the prediction of hospital readmission within 30 days of discharge. (Int J Cardiovasc Sci. 2020; 33(2):175-184)

Keywords: Heart Failure; Hospitalization; Patient Readmission; Patient Discharge/trends.

Introduction

Heart failure (HF) is a chronic disease associated with high morbidity and mortality and is known worldwide as a public health issue due to its significantly increased incidence, especially amongst the elderly population. It is estimated that the prevalence of HF varies from 1% of people under 50 to 10% of people over 80 years of age.[1]

According to North American data, HF affects around 5.5 million patients. Annually, it presents an incidence of 660,000 new cases, with 800,000 to 3.6 million hospitalizations, 300,000 deaths per year and related costs of around 35 billion dollars, being the fifth most frequent cause of hospitalization and the most common amongst the elderly.[2]

In Brazil, according to data from the National Health System – DATASUS (2017), in 2016, there were around 214,000 hospitalizations due to HF, which is 19% of the hospitalizations for cardiovascular diseases, with in-hospital mortality of 11% and costs related to

hospitalization alone of around BRL 334 million. In same year, in the Northeast of Brazil, hospitalizations for HF were around 48,000, including more than 8,000 in the state of Pernambuco, with 13.7% mortality.[3] In First Brazilian Registry of Heart Failure — BREATHE — in-hospital mortality was 12.6% of 1,263 patients distributed in 51 urban centers in Brazil.[4]

One of the greatest problems related to the outcome of HF refers to high rates of hospital admissions caused by clinical decompensation, generating intense stress to patients and relatives, with high economic cost and great impact on the health system, in addition to worsening of ventricular function.[5] Studies have demonstrated that each event of clinical decompensation results in additional worsening of ventricular remodeling in HF, resulting in worse heart function and clinical manifestations of heart failure.[6]

The objective of this study is to calculate hospital readmission rate within 30 days of discharge, as well as to identify the main predictors of re-hospitalization of patients with acute decompensated heart failure (ADHF), in order to assist the development of public health policies, with positive impact on the reduction of morbimortality among those patients.

Methods

Retrospective study with historic cohort of patients assisted at a private hospital from Recife/PE (Brazil), who were in hospital for over 24 hours, from January 2008 to February 2016.

Admitted patients had primary diagnosis of decompensated heart failure, were 18 years of age or older, Functional Class III and IV according to the Classification of the New York Heart Association – NYHA. Decompensated heart failure was diagnosed according to the Framingham Study.[7] Patients with incomplete or unavailable data on their electronic charts, patients submitted to transplantation and minors of 18 years of age were excluded.

Data collection included hospital admission information from the date of admission to medical discharge or in-hospital death, and hospital readmission within 30 days of discharge. Information was obtained from medical records, then complemented, when necessary, by consultation with the medical assistant. Data collection instrument was a structured questionnaire, including demographic and clinical variables, complementary tests

and the therapy used, besides information about clinical outcomes and post-discharge outcome.

The outcome of interest was hospital readmission within 30 days of discharge. Only hospital readmissions due to cardiac causes were considered in this study. HF etiologies were defined as: a) ischemic heart disease due to previous heart attack, chest angina, previous coronary artery bypass grafting surgery or percutaneous angioplasty, or coronary angiography showing major artery obstructions (> 70%) in epicardial branches; b) hypertension heart disease, defined as long-term history of systemic hypertension without adequate blood pressure control or long-term use of anti-hypertensive medication associated with the presence of left ventricular hypertrophy on electrocardiogram or echocardiogram; c) valvular heart disease defined as history of previous valvular disease or based on echocardiogram results; d) idiopathic cardiomyopathy in the presence of dilatation and ventricular dysfunction, in the absence of any other evident cause.

Left ventricular ejection fraction (LVEF) was measured by echocardiogram, using the Teichholz formula for records on mode M or modified Simpson's rule for final left ventricular systolic and diastolic diameter measurements on apical four-chamber view, according to the regulations applicable. All tests were conducted at the echocardiography section of the hospital.[8]

The variable hospital-acquired complication was made by the composition of in-hospital events (dialysis procedure, ventricular arrhythmia, infection, pulmonary embolism and cardiogenic shock), that is to say, if the patient had at least one of the described events, it was considered hospital-acquired complication.

Some of the continuous variables were changed to categorical variables for analytical purposes:[9] age (< 65 and ≥ 65 years), systolic blood pressure (< 115 mmHg and ≥ 115 mmHg), heart rate (≤ 80 bpm and > 80 bpm), hospitalization period (≤ 7 days and > 7 days), creatinine (abnormal: > 1.3 mg/dl men and > 1.1 mg/dl women), plasma sodium (altered — hyponatremia: < 130 mEq/L), blood urea nitrogen (abnormal: ≥ 92 mg/dL) and LVEF (< 40% and ≥ 40%). Presence of anemia was based on the World Health Organization (hemoglobin < 13 g/dl men and hemoglobin < 12 g/dl women).

Statistical analysis

Demographic and clinical characteristics of patients were analyzed using descriptive statistics: mean and

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standard deviation (SD) for quantitative variables and absolute and relative frequencies for qualitative variables. Bivariate analysis, by Pearson's Chi-Square test, was conducted as a strategy to evaluate the correlation between outcome (readmission within 30 days) and the independent variables studied. In order to build a multivariable logistic regression model, we considered all the variables which, in the bivariate analysis, presented an association with readmission with $p < 0.20$. The stepwise forward method was applied to select the final model. The selected variables had their interactions, if any, examined by correlation matrix, interactions with correlation coefficient greater or equal to 0.5 were included in the model. Once the final model was defined, model calibration was evaluated by the Hosmer-Lemeshow Goodness-of-fit test. Discrimination capability of the final model was studied by the C-statistic, that is, the area under the curve built from the receiver operating characteristic curve. The program SPSS for Windows, version 21.0 – Statistical Package for Social Sciences (IBM, Armonk, NY) was used to do the statistics calculations. The level of significance assumed was 5%.

The project was approved by the Research Ethics Committee of Centro de Pesquisas Aggeu Magalhães (CPqAM) of Fiocruz/PE, with CAAE registration number 67404216.8.0000.5190, in accordance with the Declaration of Helsinki.

Results

This study included 372 patients that met the criteria of inclusion and exclusion from 2008 to 2016. The analyzed sample of 312 patients was created according to Figure 1. Of those patients, 71 (22%) were readmitted within 30 days after hospital discharge. The age of the patients varied from 26 to 99 years of age, with mean 73 (SD = 14) years, with 232 (74%) patients aged 65 or older, the majority of men (62%), NYHA-Class III (50%), ischemic etiology (58%), LVEF ≥ 40% (57%) and hospital admission period over 1 week (64%).

Among previous comorbidities, systemic arterial hypertension (SAH) was present in 86% of the patients, diabetes mellitus (DM) in 49%, severe kidney disease in 30% and chronic obstructive pulmonary disease (COPD)/asthma in 18%. The main cause of decompensation was acute coronary syndrome (ACS) (46%), followed by arrhythmia (25%) and infection (23%). Regarding drug therapy during hospitalization,

Figure 1 - Flowchart of the sample selection process analyzed.
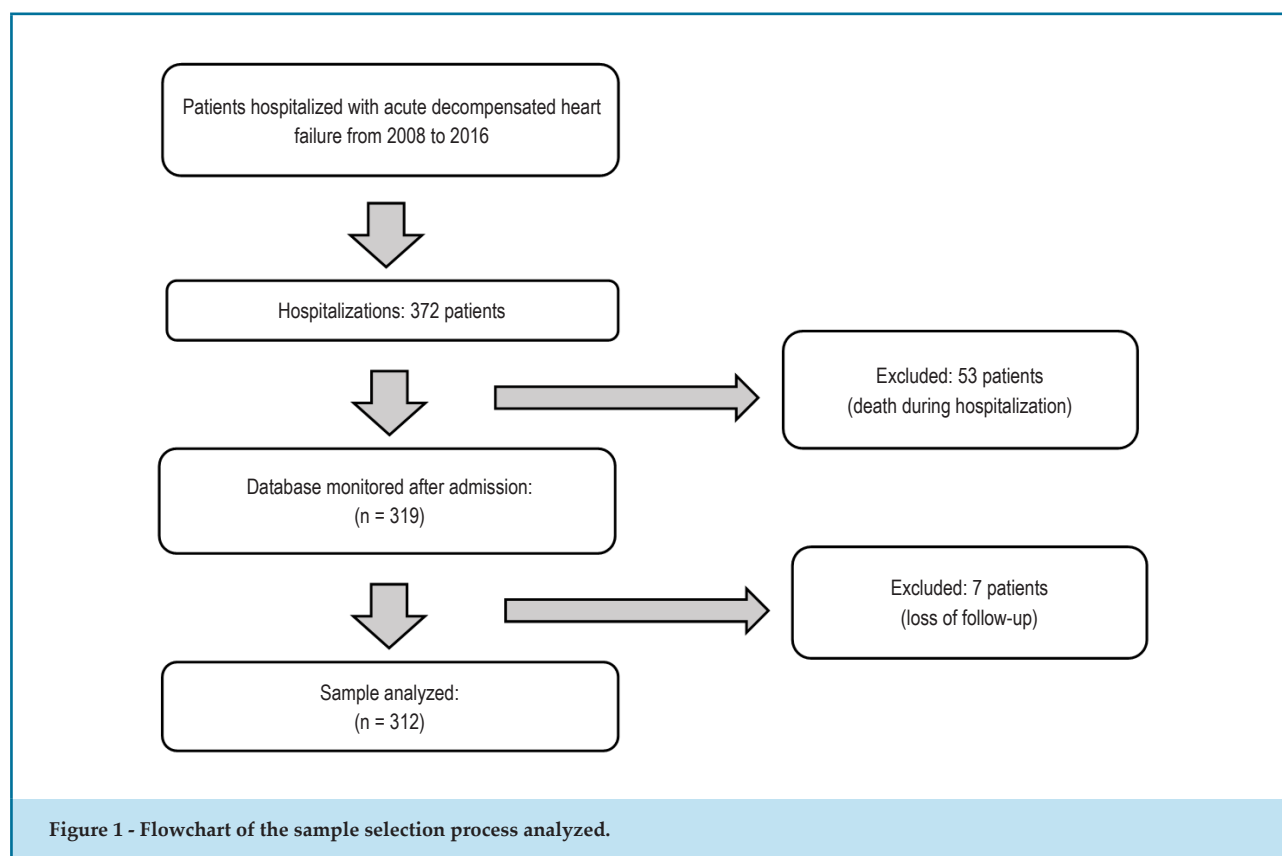
the use of betablockers was seen in 77% of the patients, as well as angiotensin-converting enzyme inhibitors (ACEI) and *angiotensin* receptor *blockers* (ARB). By analyzing only the patients with HF, with reduced ejection fraction (LVEF < 40%), that percentage increases to 82% regarding ACEI/ARB and 84% regarding betablockers. High levels of creatinine were found in 41% of the patients. Anemia was found in more than half of the analyzed sample (53%), as 15% of the patients had abnormal urea levels, and only 8% had abnormal sodium levels (hyponatremia) on admission (Table 1).

According to the bivariate analysis, the variables with significant correlation with hospital readmission were: ACS as a cause of decompensation (p = 0.032), LVEF (p = 0.004) and hyponatremia on admission (p = 0.022). Previous comorbidities, such as HAS, coronary artery disease, stroke, peripheral vascular disease (PVD) and smoking had a statistical tendency (p < 0.20) and, therefore, were included in the logistic regression model (Table 1).

Multivariable logistic regression detected the following independent risk factors for hospital readmission: left

Table 1 - Univariable predictors of rehospitalization within 30 days after discharge

Variable	Overall cohort (n = 312)	No readmission (n = 241)	Readmission (n = 71)	OR univariate 95% CI	p-value
Age ≥ 65 years	232 (74.4%)	176 (73.0%)	56 (78.9%)	1.38 (0.73 – 2.61)	0.322
Male gender	194 (62.2%)	151 (62.7%)	43 (60.6%)	0.92 (0.53 – 1.58)	0.749
Etiology					
Ischemic	179 (57.6%)	133 (55.4%)	46 (64.8%)	1.0	-
Hypertensive	54 (17.4%)	45 (18.8%)	9 (12.7%)	0.58 (0.26 – 1.27)	0.274
Idiopathic	32 (10.3%)	25 (10.4%)	7 (9.9%)	0.81 (0.33 – 1.99)	0.646
Valvar	19 (6.1%)	16 (6.7%)	3 (4.2%)	0.54 (0.15 – 1.95)	0.348
Others	27 (8.7%)	21 (8.8%)	6 (8.5%)	0.83 (0.31 – 2.17)	0.699
NYHA - Class IV	154 (49.5%)	119 (49.6%)	35 (49.3%)	0.99 (0.58 – 1.68)	0.966
ACS cause of decompensation	140 (45.9%)	100 (42.6%)	40 (57.1%)	1.80 (1.12 – 3.16)	0.032*
Hypertension	268 (85.9%)	203 (84.2%)	65 (91.5%)	2.03 (0.82 – 5.01)	0.120
Diabetes mellitus	153 (49.0%)	115 (47.7%)	38 (53.5%)	1.26 (0.74 – 2.14)	0.390
Coronary disease	202 (64.7%)	150 (62.2%)	52 (73.2%)	1.66 (0.92 – 2.99)	0.088
Kidney disease	94 (30.1%)	69 (28.6%)	25 (35.2%)	1.32 (0.77 – 2.38)	0.288
Valvar disease	22 (7.1%)	19 (7.9%)	3 (4.2%)	0.55 (0.15 – 1.79)	0.290
COPD/asthma	57 (18.3%)	47 (19.5%)	10 (14.1%)	0.68 (0.32 – 1.42)	0.299
Neoplasia	28 (9.0%)	22 (9.1%)	6 (8.5%)	0.92 (0.36 – 2.37)	0.861
Stroke	31 (9.9%)	21 (8.7%)	10 (14.1%)	1.72 (0.77 – 3.84)	0.184
Peripheral vascular disease	60 (19.2%)	42 (17.4%)	18 (25.4%)	1.61 (0.56 – 3.02)	0.136
Alcohol use	69 (22.1%)	57 (23.7%)	12 (16.9%)	0.66 (0.33 – 1.31)	0.231
Smoking	76 (24.4%)	63 (26.1%)	13 (18.3%)	0.63 (0.23 – 1.23)	0.277
Systolic BP on admission < 115 mmHg	73 (23.4%)	58 (24.1%)	15 (21.1%)	0.85 (0.45 – 1.61)	0.607
Heart rate on admission ≤ 80 bpm	139 (44.6%)	106 (44.0%)	33 (46.5%)	1.11 (0.65 – 1.88)	0.710

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Cont. Table 1 - Univariable predictors of rehospitalization within 30 days after discharge

Variable	Overall cohort (n = 312)	No readmission (n = 241)	Readmission (n = 71)	OR univariate 95% CI	p-value
Betablockers in hospital	237 (76.9%)	179 (75.5%)	58 (81.7%)	1.45 (0.74 – 2.83)	0.279
ACEI/ARB in hospital	239 (77.3%)	187 (78.6%)	52 (73.2%)	0.75 (0.41 – 1.37)	0.342
LVEF < 40%(+)	126 (43.0%)	85 (38.3%)	41 (57.7%)	2.20 (1.28 – 3.79)	0.004*
Hyponatremia on admission	24 (7.7%)	14 (5.8%)	10 (14.1%)	2.65 (1.12 – 6.25)	0.022*
Abnormal blood urea nitrogen on admission	47 (15.2%)	36 (15.1%)	11 (15.5%)	1.03 (0.49 – 2.14)	0.940
Abnormal creatinine on admission	126 (40.5%)	97 (40.4%)	29 (40.8%)	1.29 (0.76 – 2.22)	0.948
Anemia on admission	163 (52.8%)	122 (51.3%)	41 (57.7%)	1.02 (0.59 – 1.75)	0.337
Complication during hospitalization	81 (25.9%)	61 (25.3%)	20 (28.2%)	1.18 (0.65 – 2.14)	0.597
Hospitalization period > 7 days	198 (63.5%)	150 (62.2%)	48 (67.6%)	1.27 (0.72 – 2.21)	0.409

OR: odds ratio; 95%CI: 95% confidence interval 95%; ACS: acute coronary syndrome; COPP: chronic obstructive pulmonary disease; BP: blood pressure; ACEI: angiotensin-converting enzyme inhibitors; ARB: angiotensin receptor blockers; LVEF: left ventricular ejection fraction; (+) = sample of 293 patients who underwent echocardiography; (*) = p-value < 0.05.

ventricular ejection fraction < 40% (OR = 2.11; 95% CI 1.21 – 3.69), hyponatremia on admission (OR = 2.87; 95% CI 1.16 – 7.07) and ACS as a cause of decompensation (OR = 1.89; 95% CI 1.08 – 3.31). The final model with these three variables presented a reasonable discrimination capability (C-statistic = 0.655 – 95% CI: 0.582 – 0.728) and good calibration (Hosmer-Lemeshow: $\chi2 = 0.892$, p = 0.925). Figure 2 shows the graphic representation of those variables and their respective odds ratio and 95% CI.

Discussion

This study contributed to the comprehension of the dynamics of hospital readmission of patients with HF, which has become more prevalent among the population, due to increase of population and life expectancy. Therefore, the concern with the improvement of clinical conditions and survival rate is justified, contributing to better planning of health actions.

The main characteristic of the studied population is the profile of high severity and complexity and advanced age: more than 70% were elderly (over 65) with many comorbidities. This configuration can be explained by the fact that the studied hospital is a reference in cardiology in the North and Northeast of Brazil. The profile is similar to the population on international records, such as ADHERE done in multiple health centers in the USA with more than 118,000 patients between 2001 and 2004, whose average age was 73 and 50% were men.[9] On the other hand, the 1st Brazilian Registry of Heart Failure — BREATHE — done in 51 hospitals (public and private) from different parts of Brazil, reported younger age on average (64 ± 16 years), majority of women and infection as the main causes of decompensation.[4]

Considering the etiology of HF, the most frequent one found in our population was ischemic etiology (58%), followed by hypertensive (17%), corroborating most of the studies.[10-12] When we looked at the northeastern states only, in the BREATHE registry, the percentage of hypertensive and valvar etiology were greater than the ones observed in that population.[4]

The average time of hospitalization for compensation, among our patients, was 13 days, which superior to that in the literature, with an average time of 9 days for the most critical cases.[12] Despite the technological progress achieved in the last decades, such as new drugs, pacemaker and resynchronizer use, the length of stay and in-hospital mortality of the patients with HF is increasing in Brazil, and, automatically, the average cost of hospitalization has increased significantly from
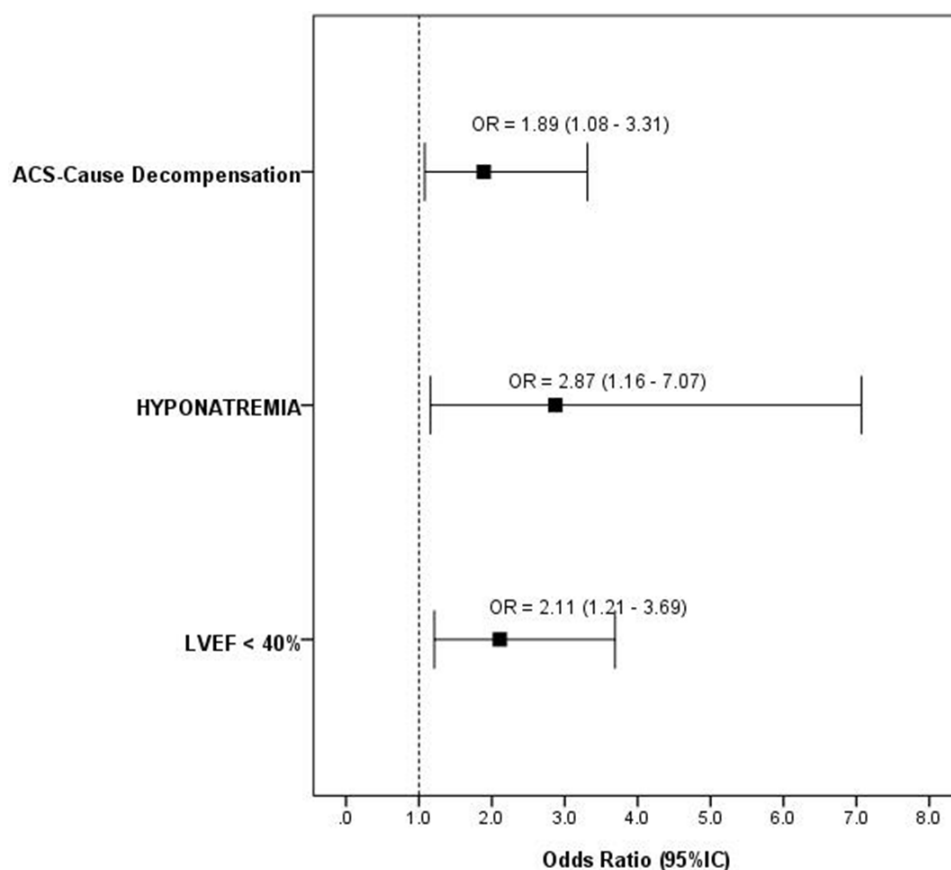
Figure 2 – Multivariable model for 30-Days readmission – Odds Ratio (95%CI).
ACS: acute coronary syndrome; LVEF: left ventricular ejection fraction.

BRL 920 in 2008 to BRL 1,559 in 2016.[13-14] A possible explanation to the increased length of stay may be due to the fact that the study was conducted at a private hospital, where there is no major issues of scarcity of hospital beds, hence less pressure from the public health system for early patient discharge.

In this study, the readmission rate of patients with DHF within 30 days of discharge was 23%, which is consistent with other published studies, in which 24% of the participants were readmitted within 30 days.[15-17]

Historically, several measurements have been proposed in order to create models of HF prognostic prediction; however, those models have presented limited predictive capabilities, as we are dealing with a chronic disease whose outcome is associated with multiple causes, including the form of presentation and severity of the disease, clinical and behavioral characteristics of the patients, in addition to factors such

as failure of the health system, which is not comparable to models from developed countries. In a systematic review of 30 studies that developed models of hospital readmission prediction, the C-statistic varied from 0.55 to 0.65, demonstrating the inexistence of predictor scores of high discriminatory power.[18]

Among 26 analyzed variables of hospital readmission within 30 days of discharge, using the multivariable logistic model, this study identified the following factors as predictors of independent risk: LVEF < 40%, hyponatremia and ACS as causes of decompensation. The final logistic model presented a reasonable discriminatory power (C-statistic = 0.655 – 95% CI 0.582 – 0.728) and good calibration (Hosmer-Lemeshow: $\chi^2 = 0.892$, p = 0.925).

It was demonstrated that patients with hyponatremia at the time of hospital admission had three times more chance of readmission (95% CI 1.01 – 11.19) in comparison with those with normal sodium levels. Notwithstanding

the wide reliability interval, this estimate could be considered as relatively early, however, this estimate is consistently present in other studies of this literature as well. A study developed in Boston in 2014 demonstrated that patients with low sodium levels presented an odds ratio of 1.45 on readmission within 30 days.[15] In a meta-analysis of observational studies, developed by Saito in 2015, including 57 articles, the importance of hyponatremia as a marker of bad prognosis of HF was also attested.[19]

Corroborating previous studies, reduced left ventricle ejection fraction (LVEF) was an independent risk predictor of readmissions.[19-20] In the American study, it was demonstrated that LVEF < 45% had a direct association with hospital readmission due to other causes, with a risk of 1.25.[21]

Data suggested that acute coronary syndrome (ACS) as a cause of decompensation is a relevant risk factor associated with readmission within 30 days of discharge. Unlike other precipitating factors of HF decompensation, such as excessive salt intake infections, lack of commitment to the treatment, among others, ACS cannot be prevented. Heart attack survivors have consistent risk of developing HF. Lower risk of HF can be related to decrease of comorbidities and/or evidence-based treatment. The possibility that the new heart injury secondary to the new acute coronary finding impacts an outcome of early hospital readmission is suggested here.[22] From this standpoint, patients with that condition can only be identified and from that, a more intensive strategy can be created at the post-discharge service.

In this study, 49% of patients declared having diabetes as a comorbidity. Of these, 25% returned within 30 days of discharge, whereas, among non-diabetics, this percentage was 21%, not showing evidence that that factor is a possible risk factor of early readmission. Nevertheless, an analysis of more than 600 individuals identified type II DM as an independent predictor of readmission, as in Huynh's study of 2015, in which DM was classified as a moderate criterion in models of short-term prediction.[19,23–24]

The variables of gender and age were not predictors of hospital readmission. Regarding social factors, there is great controversy if those are or not predictors of HF prognosis. Some studies demonstrated the correlation of those variables with clinical outcomes, such as death and readmissions.[15] Paradoxically, a study conducted at a hospital in Tasmania tested two models of rehospitalization prediction: one including clinical data and another with non-clinical data such as gender, age, whether the person lives alone, and so on. The author demonstrated that the model with clinical data reported a better discriminatory power for hospital readmission.[25]

High levels of creatinine and urea are associated with worse in-hospital survival and outcome after discharge.[15,26] The risk score ADHERE — a globally accepted score for the prediction of in-hospital mortality due to HF — takes in consideration only those two markers, in addition to systolic blood pressure.[9] Nevertheless, in this study, although creatinine and urea levels are biologically plausible, they did not present any relevant association with readmissions, possibly due to no statistical power detected in such correlations. As in the HF spectrum, in systolic blood pressure on admission, there was no confirmed association with readmission.

In this study, betablockers (BB), as well as the association of angiotensin-converting enzyme inhibitors (ACEI) and angiotensin receptor blockers (ARB), were prescribed during hospitalization to the majority of the patients (77%), a much higher number than the ones announced by the BREATHE registry, which were 57% of BB, 42% of ACEI and 24% of ARB. Considering HF patients, with reduced LVEF, the indication was higher: 82% in the case of ACEI/ARB and 84% for betablockers. These findings highlight the practice of the studied center in following the recommended standards, in line with the guidelines from several countries, as well as the Brazilian Guideline for Chronic HF, in which there is a consensus on the therapeutic use of BB drugs related to ACEI and ARB, their well-established clinical benefits on death caused by HF, besides the improvement of symptoms and reduction of readmission due to HF.[4,27-29] Nevertheless, in our specific population, the use of those medications during hospitalization was not confirmed as a protection factor against readmissions in the short-run. This might be explained by the fact that commitment and continuous use of therapeutic are largely associated with patient evolution than with its prescription during hospitalization.

The biochemical marker troponin as well as B-type natriuretic peptide (NT-proBNP) were validated in previous studies as relevant predictors of readmissions, however in this study, they were not analyzed due to the limited number of patients with those information from exams, as in our Brazilian reality, both troponin and NT-proBNP are not requested from all patients.[30]

Economic and social aspects were not considered in this study, since it was based on a historical cohort, with medical record data. The operation of these variables, from the quantitative point of view, was limited both by the inexistence of information and by the quality and reliability of the information present on the medical records.

Ziaian concluded, in his article, that the risk of hospital readmission is also related to the behavior of healthcare professionals, such as strategies that lead to greater support to discharging patients, better communication and earlier outpatient care.[29] Another factor that has an influence on hospital readmission rates is the hospital structure. In the Bergethon study, university hospitals presented higher relative readmission rate in comparison with their peers, and the hospitals that used disease management programs had lower relative readmission rates.[31]

It is very important to validate the reproduction of literature findings in our own population, as we are dealing with patients from the private health system and it is well known that their socio-economic and clinical profile differ from those of the patients seen by the public health system, besides the access to healthcare, which is very distinct between the two groups of patients. According to official data from the National Health Agency of Brazil, in 2003, the private health system received around 35 million beneficiaries. In 2016, this number raised to 48 million, an increase of 37% in 13 years.[32] The private health system has been crucial to the State, as it supports the National Health System itself, helping to meet the national demand for healthcare.

The data must be interpreted from the light of its limitations. The study was based on only one hospital facility, even though that facility is a reference in cardiology treatments in the North and Northeast of Brazil, where there is still some lack of information. The size of the sample group was limited, and the data was taken from medical records, implying that all relevant data were registered precisely, however, unknown prognostic factors or the ones not registered may have influenced the results.

As stated previously, it is possible to recognize that, according to several discussed studies, there is no single model of risk prediction of hospital readmission from HF. The epidemiological and clinical characteristics of each population require local validation of those risk tools as a way to find out the relevant predictors to complement clinical practice in determining the best care to be given to patients with that syndrome. From this perspective, in the context of a healthcare system with a multidisciplinary profile capable of offering full patient assistance, taking in consideration all biological, psychological and social determinants, it is important to have a follow-up plan to support patients and families.

In a sample of patients admitted at the private health system with DHF, the readmission rate was over 20%, and factors such as reduced left ventricular ejection fraction, hyponatremia and ACS as causes of decompensation were strong markers of hospital readmission within 30 days of discharge. Acknowledgement and evaluation of these findings are helpful for policymaking in the public healthcare system, with actions aiming at treatment and care for those patients. The healthcare and scientific communities must practice critical epidemiology based on a wider comprehension of reality, seeking better evidence in order to protect life and not only health.

Author contributions

Conception and design of the research: Sarteschi C, Cesse EAP, Martins SM. Acquisition of data: Sarteschi C, Medeiros C. Analysis and interpretation of the data: Sarteschi C, Martins SM. Statistical analysis: Sarteschi C. Obtaining financing: Sarteschi C. Writing of the manuscript: Sarteschi C. Critical revision of the manuscript for intellectual content: Sarteschi C, Cesse EAP, Martins SM, Souza WV. Supervision / as the major investigador: Sarteschi C.

Potential Conflicts of Interest

There are no relevant conflicts of interest to be declared.

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Ethics approval and consent to participate

This study was approved by the Ethics Committee of the *Universidade Católica de Pernambuco* under the protocol number 70891517.8.000.5206. 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.

Erratum

Int J Cardiovasc Sci. 2022 Issue vol 33(2), pages 175-184.

In Original Article "Predictors of Post-Discharge 30-Day Hospital Readmission in Decompensated Heart Failure Patients", with DOI number: https://doi.org/10.36660/ijcs.20180088, published in International Journal of Cardiovascular Science, 33(2) in page 175-84. Correct the author's name "Wayner Viera de Souza" to "Wayner Vieira de Souza".

References

1. Schmidt MI, Duncan BB, Azevedo e Silva G, Menezes AM, Monteiro CA, Barreto SM, et al. Chronic non-communicable diseases in Brazil: burden and current challenges. Lancet. 2011;377(9781):1949-61.

2. Cleland JG, Khand A, Clark A. The heart failure epidemic: exactly how big is it? Eur Heart J. 2001;22(8):623-6.

3. Ministério da Saúde [internet].Departamento de Informática do SUS. Sistema de Informações Hospitalares do SUS. Brasília; 2004. [acesso em 16 maio 2017]. Disponível em: http://www.datasus.gov.br.html.

4. Albuquerque DC, Souza Neto JD, Bacal F, Rodhe LEP, Pereira SB, Berwanger O, et al. I Brazilian Registry of Heart Failure - Clinical Aspects, Care Quality and Hospitalization Outcomes. Arq Bras Cardiol. 2015;104(6):433-42.

5. Cowie MR, Fox KF, Wood DA, Metcalfe C, Thompson SG, Coasts AJ, et al. Hospitalization of patients with heart failure: a population-based study. Eur Heart J. 2002;23(11):877-85.

6. Felker GM, Benza RL, Chandler AB, Leimberger JD, Cuffe MS, Califf RM, et al. Heart failure etiology and response to milrinone in decompensated heart failure: results from the OPTIME-CHF study. J Am Coll Cardiol. 2003;41(6):997-1003.

7. Ho KK, Pinsky JL, Kannel WB, Levy D. The epidemiology of heart failure: the Framingham study. J Am Coll Cardiol. 1993;22(4 Suppl A):6A-13A.

8. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, et al. Recommendations for cardiac chamber quantification by echocardiography in adult: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. Eur Heart J Cardiovasc Imaging. 2015;16(3):233-70.

9. Fonarow GC, Heywood JT, Heidenreich PA, Lopatin M, Yancy CW, ADHERE Scientific Advisory Committee and Investigators. Temporal trends in clinical characteristics, treatments, and outcomes for heart failure hospitalizations, 2002 to 2004: findings from acute decompensated Heart Failure National Registry (ADHERE). Am Heart J. 2007;153(6):1021-8.

10. Abraham WT, Fonarow GC, Albert NM, Stough WG, Gheorghiade M, Greenberg BH, et al. Investigators and Coordinators. Predictors of in-hospital mortality in patients hospitalized for heart failure: insights from the Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure (OPTIMIZE-HF). J Am Coll Cardiol. 2008;52(5):347-56.

11. Pocock SJ, Wang D, Pfeffer MA, Yusuf S, McMurray JJ, Swedberg KB, et al. Predictors of mortality and morbidity in patients with chronic heart failure. Eur Heart J. 2006;27(1):65-75.

12. Rohde LE, Clausell N, Ribeiro JP, Goldraich L, Netto R, William Dec G, et al. Heath outcomes in decompensated congestive heart failure: a comparison of tertiary hospitals in Brazil and United States. Int J Cardiol. 2005;102(1):71-7.

13. BRASIL. Ministério da Saúde [internet]. Departamento de Informática do SUS. Sistema de Informações Hospitalares do SUS. Brasília; 2004. [acesso em 05 junho 2017]. Disponível em: http:www.datasus.gov.br.html.

14. Kaufman R, Azevedo VMP, Xavier RMA, Geller M, Chaves RBM, Castier MB. Evolution of Heart Failure-related Hospital Admissions and Mortality Rates: a 12-Year Analysis. Int J Cardiovasc Sci. 2015;28(4):276-81.

15. Fleming LM, Gavin M, Piatkowski G, Chang JD, Mukamal KJ. Derivation and validation of a 30-day heart failure readmission model. Am J Cardiol. 2014;114(9):1379–82.

16. Bottle A, Goudie R, Cowie MR, Bell D, Aylin P. Relation between process measures and diagnosis-specific readmission rates in patients with heart failure. Heart. 2015;101(21):1704-10.

17. Krumholz HM, Chen YT, Vaccarino V, Wang Y, Radford MJ, Bradford WD, et al. Correlates and impact on outcomes of worsening renal function in patients ≥ 65 years of age with heart failure. Am J Cardiol. 2000;85(9):1110–3.

18. Kansagara D, Englander H, Salanitro A, Kagen D, Theobald C, Freeman M, et al. Risk prediction models for hospital readmission: a systematic review. JAMA. 2011;306(15):1688-98.

19. Saito M, Negishi K, Marwick TH. Meta-analysis of risks for short-term readmission in patients with heart failure. Am J Cardiol.2016;117(4):626-32.

20. Rahimi K, Bennett D, Conrad N, Williams TM, Basu J, Dwight J, et al. Risk prediction in patients with heart failure. JACC Heart Fail. 2014;2(5):440-6.

21. Chaudhry SI, McAvay G, Chen S, Whitson H, Newman AB, Krumholz HM, et al. Risk factors for hospital admission among older persons with newly diagnosed heart failure: findings from the cardiovascular health study. J Am Coll Cardiol. 2013;61(6):635-42.

22. Desta L, Jernberg T, Spaak J, Hofman-Bang C, Persson H. Risk and predictors of readmission for heart failure following a myocardial infarction between 2004 and 2013: a Swedish nationwide observational study. Int J Cardiol. 2017 Dec 1;248:221-6.

23. Cubbon RM, Woolston A, Adams B, Gale CP, Gilthorpe MS, Baxter PD, et al. Prospective development and validation of a model to predict heart failure hospitalisation. Heart. 2014;100(12):923–9.

24. Cavender MA, Steg PG, Smith SC Jr, Eagle K, Ohman EM, Goto S, et al. Impact of diabetes mellitus on hospitalization for heart failure, cardiovascular events, and death. outcomes at 4 years from the Reduction of Atherothrombosis for Continued Health (REACH) Registry. Circulation. 2015;132(10):923-31.

25. Huynh QL, Saito M, Blizzard CL, Eskandari M, Johnson B, Adabi G, et al. Roles of nonclinical and clinical data in prediction of 30-day rehospitalization or death among heart failure patients. J Card Fail. 2015;21(5):374–81.

26. Millane T, Jackson G, Gibbs CR, Lip GY. ABC of Heart Failure. Acute and chronic management strategies. BMJ. 2000;320(7234):559-62.

27. Bocchi EA, Marcondes-Braga FG, Bacal F, Ferraz AS, Albuquerque D, Rodrigues D, et al. Atualização da Diretriz brasileira de insuficiência cardíaca crônica - 2012. Arq Bras Cardiol. 2012;98(1 supl. 1):1-33.

28. Montera MW, Almeida DR, Tinoco EM, Rocha RM, Moura LAZ, Réa-Neto A, et al. II Diretriz Brasileira de Insuficiência Cardíaca Aguda. Arq Bras Cardiol. 2009;93(3 supl.3):1-65.

29. Ziaeian B, Fonarow GC. The prevention of hospital readmissions in heart failure. Prog Cardiovasc Dis. 2016;58(4):379-85.

30. Xin W, Lin Z, Mi S Does B-type natriuretic peptide-guided therapy improve outcomes in patients with chronic heart failure? A systematic review and meta-analysis of randomized controlled trials. Heart Fail Rev. 2015;20(1):69-80.

31. Bergethon KE, Ju C, DeVore AD, Hardy NC, Fonarow GC, Yancy CW, et al. Trends in 30-day readmission rates for patients hospitalized with heart failure: findings from the get with the guidelines-heart failure registry. Circ Heart Fail. 2016;9(6): e002594.

32. Brasil. Ministério da Saúde [internet]. Agencia Nacional suplementar de Saude. Informação em Saúde Suplementar. [acesso em 15 marco 2017]. Disponível em: http:www.ans.gov.br/perfil-do-setor/dados-e-indicadores-do-setor.

VIEWPOINT

A Different Heart in Children´s Literature: The Juvenile Literature in Medical Education

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Abstract

José Saramago, Nobel Prize in Literature, is the author of a statement that provokes adult readers: "What if children's stories become mandatory reading for adults? Would they really learn what they've been teaching for so long?".[1] It is in this context that literary texts dedicated to children have been used at times in medical education and clinical practice to bring up often invisible subjectivities.

Introduction

The scope of children's literature has exceeded the recommended age groups, and it is now accepted that the same book can be appreciated by different ages, depending on readers' demands and needs of each reader.

Supported by the Narrative Medicine reports,[2-4] the possibility of using the so-called children's literature has been investigated as a tool in the approach of topics related to medical practice. The heart, for example, has often been addressed in children's literature. It is almost always presented as an organ linked to tenderness, benevolence and care, often tending to a certain stereotype. In this article, we intend to present four children's books, selected by the way in which they present the heart. We believe they can be used by both undergraduate medical students and health professionals, as support for multidisciplinary teams.

The following books will be approached: Daddy's heart is outside the compass,[5] Hearts to millions,[6] The man's heart of popp[7] and The heart and the bottle.[8]

In *Daddy's heart is outside the compass*, the mother's heart that "beats quiet and constant" is a safe place for the boy trembling for fear of the storm. The father, carrying a laptop and a cell phone, complained of a burning feeling on the left side of his chest, and of pain going down to the left hand. The mother then calls an ambulance and an examination is made: "ten cables coming out from the device... six cables placed on the chest, around the heart, and four in the arms and legs" – an electrocardiogram ("This strip of paper with zigzag lines is called electrocardiogram"). The doctor gives the diagnosis: "Unfortunately, you have suffered a heart attack," and the treatment has already begun: "We need to inject it directly into the blood, so it can be quickly effective", explains the doctor. While the mother cries, Joaquim realizes that his father's heart is also beating fast. "I think he is sad" (the heart, but also the father), thought Joaquim. In the hospital, the mother explains to Joaquim that "Daddy's heart no longer jumps with joy to live. They are both sad." But even with the boy's effort, the father doesn't smile.

One week after hospital discharge, the father exercises on a stationary bike and starts a healthy diet composed of vegetables and fruits, despite his preference for juicy roast pork. During a walk with his dad, Joaquim, feeling him very sad and distant, approached him by asking childish questions: "Does the goldfinch have a heart too?", "Can birds suffer a heart attack too?" For the first time since the heart attack, the father smiles with the boy's innocence. The book ends when, after a walk in the rain, the father feels touched when his son snuggles up to him and says "I'm hearing your heart beats." A tear falls from his father's eye. He starts a conversation with Joaquim about the heartbeats, the joy and sorrow in life. Joaquim is the center of the book, and the only character with a proper name. His father and mother are presented to highlight the repercussions of the situation for the boy. Despite the

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book's somewhat didactic approach, it can help students to realize the whole network of repercussions behind a patient who suffers a heart attack. In this case, an event in a young patient with a child. And this situation can bring consequences not only from the emotional point of view, but also from social and economic ones. This didactic approach becomes even more explicit when, at the end of the book, we find the information on how to prevent and how to treat a heart attack, and what is a defibrillator, for instance. Besides, there are moments of poetry in the daily process in which father and son (re) approach and how Joaquim "finds a way to his father's heart," which "returned to beat normally".

Hearts to millions presents the heart with more subtle and poetic metaphors and situations. From a duality between what a child feels about the heart and what his older brother thinks, we can discuss an (false?) opposition between art and science. At first, the older boy, under the influence of teachers and school, considers the heart only as a muscle "with auricles, ventricles and other complicated names", the size of a closed hand and a constant heartbeat, even if varying with emotions. The younger boy asks: "If my heart is so small, how do so many things fit in it?". The illustration of the book follows the text: on the one hand the small heart muscle inside a pot, ready to be studied in an anatomy class. On the other hand, hearts of varying sizes and colors in contact with nature and life. The younger boy has a richer vision - he notices the differences in heartbeats when he's quiet: "when mom caresses my hair, my heart gets serene and beats slower"; he also starts to question the size of the heart: "sometimes I even think my heart is elastic. When I'm happy it gets huge, when I'm sad it seems to shrink and gets so tiny the size of a point." Some of everyday metaphors are translated by a child's innocence to: "... I'm suspicious that my aunt has a heart that is a safe as he heard his mother on the phone telling his aunt that she had to open her heart. The boy thought "my aunt locked her heart in such a way that she can't open it now. Poor thing... this must cause her affliction." And he also hears that the girl who works at the bakery has a "butter heart" and that "anyone who has heard of butter hearts has certainly heard of stone hearts." And the young boy sadly notes: "I try to explain these things to my brother, that the heart is not only a muscle, but he does not understand... Does he not understand that a heart has so much to tell!... of one thing I'm sure: there are no two hearts alike!". And he decides that "... if his heart is a muscle, my heart, that beats like a drum, is a

box where I keep the things I feel every day!" And even a child realizes that "things can be joyful and sad at the same time and hearts can mix everything and disorganize them like dressing drawers."

In the third book, *The man's heart of popp*, a pop-up book of incredible beauty, the boy José Francisco says that his father was a good man and a "carpenter, although he would like to be a fisherman, as he felt tightly held by the waves". But..."my father was born with a weak heart... the days passed and he did not improve, he was weaker and weaker." His father missed people but "people didn't greet him anymore, because he wouldn't get out of bed. The heartbeat cluttered like a moth closed in a jar looking for the air." But the father was good with his hands and thought of "building a poplar heart to replace his, that was faltering." The doctor called him crazy because this had never been tempted. But the father, "slowly, not to get tired, carved a wooden heart." The poplar's heart had "small roots coming out of it, resembling small veins and arteries". The doctor still found it a silly idea but "had no choice than to try the risky operation" because the father's heart stopped working for a moment. The doctor, in despair, had no other choice, and it was not a surprise, "the operation was a success!". "His life resumed, he returned to work in carpentry, and dream of the sea... that was when he met my mother and fell in love." But, with time, his mother realized his father was changing, roots started to grow from his feet and one morning, his father "left home to walk in the woods and never came back." This story was told by a boy who did not

Figure 1 - Book cover "The man with the poplar heart" - authorized by author Marco Taylor.

actually met his father but created his own story from reports of others and his imagination, and touchingly illustrates an approach of heart failure disease and heart transplantation through a child's eyes.

In *The heart and the bottle*, a girl full of life and energy keeps her heart in a supposedly safe place – a bottle – after a great loss, which is represented in the book by an empty chair. In the story, one day, the girl felt very insecure as she found the chair empty. The girl then thought the best thing to do was to put her heart in a safe place, "just for a while." She put her heart in a bottle, which she hung around her neck; "it seemed to fix things", thought the girl. But since then, the girl stopped paying attention at the sea, and even forgot the stars... the bottle started to become heavy, "but at least her heart was safe." Many years later, as she strolled on the beach, she meets a child, "curious about the world" as she herself used to be. The child asked her things she couldn't answer anymore, not without her heart. At that point she decides to rescue it from the bottle but did not know how to: she tried to saw the bottle, to throw it from a great height, she used a stick... but nothing worked. But the "little girl, still curious about the world thought that maybe there was a way." Her little hand managed to take the heart out of the bottle and "the chair was no longer empty". This is beautifully illustrated in the book. We have been used the image of the empty chair with students and health professionals in a technique called visual literacy:[9] after the analysis of the image for a few minutes, participants are asked to write a text from a trigger phrase. In our case, the excerpt "the presence of absence" is used as the trigger in the dynamics.

Conclusion

In these four children's books, the heart has been associated with topics little addressed in children's literature: heart attack and infarction, the dichotomy emotional heart and biological heart, heart failure and heart transplantation, death and mourning. The use of this material in medical undergraduate programs can help promote a broader view of the impact of any of these events on someone's life, especially a child.

Considering that cardiovascular diseases are the leading cause of death in our country and that, unlike most of developed countries, they affect younger adults, their economic and social consequences may be more traumatic in a family's life. Maybe simple and poetic texts have the power to expand the perception of these conditions and their impact, by touching sensitive aspects of medical practice, and stimulating a critical posture in all the readers.

Author contributions

Conception and design of the research: Mallet A, Geovanini F, Andrade L, Kestenberg D. Obtaining financing: Mallet A. Writing of the manuscript: Mallet A, Geovanini F, Andrade L, Kestenberg D. Critical revision of the manuscript for intellectual content: Mallet A, Geovanini F, Andrade L, Kestenberg, D.

Potential Conflict of Interest

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References

1. Saramago J. The largest flower in the world. São Paulo: Companhia das Letrinhas; 2001.

2. Charon R. Narrative medicine: a model for empathy, reflection, profession, and trust. JAMA.2001; 286(15):1897-902.

3. Charon R. Narrative medicine: honoring the stories of illness. New York: Oxford University Press; 2006.

4. Charon R, Dasgupta S, Hermann N, Irvine C, Marcus ER, Colón ER, Spencer D, Spiegel M. The principles and practice of narrative medicine. New York: Oxford University Press; 2017. 347 p.

5. Huainigg FJ; Ballhaus V. Daddy's heart is outside the compass. São Paulo: Editora Scipione; 2010.

6. Lopes J, Marques CC. Hearts to millions. Lisboa(Portugal):Editora Livros Horizonte; 2018.

7. Taylor M. The man's heart of popp.[Internet] {Cited in 2019 Jun 10]. Available from: www.marcotaylorautor.com

8. Jeffers, O. The heart and the bottle. São Paulo: Editora Salamandra; 2012.

9. Capeloa Gil I. Literacia visual. Estudos sobre a inquietude das imagens. Lisboa:Edições 70;2011.

Quantification of Myocardial Ischemia: Comparison between Myocardial SPECT and $^{13}NH_3$ PET/TC

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Introduction

Myocardial perfusion is a very important tool to diagnose and quantify hypoperfusion related to coronary artery disease (CAD). Single-photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI) is a widely available nuclear medicine imaging tool. Cardiac ^{13}N-ammonia positron emission tomography/computed tomography ($^{13}NH_3$ PET/CT) has increased its capability to provide quantitative measures of myocardial blood flow at rest and under stress, as well as of coronary flow reserve (CFR), in addition to better image quality.

Case report

A 61-year-old male patient with a history of hypertension, dyslipidemia and previous atrial fibrillation underwent a kidney transplant in 2001 because of post-pyelonephritic chronic kidney disease.

In 2007, in the presence of typical angina with anterior ST-depression, he underwent coronary angiography, which showed critical stenosis in the Left Anterior Descending Artery (LAD). He also underwent percutaneous transluminal coronary angioplasty (PTCA) and stenting.

From 2007 to 2017 he remained asymptomatic and all cardiac examinations he underwent did not reveal any abnormalities.

Keywords

In January 2018, a treadmill stress test demonstrated ST-depression in the anterior and lateral leads that appeared only during the recovery and disappeared after 3 minutes. Therefore, he was submitted to a pharmacological stress-rest SPECT-MPI using a CZT gamma camera; an intravenous infusion of 400 µg regadenoson was performed, followed by the ^{99m}Tc-tetrofosmin injection at 7 minutes. Stress acquisition started 15-25 minutes after the radiotracer administration. Rest injection was administered 2 hours later, and images were obtained about 15-30 minutes later. Both stress and rest studies were acquired in list mode for 9 minutes using a gated 16 frame-per-cycle acquisition.

The images showed a small hypoperfusion area in the lateral wall, while it was not possible to evaluate the inferior wall because of the presence of artifacts due to persistent diaphragmatic attenuation (Figure 1). The inducible ischemia in the LCX coronary territory was reported as 16%. CFR was also evaluated during the test : it was normal in the LAD and CDX territory, whereas it was 1.58 in the LCX territory.

A subsequent $^{13}NH_3$ PET/CT study was performed to better define the perfusion and coronary blood flow measurement of the left ventricular inferior wall (Figure 2). The examination was performed again at stress and at rest with 400 µg of regadenoson and the dose was 370 MBq of $^{13}NH_3$ both at stress and at rest. The PET studies were acquired in 3D and list mode for 10 minutes, starting acquisition immediately before $^{13}NH_3$ injection using a Discovery PET/CT 690 (GE Healthcare, Milwaukee, Wisconsin, USA). A low-dose CT attenuation correction (140 kV, 120-150 mA) was acquired for optimal imaging position on a CT scout scan and for attenuation correction. The examination result was an increased area of inducible ischemia in the LCX coronary territory of 46%. The global CFR was also evaluated during the PET/

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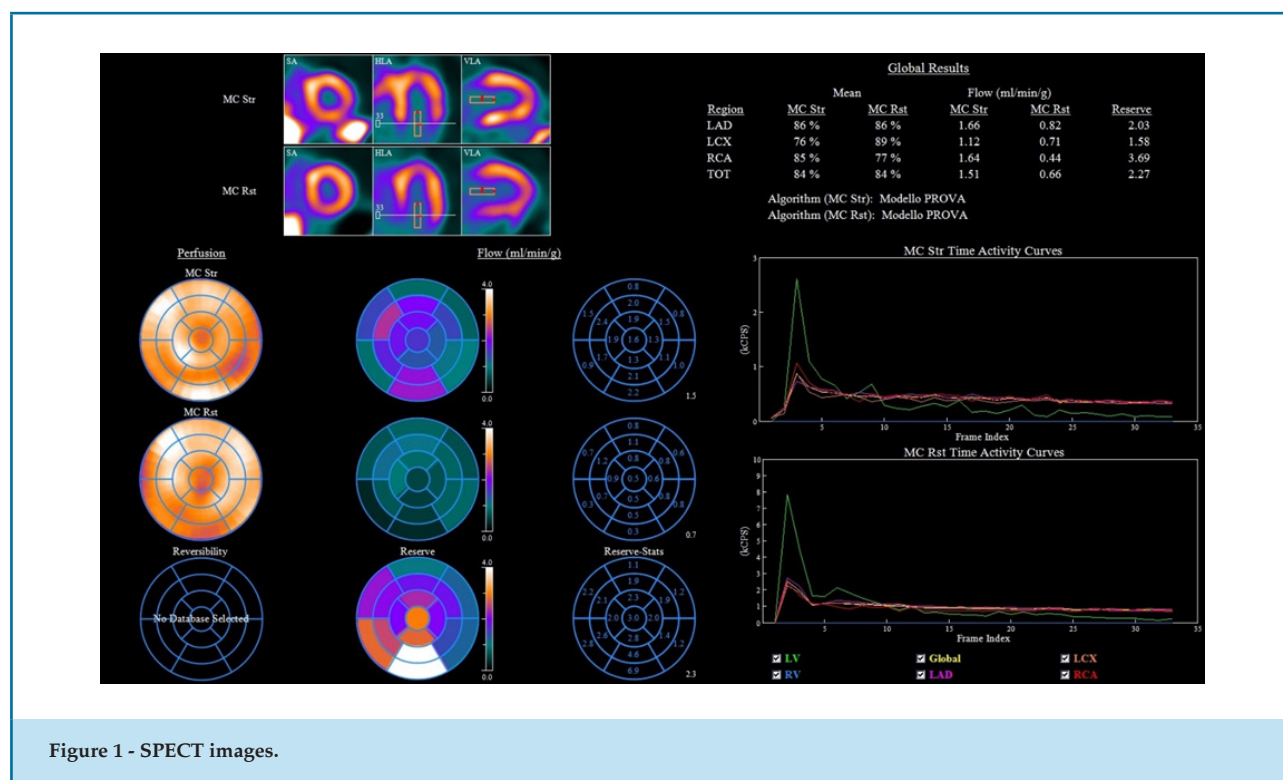E-mail: mazzolettiangelica@gmail.com

Figure 1 - SPECT images.

CT test : the values were normal in the LAD and CDX territories, but pathological in the LCX territory (1,45). The patient was asymptomatic during the examination and there were no alterations in the ECG.

Discussion

Coronary anatomy and myocardial blood flow have been identified as independent prognostic factors in patients with stable CAD.[1] Frequently, these anatomical and physiological assessments are used as complementary techniques for risk stratification and clinical decision-making.[2] Nuclear methods such as SPECT with ^{99m}Tc-tetrofosmin and cardiac PET/CT with ^{13}NH$_3$ are among the most frequently used tools for myocardial perfusion assessment. However, some disadvantages of the SPECT imaging related to the presence of image artifacts, long duration of the examination and the possibility of underestimating the ischemic severity in patients with multivessel disease should be considered.[3] These negative issues can be avoided by using cardiac PET/CT study, which has shown high accuracy and enables the quantification of perfusion and determination of CFR, which means high sensitivity and high predictive value in coronary artery disease detection and small vessel disease.

Myocardial perfusion PET is an important and appropriate test for patients in which CFR quantification is useful for patient management.[4] CFR has an important impact on the prognosis of the patient: an analysis of the association between CFR and cardiac mortality suggests an excellent prognosis for a CFR > 2 and a steady increase in cardiac mortality for a CFR lower than this value.[5]

Much attention now is being devoted to the possibility of evaluating CFR with CZT-SPECT. This technique is very promising and recently, the WATERDAY study results were published demonstrating that the sensitivity, specificity, accuracy, positive and negative predictive value of CZT-SPECT were, respectively, 83.3, 95.8, 93.3, 100 and 85.7% for the detection of ischemia in comparison with ^{15}O-H$_2$O PET.[6] Unfortunately, in our case, the results of CZT-SPECT images were not completely accurate because of the presence of diaphragmatic attenuation and the identification of a small area of inducible ischemia in the LCX territory.

Therefore, it was suggested to the patient to undergo a ^{13}NH$_3$ PET/CT study, which was able to better define the results of the quite unclear SPECT MPI test. The PET scan result showed an important area of inducible ischemia in the LCX coronary territory (46%) and the CFR of this territory was estimated at 1.45, which confirmed
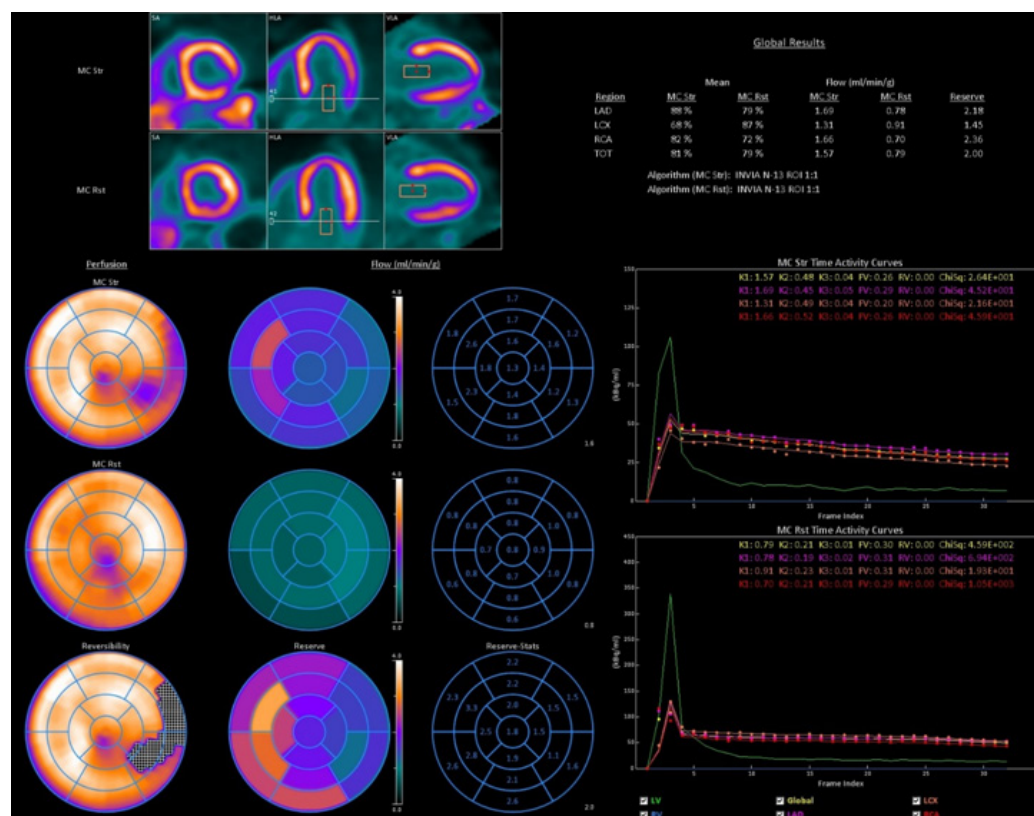
Figure 2 - ^{13}N-NH$_3$ PET/CT images.

the significant diagnosis of ischemia: this information has an important impact on patient prognosis and management. We believe that this case highlights the need to perform more studies evaluating the role of CZT-SPECT in myocardial blood flow reserve assessment with a larger number of subjects using attenuation and scatter correction. Until further proven, PET results should be considered the gold standard for the quantification of myocardial blood flow.

Author contributions

Conception and design of the research: Mazzoletti A, Mesquita CT, Giubbini R. Acquisition of data: Mazzoletti A, Dondi F. Analysis and interpretation of the data: Mazzoletti A, Dondi F, Giubbini M. Statistical analysis: Giubbini M. Writing of the manuscript: Mazzoletti A, Dondi F. Critical revision of the manuscript for intellectual content: Mesquita CT, Giubbini R.

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. Douglas PS, Hoffmann U, Patel MR, Mark DB, Al-Khalidi HR, Cavanaugh B, et al. Outcomes of anatomical versus functional testing for coronary artery disease. N Engl J Med 372(14):1291–300.

2. Cremer P, Hachamovitch R, Tamarappoo B. Clinical decision making with myocardial perfusion imaging in patients with known or suspected coronary artery disease. Semin Nucl Med 44(4):320–9.

3. Yoshinaga K, Katoh C, Manabe O, Klein R, Naya M, Sakakibara M, et al. Incremental diagnostic value of regional myocardial blood flow quantification over relative perfusion imaging with generator-produced rubidium-82 PET. Circ J. 2011,75(11):2628-34.

4. American Society of Nuclear Cardiology and Society of Nuclear Medicine and Moleclar Imaging Joint Statement on the Clinical Indications for Myocardial Perfusion PET. J Nucl Med, 2016;57(10):1654-6.

5. Murthy VL, Lee BC, Sitek A, Naya M, Moody J, Polavarapu V, et al. Comparison and progrnostic vaildation of multiple methods of quantification of myocardial blood flow with 82Rb PET. J Nucl Med. 2014;55(12):1952-8.

6. Agostini D, Roule V, Nganoa C, Roth N, Baavour R, Parienti JJ, et al. First validation of myocardial flow reserve assessed by dynamic (99m) Tc-sestamibi CZT-SPECT camera: head to head comparison with (15) O-water PET and fractional flow reserve in patients with suspected coronary artery disease. The WATERDAY study. Eur J Nucl Med Mol Imaging. 2018l;45(7):1079-90.

Coronary Artery Disease Associated with Coronary Anomaly and Situs Inversus Totalis in Man Submitted to Angioplasty

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Instituto Estadual de Cardiologia Aloysio de Castro (IECAC),[2] Rio de Janeiro, RJ - Brazil

Introduction

Dextrocardia associated with situs inversus totalis is a rare condition with an incidence of 1:10,000 in the general population.[1,2] It is characterized by a complete left-to-right reversal of the abdominal organs, including the abnormal position of the heart, resulting from changes in embryological development during the gastrulation stage (third week), characterized by the establishment of the craniocaudal, dorsoventral and right-left axes in the embryo.

This condition is transmitted by autosomal recessive genes, located in the long arm of chromosome 14, which affects the genetic cascade responsible for left-right differentiation. It should be noted that most affected individuals can have normal lives.[3]

The association of situs inversus totalis with coronary atherosclerotic diseases have similar incidence to the general population. However, the surgical approach in an event of acute infarction has significant statistical difference, since in patients with the anatomical condition mentioned before, there are more reports in the literature of myocardial revascularization surgery than percutaneous coronary intervention.[4] The exceptional nature of the case was more evident after the coronary angiography showed right coronary artery originating from the left coronary sinus and anomalous pathway, which is a rare congenital coronary anomaly. Coronary

Keywords

Coronary Diseases/complications; Dextrocardia; Situs Inversus; Heart Defects, Congenital; Angioplasty,Balloon, Coronary; Stent; Thromboytic Terapy.

artery anomalies can be found in 0.3% to 5.6% of the population.[5] Congenital changes are associated with early morbidity and mortality in young adults, and there are reports of sudden deaths either during or after extenuating physical activity.[6] It is estimated that this is the second more frequent cause of sudden death of cardiovascular origin among athletes, occurring between 12.2% to 17.2% in Europe and in the United States and dividing expert opinion, especially in regards with the therapeutic approach.[7]

Case report

A 46 year-old white male patient, natural from Rio de Janeiro, previously healthy, with a Framingham score of 11.7% (dyslipidemia, previous history of CAD) and dextrocardia associated with situs inversus totalis, reported that in September 2017 he started with dyspnea to medium efforts, which subsequently evolved to small efforts. On October 14, 2017, when he was making physical effort while repairing his house, he started with oppressive chest pain radiating to interscapular region associated with dyspnea and palpitation. Thus, he went to the emergency care unit, where he had a syncopal episode. Laboratorial tests were performed and the results showed positive myocardial necrosis markers, with a significant curve and a peak CK-MB 17.4 ng/mL and a troponin of 0.6 ng/mL. He was diagnosed with acute ST-segment elevation myocardial infarction (STEMI), presenting reperfusion criteria, and treated with thrombolytic therapy.

He was transferred to the State Institute of Cardiology Aloysio de Castro (IECAC), on October 16, 2017, where he underwent coronary angiography, which showed a severe 90% (ninety percent) lesion in the proximal

segment of the right coronary artery and also revealed the anomalous origin of the right coronary artery from the left sinus. On the following day, the patient underwent successful angioplasty with stent implantation. He evolved with clinical improvement and was discharged with a prescription for the following medications: ASA, atenolol, enalapril and simvastatin. Two weeks after this procedure, the patient was in good general condition and asymptomatic. To the physical examination, he presented with a heart rate of 53 bpm, a respiratory rate of 18 breaths/min and blood pressure of 135/90 mmHg. The heartbeat was regular with two clicks and normal sound without murmurs. The conventional electrocardiogram (ECG) performed after the angioplasty showed typical dextrocardia pattern and electrocardiographic changes characteristic of inferior wall infarction. A nuclear magnetic resonance (NMR) imaging of the abdomen confirmed situs inversus totalis, with the liver on the left side and the spleen on the right side.

An important aspect to point out is the patient's lack of risk factors for coronary events.

Discussion

The importance of the electrocardiographic diagnosis of dextrocardia is essential in the acute phase of coronary heart disease, especially in cases of clinical emergency, in which there is a need for immediate treatment with direct prognostic implications. Other aspects of importance are clinical reasoning and semiologic diagnosis, essentially by physical examination, in pathologies that involve dextrocardia and/or situs inversus totalis.

In these specific cases, we highlight the relevance of the epidemiology, clinical features, hemodynamics and anatomic abnormalities, through which we verify: frequency and disease-association in the population in general; the presence of coronary artery disease; acute coronary events and primary percutaneous intervention and, finally, right coronary artery originating from left coronary sinus and anomalous pathway. In other words, the association of benign and malignant anomalies in the same patient. Hence the need for early identification and the importance of clinical reasoning.

Coronary angiography and percutaneous coronary intervention (PCI) in these patients are technically difficult and require certain modifications, such as mirror image angiographic angulation, proper catheter selection and catheter manipulation for selective cannulation of coronary arteries.[8] Regardless of the unusual anatomy, percutaneous coronary intervention in patients with coronary artery disease and dextrocardia is normally successful.[9]

PCI can be safely performed using femoral or radial approaches, although as shown by previous case reports of PCI for AMI in patients with the mirror-image dextrocardia, it is conventionally performed with femoral arterial access.[10]

In this case, the coronary angiography was performed via the right radial artery. Contrast injection into the aorta revealed dextrocardia and anomalous origin of right coronary artery from left coronary sinus. Catheterization of left coronary artery was performed using a JL4 catheter and showed absence of severe obstructive atherosclerotic lesions. Due to the anomalous origin of the right coronary artery, an AL2 catheter was used for characterization, which showed a 90% lesion in the proximal segment of the right coronary artery. We decided to perform a coronary angioplasty and to implant a conventional stent, 3.5/14 mm with a pressure of 14 atm, followed by dilating force at the target lesion with a 4.0/10 mm balloon, inflated to a pressure of 12 atm. Control angiography shows a good final angiographic result.

Dextrocardia accompanied by atherosclerotic coronary disease has been poorly described in the literature, but it can be treated with percutaneous coronary intervention. The procedure was performed with movements contrary to the usual, showing that coronary angioplasty can be used to treat these patients.

Author contributions

Conception and design of the research: Fuchs A. Acquisition of data: Cunha IAT, Mourão JRC, Lora LB, Duarte FCC. Analysis and interpretation of the data: Cunha IAT, Mourão JRC, Lora LB, Duarte FCC. Statistical analysis: Catanheda CRO. Writing of the manuscript: Cunha IAT, Mourão JRC, Lora LB, Duarte FCC. Critical revision of the manuscript for intellectual content: Fuchs A, Catanheda CRO. Supervision / as the major investigador: Catanheda CRO.

Potential Conflict of Interest

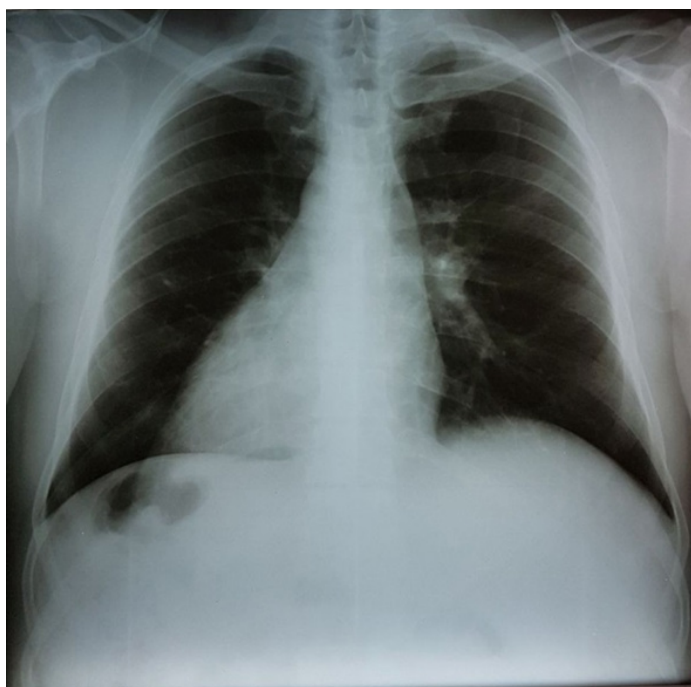No potential conflict of interest relevant to this article was reported.

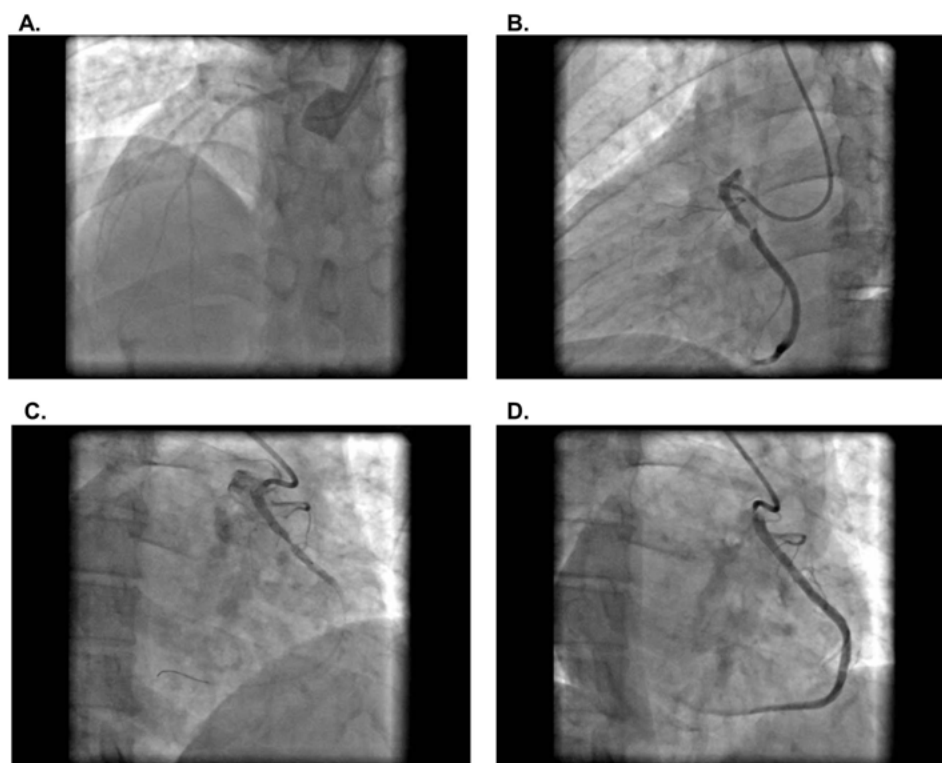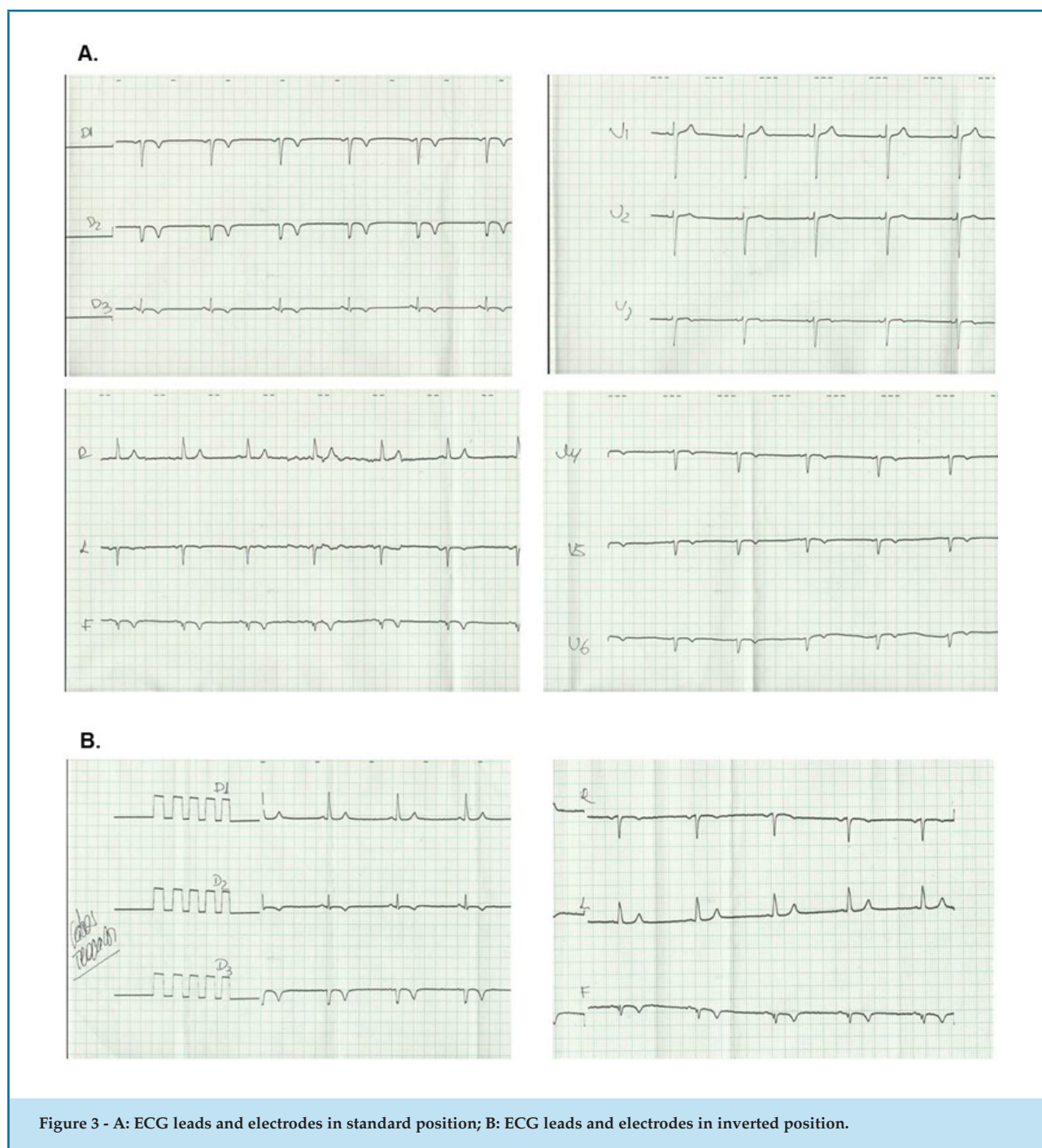**Figure 1 - PA Chest x-ray – Dextrocardia.**

Figure 2 - A: anomalous origin of the right coronary artery from the left sinus; B: pre-angioplasty; C: positioning of stent; D: post-angioplasty.

Figure 3 - A: ECG leads and electrodes in standard position; B: ECG leads and electrodes in inverted position.

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.

Erratum

Int J Cardiovasc Sci. 2022 Issue vol 33(2), pages 192-6.

In Case report "Coronary Artery Disease Associated with Coronary Anomaly and Situs Inversus Totalis in Man Submitted to Angioplasty", with DOI number: https://doi.org/10.5935/2359-4802.20190022, published in International Journal of Cardiovascular Science, 33(2) in page 192-6. Correct the author's name "Claudia Regina de Oliveira Catanheda" to "Claudia Regina de Oliveira Cantanheda".

References

1. Rosenberg HN; Rosenberg IN. Simultaneous association of situs inversus, coronary heart disease and hiatus hernia. Ann Intern Med .1949;30:851-9.

2. Torgersen J. Genetic factors in visceral asymmetry and in the development and pathologic changes of lungs, heart and abdominal organs. Arch Pathol. 1949;47:566-93.

3. Pêgo-Fernandes PM, Serro Azul JB, Matheus F, Maehara BS. Myocardial revascularization in a patient with situs inversus totalis. Arq Bras Cardiol. 2007:88(5):e103-e106

4. Mesa JM, Aroca A, Frutos A, Centeno J, Silvestre J, Baset F. Situs inversus and myocardial revascularization: case report. J Cardiovasc Surg (Torino). 1995;36(6):571-2.

5. Angelini P. Coronary artery anomalies: an entity in search of an identity. Circulation. 2007;115(10):1296-305.

6. Angelini P, Velasco JA, Flamm S. Coronary anomalies: incidence, pathophysiology, and clinical relevance. Circulation. 2002;105(20):2449-54.

7. Neves PO, Andrade J, Monção H. Coronary anomalies: what the radiologist should know. Radiologia Brasileira. 2015;48(4):233-41.

8. Vijayvergiya R, Grover A. Percutaneous coronary intervention for acute myocardial infarction in a patient with dextrocardia. World J Cardiol. 2010;2(4):104-6.

9. Wester JP, Ernst JM, Mast EG, Plokker HW, Bal ET, Verzijlbergen JF. Coronary angioplasty in a patient with situs inversus totalis and a single coronary artery. Cathet Cardiovasc Diagn. 1994;31(4):304-8.

10. Dhanjal TS, Davison P, Cotton JM. Primary percutaneous coronary intervention for acute myocardial infarction in a patient with dextrocardia. Cardiol J. 2009;16(2):168-71.

Calendar

22º Congresso de Cardiologia de Brasília e 10º Congresso de Imagem Cardiovascular

Centro Internacional de Convenções de Brasília

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32º Congresso de Cardiologia do Estado da Bahia

Hotel Deville Prime Salvador

De 30 abril a 02 de maio de 2020

37º Congresso De Cardiologia da SOCERJ

Centro de Convenções SulAmérica

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47º Congresso da Sociedade Brasileira de Cirurgia Cardiovascular

PUCRS - POA

De 15 e 16 de maio de 2020

41º Congresso da Sociedade de Cardiologia do Estado de São Paulo

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Expominas - BH/MG

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DEIC 2020

Hotel Royal Palm Plaza - Campinas

De 25 a 27 de junho de 2020

30º Congresso do Sociedade Mineira de Cardiologia

Ouro Minas Palace Hotel

De 02 a 04 de julho de 2020

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De 14 e 15 de agosto de 2020

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Goiânia

De 22 a 24 de outubro de 2020

XXVI Congresso Nacional do DERC - da prevenção ao tratamento

Centro Fecomércio de Eventos - SP

De 26 e 28 de outubro de 2020

XVII Congresso Brasileiro de Cardiogeriatria - DECAGE 2020

Hotel Plaza São Rafael - POA

De 30 e 31 de outubro de 2020

SOBRAC 2020

Hotel Sharaton Santos - SP

De 5 a 7 de novembro de 2020

26º Congresso Brasileiro de Cardiologia e Cirurgia Cardiovascular Pediátrica

Royal Tulip Brasília Alvorada

De 26 a 28 de novembro de 2020

Vol. 33, Nº 3, May and June 2020

Evaluation of Polymorphisms in IL8 and IL16 Genes in Patients with Acute Coronary Syndrome

Lílian Caroliny Amorim Silva, Romário Martins Araújo, Fábia Carla Silva Soares, Roberto Pereira Werkhauser, Sergio Tavares Montenegro, Tetsuo Tashiro, Viviane do Carmo Vasconcelos Carvalho, Silvia Maria Lucena Montenegro

QT Interval Dispersion Behavior in Patients With and Without Obstructive Coronary Artery Disease Undergoing Exercise Test

Alexandre Maulaz Barcelos, Marcelo Perim Baldo, Sérgio Lamego Rodrigues, José Geraldo Mill

Plasma Renin in Women Using and not Using Combined Oral Contraceptive

Sidney de Souza Oliveira, Jefferson Petto, Diego Passos Diogo, Alan Carlos Nery dos Santos, Marvyn de Santana do Sacramento, Ana Marice Teixeira Ladeia

Evaluation of Cardiovascular Risk in Hypertensive Individuals Attending a Primary Health Care Center

Tiago Ricardo Moreira, Luana Vieira Toledo, Érica Toledo Mendonça, Renata Maria Colodette, Luciana Saraiva Silva, Rosângela Minardi Mitre Cotta

Diagnostic and Prognostic Role of Liver Elastography in Heart Failure

Diane Xavier Ávila, Priscila Abreu Matos, Gabriel Quintino, Wolney de Andrade Martins, Dalmo Machado, Claudio Tinoco Mesquita, Humberto Villacorta Junior

A Retrospective Study on Unfractionated Bovine Heparin Safety in On-Pump Cardiac Surgery

Fernando Antonio de Lima Torres, Andressa C. B. Torres, Allinson Ribeiro, Cauê O. Maia, Fernanda P. Almeida, João Roceto, Jorge A. Matkovski, Matheus G. Kovalski, Vanessa A. Pizato, Tatiana M. G. Cordeiro

Analysis of Adherence to Antihypertensive Drug Treatment in an Argentinean Cohort

Walter Gaston Espeche, Rodrigo Sabio, Alejandro Diaz, Roberto Parodi, Carlos Enrique Leiva Sisnieguez, Roberto Antonio Flores, Silvia Poppe, Javier Altube, Diego Grimaldi, Martin Rogelio Salazar

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