

## ORIGINAL ARTICLE

# Associated Factors to the Risk of Obstructive Sleep Apnea in the Acute Phase of Myocardial Infarction

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## Abstract

**Background:** Obstructive sleep apnea (OSA) promotes endothelial dysfunction and systemic inflammation, and it is associated with shorter long-term survival and unfavorable clinical outcomes in patients with ST-segment elevation myocardial infarction (STEMI).

**Objectives:** To investigate the factors associated with the risk of OSA in the aftermath of STEMI.

**Methods:** A cross-sectional, quantitative study conducted with 145 individuals with STEMI in a large Brazilian teaching hospital. Anthropometric measurements were performed in addition to collecting sociodemographic/clinical data and lifestyle habits. The STOP-BANG questionnaire was used to determine the risk of OSA. The results were analyzed using descriptive statistics, association tests, and logistic regression. A significance level of 5% was adopted for the statistical analysis.

**Results:** The mean age of the participants was  $62 \pm 12$  years, with a predominance of males (71%), white individuals (57.2%), and those at high risk of OSA (58.6%). Moderate to high risk of OSA was associated with male gender, hypertension, and dyslipidemia. Gender (HR = 6.13, 95% CI [1.88, 20.03],  $p = 0.003$ ) and hypertension (HR = 4.31, 95% CI [1.27, 14.63],  $p = 0.019$ ) were factors influencing the risk of OSA after acute myocardial infarction.

**Conclusions:** Hypertension and male gender were significant factors for a moderate/high risk of OSA in infarcted patients.

**Keywords:** Obstructive Sleep Apnea; Myocardial Infarction; Risk Factors.

## Introduction

The sudden interruption of breathing during sleep, causing airway collapse for a time greater than or equal to 10 seconds, is defined as obstructive sleep apnea (OSA). Non-restorative sleep, snoring, nocturia, and daytime sleepiness are the most frequently reported signs and symptoms.<sup>1,2</sup> Among the main comorbidities related to OSA are hypertension, cardiac arrhythmias, coronary artery disease (CAD), stroke, heart failure, obesity, and sedentary lifestyle.<sup>2-4</sup> Numerous authors show OSA as an independent risk factor for CAD, with moderate and severe OSA having a higher incidence in STEMI.<sup>2,5-8</sup>

OSA is linked to the origin and progression of STEMI cardiac ischemia through physiological mechanisms, including severe intermittent hypoxemia, acidosis, increased blood pressure, and sympathetic vasoconstriction. These factors, along with changes in transmural, intrathoracic, and cardiac pressures, combined with endothelial dysfunction and systemic inflammation, may compromise arterial structures.<sup>6</sup> Consequently, untreated severe OSA is associated with shorter long-term survival in patients with STEMI.<sup>9,10</sup>

OSA is an underdiagnosed disease, and patients are rarely investigated and treated properly.<sup>11</sup> The gold standard method for the diagnosis of OSA is

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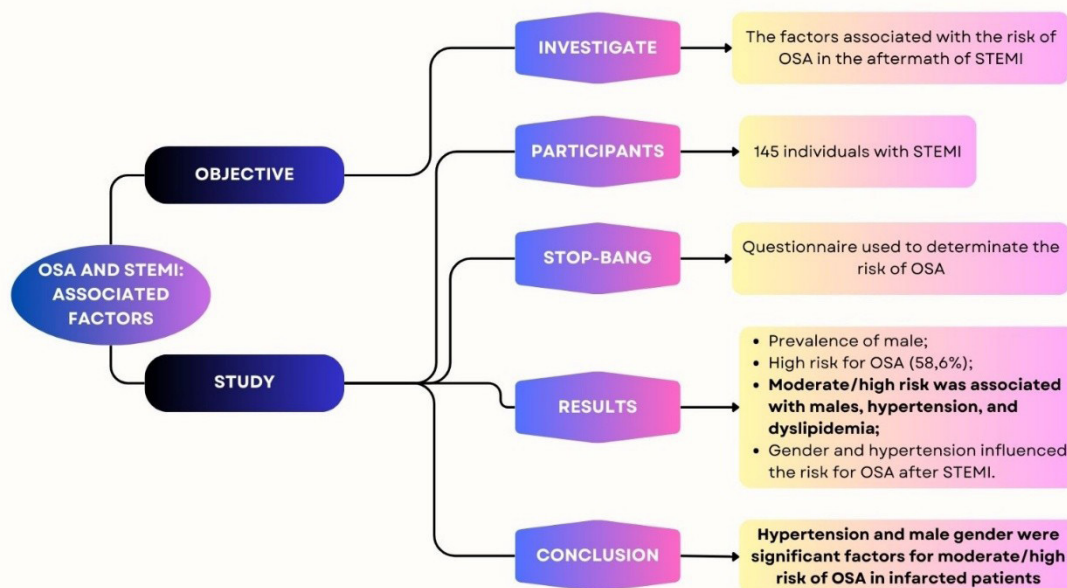
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### Central Illustration: Associated Factors to the Risk of Obstructive Sleep Apnea in the Acute Phase of Myocardial Infarction

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OSA: Obstructive sleep apnea; STEMI: ST-segment elevation myocardial infarction.

polysomnography (PSG); however, due to the high cost and limited availability of health services, PSG performs a small role in the Brazilian public health system.<sup>2,11-13</sup> On the other hand, there are validated screening tools with high sensitivity and positive predictive value for early detection of OSA, allowing its risk stratification.<sup>4</sup> Among these, there is the STOP-BANG questionnaire (snoring, tiredness, observed apnea, high blood pressure, body mass index (BMI), age, neck circumference, and gender), a simple tool, easy to apply and with excellent performance for the identification of moderate to high risk of OSA.<sup>4,14,15</sup>

Considering the incidence of OSA in patients with STEMI,<sup>10</sup> being associated with unfavorable clinical outcomes, this study aimed to verify the factors associated with the risk of OSA in the acute phase of myocardial infarction.

## Methods

This is an observational, cross-sectional study with a quantitative approach developed in the Emergency Room, Medical Clinic, Coronary Intensive Care Unit, and Chest Pain Unit of a large Brazilian teaching hospital.

Individuals aged 18 or older, of both genders, with a medical diagnosis of STEMI confirmed by ischemic symptoms lasting more than 30 minutes but less than 24 hours, ST-segment elevation of at least 1 mm in the frontal plane or 2 mm in the horizontal plane in two contiguous leads, and an elevation followed by a decline in biochemical markers of myocardial necrosis with a peak above the 99th percentile were included.

The exclusion criteria were cognitive impairment and the Killip III and IV classification.<sup>16,17</sup>

This sampling was a non-probabilistic type; the participants were selected according to the admission flow at the hospitals and observing the inclusion/exclusion criteria.

Data collection took place from July 2020 to June 2022, and the period observed was from the 1st to the 5th day after STEMI.

Initially, data were collected regarding the individual's cognitive ability using the Mini-Mental State Examination, a questionnaire composed of 19 questions that propose to evaluate orientation in time and space, immediate and delayed evocation, attention, naming, repetition, command in three stages, reading, copying, and writing. It has a maximum score of 30

points, with 21 points being the minimum necessary to consider oneself cognitively fit.<sup>18</sup>

To identify and classify the risk of OSA, the STOP-BANG instrument was applied based on eight dichotomous questions referring to snoring, tiredness, fatigue, drowsiness, observation of stopped breathing during sleep, blood pressure, BMI, age, neck circumference, and gender. The instrument, valid in Portuguese and available for free, consists of yes or no questions/answers (scores 1 and 0, respectively), with a total score ranging from 0 to 8, representing low (0-2), moderate (3-4), and high risk (5-8) groups for OSA, respectively.<sup>19</sup>

The survey of risk factors was carried out using an instrument developed by the researchers themselves, with questions about sociodemographic data (age, gender, and self-reported skin color), anthropometric data (weight, height, BMI), clinical data (blood pressure systolic blood pressure [SBP]; diastolic blood pressure [DBP]; heart rate [HR]; re-infarction, previous cerebrovascular accident [CVA], drowsiness, and comorbidities) and life habits (smoking, use of alcohol, and physical activities). The instrument was submitted for content validation by five experts.

The selected tool to measure the anthropometric data was a digital electronic scale, platform type, brand Omron HBF-214, 150 kg capacity, and sensitivity of 50 g. Height was measured with an inextensible measuring tape on a wall at ninety degrees relative to the floor, with the participant in the orthostatic position. BMI calculation is the weight (kg) / height<sup>2</sup> (m) ratio. BMI was categorized as normal (BMI between 18.5 and 24.9 kg/m<sup>2</sup>), overweight (BMI between 25 and 29.9 kg/m<sup>2</sup>) and obesity (BMI  $\geq$  30 kg/m<sup>2</sup>).<sup>20</sup> BP and HR were checked using automatic portable BP measuring devices (model HEM-7113 Omron®). BP was checked three times; the first one being discarded and the last two times being averaged. BP checks were performed according to the Brazilian Guidelines on Hypertension.<sup>21</sup>

For the evaluation of excessive daytime sleepiness, the Epworth Sleepiness Scale (ESS) was used. This is a questionnaire that assesses the probability of falling asleep in eight situations involving daily activities (sitting and reading, watching television, sitting in a public place, being a passenger in a car for an hour with no breaks, lying down to rest after lunch, sitting and talking to someone, sitting after lunch without drinking alcohol, driving in slow traffic). ESS score varies between 0 and 24, and a score greater than 10 suggests a diagnosis of excessive daytime sleepiness.<sup>22</sup>

Hypertensive and diabetic individuals are, according to information recorded in the medical records, in use of antihypertensive and hypoglycemic agents and/or insulin, respectively, prior to STEMI. Dyslipidemia patients have alterations in at least one of the components: HDL-C, LDL-C or triglycerides, or those in use of statins. Sedentary people do not practice physical exercise or do it twice a week or less. As for the use of alcohol, all those who reported using alcoholic beverages were considered, regardless of type, quantity or frequency. As smokers, those who smoked at least one cigarette per day were considered.

## Statistical Analysis

Collected data were submitted to double typing (Microsoft Office Excel for Windows) with subsequent validation and analyzed using the Statistical Package for the Social Sciences (SPSS) for Windows software, version 25. The Kolmogorov-Smirnov test was used to assess normality of continuous variables, data with normal distribution being presented as mean  $\pm$  standard deviation (SD). Categorical variables were described using absolute and relative frequencies. To assess the association between sociodemographic/clinical variables, lifestyle habits, and risk of OSA, the Chi-square test was used, along with measures of association in contingency tables (relative risk, odds ratio, and respective confidence intervals), followed by logistic regression, adjusting for other potentially relevant variables (age, gender, diabetes, hypertension, dyslipidemia, sedentary lifestyle, and obesity). Inferential analyses considered a significance level of 5% ( $\alpha = 0.05$ ).

## Ethical Aspects

The local Ethics Committee approved this work, registered under feedback no. 3.848.998 and CAAE: 23136219.0.0000.5152, meeting the requirements of the National Health Council for carrying out research with human beings. Informed consent from all persons with STEMI was obtained prior to their inclusion in the study.

## Results

A total of 145 individuals with STEMI and mean ( $\pm$ SD) age 62 $\pm$ 12 years were included. There was a prevalence of males (103; 71%), white (83; 57.2%), and with a high risk of OSA (85; 58.6%). Table 1 presents the sociodemographic, anthropometric, clinical, and lifestyle characterization of the participants distributed by OSA risk classification.

**Table 1 - Distribution of study participants (n = 145) according to sociodemographic, anthropometric, clinical data, and lifestyle according to risk of OSA. Uberlândia, Minas Gerais, Brazil, 2022.**

	Low risk of OSA (n = 19)	Moderate risk of OSA (n = 41)	High risk of OSA (n = 85)
Age, years	59±15	64±10	62±12
Male, n (%)	9 (8.7%)	24 (23.3%)	70 (68%)
White, n (%)	12 (14.5%)	22 (26.5%)	49 (59%)
BMI, kg/m <sup>2</sup>	24.06±4.3	25.80±4.6	28.00±6.2
SBP, mmHg	110±15	118±23	122±18
DBP, mmHg	64±12	69±13	71±14
HR, bpm	75±10	77±10	76±15
History of hypertension, n (%)	7 (7.1%)	21 (21.2%)	71 (71.7%)
History of DM, n (%)	2 (4.7%)	0 (23.3%)	31 (72.1%)
Re-infarction, n (%)	2 (6.1%)	9 (27.3%)	22 (66.7%)
Stroke, n (%)	0 (0%)	2 (33.3%)	4 (66.7%)
Smoker, n (%)	10 (16.7%)	20 (33.3%)	30 (50%)
Sedentary lifestyle, n (%)	14 (12.3%)	33 (28.9%)	67 (58.8%)
Use of alcoholic beverages, n (%)	7 (11.9%)	14 (23.7%)	38 (64.4%)
Abnormal sleepiness, n (%)	9 (12.7%)	18 (25.4%)	44 (62%)

*Values are expressed in absolute and relative numbers (%) or mean ± SD. OSA: Obstructive Sleep Apnea; BMI: Body Mass Index; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; HR: Heart Rate; DM: Diabetes mellitus.*

In the group of participants at moderate/high risk of OSA, it was observed that men, individuals with a history of hypertension, and those with dyslipidemia exhibited a higher likelihood of OSA (Table 2).

Analyzing the impact of predictive variables (including age, gender, obesity, history of diabetes, hypertension, and dyslipidemia) on the occurrence of moderate and high risk of OSA using logistic regression, it was found that gender and hypertension significantly influenced the likelihood of OSA after STEMI (Table 3 and Central figure).

## Discussion

The prevalence of a high risk of OSA assessed by the STOP-BANG questionnaire among patients with STEMI in this study was 58.6%. The result of the present study meets the results of other researchers, who also reported a high percentage of infarcted individuals at high risk of OSA (58.7%).<sup>11</sup> American Heart Association statement shows that the prevalence of OSA varies from

40% to 80% in patients with CAD and that patients with myocardial infarction may be prone to having OSA as a comorbidity.<sup>10</sup> The impact of OSA on CAD is greater in its most severe form, leading to a worse prognosis for this group of patients, associated with a lower survival rate.<sup>9</sup> Patients with STEMI who have severe OSA as a comorbidity have a higher chance of having another cardiovascular event in the 18-month period after the ischemic event. However, mild to moderate OSA was not associated with increased mortality.<sup>10</sup> In addition, a multicenter study involving five countries showed that, in patients undergoing percutaneous coronary intervention, OSA was an independent predictor of major adverse cardiovascular and cerebrovascular events (HR = 1.57, 95% CI [1.10, 2.24], p = 0.013).<sup>23</sup> Conditions such as hypertension, diabetes mellitus (DM) and dyslipidemia may favor adverse effects of OSA on the cardiovascular outcome. On the other hand, OSA is treatable, so, when confirmed, it can be a controllable CAD determinant.<sup>6</sup>

In this study, gender and hypertension were variables correlated with high risk of OSA. Male gender is known

**Table 2 – Association between sociodemographic, anthropometric, clinical parameters, lifestyle, and risk of OSA. Uberlândia, Minas Gerais, Brazil, 2022.**

Variables	Low risk of OSA	Moderate/High Risk of OSA	RR* (CI $\pm$ )	p $\pm$
Age				
Adult, n (%)	10 (16.4%)	51 (83.6%)	1.63 (0.62-4.30)	0.331
Elderly, n (%)	9 (10.7%)	75 (89.3%)		
Gender				
Female, n (%)	10 (23.8%)	32 (76.2%)	3.26 (1.21-8.74)	0.027
Male, n (%)	9 (8.7%)	94 (91.3%)		
History of DM				
No, n (%)	17 (16.7%)	85 (83.3%)	4.10 (0.90-18.59)	0.060
Yes, n (%)	2 (4.7%)	41 (95.3%)		
History of Hypertension				
No, n (%)	12 (26.1%)	34 (73.9%)	4.63 (1.68-12.75)	0.003
Yes, n (%)	7 (7.1%)	92 (92.9%)		
History of Dyslipidemia				
No, n (%)	16 (19.3%)	67 (80.7%)	4.69 (1.30-16.92)	0.012
Yes, n (%)	3 (4.8%)	59 (95.2%)		
Physical Activity				
Not sedentary, n (%)	5 (16.1%)	26 (83.9%)	0.72 (0.24-2.0)	0.557
Sedentary, n (%)	14 (12.3%)	100 (87.7%)		
Obesity				
No, n (%)	17 (15.7%)	91 (84.3%)	3.17 (0.69-14.48)	0.158
Yes, n (%)	2 (5.6%)	34 (94.4%)		
Sleepiness				
Norma/Average, n (%)	10 (14.3%)	60 (85.7%)	1.14 (0.43-3.02)	0.810
Abnormal, n (%)	9 (12.7%)	62 (87.3%)		

OSA: Obstructive sleep apnea; DM: Diabetes mellitus; RR\*: Crude relative risk (unadjusted); CI $\pm$ : Confidence interval; p $\pm$ : Probability ( $p < 0.05$ ).

to be an established and significant risk factor for OSA,<sup>4,5,10,15,24-26</sup> being prevalent in this population. These findings are in line with the result of the present study, where men represented 71% of the participants, of which 68% were at high risk of OSA. In this research, the male gender was independently associated with a high risk of OSA ( $p = 0.003$ ). Furthermore, it was observed that the outcome of OSA is equally severe in men and women.<sup>27</sup> In a systematic review, it was shown that, in the general population, the ratio of OSA ranges from

2:1 to 3:1, and in men, there is a greater association between OSA and myocardial infarction. At the same time, in women, these values were less significant.<sup>6</sup> However, there is little understanding of the impact of pathophysiological distinctions between genders on OSA.<sup>28</sup> Knowing the different relationships between OSA and gender can improve the diagnosis of OSA, and gender-specific considerations should be incorporated in the application, analysis and interpretation of the instrument.<sup>29</sup>



**Table 3 – Logistic regression model with adjusted relative risk and confidence interval for the risk of OSA in patients with STEMI (n=145). Uberlândia, Minas Gerais, Brazil, 2022.**

	HR*	CI†	p‡
Age	1.01	0.32-3.17	0.981
Gender	6.13	1.88-20.03	0.003
History of Hypertension	4.31	1.27-14.63	0.019
History of Dyslipidemia	3.64	0.86-15.33	0.079
Sedentary Lifestyle	0.54	0.15-1.95	0.350
Obesity	1.95	0.35-10.86	0.447
History of Diabetes	1.76	0.31-10.10	0.524

HR\*: Adjusted relative risk (hazard ratio); CI†: Confidence interval; p‡: Probability ( $p < 0.05$ ).

This study proved that hypertension was independently associated with a high risk of OSA ( $p = 0.019$ ). Hypertension is associated with a high prevalence of OSA,<sup>10,25,27</sup> and 30 to 50% of hypertensive patients are subject to presenting OSA as a comorbidity.<sup>10</sup> OSA and hypertension have multifactorial causes and often coexist. However, hypertension is not necessarily attributable to OSA.<sup>10</sup> OSA has the potential for negative feedback, as it can worsen hypertension, which then can worsen OSA.<sup>10</sup> Hypertension and myocardial infarction were reported in a systematic review as a common comorbidity in patients with OSA.<sup>25</sup> Intermittent and chronic hypoxia caused by OSA generates increased sympathetic activity, endothelial dysfunction, systemic inflammation, oxidative stress and metabolic abnormalities, which are mechanisms that cause myocardial damage and promote the development of hypertension.<sup>25</sup> The prevalence of high risk of OSA in another study was twice as high in the presence of hypertension as comorbidity than in normotensive individuals.<sup>3</sup> According to present results, 92.9% of the hypertensive individuals in the trial were at moderate to high risk of OSA. In a similar study, the prevalence of hypertension was 73% in the same risk group.<sup>7</sup>

The role of dyslipidemia in the pathogenesis of cardiovascular disease is essential since the accumulation of LDL-C initiates the formation of atherosclerotic plaques in arterial walls.<sup>30</sup> Dyslipidemia belongs to the group of risk factors that influence the evolution of myocardial infarction.<sup>31</sup> This study presents 95.2% of participants classified as moderate/high risk of OSA were dyslipidemic ( $p = 0.003$ ); however, in multivariate

analysis, dyslipidemia was not an independent predictor of high risk of OSA ( $p = 0.079$ ).

OSA and DM are two interconnected non-communicable diseases, and diagnosing one of these conditions may lead to screening for the other.<sup>1</sup> Given the relevance of OSA in cardiovascular risk, and that patients with DM already have an increased cardiovascular risk, this category of individuals should be screened for OSA.<sup>13</sup> OSA has been linked to a high probability of DM, regardless of the level of adiposity.<sup>10</sup> In a systematic review, it was shown that DM is among the various comorbidities present in individuals with OSA.<sup>6</sup> Increased catecholamines, along with sleep deprivation caused by OSA, are related to insulin resistance.<sup>6</sup> Researchers observed a moderate prevalence of DM in patients at high risk of OSA.<sup>7</sup> In this study, despite the high prevalence of DM (72.1%), no association with an independent risk factor for OSA was observed ( $p = 0.524$ ).

### Limitations of the Study

Because it is a cross-sectional study, it is known that it is impossible to establish a cause-and-effect relation between risk factors and OSA in STEMI. In addition, polysomnography, the gold standard method to confirm the diagnosis of OSA, was not performed. Lastly, individuals were classified as hypertensive, diabetic, or dyslipidemic based on information recorded in their medical records, including those using antihypertensive, hypoglycemic, and/or antidyslipidemic medications. Therefore, selection bias may arise from individuals who have these comorbidities but are unaware of them.

## Conclusion

The present study reveals a notable prevalence of high risk of OSA among patients with STEMI. Notably, hypertension and gender emerged as significant variables, representing significant risk factors for the development of moderate to high risk of OSA. These findings underscore the importance of OSA screening in post-myocardial infarction patients to mitigate potential adverse clinical outcomes associated with its presence.

## Author Contributions

Conception and design of the research: Carrijo LSS, Magnabosco P, Raponi MBG, Figueiredo VN; acquisition of data: Carrijo LSS, Figueiredo VN; analysis and interpretation of the data: Carrijo LSS, Magnabosco P, Raponi MBG, Oliveira MAM, Araújo SA, Figueiredo VN; statistical analysis: Magnabosco P, Raponi MBG; writing of the manuscript: Carrijo LSS, Oliveira MAM, Araújo SA, Martins LC, Figueiredo VN; critical revision of the manuscript for intellectual

content: Magnabosco P, Raponi MBG, Oliveira MAM, Araújo SA, Martins LC, Figueiredo VN.

## 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 Federal de Uberlândia under the protocol number 23136219.0.0000.5152. 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.

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