## **ORIGINAL ARTICLE**

# Risk Factors for In-Hospital Mortality from Cardiac Causes After Acute Myocardial Infarction

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#### Abstract

**Background:** Risk stratification on admission of patients with acute ST-elevation myocardial infarction (STEMI) is considered a clear strategy for effective treatment, early intervention, and survival.

**Objective:** The purpose of this study was to determine the risk factors for in-hospital mortality from cardiac causes after STEMI.

**Methods:** Observational, retrospective, longitudinal study, with a quantitative approach, based on data from the medical records of individuals diagnosed with STEMI treated at the Emergency Room of a large hospital in the state of Minas Gerais, Brazil, from January 2011 to July 2016. The outcome of interest was 30-day in-hospital mortality from after STEMI. For statistical analysis, the Pearson's chi-square test, Spearman's correlation and multivariable Cox-regression analysis were used, with a significance level of  $\alpha = 0.05$ .

**Results:** Of the 459 patients, 55 (12%) died from cardiac causes within 30 days after STEMI. Mean admission SBP of these patients was 109.08mmHg. The incidence of death was higher in women (23.7%), patients with systemic arterial hypertension (SAH) (13.8%) and elderly patients (16.5%). The elderly — heart rate (HR) = 3.54 — and women — HR = 2.55 — had a statistically significant higher risk of progressing to death when compared to younger adults and men. The highest admission SBP had a protective effect (HR = 0.97), reducing the chance of death by 3%.

**Conclusion:** SBP on admission, female gender and advanced age were significant risk factors for death within 30 days after STEMI.

Keywords: Myocardial Infarction; Blood Pressure; Mortality; Risk Factors.

#### Introduction

Cardiovascular disease is the leading cause of death worldwide<sup>1</sup> and the second leading cause of death in Brazil.<sup>2</sup> Despite continuous efforts by health services with actions to prevent risk factors, promote health and develop technological care, hospital mortality in patients with acute myocardial infarction (AMI) remains high.<sup>3</sup>

Risk stratification upon admission of patients with AMI is considered an effective strategy as it enables early intervention, more effective treatment and, consequently, longer patient survival.<sup>4</sup> In this context, different factors have been proposed as risks for cardiovascular mortality, including advanced age, high Killip class, hyperglycemia, tachycardia, renal dysfunction, atypical chest pain,<sup>5,6</sup> and admission systolic blood pressure (SBP).

Studies involving millions of patients with AMI have shown that the mortality rate from cardiovascular causes within one year after AMI was significantly lower among patients with SBP ≤108mmHg<sup>7</sup> or <120mmHg<sup>8,9</sup> on admission compared to those with SBP greater than 108mmHg<sup>7</sup> or 125mmHg.<sup>8,9</sup> On the other hand, in another study involving 13,104 participants with AMI,

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a significant association was shown between admission SBP <90mmHg and higher in-hospital mortality.<sup>10</sup>

It is understood that the identification of risk factors can support the planning of care to reduce morbidity and mortality in patients with AMI. In this context, the following question was formulated: what are the contributing factors for in-hospital mortality from cardiac causes in patients with AMI? The aim of the present study was to determine the risk factors of in-hospital death from cardiac causes after AMI with STEMI.

## Material and methods

## Type and place of study

This was an observational, longitudinal, retrospective study with a quantitative approach carried out in a large teaching hospital in the countryside of the state of Minas Gerais, Brazil.

#### **Research Participants**

The study population consisted of users of the Emergency Care services of the aforementioned hospital from January 2011 to July 2016. The recruitment process was non-probabilistic.

A list of the medical records of all patients hospitalized during the study period and classified as I21 – AMI, according to the International Code of Diseases (ICD-10) was obtained from the medical records department and the inactive medical records department. From a total of 1318 medical records, 459 (34.82%) were considered eligible, according to the inclusion criteria: age greater than or equal to 18 years; of both sexes; medical diagnosis of STEMI, confirmed by symptoms of ischemia lasting more than 30 minutes for less than 24 hours, ST segment elevation of at least 1 mm (frontal plane) or 2 mm (horizontal plane) in two contiguous leads and elevation followed by decline in biochemical markers of myocardial necrosis with the peak above the 99th percentile; and medical records with complete information of interest.

#### **Data collection**

Data were collected using an instrument developed by the researchers themselves, and consisted of sociodemographic (gender, self-reported skin color and age), clinical data — SBP; diastolic blood pressure (DBP); heart rate (HR); comorbidities; cardiac enzymes; Killip classification — and tobacco use. The instrument was submitted to face and content validation by five experts.

The outcome of interest was in-hospital death within 30 days after STEMI from cardiac causes — recurrent AMI, stroke, heart failure, sudden death or fatal arrhythmia. Hypertensive individuals were considered those who, according to information recorded in the medical record, were using antihypertensive drugs prior to STEMI.

For the classification of heart failure severity in STEMI, the classification proposed by Thomas Killip and John T. Kimball was used, namely: Killip I: no signs of cardiac decompensation; Killip II: with pulmonary crackling rales, third heart sound and high jugular venous pressure; Killip III: with acute pulmonary edema; and Killip IV: with cardiogenic shock or hypotension.<sup>11</sup>

#### Data analysis

Data were analyzed using the Statistical Package for Social Science (SPSS) for Windows software. Quantitative variables showed normal distribution by Table 1 – Sociodemographic and clinical characteristics of patients with STEMI (n = 459). Uberlândia, Minas Gerais, Brazil, 2019

Variables	
Male, n (%)	345 (75.2)
White, n (%)	276 (57.2)
Age, years	63.6 ± 12.8
SBP, mmHg	125.7 ± 25.9
DBP, mmHg	78.1 ± 16.5
PP, mmHg	47.6 ± 16.1
HR, bpm	79.8 ± 18.3
Hypertensive, n (%)	290 (63.2)
Diabetics, n (%)	106 (23.1)
Obesity, n (%)	66 (14.4)
Brain stroke, n (%)	16 (3.5)
Smokers, n (%)	198 (52.8)
Total cholesterol, mg/dl	$191 \pm 47.0$
CKMB, ng/ml	169.3 ± 183.9
Troponin, ng/ml	$4.47 \pm 13.17$
LVEF, %	$50.9 \pm 10.7$
Killip I, n (%)	200 (74.6)
Killip II, n (%)	42 (15.6)
Killip III, n (%)	8 (3.0)
Killip IV, n (%)	18 (6.7)

Values are expressed as percentage or mean ± standard deviation (SD). SBP: systolic blood pressure; DBP: diastolic blood pressure; PP: pulse pressure; mmHg: millimeters of mercury; HR: heart rate; bpm: beats per minute; Min: minute; LVEF: left ventricular ejection fraction; CKMB: creatine kinase.

the Kolmogorov-Smirnov test and were expressed as mean and standard deviation. Qualitative variables were expressed as frequency and percentage. The association of sociodemographic and clinical variables with death was verified by bivariate analysis (Pearson's chi-square test) including measures of association in contingency tables (relative risk and respective confidence intervals) and Spearman's correlation; adjustment for potential confounders included Cox multiple regression analysis. The statistical tests were conducted with a significance level of  $\alpha$  = 0.05 and 95% confidence interval.

## Results

Characteristics of participants (n = 459) are described in Table 1.

Considering the mortality from cardiac causes in the first 30 days after STEMI, it was observed that 55 (12.0%) patients died. Mortality rate was higher in women, patients with hypertension and elderly (Table 2).

Mean (±SD) SBP on admission was  $109.08 \pm 28.21$ mmHg in patients who died and  $127.96 \pm 24.87$ mmHg among survivors. A positive and significant correlation (r = 0.25; p<0.001) was observed between SBP on admission and survival time up to 30 days after STEMI.

Using Cox regression analysis, of the variables evaluated (gender, age, SBP on admission, and obesity), age and sex influenced the occurrence of death. The elderly had 3.54 times greater risk of dying when compared to adults. In addition, females had a 2.55 times greater risk of progressing to death when compared to males. Admission SBP acted as a protective factor, that is, for each additional point on SBP, the risk of the patient progressing to death was reduced by 3% (Table 3).

## Discussion

In a prospective study<sup>12</sup> involving 2369 post-STEMI individuals, the authors analyzed the prevalence and the accumulated number of cardiovascular risk factors, such as SAH, hypercholesterolemia, smoking, diabetes, and obesity, and found that most participants had multiple concomitant factors.12 This is in line with the findings of the present study, which highlights the high prevalence of SAH in this population; although there was no significant association between SAH and mortality (p = 0.07), there was a higher prevalence of this comorbidity in patients who died after STEMI than those who survived. The high prevalence of SAH may be at least in part justified by the aging of the population and the increase in obesity.<sup>13</sup> It is noteworthy that SAH, especially in the elderly, can be related to severe adverse cardiovascular outcomes, such as AMI and death.13

In this study, post-STEMI mortality rates were higher among females and older people, corroborating other

Minas Gerais, Drazii, 2019						
Variables	Dead patients n (%)	Survived patients (n %)	RR* (IC+)	p¶		
Female	27 (23.7%)	87 (76.3%)	2.02(1.70, 4.72)	<0.001		
Male	28 (8.1%)	317 (91.9%)	2.92 (1.79 – 4.73)	<0,001		
Obese	05 (7.6%)	61 (92.4%)	0.50 (0.24 1.42)	0.1/		
Non obese	50 (12.7%)	343 (87.3%)	0.39 (0.24 - 1.43)	0.16		
Hypertensive	40 (13.8%)	250 (86.2%)	1 55 (0.88 - 0.50)	0.07		
Non-hypertensive	15 (8.9%)	154 (91.1%)	1.55 (0.88 – 2.72)	0.07		
Elderly	48 (16.5%)	243 (83.5%)	1.14 (1.08 – 1.21)	< 0.001		
Non-elderly	07 (4.2%)	161 (95.8%)				
*RR: gross relative risk (not adjusted); †IC: confidence interval; p¶: probability ( $p \le 0.05$ ). Pearson's chi-square test.						

Table 2 – Association of sex, obesity, hypertension and age with 30-day mortality after STEMI (n = 459), Uberlândia, Minas Gerais, Brazil, 2019

studies.<sup>14-18</sup> In addition, previous reports<sup>18-20</sup> have shown that, when suffering from AMI, women were older and had a higher prevalence of cardiovascular risk factors, such as diabetes mellitus, hypercholesterolemia and SAH, when compared to men. A survey carried out with 31,698 patients who suffered STEMI showed that, although women had a higher in-hospital mortality rate than men, this difference did not seem to be caused by sex itself, but due to comorbidities and age differences.<sup>15</sup>

As the population ages and the prevalence of risk factors associated with lifestyle increases, the incidence of AMI in women will likely be more similar to that of men.<sup>21</sup> Gender differences in cardiovascular risk have become more evident, indicating the importance of addressing risk factors for preventive strategies and policies.

It is evident that increasing age is an important influencing factor in the mortality of post-AMI patients.<sup>19</sup> In a study that evaluated the impact of age on the patient's prognosis after the event, a worse prognosis was observed for those with more advanced age.<sup>22</sup> At 60 years of age, men are at greater risk of suffering an AMI, but after 70 years of age both sexes have the same chance.<sup>8</sup> Aging results in several structural and functional changes in the arterial vasculature. A study investigated the effects of arterial stiffness on left ventricular (LV) function in a period from three and six months after AMI and observed that arterial stiffening can result in a less effective recovery of LV function.<sup>23</sup> Increased wave velocity pulse rate and age are associated with changes in metabolic syndrome components, inflammatory markers and oxidative

stress.<sup>24</sup> However, each of these components has a different and specific impact on arterial stiffness according to age. In particular, oxidative stress may be independently associated with arterial stiffness in individuals over 45 years of age.<sup>25</sup>

In risk stratification of patients with AMI on admission, BP has been an important prognostic factor. In our study, we observed that admission SBP values influenced the post-STEMI mortality. Similar results were demonstrated in other studies that indicated admission SBP <106 mmHg as an independent predictor of hospital mortality after STEMI, and admission

Table 3 – Cox multivariate regression model, with relative risk and confidence interval for 30-day mortality after STEMI (n = 459), Uberlândia, Minas Gerais, Brazil, 2019.

Variables	HR*	IC†	p¶
Sex	2.55	1.44 - 4.54	0.001
Age	3.54	1.47 - 8.51	0.005
SBP admission	0.97	0.96 - 0.98	< 0.001
HBP	1.16	0.61 – 2.20	0.64
Obesity	0.63	0.22 – 1.78	0.38

\*HR: adjusted relative risk (hazard ratio); †IC: confidence interval; p¶: probability ( $p \le 0.05$ ); SBP: systolic blood pressure. Reference Category: Male; Adult; Non-hypertensive; Non-obese; high blood pressure

SBP <125mmHg as an independent predictor of cardiovascular mortality one year after STEMI.<sup>8,26</sup> These results suggest that high admission SBP can be considered an important protective factor in post-STEMI mortality.

A study conducted with 1475 patients with STEMI showed that an admission SBP between 141-158mmHg could be correlated with a better in-hospital prognosis, while an admission SBP <105mmHg was associated with in-hospital death.<sup>26</sup> In this study, as the sample was not homogeneous, we chose to investigate mean admission SBP values of individuals who progressed to death instead of determining a cutoff for admission SBP that would predict mortality. A prospective study with 167 patients found that an admission SBP lower than 95mmHg was a significant predictor of 30-day mortality in patients with STEMI.<sup>27</sup>

The impact of BP on STEMI prognosis is still a matter of debate. Researchers have found that increased admission SBP values in the acute phase of AMI indicate that the heart still responds to stress, suggesting that the use of drug classes such as nitrates, beta blockers and angiotensin-converting enzyme inhibitor would be safe in this context.<sup>7</sup> Therefore, admission BP values after AMI should be interpreted in contrast with the conventional, preventive point of view, and low admission BP values should serve, therefore, as a warning sign in these patients.<sup>28</sup>

#### Limitations of the study

This study has limitations. The study did not include data that may influence post-STEMI mortality, such as the time from symptom onset to admission, or pre-hospital and hospital treatment information.

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## Conclusion

Results of the present study add evidence to the clinical practice of health professionals, by demonstrating that female gender, advanced age, and admission BP influence post-STEMI mortality. This is an important finding considering that the professional's decision-making, when based on risk assessment, results in the prevention of cardiovascular complications, better quality of care and patient safety.

## **Author Contributions**

Conception and design of the research, acquisition of data, Analysis and interpretation of the data, statistical analysis, obtaining financing writing of the manuscript and critical revision of the manuscript for intellectual content: Oliveira GV, Raponi MBG, Magnabosco P, Oliveira MAM, Araújo SA, Haas VJ, 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 2.032.101

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