

## Preinfarction Angina and In-hospital Outcome of Elderly Patients with Acute Myocardial Infarction

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### Summary

**Background:** Preinfarction angina (PIA) may be a marker of ischemic preconditioning. A decrease in infarct size, ventricular remodeling, congestive heart failure, cardiogenic shock or death was demonstrated in the presence of preinfarction angina. These findings were more evident in adults, but not in the elderly.

**Objective:** To assess the relationship between PIA and the clinical course of elderly patients with acute myocardial infarction (AMI).

**Methods:** This was a case-series study with a comparison group. A total of 36 patients with ST-segment elevation AMI were included in the study and divided into two groups: group A (21 patients with PIA) and group B (15 patients without PIA).

**Results:** Mean age of the study population was 70.5 years, and there was a predominance of males (73%). Mean body mass index was 25.3 Kg/m<sup>2</sup>. Hypertension was present in 77.8%, diabetes in 27.8% and dyslipidemia in 32.4%. Type-A chest pain was reported by 71.4% of patients, and the majority of them (72.2%) were in Killip class I. Clinical endpoints for groups A and B were as follows: postinfarction angina 9.5% versus 20%,  $p = 0.630$ ; heart failure 23.8% versus 13.3%,  $p = 0.674$ ; urgent revascularization 4.8% versus 6.7%,  $p = 1$ ; and cardiac arrhythmia 0% versus 6.7%,  $p = 0.417$ . There was no case of reinfarction, cardiogenic shock or death within 30 days of follow up in either group.

**Conclusion:** In this case series, preinfarction angina was not associated with better clinical course in elderly patients with AMI. (Arq Bras Cardiol 2007;89(6):334-340)

**Key words:** Angina unstable; myocardial infarction; aged.

### Introduction

The clinical course after coronary occlusion depends mostly on myocardial vulnerability. Murry et al<sup>1</sup>, reported that short periods of myocardial ischemia rendered the heart more resistant to subsequent, longer ischemic insults, thereby limiting infarct size. This phenomenon, called ischemic preconditioning (IPC), is considered a powerful endogenous protective mechanism against myocardial ischemia<sup>1</sup>.

The warm-up phenomenon that occurs in more than 50% of patients with coronary artery disease (CAD) strongly suggests that IPC exists in humans. These patients report angina symptoms that are more severe in the morning and subside during the course of the day, providing evidence that myocardial metabolism becomes more efficient during subsequent efforts<sup>2</sup>. Angina pectoris prior to acute myocardial infarction (AMI), called preinfarction angina (PIA), is likely to be a marker of IPC<sup>3-9</sup>.

The presence of PIA was associated with better clinical course after AMI and reduction in infarct size, as assessed indirectly by measurement of myocardial necrosis markers<sup>3</sup>

or quantitative SPECT (single-photon emission computed tomography)<sup>4</sup>. Other authors have found a decrease in ventricular remodeling<sup>5</sup>, as well as in the incidence of ventricular arrhythmias, congestive heart failure (CHF), cardiogenic shock, and death<sup>6-8</sup>. Reperfusion of the infarct-related artery was also found to be faster after thrombolytic therapy when AMI was preceded by PIA<sup>9</sup>.

The protective effect of IPC in elderly patients is still a matter of debate. Ishihara et al<sup>10</sup> have found that PIA was associated with smaller infarct size and improved short- and long-term survival. The same benefits were not demonstrated in patients older than 70 years of age<sup>10</sup>. Abete et al<sup>11</sup> also found favorable effects of preinfarction angina in adults; these effects, however, were less obvious in elderly patients<sup>11</sup>.

The aim of this study was to evaluate the association between PIA and the clinical course (postinfarction angina, urgent surgical or percutaneous revascularization, heart failure, complex arrhythmias, cardiogenic shock, and death) of elderly patients with ST-segment elevation myocardial infarction (STEMI).

### Methods

This is a case-series study using a comparison group. From March to October 2005, a total of 36 elderly patients (60 years or older, according to the definition proposed by the World

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Health Organization for developing countries<sup>12</sup>) were recruited from the Coronary Care Unit of Agamenon Magalhães Hospital and prospectively evaluated for the study endpoints. These patients were divided into two groups: group A, comprising 21 patients with PIA; and group B, comprising 15 patients without PIA.

Patients with previous history of AMI and myocardial revascularization, either surgical or percutaneous, were excluded from the study, as were those who failed to provide reliable information or were lost to follow-up. The presence of PIA was considered an independent variable, and the dependent variables were the following clinical endpoints: postinfarction angina, reinfarction, need for urgent revascularization (surgical or percutaneous), malignant ventricular arrhythmias, CHF, cardiogenic shock, and death within 30 days after AMI.

Patient data, including personal identification, present history of disease, systems review, history of diseases, and physical examination, were collected by a single investigator using a standard form. Patients were treated according to the standard hospital protocol without interference from the investigators. Information about treatments used, clinical outcomes, and results of additional examinations was retrieved from medical records.

Data were processed using Excel 2000 spreadsheet, and statistical analyses were performed using the Minitab 14.1 software. Continuous variables were expressed as mean and standard deviation and categorical variables, as absolute and relative frequencies. The Fisher-Freeman-Halton exact test was used to compare frequencies between both groups for categorical variables, and the Student's *t*-test was used for continuous variables. A 95% confidence interval was used, and the significance level was set at 5% ( $p \leq 0.05$ ).

The study protocol was approved by the Research Ethics Committee of Agamenon Magalhães Hospital in accordance with regulations for research involving human subjects (Resolution 196/96), and all patients signed an informed consent form.

As data were not collected continuously 24 hours per day, there may have been selection bias. This research relied on information provided by the patients themselves; therefore, memory bias cannot be discarded, particularly when data were not collected on the first day of admission. The investigator was not blinded to the presence or absence of PIA, and this may have resulted in measurement bias.

## Results

Demographic features were similar in both groups (Table 1). There was a male preponderance in group B, but without statistical significance ( $p = 0.096$ ). Patients' age ranged from 60 to 92 (mean age 70.5 years). There was no statistically significant difference between both groups regarding clinical characteristics. Chest pain, graded as type C and D, was not present in the study sample. Symptoms most frequently associated with anginal pain are shown in Figure 1. In the PIA group, 19% of the patients arrived at the emergency room more than 12 hours after symptoms onset, as compared with 26% in the non-PIA group. Table 2 summarizes the main

cardiovascular risk factors of the study sample. Only 25% of the hypertensive patients were on antihypertensive medication. Among the diabetic, 8.3% were taking glucose-lowering drugs, and no dyslipidemic patient was taking lipid-lowering drugs.

Fifteen patients (71.4%) in group A and eight (53.3%) patients in group B had anterior ST-segment elevation, and six (28.6%) patients in group A and seven (46.7%) patients in group B had inferior ST-segment elevation,  $p = 0.310$ . There was no case of ST-segment elevation in the other left ventricular walls. Treatments given to the patients are shown in Table 3. No patient in either group underwent primary angioplasty as first-choice treatment, because Agamenon Magalhães Hospital did not have a hemodynamic laboratory to perform percutaneous intervention for AMI patients. Length of hospital stay was  $31.0 \pm 21.1$  days for patients in group A and  $31.1 \pm 35.5$  days for patients in group B ( $p = 0.983$ ). Echocardiographic findings during hospitalization are summarized in Table 4. Patients in group A had, on average,  $1.8 \pm 1$  coronary arteries with stenosis  $> 50\%$ , as compared to  $2.0 \pm 1.3$  in group B ( $p = 0.728$ ).

In-hospital clinical outcomes are shown in table 5. There was no case of cardiogenic shock, reinfarction or death in either group.

## Discussion

This study assessed patients aged 60 or older (mean age  $70.5 \pm 7.4$ ), according to the WHO definition of elderly people for developing countries<sup>12</sup>. Other studies assessing PIA in the elderly used different definitions and included patients with more advanced age, but achieved results similar to those of this subset of patients regarding the absence of the protective effect of PIA<sup>10,11</sup>. Our sample was predominantly male, in agreement with literature data, which report higher prevalence of AMI in this population<sup>6,10,11,13</sup>, as well as greater risk for developing AMI<sup>14</sup>.

Mean time interval between the onset of symptoms and the diagnosis of AMI was high in both groups, beyond the optimal time window for thrombolytic therapy. This may be explained by the fact that some patients were included in the study during the subacute phase of AMI. Other factors that may have contributed to this finding are: neglect of symptoms by the patients, which led them to delay seeking medical attention and the logistics of medical care, particularly for those from cities located in the interior of the state that provided low-complexity services. The higher number of patients admitted more than 12 hours after the onset of symptoms in the non-PIA group suggests that the presence of painful symptoms prior to AMI could have prompted them to seek medical attention more quickly.

Even though CAD is a highly prevalent disease, its diagnosis in elderly people is not that simple<sup>15</sup>. This population often experiences atypical chest pain during AMI. Some hypotheses to explain this finding include diminished cognitive function, increased collateral circulation, and reduced pain perception due to comorbid conditions or localized autonomic dysfunction<sup>16</sup>. In the Framingham study, more than 40% of the AMI cases were unrecognized, that is, were clinically silent in patients aged 75 or older, especially in women<sup>14</sup>. In

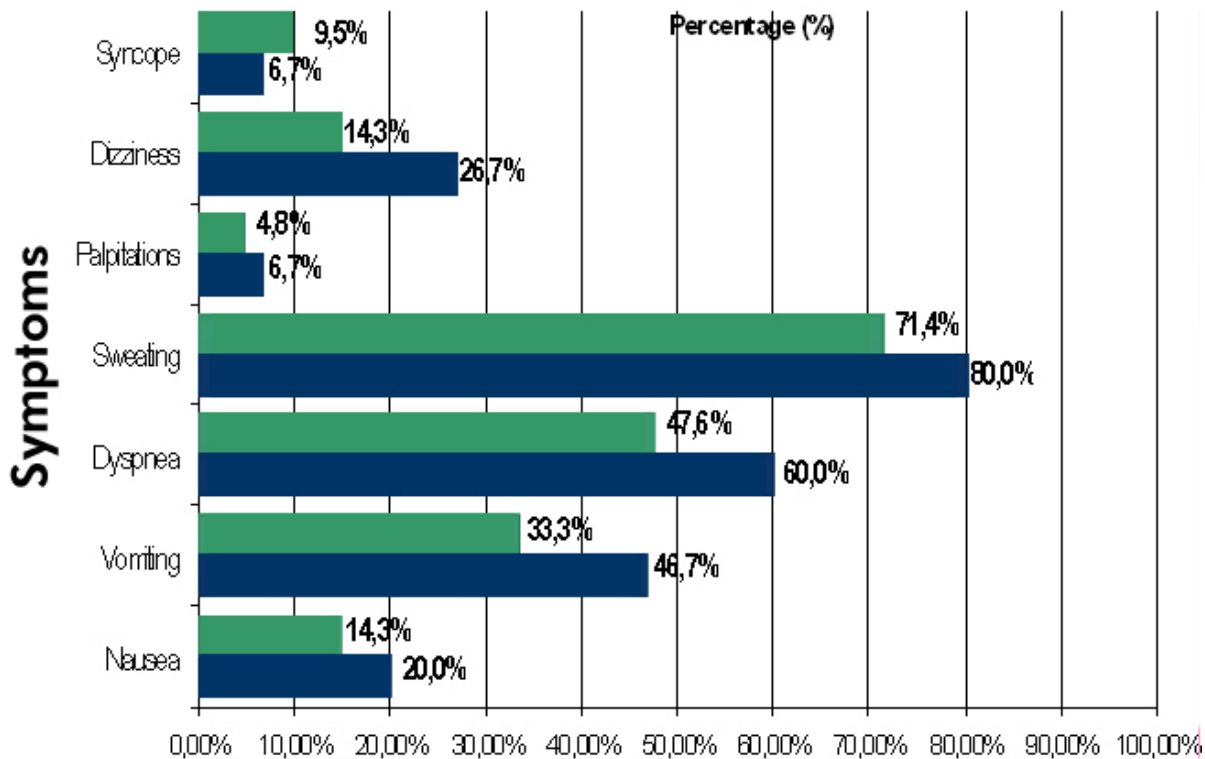


Fig. 1 - Distribution of angina-related symptoms in elderly patients with AMI. Agamenon Magalhães Hospital ; 2005.

Table 1 – Distribution of clinical and demographic characteristics of elderly patients with AMI. Agamenon Magalhães Hospital; 2005

Preinfarction angina				
Characteristics	Yes (n = 21)	No (n = 15)	Total (n = 36)	p value
Male	9 (43.0%)	11 (73.0%)	20 (55.6%)	0.096*
Age (in years)	69.8 ± 6.6	71.5 ± 8.6	70.5 ± 7.4	0.525**
BMI	25.1 ± 3.7†	25.7 ± 4.6	25.3 ± 4.0	0.661**
<b>Chest pain</b>				<b>0.474*</b>
A	16 (76.2%)	9 (64.3%)	25 (71.4%)	
B	5 (23.8%)	5 (35.7%)	10 (28.6%)	
Chest pain interval (in hours)	15.9 ± 35.1	12.3 ± 17.9	14.4 ± 28.9	0.685**
SBP (mm Hg)	142.4 ± 21.9	142.0 ± 29.1	142.2 ± 24.7	0.966**
DBP (mm Hg)	83.8 ± 12.8	90.7 ± 21.2	86.7 ± 16.9	0.277**
<b>Killip classification</b>				
I	16 (76.2%)	10 (66.7%)	26 (72.2%)	0.745*
II	4 (19.0%)	3 (20.0%)	7 (19.4%)	
III	1 (4.8%)	2 (13.3%)	3 (8.3%)	

BMI - body mass index; SBP - systolic blood pressure; DBP - diastolic blood pressure. \*Fisher exact test; \*\*Student's t-test; †n - 20.

Table 2 – Cardiovascular risk factors in elderly patients with AMI. Agamenon Magalhães Hospital; 2005

Preinfarction angina				
RISK FACTORS	Yes (n = 21)	No (n = 15)	Total (n = 36)	p*
Hypertension	17 (81.0%)	11 (73.3%)	28 (77.8%)	0.694
Diabetes	6 (28.6%)	4 (26.7%)	10 (27.8%)	1.000
Dyslipidemia	8 (42.1%)	3 (20.0%)	11 (32.4%)	0.271
Smoking	9 (42.9%)	7 (46.7%)	16 (44.4%)	1.000
Family history of CAD	9 (42.9%)	7 (46.7%)	16 (44.4%)	1,000

CAD = Coronary artery disease (\*) Fisher's exact test.

Table 3 – Treatments given to elderly patients with AMI. Agamenon Magalhães Hospital; 2005

Preinfarction angina				
Treatment	Yes (n = 21)	No (n = 15)	Total (n = 36)	p value
Conservative	8 (38.1%)	7 (46.7%)	15 (41.7%)	0,736*
Thrombolytic	13 (61.9%)	8 (53.3%)	21 (58.3%)	

(\*) Fisher's exact test

this study, all patients had chest pain as part of the clinical manifestation of acute myocardial infarction. Type-A chest pain was reported by 71.4% of the patients, and type-B chest pain, by 28.6%. This discrepancy with the literature may be explained by methodological differences, as well as by the fact that the hospital in which the study was conducted was a tertiary reference center for cardiology; therefore, many patients had been to other medical institutions before being admitted to this hospital.

This sample included more PIA patients than non-PIA patients. The presence of PIA reported in the literature varies widely, with some studies even showing an inverse proportion<sup>5-9</sup>.

Most patients were in Killip classes I (72.2%) and II (19.4%). Killip's classification system<sup>17</sup>, originally described in 1967, stratified the risk of patients admitted to the coronary care unit according to the severity of CHF and the presence of cardiogenic shock. This author found that 67% of the patients were between classes II and IV. Twenty years later, the GISSI study (*Gruppo Italiano per lo Studio della Streptochinasi nell'Infarto Miocardico*) found that 71% of patients were in Killip class I and 23% were in Killip class II on admission<sup>13</sup>.

The present study included patients who underwent reperfusion therapy and conservative therapy. However, no statistically significant difference was found between these therapeutic strategies. All patients with indication for reperfusion therapy (58.3%) underwent chemical thrombolysis with streptokinase or tenecteplase. When both groups were compared, a greater number of patients in group A (61.9%) had undergone thrombolytic therapy than in group B (53.3%), but this difference did not reach statistical significance.

Length of hospital stay (31.1 + 27.6 days) far exceeded the average published by the Sistema de Informações Hospitalares

of the SUS (Hospital Information System of the Unified Health System [SIH/SUS]) for cardiovascular diseases in the same period, which was approximately 10 days<sup>18</sup>.

This may be explained by the difficulty in scheduling examinations due to the great number of inpatients and outpatients, as well as the fact that some patients had to stay in hospital before undergoing CABG surgery because of the severity of their angiographic findings.

Our study failed to establish an association between preinfarction angina and echocardiographic results. No statistically significant difference was found between left ventricular diameters (LVDD and LVSD) when both groups were compared. In contrast, left ventricular ejection fraction (LVEF) was unexpectedly greater in group B ( $p = 0.04$ ). Echocardiographic examinations were performed by more than one echocardiographer, and there may have been interobserver variability during image acquisition for LVEF measurement. In most cases, LVEF was calculated using the Teichholz formula, which considers the existence of a constant relationship between left ventricular (LV) major and minor axes. However, when the basal parts of the inferior wall or the interventricular septum are hypokinetic and the rest of the LV contracts normally, the systolic function is underestimated<sup>19</sup>. Simpson's rule was rarely used by the echocardiographers involved in this study. When large akinetic regions of the LV were present, estimation was done visually.

In the present study, mitral regurgitation (MR) was more common in the PIA group (44% vs. 35.7;  $p=0,725$ ), but without statistical significance. In addition, we could not determine whether MR occurred before or after the AMI, since echocardiographic examinations prior to the event were not available for comparative analysis. Mitral regurgitation, even of mild degree, detected by color Doppler echocardiography,

Table 4 – Echocardiographic data of the elderly patients with AMI. Agamenon Magalhães Hospital; 2005

Characteristics	Preinfarction angina			p value
	Yes (n = 21)	No (n = 15)	Total (n = 36)	
Mitral regurgitation	8 (44.4%) <sup>†</sup>	5 (35.7%) <sup>‡</sup>	13 (40.6%)	0.725*
LVDD (mean ± SD)	5.2 ± 0.8 <sup>§</sup>	5.5 ± 0.4 <sup>//</sup>	5.3 ± 0.6	0.117**
LVSD (mean ± SD)	3.8 ± 0.6 <sup>§</sup>	3.9 ± 0.6 <sup>‡</sup>	3.9 ± 0.7	0.823**
LVEF (mean ± SD)	47.1 ± 8.4 <sup>†</sup>	55.2 ± 11.7 <sup>‡</sup>	50.1 ± 10.6	0.040**

\*Fisher's exact test; \*\*Student's t-test; <sup>†</sup>n = 18; <sup>‡</sup>n = 14; <sup>§</sup>n = 17; <sup>//</sup>n = 15

Table 5 – In-hospital outcome of elderly patients with AMI. Agamenon Magalhães Hospital 2005

Clinical endpoints	Preinfarction angina			p value	COST, R\$	95% CI for OR
	Yes (n = 21)	No (n = 15)	Total (n = 36)			
Preinfarction angina	2 (9.5%)	3 (20.0%)	5 (13.9%)	0.630	0.4	0.03 to 4.35
Urgent revascularization (PTCA or CABG)	1 (4.8%)	1 (6.7%)	2 (5.6%)	1.000	0.7	0.01 to 58.8
Heart failure	5 (23.8%)	2 (13.3%)	7 (19.4%)	0.674	2.0	0.27 to 24.2
Complex arrhythmias (VT/VF)	0 (0%)	1 (6.7%)	1 (2.8%)	0.417	0.0	0.00 to 27.9

PTCA = percutaneous transluminal coronary angioplasty; CABG = coronary artery bypass graft surgery; VT = ventricular tachycardia; VF = ventricular fibrillation; \*Fisher exact test; \*\*Odds ratio for clinical outcomes and preinfarction angina.

has been associated with higher morbidity and mortality<sup>20</sup>. Pre-AMI mitral regurgitation was also associated with worse clinical outcome<sup>21</sup>.

ST-segment elevation, on ECG, was more frequent in anterior wall leads in patients who reported PIA and in inferior wall leads in those who did not. Anterior myocardial infarctions involve a larger mass of the myocardium and are associated with increased morbidity and mortality. In fact, heart failure was more prevalent in the PIA group than in the non-PIA group, although without statistical significance. The possibility that the protective effect of PIA has been "masked" by the greater number of patients with anterior AMI in group A, albeit speculative, cannot be excluded. Nevertheless, Kosuge et al<sup>22</sup> reported that the beneficial effects of PIA were more evident in patients with anterior infarction than in those with non-anterior infarction<sup>22</sup>.

As far as clinical endpoints are concerned, the number of patients who experienced postinfarction angina was lower in the PIA group than in the non-PIA group (9.5% vs. 20%), with odds ratio (OR) of 0.4 [95% CI: 0.03-4.35]. The same was true for urgent revascularization (4.8% vs. 6.7%), OR = 0.7 [95% CI: 0.01-58.8], and complex arrhythmias (0% vs. 2.8%), OR = 0 [95% CI: 0-27.9]. There were no cases of cardiogenic shock, reinfarction or death in either group. An OR less than 1 for postinfarction angina, urgent revascularization, and complex arrhythmias would lead to the speculation that this better clinical course was due the presence of PIA. However, as the confidence interval included unity, such inference could not be made. Our results failed to reach statistical significance, probably because of the small sample size.

Abete et al<sup>23</sup> have demonstrated that the incidence of CHF

or cardiogenic shock (3.3% vs. 10.7%, p < 0.05), in-hospital mortality (2.6% vs. 10%, p < 0.01), and the combined events of death and CHF (5.9% vs. 20.7%, p < 0.0003) was lower in adult AMI subjects with PIA. This beneficial effect, however, was not demonstrated in elderly patients. This result was independent of thrombolytic therapy, even with the PIA group receiving more lytic therapy than the non-PIA group. After logistic regression analysis for potential confounders, the results remained unchanged<sup>11</sup>.

Based on animal model studies showing that caloric restriction restored IPC, the same authors assessed the influence of body mass index (BMI) on the protective effect of PIA in the elderly and concluded that such protection was preserved only in the subset of elderly patients with the lowest BMI<sup>23</sup>. Ishihara et al<sup>10</sup> also reported absence of the protective effect of PIA in elderly people<sup>10</sup>. On the other hand, Kloner et al<sup>24</sup> conducted a retrospective study of the patients of the TIMI-4 study and found that elderly patients with PIA had lower rates of the combined endpoints of death, CHF/cardiogenic shock and/or reinfarction, compared with those without PIA<sup>24</sup>. Jimenez-Navarro et al<sup>25</sup> found that PIA protected against in-hospital adverse outcomes and preserved LV function in older patients<sup>25</sup>. Kosuge et al<sup>26</sup> reported that PIA was associated with smaller myocardial infarct size and better in-hospital survival in both elderly and non-elderly patients<sup>26</sup>.

Rezkalla et al<sup>27</sup> pointed out that the protective effect of IPC in humans is characterized by marked individual variations and seems to be attenuated in women, people with diabetes and the elderly<sup>27</sup>. The high mortality rate found in elderly patients who have AMI may be partly explained by the age-related reduction in ischemic preconditioning. The following

speculations might explain this reduction: decreased capacity to release mediators that activate the endogenous protective mechanism<sup>28</sup> and less probability of reperfusion<sup>11</sup>. According to Abete et al<sup>29</sup>, ischemic preconditioning may be preserved in elderly patients with high levels of physical activity<sup>29</sup>. In this respect, it is noteworthy that the population studied by Kosuge et al<sup>26</sup>, mentioned above, consisted of elderly patients with higher levels of physical activity.

A potential limitation of this study was our failure to diagnose silent ischemia prior to AMI, as a possible equivalent of preinfarction angina. Ambulatory ECG (Holter monitoring) might have detected silent ischemia, but it was not possible to select patients prior to AMI, making this procedure impracticable.

Understanding the IPC phenomenon, particularly in humans, opens up a new horizon in CAD management, and further prospective and experimental clinical trials may help to expand our knowledge on the subject, which will be translated into benefits for the elderly population.

## References

1. Murry CE, Jennings RB, Reimer KA. Preconditioning with ischemia: a delay of lethal cell injury in ischemic myocardium. *Circulation*. 1986; 74: 1124-36.
2. Tomai F. Warm up phenomenon and preconditioning in clinical practice. *Heart*. 2002; 87: 99-100.
3. Ottani F, Galvani M, Ferrini D, Sorbello F, Limonetti P, Pantoli D, et al. Prodromal angina limits infarct size: a role for ischemic preconditioning. *Circulation*. 1995; 91: 291-7.
4. Yamagishi H, Akioka K, Hirata K, Sakanoue Y, Toda I, Yoshiyama M, et al. Effects of preinfarction angina on myocardial injury in patients with acute myocardial infarction: a study with resting 123I-BMIPP and 201Tl myocardial infarction SPECT. *J Nucl Med*. 2000; 41: 830-6.
5. Solomon SD, Anavekar NS, Greaves S, Rouleau JL, Hennekens C, Pfeffer MA, HEART Investigators. Angina pectoris prior to myocardial infarction protects against subsequent left ventricular remodeling. *J Am Coll Cardiol*. 2004; 43 (9): 1511-4.
6. Kloner RA, Shook T, Antman EM, Cannon CP, Przyklenk K, Yoo K, et al. Prospective temporal analysis of the onset of preinfarction angina versus outcome: an ancillary study in TIMI-9B. *Circulation*. 1998; 97: 1042-5.
7. Anzai T, Yoshikawa T, Asakura Y, Abe S, Akaishi M, Mitamura H, et al. Preinfarction angina as a major predictor of left ventricular function and long-term prognosis after a first Q wave myocardial infarction. *J Am Coll Cardiol*. 1995; 26: 319-27.
8. Kloner RA, Shook T, Przyklenk K, Davis VG, Junio L, Matthews RV, et al. Previous angina alters in-hospital outcome in TIMI 4: a clinical correlate to preconditioning? *Circulation*. 1995; 91: 37-47.
9. Andreotti F, Pasceri V, Hackett DR, Davies GJ, Haider AW, Maseri A. Preinfarction angina as a predictor of more rapid coronary thrombolysis in patients with acute myocardial infarction. *N Engl J Med*. 1996; 334: 7-12.
10. Ishihara M, Sato H, Tateishi H, Kawagoe T, Shimatani Y, Ueda K, et al. Beneficial effect of prodromal angina pectoris is lost in elderly patients with acute myocardial infarction. *Am Heart J*. 2000; 139 (5): 881-8.
11. Abete P, Ferrara N, Cacciatore F, Madrid A, Bianco S, Calabrese C, et al. Angina-induced protection against myocardial infarction in adult and elderly patients: a loss of preconditioning mechanism in the aging heart? *J Am Coll Cardiol*. 1997; 30: 947-54.
12. Report of the World Health Organization. Active ageing: a policy framework. *Aging Male*. 2002; 5 (1): 1-37.
13. Gruppo Italiano per lo Studio della Streptochinasi nell'Infarto Miocardico (GISSI). Effectiveness of intravenous thrombolytics treatment in acute myocardial infarction. *Lancet*. 1: (8478): 397-402.
14. Kannel WB, Abbott RD. Incidence and prognosis of unrecognized myocardial infarction: an update on the Framingham study. *N Engl J Med*. 1984; 311: 1144-7.
15. Lie JT, Hammond PI. Pathology of the senescent heart: anatomic observation on 237 autopsy studies of patients 90 to 105 years old. *Mayo Clin Proc*. 1998; 63: 552-64.
16. Gregoratos G. Clinical manifestations of acute myocardial infarction in older patients. *Am J Geriatr Cardiol*. 2001; 10: 345-7.
17. Killip T, Kimball JT. Treatment of myocardial infarction in a coronary care unit: a two year experience with 250 patients. *Am J Cardiol*. 1967; 20 (4): 457-64.
18. Ministério da Saúde – Sistema de Informações Hospitalares do SUS (SIH/SUS) 2006. [Acesso em 2006 mar 5]. Disponível em: <<http://www.datasus.gov.br>>.
19. Teichholz LE, Kreulen T, Herman MV, Gorlin R. Problems in echocardiographic volume determinations: echocardiographic-angiographic correlations in the presence of absence of asynergy. *Am J Cardiol*. 1976; 37: 7-11.
20. Feinberg MS, Schwammenthal E, Shlizerman L, Porter A, Hod H, Friemark D, et al. Prognostic significance of mild mitral regurgitation by color Doppler echocardiography in acute myocardial infarction. *Am J Cardiol*. 2000; 86 (9): 903-7.
21. Zamorano J, Isla LP, Oliveros L, Almeria C, Rodrigo JL, Aubele A, et al. Prognostic influence of mitral regurgitation prior to a first myocardial infarction. *Eur Heart J*. 2005; 26 (4): 319-21.
22. Kosuge M, Kimura K, Kojima S, Sakamoto T, Ishihara M, Asada Y, et al. Effects of preinfarction angina pectoris on infarct size and in-hospital mortality after coronary intervention for acute myocardial infarction. *Am J Cardiol*. 2003; 92 (7): 840-3.
23. Abete P, Cacciatore F, Ferrara N, Calabrese C, de Santis D, Testa G, et al. Body mass index and preinfarction angina in elderly patients with acute myocardial infarction. *Am J Clin Nutr*. 2003; 78: 796-801.
24. Kloner RA, Przyklenk K, Shook T, Cannon CP. Protection Conferred by Preinfarction Angina is Manifest in the Aged Heart: Evidence from TIMI 4 Trial. *J Thromb Thrombolysis*. 1998; 6 (2): 89-92.
25. Jimenez-Navarro M, Gomez-Doblas JJ, Alonso-Briales J, Hernandez Garcia JM, Gómez G, Alcantara AG, et al. Does angina the week before protect against first

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- myocardial infarction in elderly patients? *Am J Cardiol.* 2001; 87 (1): 11-5.
26. Kosuge M, Kimura K, Kojima S, Sakamoto T, Ishihara M, Asada Y, et al. Beneficial effect of preinfarction angina on in-hospital outcome is preserved in elderly patients undergoing coronary intervention for anterior acute myocardial infarction. *Circ J.* 2005; 69: 630-5.
27. Rezkalla SH, Kloner RA. Ischemic preconditioning and preinfarction angina in the clinical arena. *Nat Clin Pract Cardiovasc Med.* 2004; 1 (2): 96-102.
28. Cribier A, Korsatz L, Koning R, Rath P, Gamra H, Stix G, et al. Improved myocardial ischemic response and enhanced collateral circulation with long repetitive coronary occlusion during angioplasty: a prospective study. *J Am Coll Cardiol.* 1992; 20: 578-86.
29. Abete P, Ferrara N, Cacciatore F, Sagnelli E, Manzi M, Carnovale V, et al. High level of physical activity preserves the cardioprotective effect of preinfarction angina in elderly patients. *J Am Coll Cardiol.* 2001; 28: 1357-65.