Infection Complication Portends Poor Prognosis in Acute Myocardial Infarction

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Objective

To determine both the incidence and impact of infectious complications of acute myocardial infarction (AMI) on length of hospital stay and mortality.

Methods

This is a retrospective, case-control clinical trial involving medical records review. The study population consisted of patients admitted to the Coronary Care Unit (CCU) of the Hospital das Clínicas Heart Institute of the University of São Paulo Medical School – FMUSP - with AMI between January 1996 and December 1999.

Results

One thousand two hundred and twenty-seven patients were analyzed, and 60 (5%) met diagnostic criteria for infectious complication of AMI (infected group). The other 1167 patients served as control group. Mean age (67.5 versus 62.6), hospital length of stay (26.6 versus 12.0 days), and in-hospital mortality (45% versus 12%) were higher in the infected group. Mortality rate was higher among patients who underwent more than three invasive procedures (68% and 32%, p = 0.006). The most frequent infections were pulmonary (63%), urinary tract (37%) and positive blood cultures with no identifiable site of infection (8%).

Conclusion

In the population studied, infectious complication rate was 5%. Prolonged hospital stay and high mortality rate suggest that infection complication has a great impact on AMI patients admitted to the coronary care unit.

Key words

Myocardial infarction, infection, complication, mortality.

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According to data from the Brazilian's public health care system (SUS), in 2000 more than 40,143 patients were admitted with acute myocardial infarction (AMI). Mean hospitalization was 7.7 days, and mortality rate was 16%[1]. Most deaths related to AMI, however, occur before hospital admission, usually secondary to severe cardiac arrhythmias[2]. After admission, AMI complications account for a significant proportion of deaths. Foremost among them are electrical, hemodynamic or mechanical, inflammatory, and infectious complications. Their associated mortality rate, as well as incidence and severity, are of great concern for all health care professionals involved in the management of AMI patients. Prompt diagnosis and appropriate treatment of these complications are crucial in the attempt to improve clinical outcomes.

Recent studies, however, suggest that the demographic profile of the population admitted with AMI is changing. The increase in these patients' age group is a most relevant data[1,3]. This phenomenon may reflect a higher prevalence of other diseases, such as comorbidities, among patients admitted with AMI. In fact, some studies have already identified a higher prevalence of diabetes mellitus associated with AMI[3], which in turn may increase the incidence of infectious complications in AMI, as with other diseases that affect elderly and/or diabetic patients[4,5,6,7] .

Both the change in demographic profile (older patients) and higher incidence of diabetes mellitus as a comorbidity in acute myocardial infarction may have contributed to these outcomes. Among other possible causes for the development of infectious complications are prolonged immobilization, invasive procedures, and other comorbidities. The lack of conclusive information in the literature about the incidence and impact of infectious complications of AMI on morbidity and mortality prompted this study.

Population - A retrospective review of medical records of all patients with AMI admitted to the Coronary Care Unit of the Hospital das Clínicas Heart Institute of the University of São Paulo from January 1996 to December 1999 was done.

Criteria for establishing the AMI diagnosis were the same as those used in earlier studies[2]. Of the 1227 AMI patients admitted during this period, 120 had nosocomial infection as comorbidity. Patients with at least one of the following were excluded: autoimmune disease or HIV infection, neoplasias, liver diseases, history of infection or fever during the two weeks prior to admission or chronic renal failure (plasma creatinine levels above 2.0 mg/dL) at admission. The 60 remaining patients comprised the infected group. The other 1167 patients formed the control group, representing the AMI patients with no infectious complication.

Methods

Demographics, patient history, clinical course during hospitalization, physical examination, laboratory tests, and cause of death were analyzed. Variables of interest were length of hospitalization and in-hospital mortality. Dichotomous categorical variables studied included gender, diagnosis of arterial hypertension or diabetes mellitus determined during history taking, white blood count with a left shift (band neutrophils > 10% of segmented neutrophils count), and interventional treatment (angioplasty or surgery). Polychotomous categorical variables were location of infarction, number of invasive procedures, site of infection, causes of death, and other complications. Invasive procedures analyzed were cardiac catheterization, urinary catheterization, orotracheal intubation, central venous access, pacemaker implantation, and tracheostomy, in addition to the use of intra-aortic balloon, peritoneal dialysis, pulmonary artery catheter, chest tube, and hemodialysis.

Continuous variables included age, length of hospital stay, body mass index, and time to infection onset. The use of interventional treatment during hospitalization (cardiac catheterization, angioplasty or coronary artery bypass grafting) was evaluated.

In regard to infection as an AMI complication, the following were surveyed: site of infection, time for onset, treatment provided, and its progression (development of renal failure, new foci of infection, death, etc.)

Nosocomial infection was defined as any infection acquired in the hospital setting within 48 hours of admission that was not in the incubation period or that was diagnosed following an invasive procedure. Infectious conditions analyzed were symptomatic urinary tract infection, asymptomatic bacteriuria, surgical site infection (superficial incisional), pneumonia, clinical sepsis, myocarditis or pericarditis, upper respiratory tract infection and hepatitis, according to criteria described in the literature[8].

Statistical analysis - Mean age of the two groups was compared by Student's t test. A chi-square test was calculated to check for any association between the gender and group variables. The variable hospital length of stay showed abnormal distribution Thus, logarithmic transformation was applied to this variable in order to achieve symmetry. Mean logarithm of hospital length of stay between the two groups was compared by Student's t test. The chi-square test was applied to check for any association between the mortality and group variables.

In the infected group, a relationship between number of procedures per patient and in-hospital mortality rate was investigated. This analysis was performed using the chi-square test.

The significance level for all tests was set at 0.05.

Results

Sixty patients (5%) experienced AMI infectious complication. Data relative to the age, length of stay, gender, and mortality variables are shown in Table 1.

Clinical features of patients with acute myocardial infarction complicated by infection (infected group) are shown in Table 2.

Mean number of invasive procedures performed in patients of the infected group was 3.38. A relationship between number of invasive procedures per patient and in-hospital mortality was investigated (Table 3).

Table 3 seems to suggest that the mortality rate rises as the number of procedures performed increases. However, the number of patients who underwent a large number of procedures was progressively lower. In other words, for these groups, high mortality rates may be related to one or two deaths only. For this reason, the relationship between mortality rate and number of procedures could not be evaluated, because the small number of patients

Table 1 – Demographics and variables of interest in the infected and control groups

	Infected	Control	p
Mean age (years)	65.57 ± 11.87	65.92 ± 12.51	0.0032
Feminine gender	25 (42%)	290 (25%)	0.0036
Length of stay (days)	26.68 ± 27.06	12.08 ± 10.74	0.0000
Mortality	27 (45%)	143 (12%)	0.0000

Table 2 - Clinical features of patients in the infected group

Features	Infected
Arterial hypertension	42 (70%)
Diabetes mellitus	26 (42%)
Mean BMI kg/m2	24,1 ± 9,2
Leukocytosis	39 (66%)
Left shift	41 (69%)
Angioplasty	29 (47%)
AMI site	
Anterior	27 (45%)
Inferior	20 (33%)
non-Q-wave	13 (22%)
Killip classification	
I - II	26 (43%)
III – IV	34 (57%)
Surgery	8 (13%)

BMI- body mass index; AMI - acute myocardial infarction; CABG - coronary artery bypass graft.

Table 3 – Mortality rate according to the number of procedures performed in the infected group

Number of procedures	Number of deaths	Number of infected patients	Mortality rate
1	3	12	25%
2	2	9	22%
3	7	17	41%
4	1	2	50%
5	9	13	69%
6	1	1	100%
7	3	5	60%
8	1	1	100%

Mean of procedures per patient: 3.38.

distributed into so many classes (eight) precluded statistical analysis. An attempt was made to reduce the number of classes by grouping adjacent classes, but only a reduction to two classes allowed statistical analysis, establishing a cut-off point that would separate them in two sets, each with a considerable number of individuals. The cut-off point chosen to separate the two classes according to the number of invasive procedures took into account one to three procedures versus four procedures or more. The number of three procedures was chosen, because it was the "mode" or the most frequent value found and the one closest to the mean value (3.38).

The chi-square test was used to check for any association between number of procedures and mortality. The chi-square statistic was 7.54 with p = 0.006, meaning that an association existed between both variables. Table 4 shows that mortality rate among infected patients is 45%. Hence, that would be the expected death rate, if no association existed between both variable, regardless of the number of procedures performed. This proportion, however, was found to be lower (29%) in the group of patients who underwent one to three procedures and higher (64%) in the group of patients who underwent at least four procedures. In other words, mortality rate is associated with the number of procedures, and is higher with a minimum of four procedures and lower with up to three procedures.

It was noted, however, that the mean number of procedures was 2.19 among patients in Killip class I or II and 4.29 among patients in Killip class III or IV. This high mortality rate reflects the greater gravidity of the condition of patients who underwent a greater number of procedures. The most severely ill patients (Killip III, IV) require more aggressive strategies, such as central venous catheterization, pulmonary artery catheterization, orotracheal intubation, and intra-aortic balloon, and the number of procedures is a marker of poor prognosis, rather than a risk factor.

Mortality, thus, was associated with the number of procedures, and was higher with a minimum of four procedures and lower with up to three procedures, as shown in Figure 1.

In-hospital mortality was higher among female patients (20% vs. 125), and patients who died were significantly older (71.24 +/- 10.92 vs. 61.59 +/- 12.24). Based on these observations, we investigated whether the relationships between age and gender with mortality were real or only influenced by the group variable, or else, if having an infectious complication were not a confounding factor. We did so by adjusting a logistic regression model in which the three variables of interest were included primarily (age, gender, and group), as well as any possible

Table 4 – Contingency table for mortality per number of procedures

		Mortality		
		Death	Hospital discharge	TOTAL
Number of procedures	1 a 3	12 (32%)	26 (68%)	38 (100%)
	4 a 8	15 (68%)	7 (32%)	22 (100%)
	Total	27 (45%)	33 (55%)	60 (100%)

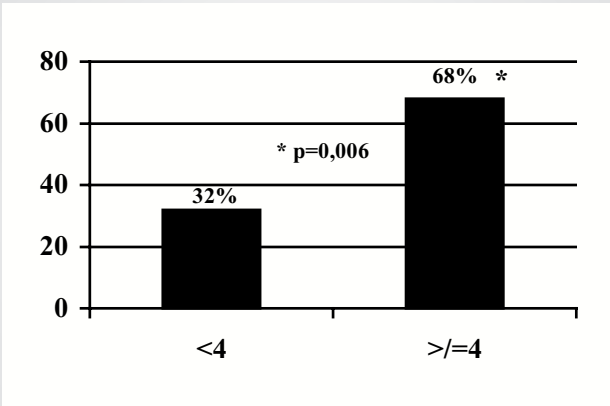

Fig. 1 – Mortality rate according to the number of procedures in the infected group.

interactions between them. The final model retained the age and group variables, as well as their interplay; that is, both age and group seem to play important roles in mortality. In addition, the presence of interaction in the model means that the effect of age on mortality is not the same in either group, or that the fact whether the patient is infected or not does not affect mortality differently, depending on the age. The final adjusted model was the following:

$$\text{Probability(death)} = \frac{1}{1+e^{-Z}}$$

where Z = – 4.5400 –2.5331 x group + 0.0516 x AGE + 0.0249 x group x AGE

(In the above equation, the group variable is –1 when the patient belongs to the infected group and 1 when the patient belongs to the control group.

Based on this model, the probability of death was calculated for patients of several ages, according to the group to which he/she belongs (Figure 2).

Obs.: na figura 1 no eixo Y o sinal de % e no eixo X a identificação Years

Therefore, the older the patient, the higher the probability of death, and this probability is always higher in the infected group. Odds ratio for death was also calculated:

- For every group, according to a given increase in patient age:

Table 5 shows that, despite higher death probability in the infected group, age increment is associated with greater increase in the odds ratio for death in the control group. In other words, the control group is more affected by age (in that it increases the odds ratio).

- Between the groups (infected and control), for different ages:

The odds ratio for death between the infected and control groups is, thus, higher among younger patients and declines as age increases. To put it differently, younger patients are more affected by the group variable (in that it increases the odds ratio).

Distribution of length of stay in hospital per age group

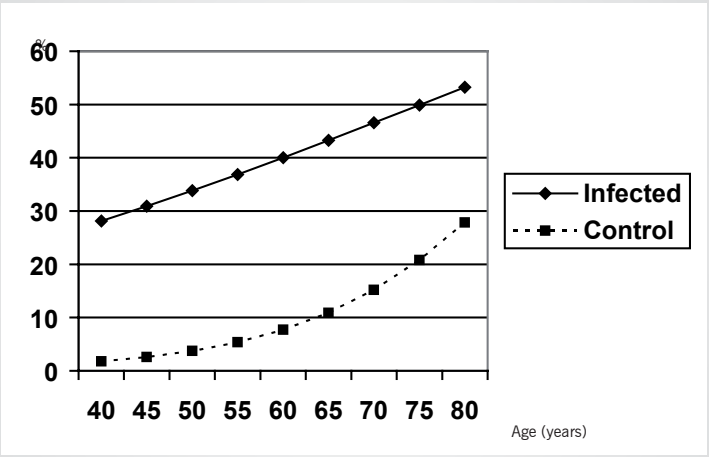

***Figure 2** – Estimated probability of death for different ages.*

Table 5 – Odds ratio for death at increasing age group

Increase in age (years)	Odds ratio	
	Infected	Control
1	1.03	1.08
5	1.14	1.47
10	1.31	2.15
15	1.49	3.15
20	1.71	4.62
25	1.95	6.77
30	2.23	9.92

Table 6 – Odds ratio for death between both groups (infected and control), for different ages.

Age	Odds ratio
40	21.63
45	16.86
50	13.15
55	10.25
60	7.99
65	6.23
70	4.86
75	3.79
80	2.95

(> 65 and ≤ 65) for patients with AMI complicated by infection was similar in both groups (28.4 ± 33.5 and 24.5 ± 17.0 days, respectively, p = 0.59). The most frequent site of infection in this population was the lung (63%), followed by urinary tract (37%), blood stream (8%), skin (7%), and liver (2%). No association was found between leukocytosis, left shift in the blood count or pulmonary infection and mortality among patients with infection as a complication of AMI.

Causes of death in the population of patients with AMI complicated by infection were cardiogenic shock (41%), septic shock (30%), ventricular fibrillation (22%), and respiratory failure (7%).

Discussion

Since the advent of the Coronary Care Unit, in-hospital mortality in acute myocardial infarction has been declining progressively[9]. Since then, treatment measures such as electric cardioversion and the use of anti-arrhythmic, vasodilator, beta-blocker, thrombolytic, antiplatelet, and ACE inhibitor agents, have significantly reduced mortality rates and are mandatory in the AMI therapeutic armamentarium[9].

With the introduction of coronary care units, some authors attempted to stratify the risk of complications for AMI patients, identifying variables or developing scores related to morbidity and mortality, such as the Killip-Kimball classification [10]. This index or score is based on variables obtained during hospitalization. According to more recent studies, in-hospital mortality in acute myocardial infarction is directly related to feminine gender, older age, previous history of infarction, anterior wall AMI, extension of the ischemic area, signs of significant left ventricular dysfunction, and arterial hypotension[11-15].

Unlike other clinical conditions, no information is available in the literature about infectious complications incidence in acute myocardial infarction or how it affects in-hospital morbidity and mortality[4,7].

No studies were found that analyzed infection incidence in coronary care units, which have distinctive characteristics, from its physical structure (individual rooms) and patient condition and their diseases to the trained professionals working there. When it comes to intensive care units (ICUs), however, a wealth of data is available regarding nosocomial infections and their impact on morbidity and mortality. The EPIC trial showed that, of 10,038 patients admitted to several ICUs in seventeen western Europe countries, 4501 (45%) had developed hospital infections. Pneumonia (47%), lower respiratory tract infection (18%), urinary tract infection (18%), and septicemia (12%) were the most frequently found.

This same study identified some risk factors for the development of infection, such as prolonged ICU stay, indwelling urinary catheter, central venous catheter, pulmonary artery catheter, and mechanical ventilation[16]. The lower incidence of infection found in our study (5% vs. 21% in the EPIC trial) may have reflected the more severe condition of patients admitted to the ICU, where the high mortality rates are in accordance with this hypothesis[17]. Although its study population was rather heterogeneous and had different clinical features, the EPIC trial shares the same base of association with this study. Both studies sought to analyze the impact of the same complication (nosocomial infection) on severely ill patients. Regardless of the underlying diagnosis, preventing nosocomial infections should be an important goal for critically ill patients in several clinical conditions.

Leu et al[18] analyzed cases of hospital-acquired pneumonia between 1979 and 1983 and found that, among other variables, advanced age, previous use of mechanical ventilatory support, and neoplasic disease were directly related to mortality. These authors suggested that nosocomial pneumonia accounts for 33% of mortality, contributing significantly to increasing costs due to prolonged hospitalization. In our study, pulmonary infection was the most frequent infectious complication (63%). Additionally, mortality rate and length of hospital stay in this population were significantly higher than in the control group (45% vs. 14% and 26 vs. 12 days). These findings indicate poorer outcomes in this group of patients, corroborating Leu et al's results.

Age is a risk variable in AMI that was described many years ago. The mechanism associated with this interrelationship is still unclear, but it is likely to be related to the small coronary and myocardial reserve seen in older individuals, since the incidence of diabetes, arterial hypertension or congestive heart failure is higher in these patients[13,19]. In the present study, increased mortality in more advanced age groups was also found. In the subgroup of patients who developed infection as a complication of AMI, however, the effect of age on mortality was attenuated, that is, mortality was more affected by age in the control group. In other words, in acute myocardial infarction, the older the patient the higher the likelihood of death, especially if an infectious complication develops.

The relationship between feminine gender and higher in-hospital mortality is also known, and some authors suggest that this is an independent variable related do mortality[13,19-23]. In our study, the number of women in the infected group was higher, indicating that they are more prone to develop infectious complication. This fact, however, may not explain the higher mortality rate among patients with infectious complication. The logistic regression model identified age, the presence of infection and their interplay as the most relevant factors

explaining mortality. As with the age variable, the fact of having an infectious complication has attenuated, or even eliminated, the influence of the gender variable on mortality in the logistic regression model.

A high prevalence of diabetes mellitus was found in the infected group (42%). This phenomenon might be explained by the older age group of these patients, since diabetes is the most prevalent disease in the oldest age groups[3,24]. In addition to being at a greater risk of developing AMI, diabetic patients show a high mortality rate in this condition, which may have contributed, at least in part, to the rate found in our study[25].

The relationship between invasive procedures (catheters, orotracheal intubation, tubes, etc.) and the development of hospital infections has already been described by several authors in different population groups[17,26-28]. In Brazil, Velasco et al[28] analyzed 370 cases of hospital infection in 623 patients admitted to the ICU for malignancies. These authors found a 50% global incidence of infection, pulmonary (29%) and urinary (26%) being the most frequent, and the rate of invasive procedures was 2%. In their sample, a strong correlation was found between hospital infection incidence and the use of invasive procedures[28].

In our study, mean rate of invasive procedure per patient was 3.38 in the infected group. This figure, much higher than that of Velasco et al's study, may be explained by the great number of patients (41%) who underwent coronary angioplasty, a procedure that requires venous and arterial catheterization. An association between mortality rate and number of procedures was also found. In this population, however, the inflated number of invasive procedures could not be classified as risk factor, because the number or procedures was greater among patients in Killip class III and IV (4.29 vs. 2.19 in patients in Killip class I and II), in which mortality rates are higher.

Wilcox & Dave[29] stated that, on average, length of stay for patients with hospital infection is 2.5-fold higher and their treatment costs £ 3,000 more, compared with their non-infected counterparts. Although data related to expenses have not been considered in our sample, length of hospital stay was around 2.1-fold higher. This information is of great interest, because it is associated with increased costs of AMI management.

In the population studied, incidence of infectious complication was 5%. Prolonged hospital stay and high mortality rate suggest that infectious complication has a great impact on AMI patients admitted to the coronary care unit. In the present study, the use of a mathematical model to calculate probabilities related to infectious complications in AMI opens a new field of investigation and discussion about the management of this population. As with patients in similar clinical conditions, prevention of nosocomial infectious complications is important for critical patients. It seems clear, therefore, that infectious complications deserve further studies, within a strategy of risk stratification following AMI.

Study limitations - Except for demographics and hospital stay, clinical features of the control group were not available for analysis in this retrospective study and thus constitute one of its limitations. This precluded an analysis to check for a possible relationship between the many clinical variables inherent to AMI (Killip class, thrombolytics therapy, etc.) and mortality and hospital stay. Nevertheless, the relationship between these variables and morbidity and mortality in AMI is already known in the literature. Although this relationship was not determined in the present study due to the lack of information about the control group, it seems plausible to suppose that these variables are also important in this specific group.

Potential Conflict of Interest

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

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