Original Article

# Temporal Tendency of in-Hospital Lethality due to Acute Myocardial Infarction. 1994-2003

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## Objective

*To analyze the temporal tendency of lethality due to acute myocardial infarction (AMI) and if the change in behavior directly interfered in such lethality.*

## Methods

*1055 non-selected patients, who were hospitalized in coronary unit from 1994 to 2003, were assessed. Clinical and therapeutic profile-related variables were analyzed. The statistic analysis used the exponential damping of temporal series and other techniques, such as the logistic linear regression.*

## Results

*The average lethality was 10.8%, being 12% in 1994 and 7% in 2002 (p=0.000), a relative reduction of 58%. There was no significant variation in the risk profile of the patients. There were 67.4% of men and 32.4% of women, with an average age of 60.93 and 64.84 years old, respectively. It was observed a significant increase in the percentage of cardiac catheterization (from 14% to 51%), in the angioplasty carried out 24 hours after the infarction (from 2% to 33%), in the surgery for myocardial revascularization (from 4% to 7%) and in the primary angioplasty (from 4% to 11%) with p=0.000, p=0.021, p=0.000 and p=0.000, respectively, for linear tendency. In the first 24 hours there was an increase of the use of aspirin and beta-blockers, from 78% to 100% and, from 33% to 76% (p=0.003 and p=0.004, respectively) along the years. After the analysis, the myocardial reperfusion therapy, the use of aspirin and beta-blocker in the first 24 hours of the AMI (p=0.010, p=0.024 and p=0.035, respectively) kept on being lethality determiners.*

## Conclusion

*There was a decrease in lethality and the change of behavior in the treatment of AMI along the years was responsible for the reduction of lethality in that temporal series.*

## Key words

*temporal tendency, in-hospital lethality, acute myocardial infarction*

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The acute myocardial infarction (AMI) is the greatest public health problem in industrialized countries. Its incidence has been dramatically increasing in developing countries[1,2].

A progressive and steady decrease in the mortality rate through AMI has been observed in the last 4 decades, from 30% to, approximately, 15%[3]. In the early 1980s, significant efforts were developed to try to limit the size of AMI, with the introduction of fibrinolysin and beta-blockers[4-6]. The disseminated use of the acetylsalicylic acid and the full development of the percutaneous coronary intervention (PCI), have contributed for the short-term reduction of the mortality rate to 6.5%[7-10].

Despite the tendency of greater use of therapies, they still have been underused[11-13]. Some studies have demonstrated that the understanding of national or international guidelines does not guarantee a scientific evidence-based medical practice[14].

There were many explanations for the changes seen in the lethality of AMI, recorded along the years: improvement of monitoring, change in hospitalization rate due to AMI, change of the risk profile of the patients and improvement of the pharmacological and interventionist treatment[15-17].

There are only a few studies that analyze the incidence, evolution and mortality due to AMI in Brazil. In the State of Rio de Janeiro, there is only one study on the in-hospital lethality due to AMI published, in 1995, and there is no study on temporal tendency of lethality due to AMI, in a coronary care unit (CCU)[18].

Within such perspective, the present study aims at studying the temporal tendency of lethality attributed to AMI, in CCU and assess whether the change of conduct has directly interfered in such lethality.

## Methods

All non-selected AMI-diagnosed patients were included in the study, regardless of age, consecutively hospitalized at the Coronary Care Unit from 03/01/1994 to 03/01/2003, prospectively followed during the hospitalization. The data on the characteristics and evolution of the infarction were stored in a database program. The diagnostic criteria for AMI were those established by the World Health Organization[19]. From the year 2000, quantitative troponin I was used as infarction serum marker.

The classic risk factors for the coronary artery disease were investigated and the in-hospital record documentation or the presence of the pathologic Q wave was regarded as myocardial infarction antecedent[20].

The eligibility criteria for myocardial reperfusion therapy were those recommended by the AHA/ACC[21]. For the pharmacotherapy the streptokinase was used and the primary angioplasty (P PCI) was introduced in the Institution from 1998. The cardiac complications assessed at CCU were the cardiac insufficiency (classification of Killip-Kimball[22]) to the hospital admission or during the hospitalization, the reinfarction, the post-AMI angina[23] and the ordinary arrhythmias in the course of AMI.

The cardiac catheterization (cine) was indicated in the presence of persistent or recurring ischemia, cardiac insufficiency, mechanical complications and serious ventricular arrhythmias. From 1998, the routine of the coronary unit began to indicate a higher frequency of cine for the patients who evolved with cardiac insufficiency, post-AMI angina, AMI without high-risk Q wave and the earliest rescue angioplasty in the failure of streptokinase (selective PCI/S PCI).

The adjuvant medications used in the acute stage of the infarction included acetylsalicylic acid, intravenous and oral beta-blockers, inhibitors of angiotensin converter enzyme, statins, inhibitors of IIb/IIIa glycoprotein (with P PCI), ticlopidine, nitroglycerin, and non-fractioned and low molecular weight heparins, used in accordance to the previously published conducts of the routine of the coronary unit[24]. The conducts were updated in 1998 and 2002 with a wider use of cine, S PCI, acetylsalicylic acid, beta-blockers and statins.

For the objective of calculation of in-hospital lethality, the deaths occurred during the CCU hospitalization due to AMI were accounted[25,26].

After a review of the values contained in the database, the lethality due to general AMI and in accordance to the type of AMI (with Q or without Q), the location (anterior or lower), the age (65 years old and < 65 years old), sex, with or without the use of reperfusion, previous infarction, cardiac insufficiency, diabetes and other variables was calculated.

In order to check if there was a significant difference among the values of those variables along the years, the chi-square method was used. It was followed by the chi-square for linear tendency, aiming to check if the change was consistent with an ascending or descending straight line. In order to assess the differences among means, the T test of Student and ANOVA were used. To measure the importance of changes in the risk profile of patients along the years, which could interfere with lethality, the multivariable analysis has been used. The logistic regression analysis was performed for the variables that showed significant differences in three distinct moments: global (1994-2002), 1st period (1994-1998) and 2nd period (1998-2002). That analysis aimed at assessing whether the treatment way determined a change in the behavior of those predictors. Through multiple linear regressions, a multiple adjustment of lethality-related clinical characteristics was done to analyze which factors were determinant, regardless of lethality change. Before each variable was added to the original model, its correlation to all other variables was assessed in order to avoid co-linearity. Then, the exponential damping of the temporal series was done, aiming at assessing the importance of lethality in the previous year in the following year and estimate the results in the 2 future years. The temporal analysis is from March/1994 to March/2003.

The STATISTICA 6.0 software was used for the chi-square and the logistic and linear regressions, and the R System 1.7.2 software was used for the exponential damping.

## Results

1,055 AMI-diagnosed patients were consecutively included. From the sample, 713 (67.4%) were men. AMIQ represented 76.5%. The average number of AMI patients was 105 (fig. 1). The average age was 62.20±12.23 years old, being 60.93±12.4 for men and 64.84±11.5 for women. The anterior wall was affected in 287 cases. Previous infarction occurred in 23.9% of the cases. The most frequent risk factors were systemic hypertension (60.8%), familial history (40.5%), smoking (38.4%), dyslipidemia (31.6%) and diabetes mellitus (22.4%). The post-AMI angina occurred in 268 patients, Killip-Kimball class ≥2 in 290 patients and the re-infarction in 42. The average lethality was 10.8%, being 12% in 1994 and 7% in 2002 (p=0.000), representing a relative reduction of 58% (fig. 2).

From the patients with ST-segment elevation, 35% (282) were submitted to the myocardial reperfusion therapy, being 26,4% through thrombolytic and 8.5% through P PCI. The cine was performed in 32.4% of the thrombolised patients and, from those, 11.7% were submitted to rescue angioplasty (almost 100% from 1998). The lethality rate was 10.8% among the thrombolised and 10.1% in those submitted to P PCI.

351 patients were sent to the cine. S PCI had a significant growth (p <0.004), from two (1.7%) performed in 1994, to 31 (19.5%) in 2002. The myocardial revascularization surgery (MRS) was performed in 55 patients.

There was an increase of the incidence of AMI without Q wave (AMIWQ) and a lower onset of the anterior wall, respectively, p=0.000 and p=0.008 (tab. I). Women were 3.92 years older than men.

From 1994 to 2003, there were increases in the performance of cine (from 14% to 51%), of S PCI (from 2% to 33%) and MRS (from 4% to 7%) with p=0.000, p=0.021 and p=0.000, respectively, for linear tendency.

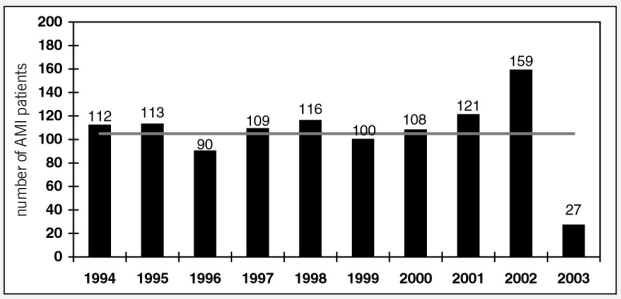


Fig. 1 – Yearly distribution of AMI admissions and the mean.

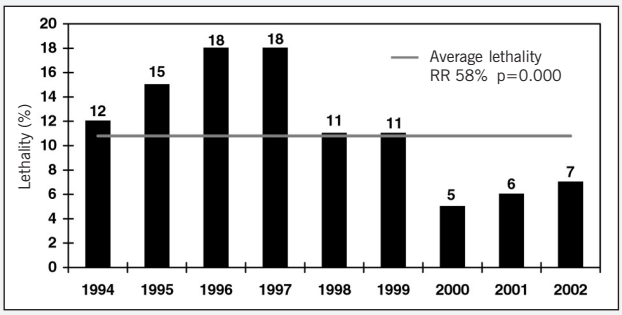


Fig. 2 – Yearly distribution and the mean of lethality due to AMI. RR: relative reduction.

**Table I – Demographic variables of the sample per year**

| Variables (%) | Year 1994 | 1995 | 1996 | 1997 | 1998 | 1999 | 2000 | 2001 | 2002 | 2003 | p* |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Global average age (years old) | 60.88 | 62.39 | 62.81 | 63.68 | 61.63 | 61.25 | 61.67 | 61.61 | 63.31 | 63.22 | 0.921 |
| Age per sex | | | | | | | | | | | |
| F | 59.64 | 61.79 | 60.76 | 63.80 | 58.47 | 58.40 | 61.68 | 59.91 | 62.25 | 62.73 | 0.342 |
| M | 63.71 | 63.62 | 69.14 | 63.32 | 67.41 | 65.53 | 61.65 | 64.49 | 65.43 | 65.40 | |
| Sex | | | | | | | | | | | |
| M | 70 | 67 | 75 | 74 | 65 | 60 | 66 | 63 | 67 | 81 | 0.274 |
| F | 30 | 33 | 25 | 26 | 35 | 40 | 34 | 37 | 33 | 19 | |
| DM | 22 | 25 | 21 | 18 | 22 | 25 | 23 | 19 | 25 | 18 | 0.929 |
| Previous infarction | 16 | 23 | 25 | 28 | 23 | 27 | 18 | 33 | 22 | 18 | 0.349 |
| With Q | 93 | 80 | 85 | 85 | 68 | 78 | 79 | 71 | 63 | 63 | 0.000 |
| Without Q | 7 | 20 | 15 | 15 | 32 | 22 | 21 | 29 | 37 | 37 | |
| Ant. Wall | 49 | 34 | 40 | 46 | 31 | 37 | 36 | 32 | 30 | 15 | 0.008 |

*p - chi-square test for linear tendency; M- male; F- female; FH- familial history; S- smoking DISL- dyslipidemia; DM- diabetes mellitus; With Q- with Q wave; Without Q- without Q wave; Ant. wall- anterior wall.

There was an increase therapy of myocardial reperfusion from 1994 to 2002 (p=0.000, for linear tendency) (fig. 3). It is important to remember that the year 2003 is represented by only the first three months in the year.

According to figure 4, a significant increase occurred in the first 24 hours in the use of acetylsalicylic acid and beta-blockers.

The cardiac insufficiency and the post-AMI angina showed significant reduction in their incidences, from 1994 to 2003, from 31% to 15% and from 21% to 11%, respectively.

Table II demonstrates the variables that compose the risk profile of the patients. Only the onset of the anterior wall and the AMIWQ showed some change along the years (p=0.008 and p=0.000, respectively, for linear tendency). In order to assess the influence of AMI on lethality, their analyses were performed along the years (tab. III). It is clear the important lethality reduction after 1998. The importance of such variables in in-hospital lethality is found on table IV. At no moment was the AMIWQ an independent predictor of lethality.

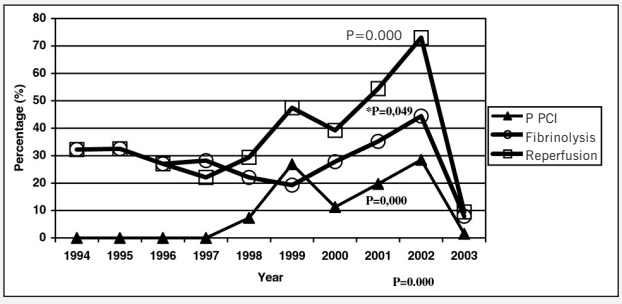


Fig. 3 - Yearly distribution of myocardial reperfusion procedures. *p= chi-square test for linear tendency; P PCI: primary angioplasty.

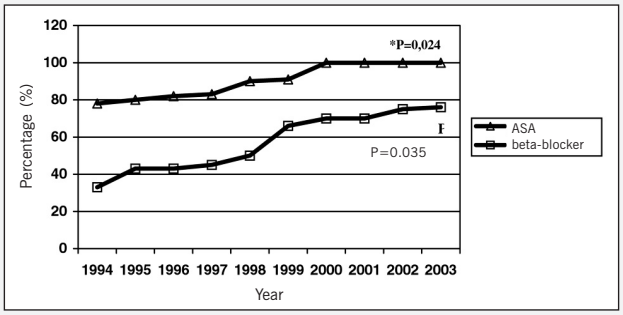


Fig. 4 - Yearly distribution of adjuvant medications used in AMI. *p= chi-square test for linear tendency; ASA: acetylsalicylic acid.

In the case of anterior wall, there was a decrease of its frequency along the years, followed by a fall in lethality rate. When analyzing that datum in three different periods, it is demonstrated that the anterior wall was an independent predictor in the global period of the study (1994-2002) and from 1994-1998. However, in the 1998-2002 period, it is not an independent predictor of in-hospital lethality.

In order to analyze which factors are independent and determinant in the change of AMI in-hospital lethality the multiple linear regression was used.

A correlation between the anterior wall AMI and the AMIQ (R=0.9173 and p=0.000) was observed, and the anterior wall AMI was chosen for biological and clinical reasons. After the analysis, the determinants of in-hospital lethality were: the therapy of myocardial reperfusion, the use of acetylsalicylic acid and beta-blocker in the first 24 hours of AMI (p=0.010, p=0.024 and p=0.035, respectively).

## Discussion

The main reasons related to the changes in in-hospital lethality due to AMI are the change in hospitalization rate, change in the risk profile of patients and the improvement of the pharmacological and interventionist treatment[15-17].

It is noted in figure 1 in this research that the average yearly hospitalization rate of AMI, along the whole period was 105 patients, with a lower number of hospitalization in 1996 and 1999 (90 and 100, respectively). However, when the general tendency of lethality due to AMI was assessed, the lethality rate in 1996 was the highest in the whole period. In 1998 and 1999 there was a plateau in the tendency curve. Such decrease of lethality, with a stable or increased hospitalization rate, is consistent with other studies published, which suggest the improvement in the treatment as responsible for the favorable tendency in lethality of AMI[17,21,27].

The in-hospital lethality due to AMI depends on the risk profile of the patients. The variables used in this sample (tab. II) were also used in many works published[28-34]. It is possible to verify that

**Table II – Risk profile of the sample**

| Variables (%) | Year 1994 | 1995 | 1996 | 1997 | 1998 | 1999 | 2000 | 2001 | 2002 | 2003 | p* |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Average Age (years old) | 60.88 | 62.39 | 62.81 | 63.68 | 61.63 | 61.25 | 61.67 | 61.61 | 63.31 | 63.22 | 0.65 |
| Sex | | | | | | | | | | | |
| M | 70 | 67 | 75 | 74 | 65 | 60 | 66 | 63 | 67 | 81 | 0.212 |
| F | 30 | 33 | 25 | 26 | 35 | 40 | 34 | 37 | 33 | 19 | |
| DM | 22 | 25 | 21 | 18 | 22 | 25 | 23 | 19 | 25 | 18 | 0.929 |
| Previous infarction | 16 | 23 | 25 | 28 | 23 | 27 | 18 | 33 | 22 | 18 | 0.349 |
| Ant. wall | 49 | 34 | 40 | 46 | 31 | 37 | 36 | 32 | 30 | 15 | 0.008 |
| Lower wall | 44 | 43 | 40 | 34 | 38 | 40 | 36 | 30 | 27 | 33 | 0.122 |
| With Q | 93 | 80 | 85 | 85 | 68 | 78 | 79 | 71 | 63 | 63 | 0.000 |
| Without Q | | 20 | 15 | 15 | 32 | 22 | 21 | 29 | /37 | 37 | |
| Killip Class ≥2 | 1 | 34 | 33 | 29 | 24 | 22 | 27 | 25 | 26 | 15 | 0.07 |

*p- chi-square test for linear tendency; M- male; F- female; DM- diabetes mellitus; ant. wall- anterior wall; lower wall- lower wall; With Q- with Q wave; Without Q- without Q wave.

**Table III – Yearly in-hospital lethality for anterior wall and AMI without Q**

| Variable | Year 1994 | 1995 | 1996 | 1997 | 1998 | 1999 | 2000 | 2001 | 2002 | |
|---|---|---|---|---|---|---|---|---|---|---|
| Ant. Wall | 16.4 | 12.8 | 25.0 | 23.5 | 22.2 | 5.4 | 7.7 | 7.7 | 8.3 | Death |
| AMIWQ | 0 | 26.1 | 7.1 | 11.8 | 5.4 | 9.1 | 0 | 2.9 | 8.5 | (%) |

%- percentage; Ant. wall- anterior wall; AMIWQ- acute myocardial infarction without Q wave.

**Table IV - Odds Ratio of clinical characteristics according to the period**

| | Anterior Wall | AMIWQ* |
|---|---|---|
| Global | 1.60 (1.04-2.5) | 1.22 (0.70-2.16) |
| 1994 a 1998 | 1.96 (1.15-3.33) | 1.02 (0.48-2.15) |
| 1998 a 2002 | 1.39 (0.72-2.71) | 1.34 (0.61-2.97) |

*AMIWQ- acute myocardial infarction without Q wave.

only the AMIWQ and the location of the infarction in the anterior wall showed significant frequency changes along the years, whereas the other variables did not change. The multivariable logistic regression demonstrated that the AMIWQ was not an independent predictor of lethality.

According to Burke et al.[35] the change in the risk profile is partly explained through changes in the policy of hospital admission and for the improvements in diagnostic techniques, by creating conditions for the detection of little infarctions. The use of troponin could have led to the admission of less serious infarctions, as well as the increase of incidence of AMIWQ. Corroborating with the logistic regression in the analysis of temporal tendency de lethality per type of AMI, we observed that it remained was practically stable along the time for the AMIWQ, whereas there was a significant decrease for the AMIQ. Such fact is due to the increase of the pharmacological and invasive interventions employed in the AMIQ, from 1998 (figs. 3 and 4), which reflected in the global lethality due to AMI. A similar result was published in 2001, in 22 years of study, in which a reduction of incidence of AMIQ and an increase of AMIWQ were verified. The in-hospital lethality of AMIQ diminished along the years (from 24% in 1975 to 14% in 1997) and the AMIWQ remained stable in 12%[36].

In the current study, the frequency of anterior AMI varied significantly (p=0.008, for linear tendency), from 49.1% in 1994 to 30.2% in 2002, a fact that could have influenced the in-hospital lethality. Associated to the decrease of frequency, a significant decrease of lethality, from 16.4% to 8.3%, was also observed, which could be a direct result from the lower number of admitted patients. In order to assess the possible confusion, the logistic regression was employed in 3 different periods, which demonstrated that in the period from 1998 to 2002 the anterior wall is not an independent predictor any longer, with an *odds ratio* of 1.39 (0.72 –2.71, tab. IV). That is a period that coincides with the most intensive use of interventions with a benefic effect on the lethality, as the reperfusion therapy (inclusion of primary PCI), the S PCI and the pharmacotherapy (figs. 3 and 4) as in other studies[21,37, 38].

In the current work we did not find any significant difference in the frequency of Killip class ≥ 2 along the years (p=0.07), corroborating with the fact that the reduction of lethality is not necessarily connected with the reduction of seriousness of the admitted patients[39].

Alexander et al.[40] reported that the in-hospital lethality due to AMI is directly related to the older age. In the present study, the proportion of elderly (around 45%) did not vary significantly (p=0.977) along the years.

This work is the first to analyze the temporal tendency of in-hospital lethality due to AMI, in 9 years, in the CCU, and the influence of therapeutic modalities in a non-selected population. The in-hospital lethality is a traditional indicator of performance of quality of attendance, and it has recently been highlighted by Dubois[41].

Therapeutic changes have occurred in the treatment of AMI in the last 2 decades and many controlled, randomized studies investigated the impact of the adjunct pharmacotherapy and the reperfusion in the in-hospital lethality[42-45]. Heidenreich et al.[46] concluded that the main reason for the decrease of early in-hospital lethality was related to the amplification of adjuvant therapy (acetylsalicylic acid, IACE, beta-blockers), the myocardial reperfusion techniques, as well as the selective angioplasty (rescue, urgency) and the MRS.

In the French records, the proportion of the use of acetylsalicylic acid increased from 63% to 89%, and the beta-blockers from 41% to 64% in the period from 1994 to 1995, with a decrease in lethality, from 12.1% to 7.7%[28]. In the American records of AMI, from 1990 to 1999, it was demonstrated a growing use of those pharmaceuticals in the first 24 hours of hospital admission[47].

A significant increase in the utilization of acetylsalicylic acid and beta-blockers (fig. 4) was noted, especially from 1998, which corroborates to the fact that the introduction and amplification of those benefic therapies participated in the reduction of in-hospital lethality.

A significant part of the reduction of lethality is related to the interventions (P PCI, early MRS, rescue angioplasty, cinecoronariography in high risk patients) performed during the acute stage[37,48].

In this sample, we noted an increase of cine and S PCI ($p=0.000$ and $p=0.021$, for linear tendency). This occurred despite of not having a change in the risk profile, but for having occurred a change in the conduct of the treatment of infarction at the acute stage through the medical routine that was introduced from 1998, by intervening more aggressive and earlier in high risk patients and in those with complications. During a recent Latin-American symposium of intensive therapy in P PCI-submitted patients from our CCU, the lethality rate was 2%[49].

In the State of Rio de Janeiro, from 23,108 AMI-diagnosed patients, assessed through authorizations for hospitalization, between 1995 and 2000, a small decreasing, but significant, tendency of in-hospital lethality, from 18.4% to 16.9%, with an average of 18%, was found, and the use of thrombolytic therapy almost doubled, going from 6.6% to 11.8% ($r^2=0.69$ and $p<0.05$). In the City of Rio de Janeiro, the in-hospital lethality did not have a significant change in the same period, going from 16.5% to 15.8%[50].

According to many authors, there is an important variation in the usage profiles of the technologies applied in AMI, with already investigated, debated and clarified indications and efficacy[51-53]. That fact is due to the existence of variable levels of adhesion or knowledge of the scientific evidence-based protocols[14,54]. At CCU the team periodically meets for the updating of the conducts in accordance to the needs and availability of therapeutic resources available. After updated, they start to be fully used by the medical team, keeping the uniformity and adhesion to the routine.

One of the limitations in this study is the low power of generalization and, therefore, its conclusions must only be applied to populations with an AMI profile similar to this one. The second limitation refers to the fact that this kind of study analyzed the general data and not the individual information of each patient. Because of that, the casualty assessment was impaired, having been minimized with the analysis of the temporal series, applied in the present study.

In conclusion, in this study it was observed that there was a reduction of in-hospital lethality due to AMI, in both sexes, and that the decrease of lethality was due to the implementation of pharmacological and interventionist clinical measures in the daily practice.

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