Relationship Between Mortality Due to Acute Myocardial Infarction and Adherence to Clinical Guidelines

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Acute myocardial infarction (AMI) is one of the main causes of death in Spain. Given its high incidence, rate of complications, and mortality, it is important to attempt to improve its prognosis.

Although some people still maintain that guidelines are there not to be followed, compliance with their recommendations does lead to a reduction in morbidity and mortality. A proportional reduction in 1-year mortality of 22% has been calculated for acute coronary syndrome when the guidelines are followed.[1] The increasingly rapid pace of scientific discovery means that guidelines are updated in ever shorter periods of time. This implies a continual effort in order to become acquainted with, assimilate, and put into practice the latest recommendations at the earliest opportunity.

When patients were selected for the Acute Myocardial Infarction Hospital Registry Project (*Proyecto de Registro de Infarto de Miocardio Hospitalario*; PRIAMHO) I[2] and II[3] registries, the definition of AMI had not yet been modified[4]; consequently, the study by Heras et al[5] in this issue of Revista Española de Cardiología relates to an old definition. The first PRIAMHO registry was undertaken in 1995 and the second in 2000. The current study, which compares the 2 registries, is of unquestionable interest since it reveals the extent of adherence to guidelines at each stage and how mortality changed in patients admitted to coronary care units (CCU) for AMI in Spain over the course of those 5 years. The raw data showed a reduction in mortality of 2.9% (14.2% to 11.3%) at 28 days and 2.1% (18.5% to 16.4%) at 1 year. Proportionally, the reduction is 12.8% at 1 year if no adjustment is made for risk

factors and 22% if the reduction is adjusted for those variables. This figure is identical to the reduction calculated by Alexander et al.[1]

There are differences between the 2 PRIAMHO registries in terms of the way that participating hospitals were selected, and these differences could bias the results. In 1995, "the majority of the 228 CCUs in Spanish hospitals were invited to participate...Of the 47 that initially expressed interest in being involved in the study…24 met all of the criteria."[2] Thus, 10.5% of the invited hospitals were ultimately included. In 2000, data were collected on the patients admitted for AMI "in the CCUs of 58 (71.6%) of the 81 Spanish hospitals that were selected at random..."[3] Those who were interested in being involved in the study were probably also those who adhered better to the guidelines, while random selection prevented this form of bias. Nevertheless, the mortality was reduced. There was a correlation between 2 of the variables studied (extent of adherence to guidelines and mortality) and one is probably responsible for the other. However, there may have been other factors that were not analyzed that would influence the increased survival.

The current study shows that there was greater adherence to the guidelines and fewer patients died due to AMI in 2000 than in 1995, despite the fact that the patients registered in 2000 were at higher risk.[5] This suggests that if the degree of adherence were increased further then there would be an even greater reduction in mortality. To test whether the differences in mortality were due to a greater adherence to the guidelines, the authors established 3 adjusted models.[5] The first model included risk factors and hospital characteristics. The second added administration of antiplatelet drugs, reperfusion, and delay prior to reperfusion, and the third added beta-blockers and angiotensin converting enzyme inhibitors (ACEI). In the first model, the difference in 1-year mortality between the 2 registries was 22%, in the second it was 13%, and in the third there was no significant difference. The authors concluded that the reduction in mortality is due to the greater frequency of administration of drugs recommended in the guidelines. Although this is plausible and probably true, another

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cause could be the lack of statistical power to detect differences due to the inclusion of too many variables.

It is clear that increasing time prior to reperfusion has a negative effect on survival. Only the door-to-needle time and not the time elapsed prior to reperfusion was found to be reduced in the period between 1995 and 2000; however, the time between the onset of symptoms and reperfusion is the most important factor, and this was not found to be reduced according to the results shown in Table 3 by Heras et al.[5] There would certainly have been a further reduction in mortality if this time had been reduced. Bearing in mind that the majority of deaths due to AMI occur prior to arrival at hospital, it may be more important to reduce the time from the onset of symptoms to arrival in the emergency department than the door-to-needle time. Although it is desirable to act more rapidly once the patient is inside the hospital, it is more important to educate the public so that patients arrive sooner.

The lesson to be learnt from the study by Heras et al[5] is that the guidelines should be followed. Although the patients included in clinical trials are not very representative of the general population, since they relate to highly selected low-risk subgroups,[6] guidelines are useful for patients from the "real world" and doctors should only omit recommended practices when there is a contraindication in the guidelines themselves. Numerous studies have shown that patients in higher risk categories receive greater benefit from aggressive treatment, despite the fact that the treatment carries increased risk.[7] A careful balance must be ensured between risk and benefit, and patients must be informed so that they can accept or reject the treatment.

Registries, unlike trials, are representative of the general population. Such studies confirm that treatment of lower risk patients in Spain tends to be more aggressive.[8] This is usually due to doctors attempting to avoid possible treatment-related complications, which the patients and their families may attribute to poor practice if they have not been informed in advance. It appears easier to accept a "natural" complication of the disease itself than an adverse effect of the treatment.

The latest clinical guidelines on AMI with ST-segment elevation published by the European Society of Cardiology in 2003 drew attention to the importance of treating groups of high-risk patients and insist that diabetic patients should receive fibrinolysis even if they have retinopathy.[9] They also advise fibrinolytic treatment in patients aged over 75 years. These recommendations were already included in the guidelines of the Spanish Society of Cardiology (SEC) published in 1999,[10] which are the guidelines that should have been followed by the hospitals included in the second registry.[3]

It is worth analyzing the extent of adherence to these guidelines,[10] not only in terms of indicators of quality,[5] but also in other areas:

1. The administration of antiplatelet drugs, which is a class I recommendation, increased from 89.1% in 1995 to 96.3% in 2000. Only 3.7% of patients did not receive them.

2. Reperfusion: 71% of patients with an indication for reperfusion received this treatment in 2000.[3] Fibrinolysis was performed in 40% of the patients included in that registry, a proportion that is slightly lower than in 1995. However, this is compensated by a rate of 5.2% for primary angioplasty. Nevertheless, reperfusion was not performed in 29% of patients.

3. Beta-blockers were administered in 51.1% of patients in 2000 compared with 30.1% in 1995. The guidelines include this treatment as a class I recommendation in the case of continuous ischemic pain or sympathetic overactivity, and as a class II recommendation (it is not clear whether this is IIa or IIb) in the remaining patients in the absence of contraindications.[10] In the same year, the American guidelines were published and included the use of beta-blockers as a class I recommendation,[11] the same as in the European guidelines published 4 years later.[9]

4. ACEI were administered in 41.6% of patients in 2000 compared with 24.9% in 1995. In the SEC guidelines, the use of ACEI is a class I indication only in patients with ventricular dysfunction and is a class IIb recommendation in all other patients.[10] In the American guidelines from the same year,[11] and in the European guidelines from 2003,[9] it is a class IIa recommendation in patients without ventricular dysfunction.

5. The proportion of echocardiograms performed in the CCU was reduced from 40.2% in 1995 to 34.1% in 2000. However, this reduction was not attributable to the increase in coronary angiography (from 8.7% to 12.4%), which is normally accompanied by ventriculography. The guidelines recommend that the procedure is performed in all patients, although it is noted that this is not always imperative.[10]

6. The proportion of patients in whom Swan-Ganz catheters were used (6.2% in 1995 and 3.3% in 2000) was very low, despite being indicated in cases of heart failure or hemodynamic instability. In the PRIAMHO II registry, more than 38% of patients in the CCU presented some degree of heart failure and 17.5% presented acute pulmonary edema or cardiogenic shock.[3] The figures were similar in PRIAMHO I.[2] The proportion of patients in whom intraaortic balloon pumps were used (0.8% in 1995 and 1.3% in 2000) is also very low, probably substantially below the proportion of patients presenting cardiogenic shock.

7. The proportion of coronary angiography performed in the CCU in 2000 was very low (12.5%), as was the proportion of primary and rescue angioplasties. Although the 1999 guidelines indicate that Spain was not prepared at that time to perform primary angioplasty, it should have been possible to perform a much greater number in 2000 than actually took place. It is one thing is for the procedure to not always be possible, it is quite another for it to hardly ever be possible.

According to these 7 points, the recommendations were only well followed for the use of antiplatelet drugs. Less fibrinolysis was performed than should have been the case. Few echocardiograms were performed and there was little use of Swan-Ganz catheters or intraaortic balloon pumps. Coronary angiography and angioplasty were rarely performed. Beta-blockers and ACEI were used more than recommended by the SEC guidelines from 1999[10] and less than recommended in the American guidelines from the same year.[11] This indicates that we follow the recommendations from other countries more (although inadequately) than those from Spain.

Of all the recommended treatments, some have a greater impact than others in terms of the reduction of mortality. A metaanalysis of the influence of treatments on mortality due to AMI between 1975 and 1995 indicated that the following (shown in order of significance) have a clear benefit in terms of survival: primary angioplasty, fibrinolysis, aspirin, beta-blockers, and ACEI.[12] When the results are adjusted for interactions between the various treatments, the order remains the same but the impact of ACEI is reduced since they have little additional benefit over other drugs. A study based on the Euro-Heart Survey revealed that adherence to the guidelines is particularly poor in relation to cardiogenic shock, which is treated much less aggressively than recommended in relation to angiography, revascularization, and use of intraaortic balloon pumps.[13] These treatments are used at the same rate in patients with cardiogenic shock as in other patients. This confirms once again that the greater the patient risk the less likely it is that the indicated treatment will be used. It is likely that better adherence to the guidelines would reduce the high mortality.

Although the study by Heras et al[5] does not refer to this point, a high degree of variability can be seen in the PRIAMHO I and II registries in terms of the practice in the selected hospitals, both for drug therapies and the use of different techniques (echocardiography, Swan-Ganz catheter, coronary angiography, etc) in AMI.[2,3] What is not clear from the available data is whether in each hospital there is uniformity in the practice of the different doctors who treat the infarction.

These points lead to various questions:

1. Why are the guidelines not adhered to? The lack of adherence seems to be due less to a lack of information on the part of the cardiologist than to inertia. There is a tendency for professionals to continue to act in the same way as they became used to years ago, and a period of time—sometimes substantial—elapses between it being known that something should be done and it being incorporated into clinical practice and used systematically. The process of receiving information, assimilating it, and putting it into practice needs to be faster. The omission of aggressive therapies in high-risk patients is probably due to a lack of communication with the patient and family members because insufficient time is dedicated to them.

2. What needs to be done to ensure better adherence to the guidelines? For many years we have attended meetings in which the level of adherence to guidelines in different hospitals and geographical areas has been presented. This method generates slow, inadequate change. There is a much more effective method that could be implemented in all hospitals.[14] It involves the use of tools to remember that patients with AMI should receive certain drugs and that a series of techniques should be employed. This can be implemented through the use of a document with the following format during the period of admission: antiplatelet drugs, *yes or no*, fibrinolysis, *yes or no*, etc. In the case of a *no* response, the doctor would have to provide an explanation, which could be written, for instance, in a box provided on the same sheet. This method is effective because it obliges the individual to explain why something recommended in the guidelines has not been implemented. If no reason can be given, it is obvious that the recommendation should be followed. Nevertheless, the format should be sufficiently flexible to allow other practices to be employed where considered appropriate by the physician. They should act as reminders of the essential points while leaving freedom in the choice of action.

3. Why are there differences in the practice of different hospitals? This question could be answered using a questionnaire similar to that used in the Euro Heart Survey ACS[15] in the hospitals that participated in the 2 registries. It is not enough to know what percentage of patients were treated in a particular way. Information is also needed on why that practice was chosen. For instance, the Euro Heart Survey ACS asked why percutaneous interventions other than primary angioplasty were performed, and the answer was that "stenotic coronary arteries are treated in the usual way," without that having been established in the guidelines.[15]

Those same questions would probably receive a similar response in Spain: practice follows that acquired in a given hospital, let us say "by intuition," despite it not having been demonstrated that this is the correct way. We live in the age of evidence-based medicine, or more accurately, medicine based on clinical trials that show statistically significant differences. It is not good practice to use treatments that show improvement in the most recent trial, since it is likely that another study will be released that reports contradictory results. Nevertheless, guidelines are prepared by a group of experts, are based on more than 1 study, include contraindications, and in the absence of conflicting evidence, their observance is beneficial to patients. Nevertheless, it should be kept in mind that "a good doctor knows the general rules provided by the guidelines and consensus statements. An excellent doctor is aware of the exceptions to these rules" (WW Hurst, personal communication).

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