

Risk Stratification in the Chest Pain Unit: an Unresolved Problem

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"I think that it is important that the doctor should study how to learn prognosis knowing and warning in advance that whoever lives and whoever dies, he will be able to avoid criticism."

Hippocrates, Aphorisms II.19¹

Since the earliest of times, knowing the prognosis of a sick individual has been a constant desire of doctors. When faced with the uncertainty that illness produces in the individual patient and their family, anguish forces us to gamble on the future. In recent years, risk stratification has acquired a new meaning as it has become the basis on which we choose the treatment for individual patients and is especially important when the treatment can save a life but entails a risk that on occasion may be greater than the expected benefit. The patient with chest pain attending an emergency department constitutes the essential paradigm: they may be at risk of imminent death or they may be suffering something quite ordinary; their treatment might involve cardiac intervention or simply require a tranquilizer. Establishing risk and prognosis, therefore, is a necessity.

With the incorporation of statistical techniques into medical investigation numerous formulae were developed to predict the prognosis of patients with coronary disease. The first algorithms, described in pa-

tients with acute myocardial infarction by Schnur (1953), Peel (1962), and Norris (1969), which included only clinical variables, had some popularity but were seen to be somewhat impractical and to have a large margin of error. Later attempts, incorporating new clinical variables and hemodynamic or angiographic parameters, are more exact but they also fail to resolve the problem of risk stratification.²

In chest pain units, the problem of risk prediction is of particular interest and even has financial consequences. Consequently, new methods of prediction have been developed in an attempt to select those high-risk patients who require hospitalization and a more aggressive treatment and to discharge low-risk patients from the emergency department; results are far from satisfactory in this situation as well.

Recently, Doukky and Calvin³ highlighted the difficulties of developing a model to predict correctly. Firstly, it would have to be based on a large patient sample, representative of the clinical condition being studied. Moreover, it should analyze all the important variables and their independent contributions using adequate statistical techniques. The events that constitute the objective of the prediction should have clinical relevance: death, myocardial infarction or stroke, for example. Moreover, the number of these events in the follow-up needs to be sufficient to permit an adequate statistical calculation; often, to achieve this goal, less important composite variables are included. Finally, the model should be tested in an independent population of similar characteristics. Recently, some of the models proposed, such as GRACE, have been shown to lose their ability to discriminate when applied in a different, less selected, population.⁴

In addition, we could add that the formula should be easy to apply and that relevant therapeutic consequences should be derived from the prediction.

Logically, the information that a new model would provide should be greater than that obtained from simple clinical examination or methods already available and this should be provable through adequate statistical analysis, for example, using ROC curves. Thus, in an analysis according to Goldman score to predict the

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presence of ischemic heart disease in patients with chest pain in an emergency department, reported the area below the curve (ROC) was 0.68 for the physicians' prediction and 0.76 for the Goldman algorithm calculated by computer. Although the study concluded that this method was better, there is no doubt that its contribution was limited.⁵

Finally, and given that all prediction models are imperfect and their sensitivity and specificity do not approach 100%, in its design the study should anticipate its objective and priorities. For example, in the chest pain unit, any formula should aim to provide a high negative predictive value if the priority is to discharge low-risk patients only or prioritize positive predictive value if it is to select patients for a complex treatment with a high level of complications.

The current issue of *REVISTA ESPAÑOLA DE CARDIOLOGÍA* presents 2 studies that deal with the problem of risk prediction in patients with chest pain attending an emergency department. In different ways, both studies are an example of the difficulties we have outlined.

In the first, García Almagro et al⁶ analyze the value of TIMI scores to evaluate prognosis in a large series of 1254 of these patients. During 6-month follow-up, 25 patients died or presented myocardial infarction. The study distinguished between 911 patients discharged from an emergency department and 343 hospitalized, 2 very different populations, as their baseline characteristics and TIMI scores show. In fact, among patients discharged, the death or infarction rate was very low: 7 discharged patients (0.7%) versus 3.7% among hospitalized patients. Among the former, the number of events is clearly too low and this probably explains the inclusion of revascularization in the composite endpoint variable, which interferes with the statistical analysis. Moreover, as the study population is of low-risk, different to that used to derive the TIMI score, the percentage of discharged patients with high scores is low: 9 with TIMI risk score 4, 1 with a score of 5 and none in the maximum risk group.

Despite these inconveniences, the TIMI score correlate significantly with prognosis, with a 2.32 increase in relative risk (95% confidence interval, 1.91-2.82) for each increase in TIMI score. However, given that only 48 of the 1254 patients had a TIMI score ≥ 5 and that among these, only 7 died or suffered myocardial infarction (15%), questions arise: should action be taken for all these patients even at the cost of operating 85% of them who do no present complications? Would more aggressive treatment improve prognosis? Is a policy based on a TIMI score in patients with coronary pain in emergency departments more cost-effective? These questions, already answered for acute coronary syndromes, require a response in the chest pain unit prior to recommending the application of a TIMI risk score in this context.

In the second study, Martínez-Sellés et al⁷ use a different approach deriving their own model to predict the presence of coronary disease from a sample of 365 patients without electrocardiographic alterations or data on ventricular dysfunction, admitted to the chest pain unit. Their analysis included 8 variables widely known to correlate with prognosis. In the multivariate analysis they selected 4 of these as independent predictors: typical pain, age >64 years, previous use of aspirin and diabetes. Scores of 0 to 4 correlated with presence of coronary disease, incidence of new events and mortality. However, as incidence of death in the follow-up was low (8 deaths, only 3 of cardiac cause), these scores suggest that aggressive management would result in a high number of patients without imminent risk undergoing coronary angiography. Here again, we need to analyze cost-effectiveness to appreciate the practical value of the model. Is it more valuable than a simple clinical observation? Would it be improved by introducing data obtained in the hours of follow-up in the chest pain unit?

Martínez-Sellés et al⁷ used a logistical regression analysis to select the variables that finally made up the score. Although this is the statistical technique used in most studies, the discriminating capacity of the resulting models is limited. In recent years, other alternative methods have been developed that could improve our predictive capacity: specifically, decision trees, and artificial neurone networks. The latter involve non-linear classification and consist of different layers of interconnected nodes (neurones). In recent studies of patients with chest pain in an emergency department, it has been shown that neurone networks can offer certain advantages: Selker et al,⁸ found that the area below the ROC curve was greater with neurone networks (0.923) than with logistical regression and decision trees.

In the future, studies of risk prediction should take advantage of new statistical and information technology. The introduction of new parameters and variables as they are obtained during patient follow-up in the chest pain unit in a computerized clinical record, permit us to continuously update risk and change decisions on therapy accordingly. Moreover, neurone network models perfect themselves automatically as new patients are introduced, achieving negative predictive values in the region of 100%.

To summarize, risk prediction in coronary disease is far from optimal. We need more studies like those presented in the current issue of the journal, which fully exploit the potential of statistic techniques and at the same time show their superiority over simple clinical observations. The consequences of coining a patient as high-risk imply, almost inevitably, their undergoing coronary angiography and eventual revascularization. These interventions entail a degree of risk and consume already-limited resources so, showing that their

use in a specific group of patients leads to an improvement in survival is a key factor to be taken into account in the decision-making process.

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