

The MASCARA Registry Reveals the True Nature of Acute Coronary Syndromes Treatment in Spain

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Acute coronary syndromes (ACS) are the most common clinical manifestation of coronary heart disease. Despite great progress in initial risk stratification, the incorporation of powerful antithrombotic agents and platelet aggregation inhibitors, and the application of more invasive strategies, the prognosis of these patients continues to be significantly poor.

The clinical practice guidelines recommend initial invasive strategies as first-line treatment in a large proportion of patients with non-ST-segment elevation acute coronary syndrome (NSTEMACS) and in patients with persistent ST-segment elevation acute coronary syndrome (STEMACS). In high-risk patients with NSTEMACS, coronary angiography followed by revascularization significantly reduces ischemic events in the long-term compared to a more conservative initial strategy (coronary angiography and revascularization only in the case of spontaneous or induced ischemia).¹⁻³ In the patients with STEMACS, primary percutaneous coronary intervention (PCI) offers greater benefits than thrombolysis, and is the recommended reperfusion method whenever it is done within the recommended time-frame.^{4,5}

The MASCARA registry was a prospective study, with a randomized selection of centers and consecutive inclusion of patients, and was designed to determine the clinical profile, management and effects of intervention strategies in patients with ACS.⁶ It was conducted in 2004-2005, and after the application of comprehensive quality controls, it provided data on the 7251 patients included in the study (56% with NSTEMACS, 38% with STEMACS, and 6% with nonclassifiable ACS) from

32 hospitals. Compared to previous registries, an increase in early PCI was observed in the patients with NSTEMACS and in primary PCI in the patients with STEMACS. However, in the total population, no association of such strategies with mortality was observed at 6 months. The authors point out that the invasive strategies were not adapted to the baseline risk of the patients due to factors related to the care process. The results of the MASCARA registry apparently diverge from those of multiple randomized studies and metaanalyses conducted in NSTEMACS and STEMACS, and which form the basis of the evidence on which the current recommendations are founded.

Differences Between Randomized Studies and Registries

Randomized studies and registries have clearly different advantages and disadvantages. Randomized studies are more accurate in determining the impact of a specific treatment on a defined population. However, if highly selected patients are included, they do not suitably reflect daily clinical practice. Almost invariably, patients at very high risk or with comorbidities are excluded from randomized studies.⁷ Registries, by contrast, are far more representative of clinical practice and more accurately reflect the clinical event rates.⁸ Registries include non-ideal and high-risk patients and show whether the guidelines are being appropriately applied. However, evaluating the impact of a specific treatment using a registry can lead to incorrect conclusions due to the influence of unassessed confounding variables. Each treatment is selected not at random but by following specific criteria, and so there is an unavoidable risk of bias regarding selection and the possible prognosis. Although risk can be adjusted, it cannot be known if these adjustments are appropriate or if the relevant characteristics have been correctly identified. Only randomization can provide a real and unbiased estimation of the effects of a treatment.^{7,8}

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The Data of the MASCARA Registry

Undoubtedly, the MASCARA registry contributes invaluable information regarding the actual nature of the

care situation in Spain in relation to how the different groups of patients with ACS are currently treated.

Patients With NSTEMACS

Among the group of patients with NSTEMACS, the coronary angiography (63%) and coronary revascularization (41%; PCI in 34% and surgery in 7%) rates were very similar to those described in recent randomized studies.⁹ However, an early intervention strategy (EIS) of coronary angiography in the first 72 h was only applied in 19.6% of the patients. Although this was followed by percutaneous or surgical coronary revascularization in 68% of the patients, early revascularization remained limited to only 13.3% of the group of patients with NSTEMACS. Even though 76% of these patients had elevated markers of myocardial injury, only 46% received glycoprotein (GP) IIb/IIIa inhibitors. Some studies¹⁰ indicate that patients who undergo an early invasive strategy together with aggressive antithrombotic treatment have a lower rate of ischemic events than patients where the invasive strategy is delayed for several days.

On the other hand, the group of patients who initially underwent a more conservative strategy had a higher baseline risk (older, greater prevalence of diabetes, hypertension, previous acute myocardial infarction, kidney failure, and advanced Killip class). Even though 64% of these patients had elevated troponin concentrations, only 15% received GPIIb/IIIa inhibitors and coronary revascularization was limited to 32% of patients. These data indicate that an EIS was not applied in a large number of high-risk patients. It is widely documented that the patient groups which gain the most benefit from revascularization strategies are the patients at higher risk.¹⁻³

The strategies followed in the patients with NSTEMACS in the MASCARA study seem to have had a particular impact on the data on initial mortality and mortality during follow-up. Similar to that observed in different metaanalyses in NSTEMACS,¹¹ the patients who underwent an EIS presented higher hospital mortality (frequently associated with the procedure), but that was subsequently compensated for by improved progress (an absolute increase in mortality during follow-up of 4.6%). In contrast, the patients initially treated with a more conservative strategy presented high mortality (an absolute increase of 8.9%) during follow-up. In randomized studies of patients with NSTEMACS which compared invasive strategies versus conservative ones, it has been found that the greater the difference in revascularization rates between the 2 strategies, the greater the benefit of the invasive strategy in the long-term.¹² In line with the nature of the registries, hospital mortality and mortality at 6 months in the MASCARA study practically duplicated the mortality rates described in randomized studies of patients with NSTEMACS.

Patients With STEACS

Similar treatment strategies were observed regarding the patients with STEACS included in the MASCARA study. A total of 68% of the included patients received reperfusion treatment, 25% of whom received primary PCI. However, the patients who did not receive reperfusion therapies were those presenting higher baseline risk (older, greater prevalence of diabetes, background of AMI, vascular disease, kidney failure, and Killip class II/III). These patients presented very high mortality initially and during follow-up. Other registries in patients with AMI have documented similar findings.¹³ Although the reasons for not receiving reperfusion therapy cannot be specified, it is possible that this group included a large number of patients who did not have initial indications for reperfusion.

On the other hand, more suitable selection criteria were applied in the patients with STEACS who underwent reperfusion therapy. Primary PCI was performed, in contrast to thrombolytic treatment, in patients who at baseline presented a greater number of factors involving worse prognosis. This aspect could explain the fact that in-hospital mortality was greater in the patients who underwent PCI. However, despite treating patients at higher risk, mortality during follow-up was similar to that among the patients who received fibrinolytic therapy. Although recorded in only a small number of patients, the time to reperfusion (door-to-balloon or door-to-needle times) was strikingly longer than the maximum times recommended in the guidelines.^{4,5}

Patients With Nonclassifiable ACS

These patients (complete left bundle branch block, Wolff-Parkinson-White syndrome, or pacemaker rhythm on ECG) are worth special mention. They are patients who have been systematically excluded from controlled studies and who represent a very high-risk group. A total of 76% of them had elevated markers of myocardial injury and in 41% an ejection fraction of less than 40% was documented. However, only 11.6% of these patients received treatment with GPIIb/IIIa inhibitors and only 23% underwent revascularization. In-hospital mortality was almost 9%, and mortality was 16% at 6-month follow-up. It is beyond question that these patients require specific identification and treatment strategies.

Why Do the Invasive Strategies in the MASCARA Registry Not Have a Determining Impact on Prognosis?

The lack of a clear impact of the invasive strategies on prognosis in the MASCARA registry is due to multiple factors, some of which may be inherent to the limitations of registries.

There were large differences in baseline characteristics among the patients who received the different types of

treatment. A total of 36% of the initial participating centers were excluded from the later analysis. The treatment rates with GPIIb/IIIa inhibitors were very low in the groups of patients where this could have produced greater benefit. The early intervention strategy was performed in a very low percentage of the patients with NSTEMI. Many high-risk patients and those in whom revascularization or coronary reperfusion could have provided greater benefit were initially treated conservatively or without reperfusion. Despite the adjustments to risk, there may have been confounding variables in the MASCARA study that were impossible control. However, and even though it seems that the most invasive strategies were not totally adapted to the baseline risk of the patients included, the follow-up data on the patients who underwent revascularization or reperfusion indicate that these strategies could have had a favorable impact on prognosis at 6 months.

The reasons for implementing an EIS in a low number of patients with NSTEMI can be highly varied.¹⁴ Other registries on ACS have documented that the proportion of patients who undergo revascularization procedures substantially decreases as risk increases.¹⁵ The logistic limitations of the centers themselves, the absence of cardiac catheterization units in the participating hospitals, and the problems regarding transfers may have affected patient selection (the youngest patients and those without comorbidities were prioritized to invasive strategies, whereas the most complex patients or those with comorbidities underwent medical treatment). Similarly, the interventionist cardiologists themselves usually prefer intervention in less complex lesions or patients, but tend to choose medical treatment for more complex lesions or patients.

Conclusions

The results of the MASCARA registry should not cast doubt on the unquestionable benefit of invasive revascularization or reperfusion strategies in patients with ACS. Randomized studies and suitably designed registries provide complementary information that allow us to analyze the characteristics of the population and the potential benefit that different treatments and strategies can produce. Registries have the potential for identifying existing gaps between scientific evidence and clinical practice.⁷

The MASCARA study data indicate that, in some Spanish centers, a significant proportion of high-risk patients with ACS are not receiving the type of treatment that could more favorably influence prognosis. Inadequate implementation of the guidelines, the lack of confidence in the benefits of specific strategies, and the existence of logistic or structural problems may explain some of the observed deficiencies. Scientific societies have a key role to play in disseminating and recommending the therapeutic strategies that can lead to the greatest benefit

in patients with ACS, while applying the maximum objectivity and clarifying the most controversial aspects.

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