

Management of Acute Coronary Syndromes: Assessing Effectiveness

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Treatment recommendations in acute coronary syndromes are experiencing rapid changes. Decades of stable therapeutic passiveness (except for treatment of arrhythmic complications) are now being followed by ever more frequent changes in recommendations and increased complexity, all leading on from the diffusion of thrombolysis and percutaneous revascularization. Furthermore, changes in nomenclature have contributed to growing uncertainty as well as to an increased perception of treatment of acute coronary syndromes as a powerful challenge. Not all aspects of cardiology can be associated so truly with Molière's woodcutter turned physician when he remarked: "*nous avons changé tout cela.*"

It is no surprise, therefore, that we have for years been trying to unravel the accumulation of norms and indications derived from clinical practice guidelines for the treatment of acute coronary syndromes, based mainly on studies of efficacy (clinical trials). Hospital databases have been created to determine the repercussion of these recommendations in daily clinical practice and evaluate their effectiveness. What, then, is the effectiveness of the management of acute coronary syndromes and what is the role of these registries in this evaluation?

CONCEPT OF EFFECTIVENESS

The apparent simplicity of this concept—results in daily clinical practice compared with the efficacy shown in the experimental world of clinical trials, always slightly unreal—contrasts with the differences seen in everyday use. Fundamentally, the concept of effectiveness refers to the evaluation of results in a

particular territorial setting, depending on local patterns of action, undertaken with an evaluative aim and with the more or less tacit intention of evaluating some aspect of quality of care compared with a particular pattern. This is the concept used by some authors¹ who include effectiveness in a conceptual algorithm which considers the difference between effectiveness (local results) and efficacy (ideal results attained in clinical trials) as an indication of quality of care. However, we do not fully share this idea, as we do not believe that clinical trials represent the ideal results (ideally attainable), but rather those results obtained in a somewhat unreal, experimental, ideal context. These results, therefore, are not representative of the pattern of daily clinical practice. But what should this pattern be?

This leads us on to another meaning of the word effectiveness. Effectiveness can be understood as the estimation of the best results realistically attainable in the whole catchment population in a wide setting. This contrasts with the situation in clinical trials, as it includes several different groups of patients barely, if at all, represented in clinical trials, such as persons who are older, or who have a different clinical profile or comorbid conditions. Furthermore, these persons may well constitute a substantial proportion of the local population. This "attainable effectiveness" is thus the pattern with which to compare more local results, i.e. effectiveness in a more restricted sense, with the more or less explicit goal of evaluating quality of care. Indeed, the concept of "attainable effectiveness" assumes the existence of adequate quality of care. As this is theoretically susceptible to improvement, the value of this "attainable effectiveness" is not inviolable, but involves relatively wide limits. Consequently, we prefer the expression "approximation to effectiveness" rather than just "measurement of effectiveness". This approximation requires three considerations:

1. Measurement of local effectiveness, i.e. the real "crude" results in different restricted settings.

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2. A random sample of the reference population is representative. In this case, patients who attend emergency services with suspected acute coronary syndromes in the absence of ST-segment elevation, for whom an acceptable standard of care can be presumed because of some particular criteria, for instance adaptation to the recommendations of clinical practice guidelines.

3. Measurement of the risk-adjusted results in the particular sample. This enables approximation to the “attainable effectiveness” and serves as a pattern with which to compare local results.

This “attainable effectiveness” obviously fails to correspond to the effectiveness seen in clinical trials, which always refer to a selected population with particular inclusion criteria and usually to better results than those obtained in daily clinical practice, where patients are seen whose clinical course is necessarily worse despite correct health care. Although this pattern has been developed acceptably in other situations, such as the conceptual basis of tools for estimating surgical risk, much remains to be done in this sense in the field of acute coronary syndromes.

ROLE OF HOSPITAL REGISTRIES IN THE EVALUATION OF EFFECTIVENESS. CONTRIBUTIONS AND LIMITATIONS OF THE PEPA STUDY

Registries are specially designed for the systematic collection of all data concerning those patients seen in a fairly wide setting, with a relatively limited number of solid variables which, ideally, are repeated or prolonged. The richness and relevance of the information collected depends on several factors, particularly the sample size, the time and quality of data collection, and the existence of well-defined objectives. The registries provide descriptive information about clinical characteristics, risk and prognosis. When they are of high enough quality, they enable identification of tendencies over time, evaluation of the effect of interventions,² and even suggestions as to causality.^{2,3}

The practice of studies using registries has become popular, both in Spain and in other countries.²⁻⁶ In Spain, especially, the effort dedicated to the elaboration of registries representative of health care in acute coronary syndromes has now achieved a meritorious tradition.³⁻⁵ The aim of these studies is to attempt to determine the clinical profiles of the patients treated, what resources were used in their diagnosis and treatment, and to what extent interventions shown to be effective in clinical trials are in fact used. Thus, these registries address a latent concern by representing a first step towards the

evaluation of effectiveness.

But which aspects of this effectiveness do these registries of acute coronary syndromes contribute to in Spain? Basically, to awareness of the clinical profiles of the patients and the procedures used (local effectiveness), as well as to a general notion about the clinical results. This initial, very valuable notion may later deepen until we can discern the attainable effectiveness and, therefore, undertake a more detailed analysis of the true situation regarding health care in Spain. It is in this sense that the study published in this issue of *REVISTA ESPAÑOLA DE CARDIOLOGÍA*,⁷ a substudy of the PEPA study,⁵ represents an interesting contribution. At the same time as it sheds light on a very important aspect of the true health care situation in Spain regarding the management of non-ST segment acute coronary syndromes (NSTEMACS), it also raises questions which can be examined in future studies. What, then, does this study contribute?

– Firstly, this study confirms that patients with suspected NSTEMACS are studied and treated in Spanish internal medicine and emergency departments with an apparently insufficient use of the procedures and interventions which have proved their efficacy in recent clinical trials.

– Nevertheless, it suggests that the difference in overall prognosis possibly associated with this different management in terms of initial risk-adjusted results is small, although not negligible in view of other characteristics of the study.

– It raises the question of whether patients with NSTEMACS, at least non-low risk NSTEMACS, should be managed in a cardiologic setting. The authors of the study, therefore, suggest the need for remodeling the care of patients with NSTEMACS in Spain with the corresponding increase in available means, such as the creation of more chest pain units.

On the other hand, and without in any way diminishing the very valuable contribution of this report, several questions still remain in this substudy of PEPA and which could perhaps be approached in future studies. For example, the analysis does not possess sufficient power to establish the true repercussions derived from the difference in admitting departments (which in the context of the study implies differences in management), both because of insufficient sample size and the type of data collected, limited by the period during which the study was undertaken. The study also uses mortality in the coronary care units as the reference value for the statistical analysis of the prognosis of survival. Although from the analytical viewpoint there is absolutely no objection to this, the reader should not think that this is equivalent to assuming that management in coronary care units is optimum. This is not necessarily the case, and the

problem of the current effectiveness of the management of NSTEMI according to current recommendations, compared with previous recommendations, is still not clear, and the values of "attainable effectiveness" have still not been established definitively. A further difficulty is that, by not specifying the date of recruitment, it is not possible to know which pattern of recommendations should be applied for analysis of the results. Furthermore, as the authors point out in the section on limitations, the study was undertaken at a time when troponin measurement was still not systematically available in clinical practice. This results in a possible discrepancy involving an upward slant in the distribution of the diagnoses compared to the current distribution and a reduction in the ability to adjust and stratify the sample according to overall risk.

The medical relevance of the question examined in this study is great. Although the study was not designed to assess medical material and personnel available in Spain for the correct care of acute coronary syndromes, they are known to be suboptimal. For patients with heart failure this problem has been somewhat alleviated, either by planning or spontaneously, by admitting these patients to non-cardiological wards, especially to internal medicine services. The ideal hospital setting for patients with heart failure has been widely debated. Their management outside cardiology wards is acceptable, provided that cardiologic examinations and consultations are readily available and the attending physician has received suitable training.⁸ However, this is not the case with NSTEMI, a syndrome which requires the immediate availability of interventions only provided by cardiologists, except for low-risk patients or patients with severe accompanying disease.

This said, it is nevertheless opportune to recall that, apart from the availability of suitable material and health care personnel, a crucial aspect is the mentality and training of the attending physician. Some of the deficiencies detected by this study in certain departments concern such simple things as the administration of antiplatelet agents, heparin or beta-blockers, which may be due to reduced awareness about the use of such interventions, independently of the possible greater proportion of patients with a doubtful diagnosis. Although the greater availability of stress tests or coronary imaging techniques may result in a better diagnostic approach for patients with acute coronary syndromes, this also demands a higher degree of information and awareness, which might be easier in cardiology departments, though not necessarily exclusive to these.⁹

PENDING QUESTIONS

Why did this study fail to demonstrate any difference in prognosis in favor of the better equipped services and departments? Several possible explanations for this exist. Firstly, the study might not have detected actual differences because the proportion of patients with an incorrect diagnosis of NSTEMI was higher in the internal medicine or emergency departments; this insufficient detection would thus be due to a poorer use of suitable diagnostic strategies. In this case, the management of NSTEMI in departments where the diagnostic strategy was inadequate might be considered inappropriate. However, the results of the study remain unchanged after elimination from the analysis of patients with non-classified chest pain, mostly in departments making less use of examinations. Secondly, the difference in prognosis derived from following a management pattern which was less adjusted to current recommendations may in fact be slight and not detectable with the sample size used in this study: if the benefit of strict compliance with evidence-based recommendations is more obvious in the high-risk patients, a larger overall sample than that used in the PEPA study is required for the effect in these patients to be detected in the overall mean. It is also reasonable to assume that certain therapeutic interventions were more effective than others. Some studies¹⁰ suggest that the greater change in prognosis may be due to those interventions which are simpler, cheaper, and better known, such as the administration of aspirin in infarction; this could be more difficult to demonstrate in patients with NSTEMI due to the increase in interventions which are more complex, expensive and less often used, such as very early revascularization or the administration of glycoprotein IIb/IIIa inhibitors.

Examination of these possibilities leads to important conceptual doubts, such as: In quantitative terms, what is the true benefit to be expected from the strict application of clinical practice guidelines if very large samples are required to detect this benefit in representative groups of patients in daily clinical practice? To what extent do each of the recommended measures lose their applicability in patients who are older or who have severe accompanying diseases? How is the incremental effect of complex interventions shown up, when these may be small or restricted to high risk patients, or when more simple or achievable measures are also taken? To rephrase this in terms of the previous paragraphs: How should we measure the effectiveness of the treatment of NSTEMI and acute coronary syndromes in general? Evidence exists that compliance with the recommendations derived from clinical trials leads to better results in true clinical practice.^{3,11} Indeed, the

degree of compliance with clinical practice guidelines is used as a marker of health care quality;¹² but this compliance, used as a marker, still just represents an intermediate or surrogate variable in the course of demonstrating a better clinical result, probably with better grounds than those which used the reduction in postinfarction ventricular premature beats as a surrogate for the reduction in death, before the CAST study showed up the error of this supposition. Nevertheless, exhaustive compliance with the recommendations in guidelines is not the same as true effectiveness and it is necessary to quantify this, particularly regarding those interventions which are more complex, costly or sophisticated. This quantification should start with risk stratification, ideally coherent with that proposed in the clinical practice guidelines. This would enable us to determine the results that can be reasonably expected, according to the risk adjustment, in the different groups of patient with acute coronary syndromes. Furthermore, this should if possible be undertaken in all the hospitals and centers which comply scrupulously with the recommendations of clinical practice guidelines for the treatment of these syndromes. This would then enable us to establish a pattern for the degree of benefit which is both desirable and attainable in our setting, and whereabouts that benefit lies on the scale of risks in the general hospital population of patients with acute coronary syndromes.

REFERENCES

1. Iezzoni LI. Risk adjustment for measuring healthcare outcomes. Ann Arbor: Healthcare Administration Press, 1997.
2. Zahn R, Schiele R, Schneider S, Gitt AK, Wienbergen H, Seidl K, et al. Primary angioplasty versus intravenous thrombolysis in acute myocardial infarction: can we define subgroups of patients benefiting most from primary angioplasty? *J Am Coll Cardiol* 2001;37:1827-35.
3. Gil M, Marrugat J, Sala J, Masià R, Elosua R, Albert X, et al. Relationship of therapeutic improvements and 28-day case fatality in patients hospitalized with acute myocardial infarction between 1978 and 1993 in the REGICOR study, Gerona, Spain. *Circulation* 1999;99:1767-73.
4. Arós F, Cuñat J, Loma-Osorio A, Torrado E, Bosch X, Rodríguez JJ, et al. Tratamiento del infarto agudo de miocardio en España en el año 2000. El estudio PRIAMHO II. *Rev Esp Cardiol* 2003;56:1165-73.
5. Bosch X, López de Sá E, López Sendón J, Aboal J, Miranda-Guardiola F, Bethencourt A, et al. Perfil clínico, pronóstico y variabilidad en el tratamiento del síndrome coronario agudo sin elevación del segmento ST. Datos del registro PEPA. *Rev Esp Cardiol* 2003;56:346-53.
6. Fox KA, Goodman SG, Klein W, Brieger D, Steg PG, Dabbous O, et al. Management of acute coronary syndromes. Variations in practice and outcome; findings from the Global Registry of Acute Coronary Events (GRACE). *Eur Heart J* 2002;23:1177-89.
7. Bosch X, Verbal F, López de Sá E, Miranda-Guardiola F, Bórquez E, Bethencourt A, et al. Diferencias en el tratamiento y la evolución clínica de los pacientes con síndrome coronario agudo sin elevación del segmento ST en función del servicio clínico de ingreso. *Rev Esp Cardiol* 2004;57:283-90.
8. Permanyer-Miralda G. Insuficiencia cardíaca: viejas preguntas, soluciones incompletas. *Rev Esp Cardiol* 2003;56:20-2.
9. Ayanian JZ, Hauptman PJ, Guadagnoli E, Antman EM, Pashos CL, McNeil BJ. Knowledge and practices of generalist and specialist physicians regarding drug therapy for acute myocardial infarction. *N Engl J Med* 1994;331:1136-42.
10. Heidenreich PA, McClellan M. Trends in treatment and outcomes for acute myocardial infarction: 1975-1995. *Am J Med* 2001;110:165-74.
11. Mukherjee D, Fang J, Chetcuti S, Moscucci M, Kline-Rogers E, Eagle KA. Impact of combination evidence-based medical therapy on mortality in patients with acute coronary syndromes. *Circulation* 2004;109:745-9.
12. Mehta RH, Montoye CK, Gallogly M, Baker P, Blount A, Faul J, et al. Improving quality of care for acute myocardial infarction. *JAMA* 2002;287:1321-3.