

Heart Failure: From Clinical Trials to Everyday Clinical Practice

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This issue of the REVISTA ESPAÑOLA DE CARDIOLOGÍA publishes two interesting articles on the clinical characteristics and management of selected patients with heart failure (HF) in two large hospitals.^{1,2} Although they do differ in their objectives and methods, the two studies coincide in showing three important, interrelated aspects.

In first place, the patients usually seen in hospitals have clinical characteristics quite different from those of the subjects generally included in clinical trials of HF therapy. As other large studies of series of unselected patients have shown,³ patients are older, generally women, with frequent comorbidity, and often without ventricular dysfunction. Since these patients usually have not been included in clinical trials, there is uncertainty regarding suitable diagnostic and treatment guidelines. For the moment, treatment has to be based on knowledge of the pathophysiology of the mechanisms of action of drugs and on a common-sense extrapolation of the results of clinical trials in patients with whom they share some characteristics. In theory, to know what treatment would be most suitable for these patients it would be necessary to carry out clinical trials in similar patients in the future.

Nevertheless, this way of obtaining knowledge, although currently the most important, is inefficient, slow and reactive. It is inefficient because it usually requires several trials to respond to each research question, which often examine a single intervention in patients with very specific inclusion criteria. In practice, hundreds or thousands of clinical trials may be needed in each field to respond to the numerous research questions that patients generate and to determine the potential effectiveness of medications.⁴ It is slow, because trials involving chronic diseases require long periods of follow-up of the subjects to demonstrate beneficial effects on morbidity and mortality. In addition, the time between generating evidence, applying

it, and ultimately obtaining benefits in the population is very long. Consider that since the design of the first therapeutic trials of angiotensin-converting enzyme inhibitors (ACEI) in HF (e.g., CONSENSUS) to the present, about 20 years have passed and, nevertheless, there has been little improvement in the vital prognosis of HF in community patients.⁵ Finally, it seems as if investigation is lagging behind problems instead of anticipating them. For understandable reasons (e.g., to maximize the conditions in which the medication can be effective), drugs are first evaluated in «atypical» patients, leaving the evaluation in the majority of patients for later.

We do not know the solution to these problems. However, a first measure might be to improve our knowledge of the pathophysiological mechanisms of diseases and the mechanisms of action of medications so that their effects can be predicted sufficiently well in patients. In addition, medications with several potentially interesting mechanisms could be developed in order to evaluate them a single time in patients with different clinical characteristics. Another possible solution would be to develop good intermediate indicators of the benefit of medications, thus obviating the need to measure morbidity and mortality. It cannot be overlooked that medicine seems to be entering a phase of individualized treatments to maximize their effectiveness and safety. This is precisely the path that has been opened by pharmacogenetics. However, while the saying «one size does NOT fit all» is common in modern medicine, it is useful to remember that millions of people dress correctly without having to go to a tailor for a custom fitting. The clothing sold at the department store, designed on mass scale models, fits most of them. Medicine should not forget this perspective if it really proposes to be effective for the general population, without having to evaluate each new medication that is developed in each and every one of the clinical subtypes of patients. We hope that this attitude will become more frequent in the future.

Secondly, both studies show that a substantial part of the patients who can benefit from echocardiography probably do not receive it. In addition, effective treatments for ventricular dysfunction, like the ACEI, are prescribed most frequently to subjects in which echocardiography is performed.¹ This study is usually carried out

SEE ARTICLES ON PAGES 571-8 AND 579-86

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less often in older patients, although the proportion of patients with normal or depressed ventricular function does not vary substantially with age. Echography was also performed less frequently in women, possibly because they reach more advanced ages than men, although the studies do not provide any specific information about the reasons for this finding. Finally, echography was carried out more frequently in subjects characterized as having a better prognosis, usually the youngest patients. It is difficult to interpret these observations, but they are probably consistent with two lines of reasoning. On the one hand, a physician guided by good criteria may decide not to dedicate healthcare resources or add additional discomfort to that of the disease itself in patients in which medicine cannot offer an appreciable clinical improvement, due to the poor prognosis of the disease even with available examinations and treatment. Nevertheless, this requires a careful and exact evaluation of the prognosis of each patient. If this were not the case, another explanation is age discrimination (what the Anglo-Saxons call *ageism*) and the sex associated with age, which restricts the access to effective treatment of patients of advanced age.⁶

Thirdly, both studies suggest that therapeutic interventions should be improved in patients with HF. Particularly, the frequency of administration of ACEI and beta blockers (BB) should be increased. It is true that the information in both studies was collected before evidence had accumulated regarding the effectiveness of BB in HF, and that the administration of these medications usually begins outside the hospital. It is also true that many patients in both studies had clinical characteristics different from those of the patients included in ACEI trials, an appreciable number of them lacked echography to guide treatment, and in some cases there were contraindications for ACEI like kidney failure and aortic stenosis. However, the high frequency of ventricular dysfunction diagnosed and the accompanying arterial hypertension suggests that some subjects not treated with ACEI could have benefited from these medications. In fact, the authors of one of the studies conclude that the patterns of treatment of the patients can clearly be improved.¹ The as yet unpublished results of the EUROHEART study,⁷ the results of the HF registry of the Spanish Society of Internal Medicine,³ and those of a recent primary care study⁸ suggest that this is the case.

What is this situation due to? We do not know. But it is possible that some physicians are unfamiliar with clinical practice guidelines for HF, do not agree with them, or lack the resources to apply them. As far as resources are concerned, the most important is probably the facility for ordering echography on patients to determine treatment. On the other hand, the «inflation» in the number of clinical practice guidelines in almost every field of medicine, the fact that many of them

have defects in their construction (they are not really based on good evidence), that they sometimes offer inconsistent recommendations and need to be adapted locally and updated periodically illustrates the difficulty of choosing an adequate guideline and may have generated certain professional skepticism with respect to the usefulness of guidelines.⁹ The best way to improve the quality of care are not entirely clear. Grol recently reviewed instruments in this field.¹⁰ Among these are classic forms and interactive continuing education sessions, educational presentations by opinion leaders, intrahospital activities to continuously improve quality, clinical audits followed by feedback to professionals, computerized clinical decision support systems (CDSS), and the so-called «multicomponent programs» that combine several of the best instruments. The CDSS and multicomponent programs seem to be the most promising, but it is not easy to generalize their use. Until this question is clarified, we venture to propose a triple formula: professional competence plus more adequate healthcare resources (including diagnostic tests, enough professionals, and time) plus more empathy and esteem for patients.

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