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EDITORIAL

Back to the future: the crucial role of clinical registries in the era of randomized controlled trials for identifying the optimal medical therapy of heart failure

Francesco Pelliccia[1]* and Giuseppe M.C. Rosano[2,3]

[1]Department of Cardiovascular Sciences, Department 'Attilio Reale', Sapienza University, Via Tommaso Inghirami 85, Rome 00179, Italy; [2]Cardiovascular and Cell Sciences Research Institute, St. George's University of London, London, UK; and [3]IRCCS San Raffaele Pisana, Rome, Italy

Heart failure (HF) remains a leading cause of morbidity and mortality in both men and women in both sides of the Atlantic. Patients hospitalized with HF are at high risk for recurrent events, hospitalizations, and cardiovascular death. In the last decades, an impressive number of randomized controlled trials has established the paramount role of several pharmacologic and non-pharmacologic strategies to reduce all-cause mortality for patients with HF and left ventricular functional impairment. Thanks to these investigations, European and American scientific societies have developed guidelines that provide evidence-based recommendations for treating acute and chronic HF,[1,2] including β-blockers, angiotensin-converting enzyme (ACE)-inhibitors, angiotensin receptor blockers (ARBs), aldosterone antagonists, hydralazine/isosorbide dinitrate, implantable cardioverter defibrillators, and cardiac resynchronization therapy. Nevertheless, the use of these therapies in daily clinical practice remains inconsistent.

The problem of poor application of evidence-based therapies as well as poor compliance to drug prescriptions has been discussing in-depth in recent years in North America,[3] whereas it still barely faced in Europe. As a consequence, the potential magnitude of benefits of optimal implementation of evidence-based therapies in HF in European countries remains unclear. One should consider, however, that determining the respective gains that optimal application of each evidence-based therapy may provide is essential in prioritizing performance improvement efforts and planning future strategies.

The current study

In the current issue, De Blois *et al.* report important data from the Norwegian Heart Failure Registry.[4] The authors aimed at assessing the adherence to guidelines for ACE-inhibitors, ARB, and β-blockers and the possible association of ACE-inhibitors or ARB, β-blockers and statins in 5761 hospital outpatients who were diagnosed with HF of any aetiology over a 10-year period. Statistical analysis showed that Norwegian patients had a high adherence to treatment according to guidelines. Cox regression analysis showed that β-blockers, higher doses of ACE-inhibitors, and statins were significantly related to improved survival. As honestly recognized by the authors,[4] this study suffers from limitations intrinsic in clinical registries. Missing data and selection bias are important drawbacks, but one should also keep in mind that statistical associations do not prove cause–effect relationships and that confounders can affect statistical computations substantially. As a matter of fact, however, the use of clinical registries is an important tool for determining the effectiveness of a therapy in routine clinical practice.[5] Observational studies allow for the inclusion of broader populations of patients than randomized controlled trials and therefore can provide clinicians and patients with a more realistic expectation for outcomes in real-world environments. When carefully applied, a registry-based research constitutes a reliable and even invaluable source for informing routine clinical practice, and are essential to translating findings from randomized controlled trials into high-quality evidence that can guide routine clinical practice.[5] Accordingly, the study by De Blois *et al.* allows us to derive two reliable, novel conclusions.[4] First, the outcome of HF patients improves consistently when the adherence to the use of drugs indicated by European Society of Cardiology guidelines is high. Second, an increased survival can be obtained if patients are given β-blockers and statins, whereas ACE-inhibitors are effective only if doses $\geq$50% of the maximal recommended target are prescribed and ARBs have not effect on survival in the real world.

Clinical implications and future perspectives

The results of the study by De Blois *et al.* confirm previous observations by North American investigators that adherence to evidence-based, guideline-recommended therapies may have a crucial role in

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* Corresponding author. Tel: +39 348 3392006, Fax: +39 06 330 62516, Email: f.pelliccia@mclink.it

survival improvement.[6] Noteworthy, the expected gains would be much smaller if class I therapies, as it is the case of ACE-inhibitors, are used at low doses rather than at if doses ≥50% of the maximal recommended target. Establishing the potential benefits of optimal implementation of these therapies is of considerable importance to underscore growing European efforts to improve the use of evidence-based therapies in patients with HF. Indeed, newer effective approaches to improve the use of evidence-based, guideline-recommended therapies for HF are urged for European healthcare system. Implementations of programs aimed at assessing the adherence to scientific guidelines are in place in Europe in association with the ESC and HFA and in the USA.[7] Numerous studies have demonstrated that adherence to clinical guidelines is associated with a better patient outcome, including significant reductions in 30-day readmissions. In conclusion, time has come that, given the substantial HF burden, the European scientific community makes extra efforts to ensure optimal implementation of each evidence-based, guideline-recommended therapy.

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