

Medical therapy versus revascularization rounds: ischemic heart failure on focus

Alda Huqi, Cardiovascular Medicine Division, Cardio Thoracic Department, University of Pisa, Pisa, Italy, and University of Alberta, Edmonton, Alberta, Canada

Correspondence: Dr. AldaHuqi, Cardiovascular Medicine Division, Cardio Thoracic Department, University of Pisa, Via Paradisa, 2, 56100 Pisa, Italy. And: 423 Heritage Medical Research Center, University of Alberta, Edmonton, Alberta T6G 2S2, Canada. Tel: +39 32972 56426, e-mail: alda_h@hotmail.com

Ischemic heart failure (HF) has long been considered potentially reversible. In this regard, a positive test for myocardial viability would make cardiologists feel more comfortable in directing patients towards revascularization, thereby constituting a guiding practice for the past two decades [1]. Importantly, such data has been extrapolated from numerous non randomized, predominantly single-center studies [2] and meta-analyses suggesting the improved survival of revascularized patients with viable myocardium on non invasive testing [3]. However, data from randomized, multicenter studies have been lacking, and moreover, both surgical and non surgical therapies for coronary artery disease (CAD) and HF have substantially improved since then.

Recently the results of the Surgical Treatment for Ischemic Heart Failure (STICH) trial, which evaluated the role of surgery plus guideline-recommended medical therapy as compared with medical therapy alone [4], together with a sub-study that also tested the role of myocardial viability [5] in patients with ischemic HF were published. Patients with CAD amenable to coronary artery bypass grafting (CABG) and reduced ejection fraction (EF) (<35%) were eligible for the study. Those patients with a recent myocardial infarction (MI), planned aortic valve replacement or percutaneous coronary intervention (PCI), or coexisting non-cardiac disease with a projected life expectancy <3 years were instead excluded. The primary end point was death from any cause. Important secondary end points included death from cardiovascular causes and hospitalization. In all, 1,212 patients were included in the main study and 601 of them underwent a viability test before randomization. During a median of 56 months of follow-up of the main study population, the primary outcome occurred in 41% in the medical-therapy group and 36% in the CABG group ($p = 0.12$). Interim analysis showed that patients with viable myocardium had lower overall rates of death (37%) than those without viable myocardium (51%). However, after adjustment for baseline prognostic variables, there was no statistically significant difference in mortality between the 2 groups ($p = 0.21$).

These were not the expected results. In fact, the main findings of this study can be summarized as follows: patients with CAD and HF do not necessarily benefit from a revascularization procedure, and most importantly, this is true even when the presence of myocardial viability is documented.

In general, the widespread acceptance of new knowledge is directly proportional to the degree of the understanding of the concept. However, given that it was not a pre-specified objective, no pathophysiological insights responsible for such results are provided in the study. However, different hypotheses can be drawn and some of them worth mentioning.

First, provided that CAD was conceivably associated with myocardial ischemia, STICH patients represent a very complicated patient population in that they contemporaneously attain two major causes of adverse cardiovascular outcomes: ischemia and left ventricular (LV) dysfunction. Importantly, because of the particular perpetuating interactions (i.e., the greater the ischemic burden, the greater the systolic dysfunction, and vice versa), the dissection of the prevalent pathophysiological mechanism leading to the fatal outcome is often impossible. Nonetheless, as noted in the accompanying editorial [6], STICH was more of an ischemic heart disease (IHD) rather than a HF trial in that patients were younger, had more angina and fewer HF symptoms than a typical HF patient population. However, if this is the case, the data would not be surprising, being in line with other, previously published large clinical trials that compared medical versus revascularization therapy in chronic angina patients [7].

In a second hypothesis, viable but dysfunctional myocardium can be explained by the concept of hibernating myocardium. Previous studies have suggested that early revascularization of hibernating myocardium may be essential to avoid irreversible dysfunction [8]. However, no data on either the presence or the timing of the clinical ischemic event(s) of patients are provided in the STICH trial. Moreover, similar to other beliefs on this topic, such findings are based on observational, single-center data.

As for the third hypothesis, by definition, HF patients with angiographically documented CAD have ischemic HF. From here, it is extrapolated that patients with reduced EF and no CAD have dilatative cardiomyopathy. However, the latter often also present with signs and symptoms of myocardial ischemia that are routinely referred to as a specific or “main disease” related. Conversely, “ischemic HF” patients may lack a clinical history or a test indicative of a previous, well-defined ischemic event. However, when association is documented, obstructive CAD is routinely regarded as the only causal mechanism of HF. A similar response to revascularization and medical therapy alone observed in this trial suggests that the distinction between the pathologies may not be so clear. On the other hand, it is clear that, in being too simplistic, we

may have cultivated some knowledge gaps, responsible for casting a shadow over other important advances, i.e., myocardial revascularization.

In conclusion, STICH results add to those of other recently published randomized trials that enclose real threats to historical dogmas in cardiology. Not all HF patients with CAD will benefit from myocardial revascularization; this is the brand new catching up with the latter! Will we be wise enough to start acting accordingly, and win the forthcoming rounds? •

References

1. Lee KS, Marwick TH, Cook SA, et al (1994) Prognosis of patients with left ventricular dysfunction, with and without viable myocardium after myocardial infarction. Relative efficacy of medical therapy and revascularization. *Circulation*. 90(6):2687–2694
2. Pagley PR, Beller GA, Watson DD, Gimble LW, Ragosta M (1997) Improved outcome after coronary bypass surgery in patients with ischemic cardiomyopathy and residual myocardial viability. *Circulation* 96(3):793–800
3. Allman KC, Shaw LJ, Hachamovitch R, Udelson JE (2002) Myocardial viability testing and impact of revascularization on prognosis in patients with coronary artery disease and left ventricular dysfunction: a meta-analysis. *J Am Coll Cardiol* 39(7): 1151–1158
4. Velazquez EJ, Lee KL, Deja MA et al (2011) Coronary-Artery Bypass Surgery in Patients with Left Ventricular Dysfunction. *N Engl J Med* 364(17):1607–1616
5. Bonow RO, Maurer G, Lee KL et al (2011) Myocardial Viability and Survival in Ischemic Left Ventricular Dysfunction. *N Engl J Med* 364(17):1617–1625
6. Fang JC (2011) Underestimating medical therapy for coronary disease... again. *N Engl J Med* 364(17):1671–1673
7. Boden WE, O'Rourke RA, Teo KK et al (2007) Optimal medical therapy with or without PCI for stable coronary disease. *N Engl J Med* 356(15):1503–1516
8. Carluccio E, Biagioli P, Alunni G et al (2006) Patients with hibernating myocardium show altered left ventricular volumes and shape, which revert after revascularization: evidence that dyssynergy might directly induce cardiac remodeling. *J Am Coll Cardiol* 47(5):969–977
9. McGill HC, McMahan CA, Zieske AW et al (2000) Association of Coronary Heart Disease Risk Factors with microscopic qualities of coronary atherosclerosis in youth. *Circulation* 102(4):374–379
10. Cubbon RM, Gale CP, Kearney LC et al (2011) Changing Characteristics and Mode of Death Associated with Chronic Heart Failure Due to Left Ventricular Systolic Dysfunction: A Study Across Therapeutic Eras. *Circ Heart Fail* doi: 10.1161/CIRCHEARTFAILURE.110.959882
11. Li P, Zhang X, Capasso JM, Meggs LG, Sonnenblick EH, Anversa P (1993) Myocyte loss and left ventricular failure characterise the long term effects of coronary artery narrowing or renal hypertension in rats. *Cardiovasc Res* 27(6):1066–1075