Non-transplant Options in Advanced Heart Failure: Emergent Need for Guidelines ?

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Abstract

Advances in revascularization techniques along with its timeliness has significantly prolonged survival in Coronary Artery Disease. Progressive heart failure is one of the complications which persists in a large scale. The challenges of surgical revascularization in such patients with left ventricular dysfunction are daunting, necessitating short cross-clamp and cardio-pulmonary bypass times. Associated co-morbidities like renal dysfunction, low cardiac output state and pulmonary vascular obstructive disease are additional significant deterrents to surgical success. In the situation where transplant options are limited, viability of high-risk surgical revascularization may need radical re-thinking.

The burden of ischemic cardiomyopathy is increasing in large proportions particularly in South East Asia reflecting the population's ethnic genotype. Most of these patients progress relentlessly to end-stage heart failure despite maximal tolerated medical therapy. Heart transplantation is limited by logistic constraints of donor in-availability and lack of funds, and is presently being carried out in less than 5% of patients.[1]

The challenges of corrective surgery for these patients would require adequate myocardial protection with short cross-clamp and cardio-pulmonary bypass times. Associated co-morbidities like renal dysfunction, low cardiac output state, pulmonary vascular obstructive disease are significant deterrents to surgical success. In the situation where transplant options are limited, the viability of corrective high-risk surgeries may need radical re-thinking. The lack of focused guidelines targeting this population makes decision making even more difficult.

Although the mortality is slightly higher with CABG in patients LV dysfunction, the 30-day mortality being 5.6% versus 1.1% for patients with normal LV function, the benefits of revascularization far exceed the benefits of medical therapy alone.[2]

Clinical non-randomized studies on CABG in patients with LV dysfunction clearly demonstrate the need for viability testing. In patients with severe left ventricular dysfunction and evidence of relatively large areas of viable myocardium, improved long-term survival with revascularization as compared with medical therapy has been clearly demonstrated.[2]

However, the degree of LV remodeling seemed more important. Improvements in LV function after CABG occurred in patients with myocardial viability who had less severe LV remodeling, whereas functional recovery seemed less likely, despite viable myocardium, in patients with severe LV remodelling.[2] Re analyzing the STICH database, it was noted that among patients with coronary artery disease and LV systolic dysfunction, lower LV end-systolic volume index did not identify patients in whom myocardial viability predicted better outcome with surgical relative to medical treatment.[3] So, the question arises in the population with larger LV ESVI and larger proportions of non-viable myocardium, whether LVAD or cardiac transplantation are more viable options than revascularization.

All the observational studies on revascularization in LV dysfunction have studied patients with a wide range of LVEF ranging from 20% to 40%; representation of patients with LVEF≤20% being <3%. Patients with an ESVI> 120 ml, severe pulmonary hypertension; mean PAP > 25 mm Hg, VO2 max <14 ml and LVEF< 20% have not been included in these studies, as are patients in NYHA class III/IV. Patients in NYHA class III/ IV in these studies constitute < 2-4%. Therefore, it is difficult to extrapolate the findings of these studies to a population who are transplant or LVAD eligible.

Although the results of randomized controlled trials are often disappointing and difficult to interpret, there is a paucity of these trials in these patients. The STICH trial was a randomized study designed to determine the benefit of CABG in patients with LV dysfunction due to ischemic cardiomyopathy.[3] These patients were in NYHA class II/III with an LVEF ≤35% and did not qualify to be transplant or left ventricular assist device (LVAD) eligible. Also, most investigators believe that the high crossover rate from medical therapy to surgery in the first year after randomization significantly confounded the interpretation of the STICH study. The post hoc analysis examining treated patients revealed a significant benefit of surgical intervention with respect to overall mortality and freedom from repeat hospitalization. Patient selection was flawed by including patients with milder degrees of heart failure which does not allow interpretation of its results for patients with severe LV dysfunction.

Transplant eligible patients undergoing CABG are different from the patients with LV dysfunction in terms of longer duration of symptoms, presence of right heart failure, and a greater incidence of previous revascularization. Although the operative risk in the coronary bypass group with LV dysfunction was significantly higher for those with a greatly increased left ventricular end-diastolic pressure (LVEDP) (> 24 mm Hg), a low preoperative cardiac output (< 2.0 l/min/m2), NYHA class

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Received: 01.03.18; Accepted: 16.08.2018

IV, there was no significant difference in hospital mortality in patients with LVEF between 10–20% versus those between 20–30%. Survival at six years was comparable between the two groups; 78.9% for the LV dysfunction versus 68.9% in the transplant group. Reinvestigation showed a significant decrease in mean pulmonary artery pressure from 28.2 ± 4.7 mm Hg to 21.2 ± 3.9 mm Hg ($p < 0.01$), pulmonary capillary wedge pressure from19.2 ± 4.3 mm Hg to 13.1 ± 2.8 mm Hg ($p < 0.01$) and mean improvements in left ventricular ejection fraction from 0.24 ± 0.03 to 0.39 ± 0.06 ($p < 0.0001$).[4] Patients eligible for transplant had surprisingly favorable mid-term outcomes when subjected to high-risk corrective surgeries.[4] However, these patients constituted a highly selected group with an LVEF < 20% with a VO2 max <14 mL/min/m2. None of these patients required inotropic support and were not on any support device. Even the transplant in-eligible patients had better outcomes although their outcomes were worse than those who were transplant eligible. The mortality associated with CABG alone was much lower than when CABG was performed with concomitant mitral valve repair or LV restoration (2.3% versus 14%). There was a significant improvement in NYHA class following CABG at mid-term. This demonstrates that patients with severe LV dysfunction due to ischemic etiology who are transplant eligible, with preserved renal function, no evidence of cardiogenic shock, and without concomitant mitral surgery have mortality benefits from CABG. This study did not address the benefits of corrective surgeries in patients who had undergone previous open-heart surgeries. These patients constitute a very difficult population and in our opinion may require LVAD or transplantation.

Although long-term evidence is lacking, high risk percutaneous coronary Intervention (HR-PCI) has shown benefits at 12 months in this population.[5] In the PROTECT 2 trial, Impella provided superior hemodynamic support in comparison with IABP, and at 90 days a trend toward decreased events was observed in the intent-to-treat population (40.6% Impella vs. 49.3% IABP, $p = 0.066$). A subsequent analysis redefining myocardial infarction as the development of new Q waves or CKMB more than eight times the upper limit of normal demonstrated lower rates of events in patients treated with Impella (composite event rate 37% vs. 49%, $p = 0.014$), respectively; and major adverse cardiac and cerebrovascular events 22% vs. 31%, $p = 0.034$).[14] The potential mechanism for late benefit may relate to more stable procedural hemodynamics allowing for greater and more complete revascularization, including allowing for more complex PCI procedures such as rotational atherectomy.

Therefore, MCS may be considered for patients undergoing high-risk PCI, such as those requiring multivessel, left main, or last patent conduit interventions, particularly if the patient is inoperable or has severely decreased ejection fraction or elevated cardiac filling pressures.

Surgical ventricular restoration (SVR) based on Laplace's law may well become a definitive solution in selected patients especially when transplant options are not available. The reasons for the decreasing numbers for SVR in developed countries may be the wide availability of timely revascularization, which is still scarce in most developing countries, making SVR applicable.

As the incidence of heart failure following an acute coronary event or chronic ischemic heart disease is increasing, high-risk revascularization and SVR need re-thinking. Although framing treatment guidelines for this population is fraught with difficulties, these may help in better management of this increasing malady.

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