Current perspective

Non-transplant surgery for heart failure and severe left ventricular dysfunction. Opportunities and limitations

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The need of alternatives to transplantation has lead to routinely reconsidering conventional surgery for selected patients with advanced heart failure.

Although the recovery of ventricular contractility with revascularization sometimes restores ventricular function almost to normality while dramatically enhancing the quality of life, only a few patients with ischemic left ventricular dysfunction exhibit the amount of hibernating myocardium required for such a spectacular outcome taking place. Advanced remodeling is a further obstacle and is currently being addressed by means of operations designed to reduce ventricular volume and restore geometry. Hemodynamic measurements raise concerns, however, as to the diastolic function and the competence of the mitral valve late after reconstructive surgery. Finally, the repair of mitral valve regurgitation has produced interesting short-to-medium term results both in terms of survival and heart failure relief. Yet, their durability is uncertain, if not disappointing when the valvular disease has an ischemic etiology.

Expectations of patients undergoing one of the aforementioned procedures, or a combination thereof, should not be averaged as they heavily depend on the specific patient profile under evaluation.

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Introduction

Limitations with organ procurement restrict the use of homologous heart transplantation in patients with advanced heart failure. Despite the increasingly selective listing, many transplant candidates will die before the opportunity of a heart donor arises. The chances of survival and the quality of life of patients eligible for transplantation therefore depend on the waiting list no less than on the operation itself.

As a consequence, and pending further progress in mechanical replacement devices and xenotransplantation, there has been a surge in the interest for non-transplant surgical procedures, including "conventional" operations – such as coronary bypass grafting and mitral valve repair or replacement – and the more innovative interventions addressing the remodeling process.

The degree of development and the effectiveness of translating these concepts into practice are variable. There are no properly designed trials which provide evidence-based selection criteria for the matching of any of these procedures with any corresponding patient profile. Economic and accessibility considerations affect the indications no less than the clinical criteria and appropriateness. We therefore reviewed the most relevant data regarding these aspects with the aim of improving the rationale of the "conventional wisdom" approach.

Coronary bypass grafting

Patients with angina and left ventricular dysfunction are likely to benefit most from revascularization even though their clinical picture may include heart failure[1]. Their clinical and prognostic benefits are largely explained by the prevention of new ischemic events and the relief of chronic ischemia – hibernation – if any. In this setting, whether the post-revascularization left ventricular functional changes affect the outcome appears to be a moot question, though at least one study suggests that an increased ejection fraction *per se* is not a prerequisite for improved survival[2].

Patients with heart failure following one or more ischemic insult, but no angina, are often characterized by an enlarged heart and severe left ventricular systolic dysfunction and probably constitute a somewhat different subset. At variance with the previous scenario, any improvement in heart failure symptoms following revascularization has been shown to be related to the recruitment of significant amounts of reversibly dyssynergic myocardium[3-5]. The latter parameter thus plays a pivotal role in the prediction of the functional recovery when recommending a revascularization procedure. This has highlighted the hibernating myocardium as the substrate linked to the post-revascularization recovery better than any other viability state. Although it is quite prevalent in patients with ischemic heart disease – and can be identified in about half of those with ischemic cardiomyopathy – hibernation is often limited in extent, to the point that only 1 out of 3-4 examined patients presents with the minimum amount of recruitable muscle necessary for an effective surgical risk/benefit ratio[6]. As a matter of fact, patients in whom less than 20% of the left ventricle may be considered as hibernating are unlikely to benefit from revascularization[3-5]. Careful diagnostic discrimination is required in every patient, therefore, as to the specific contribution of hibernation compared to other different myocardial viability states such as stunning, inducible ischemia, remodeling and normalcy, since only the former allows the reliable prediction of the revascularization-mediated functional recovery[7]. Unfortunately, detailed viability assessment at the resolution level of some elegant research study[8] is not commonly available for clinical purposes, nor has the discriminating ability of the ventricular volumes been incorporated into routine diagnostic work-up despite some quite compelling evidence[9,10].

Those few studies assessing the value of revascularizing the failing heart suggest that when the coronary graftability[11] and myocardial viability criteria are satisfied[12-14] bypass grafting procedures compare quite favorably with heart transplantation in the short-to-medium term follow-up. Louie et al.[12] achieved a 72% 3-year survival in 22 patients revascularized for severe congestive heart failure due to ischemic cardiomyopathy (the mean ± SD end-diastolic left ventricular diameter was 70 ± 7 mm in this series). Postoperatively, the left ventricular ejection fraction increased (from 26 ± 9 to 36 ± 9%) and the functional capacity improved (from NYHA class 3.9 ± 0.3 to 1.2 ± 0.4) in the majority of their patients. The small population sample did not prevent the authors from identifying the key role of myocardial viability for patient selection while, at the same time, pointing to the adverse implications of advanced remodeling (i.e. a left ventricular end-diastolic diameter > 75 mm or a left ventricular ejection fraction < 20%).

The short-term outcome was similarly good in a series of 32 patients referred for transplantation but eventually submitted to revascularization because of "significant" myocardial viability, as reported by Dreyfus et al.[13]. The heart failure symptoms improved (average NYHA class 2 from 3.2 preoperatively) and an 84% survival rate was recorded at a mean of 18 ± 6 months of follow-up. Finally, Paolini et al.[14] selected, on the basis of viability criteria, a small group of 9 patients with severe left ventricular dysfunction and congestive heart failure but no angina nor inducible ischemia. All patients survived and clinically improved (average NYHA class 1.9 from 3.1 preoperatively) at a 28 ± 10 month follow-up, while the left ventricular ejection fraction increased from 27 to 43%.

The longer-term outcome after revascularization for congestive heart failure can only be inferred from some surgical series of patients selected on the basis of severe left ventricular dysfunction though with a variable clinical presentation. For instance, Lorusso et al.[15] reported an 8-year follow-up for such a series including 30% of cases classified as being in NYHA class III-IV preoperatively. At multivariable analysis, both old age and congestive heart failure were independent predictors of an increased mortality suggesting that, in patients with a congestive heart failure history preoperatively, the long-term survival might have been significantly lower than the overall survival rate of 60 ± 9% reported in that series. As a reference, the 8-year follow-up in the UNOS Registry[16] recorded a 54% survival rate after heart transplantation, though in a younger population sample. In another series with a somewhat more severe left ventricular dysfunction (ejection fraction 18 ± 5%) Mickleborough et al.[17] achieved a 72% 5-year survival rate following revascularization, while confirming the adverse predictive role of old age and of a congestive heart failure history. It is worth emphasizing that the preoperative NYHA class IV status was associated with a 5-year survival rate which was < 40% in this series. In contrast, the UNOS Registry[16] 5-year survival rate was 67%. It is fair to point out that the unfavorable predictive role of congestive heart failure was not confirmed by Luciani et al.[18], who reported a 75 ± 8% survival 7 years following revascularization for severe left ventricular dysfunction.

Of course, rehabilitation is at least as relevant as survival when comparing alternative treatments in this clinical setting, and that is where the limitations of coronary revascularization are best appreciated. As reported by the UNOS Registry[16], 91% of transplanted patients have no functional limitation at 5 years while, on the other hand, about half of the revascularized patients surviving through 7-8 years suffer from recurrent heart failure[15,18]. Besides the clinical outcome, the financial advantages favoring revascularization[19] may therefore be erased by subsequent multiple re-hospitalizations for congestive heart failure.

To summarize, myocardial revascularization appears to be an effective and appropriate first-line approach to ischemic cardiomyopathy though, when heart failure prevails over the ischemic symptoms and signs, significant amounts of functionally recruitable myocardium are required if the results of heart transplantation are to be emulated. It should be appreciated that advanced remodeling[9,10], unstable hemodynamics, acute coronary syndromes, a low cardiac output, pulmonary hypertension and "right ventricular" failure[11,13,17,20,21], have all been associated with a poor surgical result and render revascularization unattractive and possibly inappropriate. Advanced age is a further risk factor[11,15,17], though the lack of alternatives will introduce a bias. This may lead to a dangerous underestimation of this risk factor. Perhaps in the elderly, more than in any other setting, one should not proceed to surgery in the absence of the criteria predicting a significantly enhanced quality of life.

Mitral valve surgery

Having established that the resection of the chordae tendineae and the consequent discontinuity of the annulo-papillary apparatus could partly explain the poor results observed after mitral valve surgery in cases with severe left ventricular dysfunction, surgeons have gone back to operating upon the incompetent mitral valve with the use of new techniques which spare the suspensory mechanism of the valve. In the majority of patients, mitral repair is quite straightforward[22,23] though, as an alternative, the eventual implantation of a prosthetic device can still be performed whilst at the same time leaving at least the posterior leaflet in place together with its chordal attachments.

Whether due to primary or ischemic cardiomyopathy, as the heart enlarges the process of remodeling attracts both leaflets into the ventricle below the annular plane – while at the same time the annulus dilates. The available suspensory and closing components of the mitral valve thus become inadequate and no longer ensure valve competence. By downsizing the annular circumference, mitral annuloplasty is quite successful in restoring proper leaflet coaptation though in an abnormal, somewhat subannular plane. Annuloplasty may also restore the base of the ventricle and the whole cavity away from the somewhat spherical shape of cardiomyopathy hearts and towards a more elliptical configuration[23]. On the other hand, mitral annuloplasty, whether alone or combined with some kind of free wall repair, may be inadequate for post-infarction aneurysms involving the base of the papillary muscles, making valve replacement unavoidable.

Provided that the difficulty of comparing the different, contemporary surgical series with the historical counterparts is fully acknowledged, the short-to-medium term outcome of mitral valve surgery in the presence of severe left ventricular dysfunction has seemingly changed for the better following the implementation of the aforesaid technical principles. At 2 years, the survival ranged from 68 to 86%, only to diverge radically at 5 years from 38 to 78% in the four most contributory series dealing with this clinical problem[22-25]. The ejection fraction cut-off for inclusion (varying from 25 to 35%), the role of active ischemia (ranging from nil to prevalent) and the proportion of replacement procedures (from 0 to 40%) were just the most evident – though by no means the only – differences between the four series. This makes it difficult to definitely foretell what can be accomplished and how with mitral valve surgery in this setting. As a working hypothesis, associated revascularization for active ischemia (but not for incidental coronary artery disease) portends a worse prognosis and annuloplasty, when feasible, is preferable to mitral replacement[24,26].

Quite importantly, patients surviving mitral valve surgery for severe heart failure and left ventricular dysfunction enjoy a greater functional capacity compared to that observed preoperatively[22-25]. Bolling at al.[23] have also shown that a significant degree of reverse remodeling does occur after reductive mitral annuloplasty. The clinical and physiologic value of correcting the mitral valve regurgitation of hearts with severe ventricular dysfunction has thus been reasonably documented, although a longer-term follow-up and additional contributions are eagerly awaited in order to improve the selection criteria for recommending this procedure. It is also critical that uncertainties as to the role of active ischemia be unraveled, and that the need and the nature of different and more innovative therapeutic strategies be clearly defined for this specific subset of patients.

Left ventricular reshaping

On the basis of Laplace's law, resection of part of the left ventricular postero-lateral wall has been investigated as a means of decreasing the radius of the left ventricular cavity and hence the wall stress in patients with end-stage dilated cardiomyopathy[27]. Although the operation may be quite successful in some patients, the result cannot be reliably predicted. This, in turn, leads to a lack of reproducibility and disappointment. Partial left ventriculectomy is therefore best set aside until additional research will improve the selection criteria and perhaps bring about some kind of technical refinement[28]. Notwithstanding this criticism, the procedure has bolstered the concept of reverse remodeling and drawn new interest in left ventricular aneurysmectomy and its variants.

Among others, left ventriculoplasty by either aneurysm or simple scar excision has emerged as a means of decreasing the left ventricular volume in patients with ischemic cardiomyopathy[29]. Though first described as a treatment for anterior wall deformities, which still constitute the bulk of eligible cases, the concept may also apply to large aneurysms in different locations. The procedure has been validated in the short-term by a large multicenter study showing an 84% 18-month survival together with an 85% freedom from rehospitalization[30]. In Dor's experience, the 10-year survival was inversely related to the preoperative left ventricular volume[31], suggesting the appropriateness of proceeding with surgery before advanced remodeling occurs.

Objective postoperative evidence of improvement following Dor's procedure has not emerged as clearly as the progression in the NYHA class. At 1 year, the left ventricular volumes were down to half the preoperative measurements, and the left ventricular ejection fraction was significantly improved. Nevertheless, that seems to have occurred at the expense of the ventricular compliance, as suggested by the increased pulmonary arterial and wedge pressures compared to the corresponding preoperative values[29]. Furthermore, the cardiac output persists at the low-normal values observed prior to surgery, and slightly more than one third of patients develop mitral regurgitation[32]. The increased ventricular sphericity has been offered as an explanation for the *de novo* mitral insufficiency, which was at least moderate in 18% of Dor's patients[32]. Finally, rewarding as it may be, left ventriculoplasty certainly owes an as yet undefined share of its merits to the frequently associated procedures such as coronary artery bypass grafting, mitral repairs and antiarrhythmic intervention. Most awaited is thus the contribution of the STICH trial (Surgical Treatment for Ischemic Heart Failure) whose aim is to compare medical treatment alone versus revascularization versus combined revascularization and ventriculoplasty[33].

New technologies also address reverse remodeling by physical left ventricular containment. One option includes the conversion of the transverse section of the left ventricle almost to a "figure of 8" shape by splitting the short axis at different planes, with the aim of reducing wall stress[34]. Alternatively, a restraining mesh may be wrapped around both ventricles to decrease diastolic stress as successfully shown in a preliminary clinical series[35].

Buckberg's trilogy and epilogue

The necessity of separately discussing these different surgical procedures should not obscure the opportunity of considering them in a complementary way as appropriate in patients with heart failure undergoing surgical evaluation[31]. Whether stand-alone or combined, they are far more accessible than heart transplantation and are definitely cheaper. In properly selected patients their results may equal those of transplantation[19], not to mention that there may be no alternative for many elderly patients who are ineligible to compete for a new heart.

Unfortunately, the scenario in which such a clinical decision is taken is further compounded by the pressure to overcome the limitations of medical treatment, and the tempting – and generally favorable – early reports of innovative approaches and new technologies. It may thus happen that sometimes, maybe just out of lack of alternatives, a choice must be made in the absence of clearly supporting evidence, and heart failure typically exemplifies that situation. For those occasionally obliged to decide in the lack of guidelines or against them it is therefore mandatory to make every aspect of such a decisional process explicit, in order to improve upon their understanding of the outcomes and to use that understanding as a preliminary step towards the development of new knowledge.

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