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Coronary artery bypass surgery for congestive heart failure: An evidence-based approach

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Despite ongoing advances in medical care, congestive heart failure (CHF) continues to be a leading cause of cardiovascular morbidity and mortality. In the USA, 400,000 new cases of CHF are diagnosed annually, with a mortality rate of 80,000 patients per year. In the fiscal year 1996-97, patients with CHF in Ontario had an annual mortality rate of 32%, not significantly different from the 34% in 1994-95.[1] Medical therapy has been the mainstay of treatment for CHF with severely compromised patients going on to heart transplantation. Despite a clear benefit to survival in NYHA class 3 to 4 patients, there are problems with heart transplantation related to organ shortage, necessitating rigorous patient selection. Consequently, the majority of patients with CHF are not candidates for heart transplantation and other therapies should be sought.

Coronary artery bypass graft (CABG) surgery is a potential form of therapy for patients with CHF who have a large component of ischemia that is responsible for their symptoms. However, accurate identification of patients who have the potential for benefit with such a procedure has proven to be difficult. In this issue, we will explore the clinical evidence for consideration of CABG in patients with CHF.

Historical data

The Coronary Artery Survival Study (CASS)[2] recruited patients who were post-myocardial infarction (MI) and either CCS class 1-2 or asymptomatic, and randomized them to surgery versus medical therapy. In a substudy of patients with EF <36%, 420 patients were assigned to the medical

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group and 231 to the surgical group. Patients selected for surgery had more angina, CHF symptoms, and presence of left main coronary stenosis. The overall operative mortality was 6.9%. Patients with an EF <26% had a significant 5-year survival advantage if they had surgery, compared to those in the medical group (64% vs. 43%). However, patients who underwent surgery had no relief of CHF symptoms. In a multivariate analysis, although bypass surgery was predictive of improved survival, it ranked below NYHA class, EF, age, and presence of left main stenosis as a predictor of outcome.

Similarly, the Veteran's Affairs (VA) study[3] enrolled 192 patients with an EF <35%; of these, 77 underwent CABG and 115 were given medical therapy. Again, more 3-vessel disease and angina was noted in the surgical group. Operative mortality was 5%; 7-year survival was 63% in the surgical group versus 34% in the medical group (p<0.001). Again, as in the CASS study, a subgroup of patients with EF <25% had a significant survival advantage over medically treated patients (p=0.0002).

Identifying the problem

Despite the benefit of surgery in historical trials, the patient populations in these trials are very different from those with predominant CHF symptoms. Likely, the benefit from surgery in this cohort is overestimated, given that the majority of patients had angina and were not severely compromised by CHF.

Intuitively, patients who would benefit most from CABG are those with the highest ischemic burden, leading to the greatest potential for recovery of left ventricular function (LVF). To accurately identify this subgroup of patients, one must have an imaging technique that is able to differentiate hibernating (Figure 1) from scarred myocardium. Furthermore, the amount of viable myocardium that is needed for benefit of surgery needs to be ascertained. This information — combined with an assessment of the risk of CABG — can then be used to develop a strategy that will lead to increased survival and improved function in patients with chronic CHF.

Figure 1: Hibernating myocardium, clinical and pathologic features

Hibernating myocardium

Clinical features

- Myocardium not contracting normally but metabolically active and "alive"
- Usually chronically ischemic and supplied by compromised vascular territory
- May be a result of recurrent "stunning"
- Has contractile reserve as noted with epinephrine, and post-PVC potentiation

Pathologic features

- Usually limited to islets of subendocardial myocardium
- Change of muscle to embryonic phenotype
- Loss of contractile proteins (sarcomeres)
- No loss of cell volume
- Glycogen-rich perinuclear zones adjacent to areas with numerous small mitochondria
- Nuclear changes with heterochromatin distributed evenly over nucleoplasm
- Substantial loss of sarcoplasmic reticulum.

Imaging techniques

Current techniques for identification of hibernating myocardium include those that image myocardial perfusion and those that assess myocardial wall motion.

Myocardial perfusion can be assessed using either single photon emission computed tomography (SPECT) and a variety of radionuclides (Tl^{201}, TC^{99}– sestamibi) or positron emission tomography (PET).

Myocardial wall motion can be evaluated with 2D-echo in the resting state, and compared to wall motion during infusion of low- and high-dose dobutamine. Improvement of wall motion during low-dose dobutamine infusion suggests myocardial hibernation, and reduction in wall motion during high-dose dobutamine suggests myocardial ischemia.

Evidence for revascularization

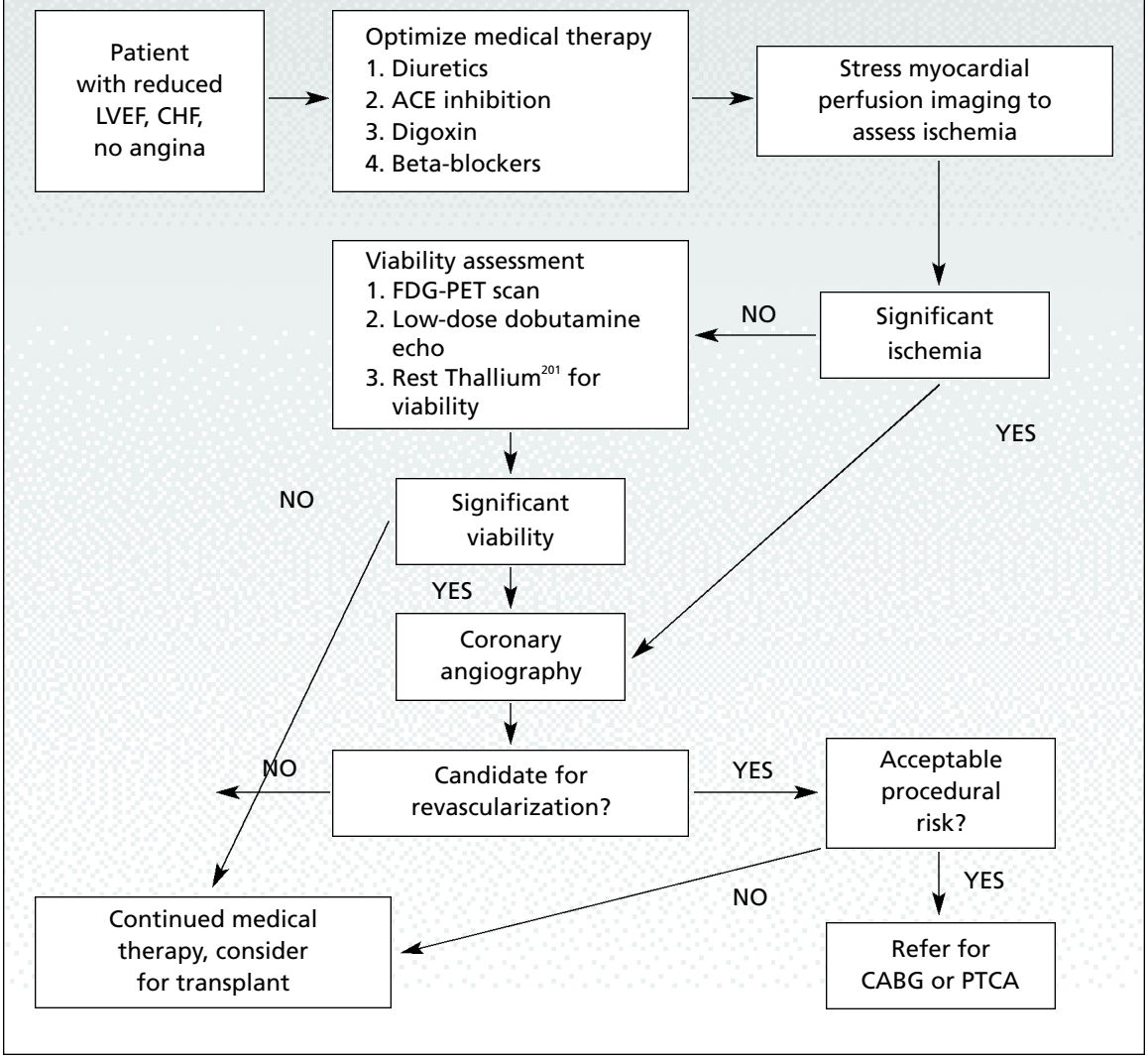
Several studies have assessed the utility of these techniques in evaluating patients with CHF prior to CABG. For the purposes of this paper, we will concentrate on several studies that have evaluated patients with severe LV dysfunction for coronary artery bypass surgery. Unfortunately, there are very few trials that have assessed patients with NYHA Class 3 to 4 symptoms, or those in which heart failure without angina is a predominant symptom.

• Pagano[4] evaluated 35 patients with NYHA 3 to 4 symptoms. Average EF was 23%, and 14 of 35 patients had symptoms of angina. No patients were on beta-blockers; the anginal group of patients was treated with a combination of nitrates and calcium channel blockers. Patients underwent 2D-echo and PET scanning prior to surgery. Viability was defined as a segment of dysfunctional myocardium on 2D-echo that had uptake of 13-FDG on PET scanning. Percentage of viable segments was greater in the angina group than in the non-angina group (94% vs. 56%). Operative mortality was 5.7%. Of 286 dysfunctional and viable segments, 190 improved after CABG, suggesting a positive predictive value (PPV) of 66% and a negative predictive value (NPV) of 96% for PET scanning. EF improved overall from 23% to 32%. A linear relationship between viability and change in EF was demonstrated ($r=0.65$, $p=0.0001$). Having 8 viable segments on PET (total of 16 segments) was the best predictor of increasing EF by 5% (previously shown to be clinically relevant). In a multivariate analysis of predictors of mortality, only EF and low viability were significant.

• Pagano[5] again reports on a very similar group of 30 patients with NYHA 3 or 4 symptoms, and compared dobutamine echo (DE) with PET scanning prior to CABG. Again, EF increased from 23% to 32%. Although both techniques had similar PPV for hibernating myocardium (68% for DE, 66% for PET), the NPV was much better for PET than for DE (96% vs. 54%, $p<0.0001$). In a stepwise linear regression for prediction of an increase in EF by 5%, only the number of viable segments on PET was a significant predictor (not preoperative EF, or viability on DE).

• A similar study by Fath-Ordoubadi[6] enrolled 47 patients with CAD and moderate-to-severe LV dysfunction. Patients were separated into two groups: group 1 (EF <30%, n=26) and group 2(EF >30%, n=21) and evaluated by PET and left ventricular radionuclide angiography (RNA). Functional status of patients was not described. There were no operative deaths. After bypass surgery, EF improved from 22% to 31% in group 1 ($p<0.0001$), but did not improve in group 2 (43% vs. 43%, p=NS). Metabolic rate of glucose uptake (MRG) — an assessment of cellular metabolic rate — was linearly related to improved wall motion score after

Figure 2: Algorithm for assessment of patients with CHF for possible CABG.



CABG (r=0.92), and dysfunctional segments that improved after CABG had a higher MRG than those that did not (0.45 vs 0.35 µmol/g/min, p<0.0001).

• A long-term follow-up study used pre-operative planar thallium to evaluate myocardial viability in 70 patients with a mean EF of 28%.[7] Viability index (VI) was defined as the sum of segmental viability scores, as assessed by planar thallium, divided by the total number of segments evaluated. Mean VI was 0.67, and patients were divided into two groups: those with a VI >0.67 and those with a VI <0.67. Operative mortality was 5.7%. Three-year freedom from death/transplant was 64.3%. Patients in group 1 did significantly better at 3 years than those in group 2 (70% vs. 54%, p=0.019). At multivariate analysis, only viability index was prognostic (χ^2=13.79, p=0.008) for increased survival.

• Thallium-201 SPECT imaging was compared to DE in a study of 38 patients with an average LVEF of 31%.[8] Thirty-six of 38 patients had angina, and although 20 of these patients had dyspnea on exertion, NYHA

class was not documented. Sensitivity and specificity for thallium SPECT imaging was 89% and 48%, while for DE was 74% and 95%. Unusually, this study did not show an improvement in EF post-operatively, although there was an improvement in angina.

• Afridi and colleagues[9] performed a retrospective analysis of 318 patients with an average EF of 27%. Patients were assessed for viability using DE and then assigned to one of four groups: patients with viability who underwent CABG (group 1, n=85), those with viability who did not have CABG (group 2, n=119), those who had no viability and underwent CABG (group 3, n=30), and those who had no viability and did not have CABG (group 4, n=84). At two years, there was a clear separation between groups, with a 92% survival in group 1, compared to an overall survival of 78% among the other 3 groups (p=0.01). There was no difference in survival between groups 2, 3 and 4. In a multivariate analysis including age, LVEF, and presence of 3-vessel CAD, not being in group 1 was the only predictor of increased mortality at 2 years (RR=3.6, p=0.05).

Summary

Although very few papers address the issue of the patient with very poor EF, minimal angina, and severe symptoms of CHF, it is clear that an assessment of viability plays an important role in decision making for this patient population. Because resources are scarce and only a select group of patients are adequate candidates, cardiac transplantation is not an option for the majority of patients with CHF. CABG surgery can be performed with an acceptable risk in this group of patients, and when carefully selected, significant improvements in long-term mortality and ejection fraction can be achieved. Clearly, only patients who have a significant amount of viability on noninvasive investigations benefit from surgery. Unfortunately, the amount of available data for patients with NYHA class 4 symptoms is limited, and application of these data to individual patients must be performed carefully.

We present an algorithm (Figure 2) that clinicians may find useful to manage patients with CHF, with a view to coronary revascularization. This algorithm is to be used as a guide only, as multiple patient factors that cannot all be accounted for, must be taken into consideration. Clearly, patients with significant 3-vessel coronary artery disease, left main stem disease, and severe proximal LAD disease benefit most from bypass surgery. However, there may be a role for direct angioplasty of a culprit vessel in patients who are either at high risk for surgery or have a limited number of involved vessels. Additionally, assessment of operative risk is an important albeit difficult aspect of this algorithm.

In conclusion, coronary artery bypass surgery is an important, though often forgotten treatment option for patients with congestive heart failure. Its application to those patients who have severe NYHA class 4 symptoms is unclear. Ongoing medical management, including ACE inhibitors, diuretics, and beta-blockers, is crucial.

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Abstracts of Interest

Survival benefit of revascularization in ischemic cardiomyopathy with viability demonstrated by low-dose dobutamine echocardiography

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Background: In ischemic cardiomyopathy, low-dose dobutamine echocardiography (LDDE) accurately predicts functional recovery and improvement in heart failure symptoms after revascularization but its prognostic value is uncertain.
Methods: Sixty consecutive patients (mean age 61 ± 9 years; 9 women) with coronary artery disease and left ventricular ejection fraction <35% were prospectively followed up after LLDE (5-15 µgm/kg/min). Wall motion score (WMS) was calculated at rest and during dobutamine infusion, using a 16 (extent) x 3 (seventy) points echocardiographic model. Viability was defined as a decrease ≥4 points in WMS during dobutamine. Patients were classified into one of four groups according to the LDDE result and performance or not of subsequent revascularization within 3 months after the test. Mean follow-up was 20 ± 13 months. Death and heart transplantation were the events considered for prognostication.
Results: Viability was present in 32 (53%) patients. Revascularization was performed in 30 patients: 26 using CABG and 4 PTCA. In the subgroup of revascularized patients, 21 had viability and 9 not (p = 0.01). During the follow-up period, 16 events occurred (5 in revascularized and 11 in non-revascularized patients; p = 0.03): 14 patients died and 2 were transplanted. In patients with viability, Kaplan-Meier estimated event-free survival was greater in the subgroup of revascularized patients (p = 0.026). Clinical outcome in patients without viability was similar whether or not revascularization was performed.
Conclusion: Revascularization improves survival in patients with ischemic cardiomyopathy and viability demonstrated by low-dose dobutamine echocardiography.

Long-term survival of patients with severe left ventricular dysfunction and multivessel coronary artery disease: 5-year results of the high risk myocardial ischemia trial

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Background: The survival benefit of revascularization for ischemic heart failure is controversial and undefined. The High Risk Myocardial Ischemia Trial (HIRMIT) was a prospective, randomized study and registry series evaluating the impact of revascularization on survival in patients with ischemic heart failure.
Methods: We prospectively identified 125 patients with low ejection fraction (EF), clinical heart failure, evidence of ischemia, and recent rejection from PTCA, CABG, or transplantation due to perceived high risk. 23 patients accepted randomization to either high-risk CABG (7), PTCA (8), or medical therapy (8). Of 102 patients who declined randomization and entered the registry, 17 underwent CABG and 20 had PTCA within 30 days. Vital status at 5 years was obtained for the entire cohort through the Duke Databank for Cardiovascular Disease or the National Death Index.
Results: The randomized and registry groups did not differ regarding baseline or outcome variables and thereby were combined for statistical analyses. Median EF for all patients was 21%. The 5-year survival rates (with 95% CI) were 38.5% (25.2-51.7%) for the revascularization group and 28.8% (18.4-39.2%) for the medical cohort (p=0.26). Survival rates for patients receiving CABG were 41.7% (21.9-61.4%), PTCA 32.1% (14.8-49.4%), and medical therapy 28.8% (18.4-39.2%)(p = 0.47 across groups).
Conclusion: HIRMIT is the only known prospective, randomized trial of revascularization in ischemic heart failure. HIRMIT shows the feasibility and necessity of a larger trial of revascularization versus medical therapy in patients with low EF, coronary artery disease, and clinical heart failure.

Abstracts from the *JACC* 1999;Feb