Original Article

Coronary Artery Bypass Surgery versus Medical Treatment in Patients with Low Ejection Fraction and Coronary Artery Disease

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Abstract

Background: *We compared the outcomes in patients with a low ejection fraction (EF) and multivessel coronary artery disease (CAD) who either underwent coronary artery bypass grafting (CABG) or received medical treatment (MT) after a viability study via dobutamine stress echocardiography (DSE).*

Methods: *We considered patients with CAD and left ventricular ejection fraction (LVEF) <40% who were referred for DSE, and enrolled 106 patients (89% male, mean age: 55.8±9.7 years) with ≥4 viable segments. According to DSE, all the 106 patients were suitable for revascularization. We compared the outcomes between the patients who underwent CABG and those who received MT at a mean follow-up time of 8 months.*

Results: *Both groups had similar baseline characteristics and rest EF. Thirty-three (31.1%) patients underwent CABG and 73 (68.9%) received MT. There was no significant difference between the CABG and MT groups in terms of mortality rate (9.1% vs. 11.0 %) and improvement in New York Heart Association functional class at follow-up. In the CABG group, patients with LVEF ≤25% had higher mortality compared to patients with LVEF >25% (100% vs. 40%, P< 0.05).*

Conclusion: *The patients with CAD and a low EF had the same survival rate after both CABG and MT at mid-term follow-up. Long-term follow-up is needed to show the survival benefit of CABG in such patients with an acceptable extent of viable myocardium.*

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Introduction

Large registries and randomized trials comparing coronary artery bypass grafting (CABG) and medical treatment (MT) have shown improved survival rates in patients with reduced left ventricular ejection fraction (LVEF) and multivessel coronary artery disease (CAD) who undergo surgery.[1-6] However, such patients have increased surgical risk and lower long-term survival rates than those with better ventricular function.[2] Further trials have demonstrated that patients with CAD and low EF benefit from CABG if there is adequate viable myocardium.[7] There is still no consensus

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about the number of viable segments that are required to perform CABG, with suggestions varying between 3 and 8 viable segments in different studies.[7,8]

Determining viability in areas of the myocardium with severe regional dysfunction may be important in patients with severe LV systolic dysfunction and multivessel CAD in whom CABG is contemplated.[9-13] Due to the scarcity of data on the relation between myocardial viability and clinical outcome, it is still a matter of debate whether survival in patients with a low EF and multivessel CAD can be predicted by dobutamine stress echocardiography (DSE).

This study was designed to compare the outcomes of patients with a low EF and multivessel CAD who either underwent CABG or received MT with an acceptable extent of myocardial viability as assessed by DSE.

Methods

Between March 2003 and January 2005, 106 patients with LVEF <40% and documented CAD underwent DSE for a clinical assessment of myocardial viability. Patients with unstable angina, congestive heart failure occurring within one month of the study, significant valvular disease, and technically inadequate echocardiographic imaging were not included in this study.

Baseline characteristics and clinical findings before the study were: age, sex, risk factors for CAD (hyperlipidemia, renal failure, family history, and diabetes mellitus), EF, left ventricular end diastolic volume (LVEDV), left ventricular end systolic volume (LVESV), New York Heart Association (NYHA) classification for heart failure, myocardial viability, and mortality rate. Patient status and NYHA functional class were obtained at follow-up for each patient.

Baseline evaluations before treatment (CABG or MT) included cross-sectional echocardiography at rest and during dobutamine infusion. According to DSE, all the patients were suitable for revascularization. All these patients were discussed in a committee comprised of a group of surgeons and cardiologists to make treatment decisions on the strength of clinical and revascularization characteristics. The patients were divided into 2 groups of CABG and MT according to the committee's decision.

Echocardiography was performed with a 2.5-MHz transducer, Toshiba, version 5000, under resting condition and during each dobutamine infusion step. Beta-blockers, calcium antagonists, and nitrates were discontinued in the patients at least 2 days before DSE.

After baseline echocardiography, dobutamine infusion was started using a mechanical pump. Dobutamine was delivered intravenously beginning at 5μg/kg/min for three minutes, followed by 5 μ/kg/min increments every three minutes and increased to 15μg/kg/min for an additional three minutes. Blood pressure was measured periodically, and 12-lead ECG was continuously monitored throughout the study and during the recovery phase. The termination of the infusion was due to severe hypotensive or hypertensive response, significant arrhythmias, prolonged angina, significant electrocardiographic changes, or completion of the protocol. The echocardiographic images were analyzed off-line, and a 16-segment model was used as suggested by the American Society of Echocardiography.[14] Segmental wall motion at rest was scored on a four-point scale: normal or mildly hypokinetic=1, severely hypokinetic=2 (decreased endocardial excursion and systolic wall thickening), akinetic=3 (absence of endocardial excursion and systolic wall thickening), and dyskinetic or aneurismal=4 (paradoxical outward movement in systole).[15]

The demonstration of wall thickening in a previously akinetic segment or normalization of thickening in a previously hypokinetic segment was considered as a criterion for myocardial viability.[16] A dysfunctional LV segment was considered viable if the infusion of dobutamine at 10 or 15μg/kg/min resulted in the improvement of wall motion of at least 1 point. A patient was considered to have adequate myocardial viability for CABG if ≥4 segments demonstrated viability. This definition was based on previous reports demonstrating that evidence of viability in ≥4 segments during DSE is associated with a significant improvement in LVEF after revascularization.[9,10,17] In addition, the viability score for each patient was calculated: segments showing viability were assigned a score of 1 and segments without viability a score of zero. By summing the grades of 16 segments, and because the maximal possible viability score was 16, the viability score was divided by 16 to yield a viability index. LVEF was measured at baseline using an available software program that applied Simpson's rule on the two-chamber and four-chamber views.

Surgery was performed by cardiac surgeons using cardiopulmonary bypass. The median number of grafts was 3 (range: 1-5). The mean cardiopulmonary bypass time was 66 minutes, and the aortic clamp time was 42 minutes.

Follow-up was commenced in April 2005 and lasted for 3 months (until June 2005). Survival status was determined by contacting all the patients or next of kin by telephone. Cardiac events during late follow-up were defined as cardiac death. Cardiovascular death was defined as death from stroke, acute myocardial infarction, and refractory congestive heart failure as well as any sudden, unexplained death.

The mortality rates and changes in NYHA functional class at follow-up were compared between the groups. Additionally, EF at rest and stress, amount of increase in EF by stress, LVESV, LVEDV, and viability index were compared between the two groups.

The numerical variables were presented as mean±SD, and the categorical variables were summarized in percentages. The continuous variables were compared using the Student's t-test or paired t-test, and the categorical variables were compared using the Fisher exact test. A P value less than 0.05 was considered statistically significant.

Results

From the 106 study patients, 33 (31.1%) underwent CABG and 73 (68.9%) received MT. The CABG group was comprised of 30 (91%) men and 3 (9%) women at a median age of 56.24±9.76 years (range: 36 to 70 years), and the MT group comprised 61(84%) men and 12 (16%) women at a mean age of 56.24±9.76 years (range: 33 to 75 years). The mean follow-up time was 8 months.

The groups had no significant difference regarding the risk factors. Table 1 depicts a comparison between the baseline and follow-up characteristics of the groups. Before treatment, the CABG group had a significantly lower NYHA score. After treatment, this difference reached a non-significant level. There was no significant difference between the mortality rates of the groups (9.1±5% vs. 11.0±3.7%). LVESV and LVEDV were not significantly different between the dead and surviving patients in both groups.

The viability index, EF at rest, and EF at stress of the dead and surviving patients were also compared between the two groups (Table 2).

Table 2. Comparison of viability and EF of dead and surviving patients in terms of CABG and Medical treatment groups prior to treatment

	group	Dead	Survive	P value*
EF_{rest} (%)	CABG	25±0	30±7	0.001
	MT	22±5	30±9	0.014
EF_{stress} (%)	CABG	31±1	37±10	NS
	MT	30±7	38±10	0.011
Viability index	CABG	0.62±0.06	0.61±0.16	NS
	MT	0.55±0.12	0.66±0.13	0.030

*Data are presented as mean±SD

**P values calculated via independent two-sample t-test for the number of viable segments for dead and surviving patients

EF, Ejection fraction; CABG, Coronary artery bypass grafting; NS, Non-significant; MT, Medical treatment

Table 1. Comparison of baseline and follow-up characteristics of patients in CABG and medical treatment groups*

Characteristics	CABG group (N=33)	MT (N=73)	P value**
Age (y)	54.82±9.15	56.24±9.76	NS
Men (%)	30 (90.9)	61 (83.6)	NS
Before treatment			
EF (%)			
at rest	29.29±6.47	28.84±8.20	NS
at stress	36.63±9.32	37.29±10.51	NS
LVEDV (cm^3)***	144.79± 8.94	141.45±5.99	NS
LVESV ($cm^{٣}$)***	103.77±7.99	100.66±5.46	NS
NYHA classification	3.24±0.75	3.53±0.52	0.05
Viability index	0.61±0.15	0.65±0.14	NS
At follow-up			
NYHA classification	1.46±0.62	1.67±0.93	NS
Mortality (%)	9.1	11.0	NS

*Data are presented as mean±SD unless specified

** P values were calculated using independent two-sample t-test or Fisher's exact test

*** Mean±standard error

CABG, Coronary artery bypass grafting; MT, Medical treatment; NS, Non-significant; EF, Ejection fraction; NYHA, New York heart association; LVEDV, Left ventricular end diastolic volume; LVESV, Left ventricular end systolic volume

The results of the comparison of the viability and EF of the dead and surviving patients between the CABG and MT groups are shown in Table 2. The improvement in NYHA functional class in the CABG and MT groups was significant (from a mean of 3.16±0.74 before, to 1.46±0.62 after CABG; P<0.0001 and from 3.53±0.53 before, to 1.67±0.93 after MT; P<0.0001).

The patients were divided into two groups on the basis of EF ≤25% and EF >25%. In the CABG group, those with EF ≤25% had higher mortality (100% vs. 40%, P<0.05) compared to the ones with EF >25%. This difference, however, was not significant in the MT group.

In both study groups, the surviving patients had a markedly higher EF at rest. In the MT group, EF at stress was markedly higher in the surviving patients; but this was not significant in the CABG group. The amount of increase in EF after dobutamine infusion had no significant effect on mortality in both groups.

It is noteworthy that the viability index was not significantly different between the dead and surviving patients in the CABG group, but the extent of viability was significantly smaller in the dead than that in the surviving patients of the MT group.

Discussion

Because ischemic LV dysfunction is the most common cause of heart failure, proper management of this group of patients is important. There are conflicting views in previous reports over whether CABG can improve survival in patients with severe LV systolic dysfunction.[18-21] The identification of patients with CAD and LV systolic dysfunction that may benefit from revascularization is, therefore, important. The presence of myocardial viability has been shown to predict improvements in LV function after coronary revascularization.[21,22] Nevertheless, it is not clear what extent of viable myocardium is needed to improve the outcome after revascularization.

Among different modalities, DSE has been shown as a strong predictor of the recovery of contractile function after revascularization.[23-27] Afridi et al. demonstrated improved survival with revascularization in patients with CAD and LV dysfunction who showed myocardial viability in four or more segments as assessed by DSE.[17] In their setting, the decision for revascularization was made by the physicians and the study groups were classified based on DSE findings and revascularization status. They reported that the main predictor of mortality among patients with multivessel CAD and severe LV dysfunction who did not undergo CABG was a low EF at rest. Our data also confirmed this notion, and the mortality rate in our study was higher in patients who underwent CABG with LVEF ≤25% at rest.

A “viability index” derived from thallium uptake during rest redistribution scintigraphy was shown to predict cardiac event-free survival after bypass surgery in 70 patients with LV dysfunction by Pagley PR et al.[28] We also used the viability index to assess the prognostic value of a viability study by DSE. The viability index was not significantly different between the dead and surviving patients in our CABG group. It is probably due to the fact that our follow-up time was not long enough to show the survival benefit of CABG. It is deserving of note that previous reports have shown increased survival among patients undergoing revascularization several months after the procedure, with the rate reaching a significant difference after 2 years.[17] We could have detected a much higher viability index in the surviving patients of our CABG group had the follow-up time been long enough. Another probable explanation is that we utilized DSE to select patients with adequate myocardial viability; be that as it may, after clinical evaluations, the patients selected for MT despite having a higher number of viable segments were considered not likely to benefit from CABG due to their clinical conditions which could render them high risk for surgery.

Conclusion

The patients with CAD and a low EF at rest had the same survival rate after both CABG and MT at a mean follow-up period of 8 months. Along with the number of viable segments, a reduced EF is also of great importance in selecting patients who are likely to benefit from CABG.

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