Effect of coronary artery bypass graft surgery on left ventricular systolic function

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Background: Changes in left ventricular (LV) systolic function in response to coronary artery bypass grafting (CABG) have not been fully assessed.

Methods: Between January 2001 and December 2014, 2,838 consecutive patients underwent isolated CABG at the Minneapolis Veterans Affairs Health Care System. Of these, 375 had echocardiographic assessment of LV function before (within 6 months) and after (3 to 24 months) CABG and were included in this analysis.

Results: While the mean LV ejection fraction (LVEF) did not change following CABG [(49±13)% vs. (49±12)%, P=0.51], LVEF decreased in the subgroup with normal (\geq 50%) pre-operative LVEF [from (59±5)% to (56±9)%, P<0.001] and improved in those with decreased (<50%) pre-operative LVEF [from (36±9)% to (41±12)%, P<0.001]. There was a significant reduction in LV internal diameter during end-diastole (LVIDd) (5.4±0.8 vs. 5.3±0.9, P=0.002) and an increase in left atrial diameter (LAD) (4.4±0.7 vs. 4.6±0.7, P<0.001). There were no perioperative changes in LV internal diameter during end-systole, LV mass, posterior wall thickness, or septal wall thickness. LVEF improved by >5% in 24% of the study population, did not change (+/- 5%) in 55%, and worsened by >5% in 21%. Patients with improved EF were less often diabetic and had lower pre-operative LVEF, and greater LV dimensions at baseline.

Conclusions: After CABG, there was a decrease in LVIDd and an increase in LAD. Also, a decrease in LV systolic function with CABG was observed in patients with normal pre-operative LVEF and an improvement in LV systolic function was observed in patients with decreased pre-operative LVEF.

Keywords: Coronary artery bypass graft surgery; echocardiography; left ventricular function

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Introduction

Coronary artery revascularization via coronary artery bypass grafting (CABG) is indicated for patients with angina and suitable coronary anatomy, especially those with stenosis of the left main coronary artery or patients with left main equivalent disease (1-5). CABG has been shown to improve survival in left main disease and in certain subgroups with multi-vessel disease (5). With regard to the latter, pivotal studies that assessed survival with CABG versus medical therapy included the Coronary Artery Surgery Study (CASS), the Veterans Administration (VA) Cooperative study, and the European Coronary Surgery Study (ECSS) (5-7). The Surgical Treatment for Ischemic Heart Failure (STICH) trial later assessed survival with CABG in patients with severe LV dysfunction (EF \leq 35%), demonstrating a significant survival benefit in the extended-follow-up results (8,9).

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The effect of CABG on LV systolic function remains to be elucidated. While the STICH trial evaluated the effect of CABG in patients with severe LV dysfunction (EF \leq 35%), to our knowledge, no large studies have assessed the effect of CABG on LV parameters in patients with normal baseline EF. The STICH trial showed a significant decrease in end-systolic volume index (ESVI) in patients with a baseline LV ESVI >90 mL/m² (10), while no significant change in LV ESVI was observed in the subgroups of patients with smaller LV cavity size (10). While LVEF significantly improved in patients with a baseline LV ESVI \geq 60 mL/m², no significant improvement in LVEF was seen in those with a baseline LV ESVI <60 mL/m².

The objectives of this study were to evaluate the effect of CABG on LV systolic function in patients with both normal and abnormal pre-operative systolic function.

Methods

Data source

The cardiac surgery database at the Minneapolis Veterans Affairs (VA) Health Care System is part of an ongoing multicenter database of prospectively collected data on all patients undergoing cardiac surgery at VA Medical Centers in the United States. The database includes information regarding patient demographics, clinical and laboratory variables, surgical details, and post-operative outcomes, including long-term survival (11,12). Additional clinical, pharmacologic, and echocardiographic variables, that were not included in the database, were extracted from electronic medical records (13). This study was approved by the Institutional Review Board at the Minneapolis VA Health Care System (No. 3949-B).

Study patients

Adult patients (\geq 18 years) who underwent isolated CABG at the Minneapolis VA Health Care System between January 1, 2001 and December 31, 2014 were identified from the cardiac surgery database. Patients who had a paired echocardiographic assessment of LV function within 6 months of surgery and between 3 to 24 months postoperatively were included in this retrospective analysis.

Echocardiographic measurements of left ventricular (LV) variables

The 2-D echocardiography studies, including chamber

quantification measurements, were performed by experienced cardiac sonographers and interpreted and verified by board-certified cardiologists certified in 2-D echocardiography. Variables of LV performance that were measured included LV internal diameter during enddiastole (LVIDd), LV internal diameter during endsystole (LVIDs), LVEF, left atrial diameter (LAD), LV mass, septal wall thickness and posterior wall thickness. Measurements were performed according to the American Society of Echocardiography chamber quantification guidelines (14).

Definitions

Improvement in LVEF was defined as >5% absolute increase in LVEF in comparison to the pre-operative echocardiogram. Consequently, LVEF that decreased by >5% compared to the pre-operative echocardiogram was categorized as worsened. All other post-operative EF measurements within $\pm 5\%$ of the pre-operative values were categorized as unchanged.

Statistical analysis

Continuous and categorical variables are summarized as mean \pm standard deviation (SD) and frequency (%), respectively. We used logistic regression analysis to examine the variables associated with peri-operative improvement in EF. Changes in pre- versus post-operative echocardiographic parameters were compared using paired *t*-test. All P values were two sided with significance of <0.05. Analyses were performed using SPSS, version 19.0 Armonk, NY: IBM Corp.

Results

Study population

Between January 1, 2001 and December 31, 2014, a total of 2,838 patients underwent isolated CABG at the Minneapolis VA Health Care System. Of these, 375 had a paired echocardiographic assessment of LV function before (within 6 months) and after (3 to 24 months) surgery and were included in this analysis.

Baseline demographic and clinical characteristics in the study population as a whole and in the subgroups of patients with normal and decreased pre-operative LVEF are presented in *Table 1*. The mean age of the study group was 66 ± 9 years and all patients were men. A substantial proportion of patients had multiple comorbidities. Pre-

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 Table 1 Baseline characteristics in the study population as a whole and in the subgroups of patients with normal and decreased pre-operative left ventricular ejection fraction

Variables	All patients (n=375)	LVEF ≥50% (n=203)	LVEF <50% (n=172)	P value*
Age, years	66±9	67±9	66±9	0.85
Male sex, %	100	100	100	1.00
Prior MI, %	72	57	90	<0.001
Hypertension, %	89	92	86	0.09
Diabetes mellitus, %	42	43	41	0.69
Atrial fibrillation, %	11	12	11	0.68
Current smoker,%	24	22	25	0.52
Body mass index, kg/m ²	30.2±5.8	30.6±6.2	29.7±5.4	0.12
COPD, %	33	30	37	0.15
CVA, %	28	31	25	0.23
PAD, %	47	46	48	0.71
Prior cardiac surgery, %	5	4	6	0.54
Permanent pacemaker, %	7	5	9	0.10
Laboratory values				
GFR, mL/min/1.73 m ²	85±36	86±38	83±34	0.40
Hemoglobin, g/dL	13.4±1.8	13.4±1.8	13.4±1.9	0.34
Medications				
Beta blocker, %	92	88	93	0.42
ACEI/ ARB, %	71	67	76	0.05
Spironolactone, %	6	2	12	<0.001
Hydralazine and ISDN, %	4	2	8	0.004
Digoxin, %	8	4	14	0.001
Diuretics, %	44	31	59	<0.001
Operative parameters				
Number of grafts	3.0±0.8	3.0±0.8	3.0±0.8	0.98
Bypass time, minutes	123±39	123±40	123±38	0.74
Ischemic time, minutes	80±27	82±27	78±26	0.87
# diseased coronary vessels [†]				0.35
1 vessel,%	5	0	10	
2 vessels,%	32	25	40	
3 vessels, %	64	75	50	
Left main disease, % [‡]	33	36	30	0.30

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; GFR, glomerular filtration rate (calculated using MDRD equation); ISDN, isosorbide dinitrate; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PAD, peripheral arterial disease; *, LVEF \geq 50% *vs*. LVEF <50%; [†], defined as having \geq 1 lesion(s) with \geq 70% stenosis; [‡], defined as having \geq 50% stenosis.



Figure 1 Scattergraph showing individual ejection fraction changes between pre- and postoperative echocardiograms at the time (days after bypass surgery) of postoperative echocardiogram.

operative medications included beta blockers in 92% of patients, an angiotensin-converting enzyme inhibitor or an angiotensin receptor blocker in 71%, diuretics in 44%, as well as spironolactone, digoxin, and hydralazine with isosorbide dinitrate combination in a minority of patients (*Table 1*). Fifty four percent of patients had normal LVEF (\geq 50%) at baseline. Patients with decreased preoperative LVEF were more likely to have a prior myocardial infarction and were treated with a more intense heart failure medication regimen (*Table 1*).

Peri-operative changes in echocardiographic LV systolic measurements

Pre-operative echocardiograms were performed at a median of 15 days [interquartile range (IQR) 4–39 days] prior to CABG. Post-operative follow-up echocardiograms were performed at a median of 291 days (IQR 147–478 days) after CABG. *Figure 1* shows the individual ejection fraction changes between pre- and postoperative echocardiograms at the time (days after bypass surgery) of post-operative echocardiogram in all 375 subjects. The time of postoperative echocardiogram did not appear to have any relation to the change in EF.

Echocardiographic measurements before and after CABG in the study population as a whole and in the subgroups of patients with normal and decreased preoperative LVEF are presented in *Table 2*. The mean LVEF did not change following CABG in the study cohort as a whole [(49 ± 13)% vs. (49 ± 12)%, P=0.51]. While there was a statistically significant reduction in LVIDd (from 5.4 ± 0.8 to 5.3 ± 0.9 cm, P=0.002) and an increase in LAD (from 4.4 ± 0.7 to 4.6 ± 0.7 cm, P<0.001), there were no peri-operative changes in other LV measurements including LVIDs, posterior wall thickness, septal wall thickness, and LV mass (*Table 2*).

With CABG, there was a statistically significant decline in LVEF in the subgroup of patients with normal preoperative LVEF [from $(59\pm5)\%$ to $(56\pm8)\%$, P<0001], resulting in a mean change in EF of -3% (range -33% to 15%). There was a significant improvement in LVEF in the subgroup of patients with pre-operative LV dysfunction [from $(36\pm9)\%$ to $(41\pm12)\%$, P<0.001], resulting in a mean change in EF of 5% (range -23% to 33%) (*Figure 2*). Similar to the overall group, LVIDd decreased and LAD increased significantly, regardless of baseline normal or abnormal LV systolic function.

Predictors of changes in LV systolic parameters and function post-CABG surgery

LVEF improved by >5% in 89 patients (24% of the study population), did not change (\pm 5%) in 207 patients (55%), and worsened by >5% in 79 (21%) patients. Pre- and post-operative LVEF was 38% \pm 12% vs. 52% \pm 12%, respectively, (P<0.001) in patients with improved EF and 55% \pm 11% vs. 42% \pm 12%, respectively, (P<0.001) in patients with worsened EF.

Patients with improved EF were less often diabetic, had lower pre-operative LVEF, and had greater LV dimensions at baseline (*Tables 3* and 4). The improved EF group had a significant reduction in mean LVIDd (5.7 vs. 5.3 mm,

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Variables Pre-CABG	atients, n=375		LVEF ≥50%, n=203			LVEF <50%, n=172			
	Pre-CABG	Post-CABG	P value	Pre-CABG	Post-CABG	P value	Pre-CABG	Post-CABG	P value
LVEF, %	49±13	49±12	0.51	59±5	56±8	<0.001	36±9	41±12	<0.001
LVIDd, cm	5.4±0.8	5.3±0.9	0.002	5.1±0.7	4.9±0.7	0.02	5.8±0.8	5.7±0.9	0.03
LVIDs, cm	4.0±1.0	3.9±1.0	0.43	3.4±0.6	3.4±0.7	0.81	4.6±0.9	4.6±0.9	0.39
LAD, cm	4.4±0.7	4.6±0.7	<0.001	4.3±0.7	4.6±0.8	<0.001	4.5±0.7	4.7±0.7	<0.001
LV mass, g	273±83	265±84	0.11	249±68	240±65	0.17	300±91	293±95	0.36
PWT, cm	1.2±0.2	1.2±0.2	0.58	1.2±0.2	1.2±0.2	0.81	1.2±0.2	1.2±0.2	0.32
SWT, cm	1.2±0.3	1.2±0.2	0.70	1.2±0.2	1.2±0.2	0.85	1.2±0.2	1.2±0.3	0.72

 Table 2 Echocardiographic measurements before and after coronary artery bypass grafting in the study population as a whole and in the subgroups of patients with normal and decreased pre-operative left ventricular ejection fraction

CABG, coronary artery bypass grafting; LAD, left atrial diameter; LVEF, left ventricular ejection fraction; LVIDd, left ventricular internal diameter during end-diastole; LVIDs, left ventricular internal diameter during end-systole; PWT, posterior wall thickness; SWT, septal wall thickness. Values presented as mean ± standard deviation.



Figure 2 Changes in left ventricular ejection fraction with coronary artery bypass graft surgery in patients with normal and decreased pre-operative left ventricular ejection fraction (EF).

P=0.03) and mean LVIDs (4.3 vs. 4.0 mm, P=0.09) preand post-CABG (data not shown). The use of angiotensin converting enzyme inhibitors or angiotensin II receptor blocking medication use did not have a statistically significant influence on peri-operative EF change (P=0.46).

In logistic regression analysis, the odds of EF improvement increased by 50% for every 5% absolute decrease in pre-operative EF (odds ratio 1.50, 95% confidence interval 1.35 to 1.66; P<0.0001). As such, patients with severe LV dysfunction (EF \leq 35%) were 7

times more likely to have improved EF (odds ratio 7.1, 95% confidence interval 4.1 to 12.4; P<0.0001) than those with a normal pre-operative EF.

Discussion

In this study, a decrease in LV systolic function with CABG was observed in patients with normal pre-operative LVEF and an improvement in LV systolic function was observed in patients with decreased pre-operative LVEF.

The assessment of changes in pre- and post-operative LV systolic indices and function after CABG is limited, perhaps due to the lack of routine echocardiography after CABG. Our study is the largest to assess pre- and postoperative echocardiograms in a population including both normal and reduced pre-operative LV function. While prior studies have similarly found an improvement in LV systolic function in patients with pre-operative LV systolic dysfunction, to our knowledge, this is the first study to show a decrease in LVEF with CABG in patients with normal baseline LV systolic function. While the magnitude of decrease in LVEF was small (mean 3% reduction), which may not have any clinical significance, the change in EF ranged from -33% to 15%, meaning that some patients had a clinically significant decline in EF. A decrease in LV systolic function with CABG surgery may result from intra-operative global ischemia (15) or myocardial stunning (16), or from early post-operative graft failure (17). These results warrant confirmation in prospective studies with unselected patients.

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Table 3 Baseline characteristics of all patients in relation to perioperative change in left ventricular ejection fraction

Variables	All patients (n=375)	Improved LVEF (n=89)	Unchanged LVEF (n=207)	Worsened LVEF (n=79)	P value*
Age, years	66±9	66±8	66±9	67±9	0.59
Male sex, %	100	100	100	100	1.00
Prior myocardial infarction, %	72	79	69	73	0.20
Hypertension, %	89	85	88	95	0.13
Diabetes mellitus, %	42	30	46	46	0.03
Atrial fibrillation, %	11	9	12	13	0.73
Chronic kidney disease stage ≥3, %	25	25	25	27	0.96
Chronic obstructive pulmonary disease, %	33	40	28	37	0.08
Cerebrovascular disease, %	28	26	29	29	0.87
Peripheral vascular disease, %	47	40	50	47	0.3
Prior cardiac surgery, %	5	8	3	6	0.23
Permanent pacemaker, %	7	9	5	9	0.39
Laboratory values					
GFR**, mL/min/1.73 m ²	85±36	84±34	84±35	86±43	0.93
Hemoglobin, g/dL	13.4±1.8	13.5±2.0	13.3±1.8	13.4±1.7	0.72
Medications					
Beta blocker, %	93	93	92	93	0.95
ACEI/ ARB, %	71	76	70	68	0.46
Spironolactone, %	6	7	7	4	0.61
Hydralazine and ISDN, %	4	7	4	4	0.43
Digoxin, %	8	9	8	10	0.73
Diuretics, %	44	51	42	41	0.31
Operative parameters					
Number of grafts	3.0±0.8	3.0±0.8	2.9±0.8	3.0±0.9	0.73
Bypass time, minutes	123±39	130±41	120±36	125±42	0.09
Ischemic time, minutes	80±27	81±26	80±25	81±31	0.94
Emergent/urgent surgery, %	25	24	26	23	0.81

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; GFR, glomerular filtration rate (**calculated using MDRD equation); ISDN, isosorbide dinitrate; LV, left ventricular; LVEF, left ventricular ejection fraction. *, P value comparing trend between improved, unchanged, and worsened LVEF groups.

Few studies have compared pre- and post-operative cardiac imaging after CABG. In patients with preserved pre-operative systolic function, Diller *et al.* prospectively followed 32 patients at 5 days, 6 weeks, and 18 months after CABG, demonstrating an improvement in LV diastolic

function. In contrast to our results, this small study did not find a significant reduction in LV systolic function immediately after CABG (18). In patients with reduced LV function, several smaller studies have shown improvement in LV function with CABG in patients with baseline LV

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Variables	All patients (n=375)	Improved LVEF (n=89)	Unchanged LVEF (n=207)	Worsened LVEF (n=79)	P value*
LV ejection fraction, %	49±13	38±12	51±12	55±11	<0.001
LVIDd, cm	5.4±0.8	5.7±0.9	5.4±0.8	5.3±0.8	0.02
LVIDs, cm	4.0±1.0	4.3±1.1	3.9±0.9	3.7±0.9	0.002
LV mass, g	275±88	291±102	273±82	261±87	0.18
Left atrial diameter, cm	4.4±0.7	4.3±0.7	4.4±0.7	4.3±0.7	0.78
Posterior wall thickness, cm	1.2±0.2	1.2±0.2	1.2±0.2	1.2±0.2	0.93
Septal wall thickness, cm	1.2±0.3	1.2±0.2	1.2±0.3	1.2±0.2	0.50

Table 4 Baseline echocardiographic parameters of all patients in relation to perioperative change in left ventricular ejection fraction

LVIDd, left ventricular internal diameter during end-diastole; LVIDs, left ventricular internal diameter during end-systole; LV, left ventricular; LVEF, left ventricular ejection fraction. *, P value comparing trend between improved, unchanged, and worsened LVEF groups.

systolic dysfunction (19-21). The STICH trial was the only prospective, randomized, controlled trial to specifically investigate the role of CABG in patients with severe LV systolic dysfunction (EF \leq 35%). A post hoc subgroup analysis of this trial showed a significant improvement in LV size and function in the subgroup of patients with higher baseline LV end-systolic dimensions (10). Similarly, the results of our study show EF improvement to be associated with greater baseline LV dimensions. Our study is also in agreement with these studies in demonstrating an improvement in LVEF in the subgroup of patients with preoperative LV systolic dysfunction.

Subject to the limitations of the study, these observations add to our understanding of the effect of CABG on LV systolic performance. The most common etiology of heart failure with decreased EF is ischemic heart disease (22). While ischemic factors and myocardial infarction are believed to be causing this ischemic cardiomyopathy, our study suggests that in patients with normal LV systolic function, factors related to CABG itself may be contributing to the development of LV systolic dysfunction. We believe that these results are worthy of further investigation as they seem to add to our understanding of the factors contributing to LV dysfunction in patients with ischemic heart disease.

There are several limitations to point out. The study has the disadvantages of being retrospective and uncontrolled and is thus hypothesis generating rather than definitive. Because echocardiograms were not routinely obtained after CABG surgery, there may be selection bias. Echocardiographic measurements in individual patients were made on only two occasions, so we cannot say whether these changes remained consistent in the longer term in their direction or magnitude. In addition, echocardiography is not the best way to assess cardiac function, with a reported ~6% inter-observer variability in the measurement of EF (23). Finally, the study was carried out at the VA Health Care System and was therefore limited to only men.

Conclusions

In patients undergoing CABG, pre-operative LVEF appears to be an important determinant of change in LV function following surgery. In our study, patients with preoperative LVEF <50% had an improvement in LV systolic function whereas those with normal pre-operative LVEF had a decline in LV systolic function. The other LV indices that changed after CABG were LVIDd, which decreased, and LAD, which increased. The present study broadens the existing knowledge on peri-operative changes in LV systolic function in patients undergoing CABG, to include a population with both normal and depressed pre-operative LV systolic function.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: This study was approved by the

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