Original Article

Assessment of Left Ventricular Function during Off-pump Coronary Artery Bypass Surgery

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Left ventricular function is commonly impaired following cardiopulmonary bypass and cardioplegic arrest. Off-pump coronary artery bypass surgery (OPCABG) offers promise of better myocardial protection, although the effect of multiple regional ischemic events on global myocardial function is unknown. Twenty-eight patients undergoing multivessel OPCABG were assessed with transesophageal echocardiography and pulmonary artery catheterization prior to and following revascularization. Both load-dependent and relatively load-independent measurements of systolic and diastolic performance were measured. Mean ± SD age was 62±8.3 years, grafts performed were 3.8±1.6, and 28% of patients had fractional area change (FAC) <50%. Blood pressure was lower following OPCABG associated with a fall in systemic vascular resistance. There was no difference in measurements of systolic functional FAC, cardiac index, or afterload-corrected FAC. Diastolic function appeared to improve based on mitral inflow and pulmonary vein Doppler measurements, but this occurred at a significantly lower pulmonary capillary wedge pressure and end-diastolic area. No change in diastolic function was found using less load sensitive indices of diastolic function (color M-mode Doppler, tissue Doppler and instantaneous end-diastolic stiffness). Left ventricular systolic and diastolic function is preserved following multivessel OPCABG. (Ann Thorac Cardiovasc Surg 2003; 9: 371–7)

Key words: transesophageal echocardiography, Doppler, systolic, diastolic, off-pump coronary artery bypass surgery

Introduction

Surgery using cardiopulmonary bypass (CPB) is associated with adverse complications, principally caused by the systemic inflammatory response generated by blood elements in contact with the foreign surfaces of the extracorporeal circulatory, and atheroembolism from aortic manipulation. Attempts to avoid the complications of CPB led to a revival of off-pump coronary artery bypass surgery (OPCABG), pioneered by Benetti et al.[1)] and Buffolo et al.[2)] in the 1980s. The potential advantages of OPCABG include reduced systemic inflammation, coagulopathy, atheroembolism, brain edema,[3,4)] and respiratory and other end-organ dysfunction.[3,5-10)] There are also potential economic benefits including reduced postoperative patient instability and faster recovery rates,[11,12)] reduced use of vasoactive drugs, less need for blood products,[13,14)] and more cost-effective resource utilization.[11)] The main disadvantage of OPCABG is the potential for acute and disastrous hemodynamic instability requiring immediate conversion to CPB.

Because of the risk of hemodynamic compromise with retraction and stabilization of the heart, many surgeons will only select patients with normal left ventricular function for OPCABG. Conventional CABG with cardioplegic arrest, however, is known to cause transient cardiac dysfunction, often requiring inotropic support to separate

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from CPB.[15] We found reduced contractility and increased myocardial stiffness following CPB.[16,17] It is possible that myocardial function is better preserved with the pulsatile coronary perfusion and intermittent partial ischemia (single coronary branch occlusion at any one time), than with global ischemia associated with cross-clamp and cardioplegia.

The aim of this study was to determine if left ventricular systolic and diastolic function were acutely compromised following multivessel OPCABG.

Methods

Following approval from the Royal Melbourne Hospital Human Ethics Committee, written informed consent was obtained from 28 patients undergoing elective OPCABG. From a previous interim analysis of data from a randomized study,[18] we determined a minimal sample size ranged from 15 for fractional area change (FAC), to 25 for right atrial pressure (RAP). We increased our sample size by 10% in case of protocol error. All operations were performed by the same surgeon and anesthesiologist. OPCABG was our routine surgical technique at this time, (98% of CABG performed with the technique described), and the patients were recruited without selection criteria. All patients were instrumented with a pulmonary artery catheter (834HF75, Baxter Healthcare Corporation, Irvine, CA), and indwelling radial artery (RA) catheter. Transesophageal echocardiography (TEE) was performed using a multiplane transducer (OmniPlane II transducer, SONOS 2500 or 5500 machine, Philips Medical Systems, Andover, MA). Patients were excluded if there was greater than mild aortic or mitral valve regurgitation, atrial fibrillation which would confound results, or concomitant valve surgery requiring CPB.

Hemodynamic and echocardiography measurements were performed during construction of the Y-graft proximal anastomosis (Pre), and immediately after the completion of the last graft when the heart was returned to normal position (Post). All measurements were obtained with the pericardium open and patients in sinus rhythm and without pacing. Hemodynamic and TEE measurements from three consecutive cardiac cycles were performed and analyzed offline by two independent observers and averaged.

Hemodynamic measurements

The following hemodynamic variables were recorded: systolic arterial pressure (SAP, mmHg); mean aterial pressure (MAP, mmHg); right atrial pressure (RAP, mmHg); pulmonary capillary wedge pressure (PCWP, mmHg); and heart rate (HR, bpm). Thermodilution cardiac output, using 10 ml of room temperature 5% dextrose solution as the injectate, was performed in triplicate and indexed to body surface area [cardiac index (CI), L/min/m^2]. For curves exceeding 10% difference, further measurements were made and the extremes excluded.[19] Systemic vascular resistance index (SVRI, dynes.s.m^2/cm^5) was calculated as SVRI = (MAP–RAP)/CI*80.

Echocardiography measurements

1. Color M-mode Doppler of left ventricular inflow propagation velocity (Vp, cm/s) was obtained from the mid-esophageal 4-chamber view by measuring the slope of the first aliasing velocity from the mitral leaflet tips to a position 4 cm into the left ventricle.[20] The Nyquist limit was set to 40 cm/s and only reduced if there was an absence of aliasing at that time. Satisfactory imaging was obtained in all patients.
2. Mitral inflow Doppler spectral display was obtained from the mid-esophageal 4-chamber view with the pulsed wave Doppler sample volume placed at the mitral leaflet tips at their apposition.[20,21] Measurements included peak early diastolic velocity (E, cm/s), peak late diastolic velocity or atrial contraction velocity (A, cm/s), deceleration time of the E wave (DT, ms), and duration of the A wave (M-duration, ms).
3. Pulmonary vein Doppler was obtained with the pulsed wave Doppler sample volume positioned within the left upper pulmonary vein (where imaging was unobtainable, the right upper pulmonary vein was used), and the duration of the atrial reversal wave measured (P-duration, ms).
4. A cine loop of the transgastric mid-papillary short axis view was obtained to determine left-ventricular end-diastolic area (EDA, cm^2) and end-systolic area (ESA, cm^2). The blood pool area (exclude papillary muscles) was measured by direct planimetry. EDA was identified at the electrocardiograph (ECG) R-wave peak and ESA at the end of the T-wave.[22]
5. Tissue Doppler velocities of the base of the lateral wall from the mid-esophageal 4-chamber were recorded. Em is the peak velocity in early diastole, and Am is the second peak coinciding with atrial contraction.

Offline determination of left ventricular performance indices

The following indices of systolic and diastolic left ventricular function were derived from data acquired above:

Systolic indices
1. FAC = (EDA–ESA)/EDA[16)]
2. Afterload-corrected FAC (FACac) = FAC × $\log_{10}$[(MAP–RAP)/CI]*100 (mmHg/L/min/m^2)[16)]
Diastolic indices
1. Instantaneous end-diastolic stiffness, IEDS = 100 × ($\log_{10}$PCWP)/EDA (mmHg/cm^2)[17)]
2. E/A ratio is the ratio of peak E and peak A mitral velocities.
3. P-Mdur (ms) is the difference between P-duration and M-duration.
4. The Canadian Consensus Score for diastolic function[23)] was rated using mitral inflow Doppler and duration of pulmonary vein atrial reversal wave. Where ambiguity was present, the PCWP and Em data were included to separate normal from pseudonormal states. A cutoff of PCWP 15 mmHg, and Em <8 cm/s, was taken as representative values for pseudonormal state.

Operative procedure

Standard midsternotomy was used and the chest wall retracted. The pericardium was opened, and arterial conduits harvested. The RA was dissected using electrocautery, from the forearm (usually left side) following assessment of collateral ulnar circulation to the hand by standard Allen's test.[24)] The RA was subjected to topical and intraluminal papaverine 1 mg/ml, but no systemic vasodilator was used. The left internal mammary artery (LIMA) was harvested as a pedicled conduit without skeletonization. Patients were anticoagulated with heparin 1 mg/kg when LIMA takedown was nearly complete. Construction of the Y-graft has previously been described.[25)] In brief, the free RA is anastomosed to the proximal part of the LIMA in a "Y" configuration, and the composite graft passed through a pericardial hole to lie just anterior to the myocardium. Retraction and stabilization of the heart was performed with the "Octopus III" stabilizer, and "starfish" apical retractor (Medtronic, Inc., Minneapolis, MN). A single surgeon performed all operations. The sequence of grafting was to perform left anterior descending artery territory grafts first, followed by sequential anastomoses to circumflex and then right coronary artery territories. The length of RA when anastomosed to the LIMA is long enough to reach the posterior descending artery in almost all cases, allowing sequential grafting to the circumflex and right coronary artery territories, without the need for additional conduit.[25)] We employed a deep pericardial suture to retract the pericardium, and placed the patient in various degrees of Trendelenburg positions and lateral rotations to help with heart displacement. No intracoronary shunts were used for any of the grafts. No patient required inotropic support during grafting, and minor hemodynamic aberrations during grafting, were treated with volume loading or vasopressor support using metaraminol or ephedrine.

Patients were anesthetized with a combined regional and general anesthetic technique. An epidural catheter was inserted prior to surgery at T2/3 or T1/2 spinal levels. Eight to 10 ml of 0.5% ropivacaine was administered prior to induction of anesthesia. Thereafter, ropivacaine 0.2% with morphine 0.02 mg/ml morphine was infused at a rate of 5-10 ml/hr, and removed on the morning of the second postoperative day. General anesthesia consisted of midazolam 0.05-1 mg/kg, fentanyl 3 μg/kg, and a target-controlled infusion of propofol set for a blood concentration of 2 μg/ml ("Diprifusor" algorithm, AstraZeneca Pty. Ltd., North Ryde, Australia), and ceased after the last skin suture. This dose represents a low target concentration, but in the presence of epidural analgesia, was typically what was required. Patients were paralyzed for intubation and mechanically ventilated throughout the procedure. The effects of the epidural technique on ventricular function and hemodynamic indices has been extensively examined in a randomized controlled trial comparing the epidural technique with a combined propofol and alfentanil anesthetic regimen.[18)] In brief, there were no differences in intraoperative hemodynamic or echocardiographic measurements between the two techniques with the exception of lower MAP with use of an epidural. Our patient population has a high incidence of hypertension and diabetes, and most patients are on a combination of β1-adrenoceptor blocking drugs and ACE inhibitors. Our practice is to continue the β-blockers up to the time of surgery, but to cease the ACE inhibitors the day prior to surgery.

Statistical methods

Continuous variables were analyzed by 2-tailed, paired samples t-tests. To minimize the type 1 error rate, each family of variables was corrected for multiple hypotheses (P') using the Ryan-Holm Bonferroni stepdown procedure.[26)] Significance was defined as $P'<0.05$. Statistical analysis for E/A ratio, Em/Am ratio, DT or to P-Mdur, was performed using an exact test for two dependent samples after performing the exact test for equality of group means. All values are expressed as mean ± standard error of the mean. The statistical analyses were performed using SPSS for Windows v11.0.0 (SPSS Inc.,

Table 1. Systolic variables

Variable	Pre	Post	*P*	*P'*
FAC	0.60±0.13	0.63±0.12	0.110	0.220
FACac	87±20	85±17.8	0.480	0.480
CI	3.08±0.99	3.37±1.0	0.070	0.210
SVRI	2,322±687	1,910±643	<0.001	<0.001
SAP	139±19	124±14	0.004	0.016
MAP	93±14	82±14	0.002	0.010
HR	64±15	77±13	<0.001	<0.001

FAC, fractional area change; FACac, afterload-corrected fractional area change; CI, cardiac index; SVRI, systemic vascular resistance index; SAP, systolic arterial pressure; MAP, mean arterial pressure; HR, heart rate. See text for units.
All values are expressed as mean ± SD. *P* is the raw 2-tailed, paired samples t-test statistic. *P´* is the statistic adjusted for 7 multiple comparisons with the Ryan-Holm Bonferroni stepdown procedure.

Table 2. Diastolic variables

Variable	Pre	Post	*P*	*P'*
Vp	42±12	44±1	0.543	>0.999
IEDS	7.6±1.6	7.6±2.1	0.944	>0.999
EDA	15.9±3.0	14.0±3.4	<0.001	<0.001
PCWP	15.3±3.8	10.5±3.2	<0.001	<0.001
RAP	9.6±2.6	7.9±3.3	0.020	0.08
E/A	1.3±0.9	0.9±0.2	<0.001	<0.001
DT	171±47	195±46	0.134	0.502
P-Mdur	0.4±37.0	–45.9±35.0	0.002	0.012
Em	9.8±2.8	9.3±2.8	0.079	0.237
Em/Am	1.2±0.5	1.0±0.28	<0.001	<0.001

Vp, left ventricular inflow propagation velocity; IEDS, instantaneous end-diastolic stiffness; EDA, end-diastolic area; PCWP, pulmonary capillary wedge pressure; RAP, right atrial pressure; E/A, ratio of E wave to A wave; DT, deceleration time; P-Mdur, P duration minus M duration; Em, tissue Doppler Em wave; Em/Am, ratio of Em wave to Am wave. See text for units.
All values are expressed, as mean ± SD. *P* is the raw 2-tailed, paired samples t-test statistic. *P´* is the statistic adjusted for 10 multiple comparisons with the Ryan-Holm Bonferroni stepdown procedure.

Chicago, IL).

Results

Twenty-two men and six women undergoing CABG were recruited to the study. Mean age was 62±8.3 years. There were no conversions to CPB, no operative mortality or perioperative myocardial infarction (new Q-wave on ECG or CK-MB rise). The number of grafts performed was 3.8±1.6. Twenty eight percent of patients had baseline FAC <50%, but 68% had Vp <45, and 57% had PCWP >15 mmHg.

Systolic variables are shown in Table 1. There was a modest decrease in SVRI, 2,322±687 to 1,910±643 dynes.s.m^2/cm^5 ($P'<0.001$) following OPCABG. Small but significant falls were noted with SAP ($P'=0.016$) and MAP ($P'=0.010$), and an increase in HR ($P'<0.001$). There was no difference in estimation of left ventricular systolic function using FAC, FACac or CI.

Diastolic variables are shown in Table 2. PCWP ($P'<0.001$) but not RAP was significantly lower following OPCABG. This was achieved at a lower EDA. Other indices of diastolic function (Vp, Em and IEDS) were not altered following OPCABG. The Canadian Consensus Score[23] for diastolic function revealed a high incidence of patients with a pseudonormal relaxation pattern

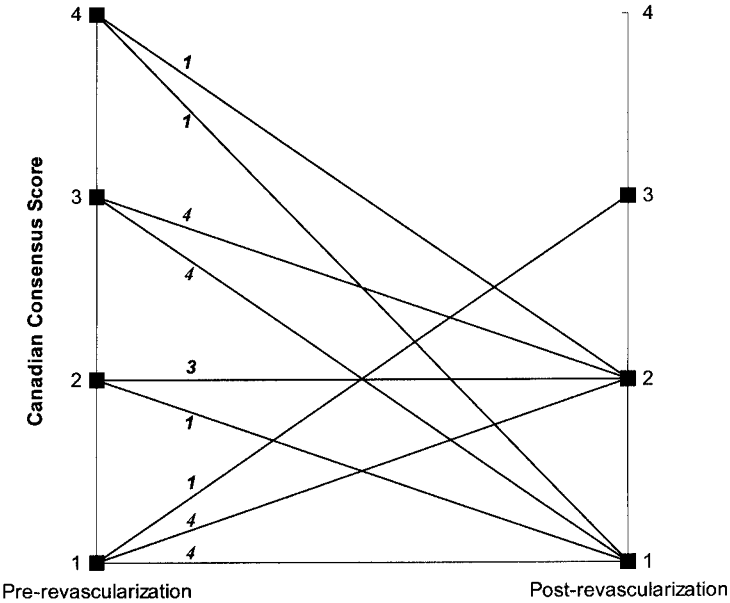

Fig. 1. Canadian Consensus Score changes following revascularization.
Canadian Consensus Score for the categorization of diastolic function (1 = normal, 2 = abnormal relaxation, 3 = pseudonormal and 4 = restrictive pattern). Scores from 1-4 are shown on both vertical axes. The numeric labels adjacent to each line in italics represent the number of patients with that trend. Twenty-three trends were analysed, even though 28 patients were recruited, because in five patients there was poor mitral inflow Doppler imaging during post-revascularization.

which improved following OPCABG (Fig. 1).

Inter-observer validation is summarized in Table 3. There was no significant difference between the two observers' measurements, except for the mitral inflow Doppler measurement DT.

Discussion

Our data shows that systolic and diastolic function is preserved following multivessel OPCABG, despite repeated intermittent regional ischemia induced during grafting.

Cardioplegia induced cardiac arrest produces a state of global ischemia, which varies in severity with the type of myocardial protection strategy employed. There is also potential for reperfusion injury with consequent exacerbation of myocardial dysfunction. In our institution we use combined antegrade and retrograde blood cardioplegia, and we have previously identified worsening of both systolic and diastolic function with cardioplegic arrest.[16,17] When developing expertise with a new technique such as OPCABG, surgeons may select patients with normal left ventricular function only. It is possible, however, that patients with impaired left ventricular function may derive more benefit from the OPCABG approach, as they have less cardiac reserve to cope, should myocardial dysfunction occur following cardioplegic arrest. OPCABG

Table 3. Inter-observer differences in echocardiography measurements

Variable	Difference	95% CI of difference	r	*P*	*P'*
Vp	–1.9	–7.4 to 3.5	0.85	0.475	>0.99
E	–6.3	–18.5 to 5.8	0.58	0.293	>0.99
DT	9.9	3.9 to 15.8	0.96	0.002	0.020
A	–3.4	–6.5 to –0.4	0.94	0.029	0.261
Mdur	–1.2	–10.7 to 8.4	0.84	0.800	>0.99
Pdur	6.4	–1.1 to 14.0	0.88	0.091	0.637
ESA	0.0	–0.4 to 0.9	0.89	0.433	>0.99
EDA	0.8	–0.4 to 1.2	0.83	0.340	>0.99
Em	0.2	–0.4 to 0.4	0.95	0.988	0.988
Am	0.4	–0.02 to 1.6	0.71	0.056	0.448

Inter-observer differences on 28 patients for echocardiography pre-grafting measurements. See text for details of measurements and units. Obs 1 and Obs 2 are the two observers, difference is Obs 1-2, 95% CI is the confidence intervals of the difference between two observers, *P* is the raw 2-tailed paired samples t-test statistic, and *P´* is the statistic adjusted for 10 multiple comparisons using the Ryan-Holm Bonferroni stepdown procedure.

may represent optimal myocardial protection during coronary artery grafting.

Our study is limited by the absence of a randomized CPB control group. We have previously shown that both systolic and diastolic function worsens with CPB. In a recent study comparing combined general and high thoracic epidural anesthesia with a combined propofol and alfentanil anesthetic,18) the same anesthetic and surgical techniques were used in this study (in the epidural arm), but with CPB. We found that systolic function was remarkably well preserved using a combination of antegrade and retrograde blood cardioplegia, but found that end-diastolic stiffness increased by about 20%. CI increased following CPB and was only slightly depressed one hour after return to the intensive care unit. Unfortunately, the wide variety of cardioplegia techniques makes it difficult to compare efficacy of myocardial preservation between different centers. Breisblatt et al,15) for example, demonstrated a significant reduction in both right and left ventricular systolic function which reached a peak at four hours following surgery, but fully resolved after 48 hours. In our institution, the apparent difference in comparing CPB with OPCABG, is perhaps better preservation of diastolic function. Our study is also limited by only one measurement of function following CPB. It provides a snapshot of ventricular function that could alter over time.

Assessment of systolic and diastolic function is limited by the load sensitive nature of most cardiovascular measurements. Traditional ejection phase indices such as CI or ejection fraction are influenced by alteration in preload or afterload. The hemodynamic states pre and post OPCABG were significantly different, though by a reasonably small magnitude. It is possible that small but significant differences in left ventricular function could be detected by more sensitive measurements such as those derived from pressure-volume loops acquired using left ventricular conductance catheters. Our population had a very high incidence of abnormal diastolic function prior to revascularization, identified by pseudonormal mitral inflow Doppler patterns. This largely improved following revascularization suggestive of improved diastolic function. Mitral inflow Doppler, however, is very sensitive to changes in preload, and there was a significant reduction in preload (EDA) and in PCWP following revascularization. The changes may therefore reflect reduced preload rather than improved diastolic function. There was no evidence, however, of impairment of either systolic or diastolic function with OPCABG.

Left ventricular systolic and diastolic function is preserved following multivessel OPCABG.

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