Heart, Lung and Circulation (2019) **28,** 1267–1276
1443-9506/04/$36.00
https://doi.org/10.1016/j.hlc.2018.06.1051

ORIGINAL ARTICLE

On-Pump Beating Heart Versus Conventional Coronary Artery Bypass Grafting Early After Myocardial Infarction: A Propensity-Score Matched Analysis From the ANZSCTS Database

Michael Z.L. Zhu, MBBS [a], Molla M. Huq, MSc [a], Baki M. Billah, PhD [a], Lavinia Tran, PhD [a], Christopher M. Reid, PhD [a,d], Kapilan Varatharajah, MBBS [a], Franklin L. Rosenfeldt, MD, FRACS [b,c*]

[a]School of Public Health and Preventive Medicine, Monash University, Melbourne, Vic., Australia
[b]Baker Heart and Diabetes Institute, Melbourne, Vic., Australia
[c]Swinburne University of Technology, Melbourne, Vic., Australia
[d]School of Public Health, Curtin University, Perth, WA, Australia

Received 13 March 2018; accepted 25 June 2018; online published-ahead-of-print 12 July 2018

Background Coronary artery bypass grafting (CABG) performed early after acute myocardial infarction (AMI) carries a high risk of mortality. By avoiding cardioplegic arrest and aortic cross-clamping, on-pump beating heart CABG (ONBEAT) may benefit patients requiring urgent or emergency revascularisation in the setting of AMI. We evaluated the early and long-term outcomes of ONBEAT versus conventional CABG (ONSTOP) utilising the ANZSCTS National Cardiac Surgery Database.

Methods Between 2001 and 2015, 5,851 patients underwent non-elective on-pump CABG within 7 days of AMI. Of these, 77 patients (1.3%) underwent ONBEAT and 5774 (98.7%) underwent ONSTOP surgery. Propensity-score matching (with a 1:2 matching ratio) was performed for risk adjustment. Survival data were obtained from the National Death Index.

Results Before matching, the unadjusted 30-day mortality was ONBEAT: 9/77 (11.7%) vs. ONSTOP: 256/5,774 (4.4%), $p < 0.001$. Preoperative factors independently associated with the ONBEAT were: septuagenarian age, peripheral vascular disease, redo surgery, cardiogenic shock, emergency surgery and single-vessel disease. After propensity-score matching, 30-day mortality was similar (ONBEAT: 9/77 (11.7%) vs. ONSTOP: 16/154 (10.4%), p = 0.85), as was the rate of major adverse cardiac and cerebrovascular events (ONBEAT: 17/77 (22.1%) vs. ONSTOP: 38/154 (24.7%), p = 0.84). ONBEAT patients received fewer distal anastomoses and were more likely to have incomplete revascularisation (ONBEAT: 15/77 (19.5%) vs. ONSTOP: 15/154, (9.7%), p = 0.03). Despite this, 12-year survival was comparable (ONBEAT: 64.8% (95% CI 39.4-82.4%) vs. ONSTOP: 63.6% (95% CI 50.5, 74.3%), p = 0.89).

Conclusions ONBEAT can be performed safely in high-risk patients requiring CABG early after AMI with similar short and long-term survival compared to ONSTOP.

Keywords Coronary artery bypass • Myocardial infarction • On-pump • Beating-heart • Cardiac surgery

*Corresponding author at: Baker Heart and Diabetes Institute, 75 Commercial Road, Melbourne, Vic. 3004, Australia. Tel: +61 3 9857 6036., Email: rosenfeldt@bigpond.com
© 2018 Australian and New Zealand Society of Cardiac and Thoracic Surgeons (ANZSCTS) and the Cardiac Society of Australia and New Zealand (CSANZ). Published by Elsevier B.V. All rights reserved.

Introduction

Urgent or emergency coronary artery bypass grafting (CABG) performed in the immediate setting of, or early after, acute myocardial infarction (AMI) carries a higher risk of mortality than if surgery can be deferred [1]. Indications for emergency CABG after AMI are generally: (1) failure of percutaneous coronary intervention (PCI) or fibrinolytic therapy, (2) unfavourable coronary artery anatomy for PCI, or (3) persistent myocardial ischaemia and angina refractory to medical therapy [1,2]. In this group of high-risk patients, conventional on-pump arrested heart CABG (ONSTOP) is typically employed for surgical revascularisation [1,2]. However, our previous research in rat [3] and canine [4] models of myocardial infarction and cardiac surgery has shown that, in the setting of recent AMI, the non-infarcted myocardium poorly tolerates the additional insult of cardioplegic arrest and associated global myocardial ischaemia. This may, in turn, lead to worse clinical outcomes. Off-pump CABG is an attractive approach, which avoids cardiopulmonary bypass (CPB), cardioplegic arrest and aortic cross-clamping. Yet, in patients with haemodynamic instability, the omission of CPB increases operative difficulty and may pose significant risks. Unplanned intraoperative conversion from off-pump to on-pump CABG is associated with a six- to seven-fold increase in risk of mortality, and confers a similarly significant increase in risk of adverse events [5]. An additional draw-back of off-pump CABG is that there remain inherent concerns over the risks of incomplete revascularisation [6].

The advantages and limitations of both conventional and off-pump CABG led to the development of a hybrid procedure, the on-pump beating heart CABG (ONBEAT) approach. Theoretically elegant in its conception, ONBEAT offers the dual advantages of maintaining haemodynamic stability and mechanical support afforded by CPB, whilst avoiding cardioplegic arrest and aortic cross-clamping. Multiple studies comparing ONBEAT to ONSTOP have shown clinical benefits associated with ONBEAT, especially among patients with a high preoperative risk profile [7–14]. These include patients with AMI and requiring prompt surgical revascularisation [9,11]. Other studies have reported non-superior outcomes [15,16], or possible disadvantage [17]. Thus, whether ONBEAT constitutes clinical benefit over ONSTOP remains unclear. Moreover, we hypothesise that the ONBEAT approach likely offers greatest benefit to patients who may poorly tolerate cardioplegic arrest, such as those undergoing CABG early after AMI. We aimed to compare the short-term outcomes and long-term survival of patients undergoing urgent or emergency CABG early after AMI, by the ONBEAT versus ONSTOP approach, using data from the Australia and New Zealand Society of Cardiac and Thoracic Surgeons (ANZSCTS) Cardiac Surgery Database. A secondary aim was to identify the preoperative risk factors independently associated with the selection of ONBEAT for myocardial revascularisation in the setting of AMI.

Methods

Patients and Data Collection

We evaluated all patients who underwent non-elective isolated CABG, within 7 days of AMI, by the ONBEAT or conventional ONSTOP techniques, at hospitals participating in the ANZSCTS Database. The period of review was from 1 July 2001 (inception of Database) to 31 December 2015. Inclusion criteria for ONBEAT were the use of CPB without cardioplegic arrest and aortic cross-clamping. Inclusion criteria for ONSTOP were the use of CPB with cardioplegic arrest and aortic cross-clamping. Patients undergoing off-pump CABG were excluded. Thirty-one (31) hospitals in Australia were involved in the prospective data collection of pre, intra and postoperative data during the study period. We have previously described the ANZSCTS Cardiac Surgery Database, including data collection, patient follow-up and data validation methods [18]. The Monash University Human Research Ethics Committee (Reference: 12184) and ANZSCTS Scientific Research Committee (Reference: 201301) approved this study.

Study Endpoints

Primary outcomes of the study were 30-day mortality and major adverse cardiac and cerebrovascular events (MACCE), defined as the composite of 30-day mortality, postoperative myocardial infarction, permanent stroke or non-elective surgical re-intervention. Other early outcomes of interest were: median intensive care unit (ICU) ventilation time; median ICU stay and new renal failure. Long-term survival was evaluated by cross-linking the ANZSCTS Database with the Australian Institute of Health and Welfare – National Death Index (NDI). Data variables from the ANZSCTS Database reflect internationally standardised definitions and are described in the ANZSCTS Database – Data Definitions Manual v3.0 [19].

Statistical Analysis

Categorical variables are expressed as frequencies, n (%) and compared using Pearson X^2 test, or Fisher's exact test if subgroups had an expected count $< 5\%$. Continuous variables are shown as mean $\pm$ standard deviation (SD) and compared using Student's unpaired *t*-tests. Data for continuous variables that did not follow a normal distribution are shown as median and interquartile range and compared using the Mann-Whitney *U* test. The Kaplan-Meier method was used to analyse survival. Two-sided $p < 0.05$ was considered statistically significant for all comparisons. All analyses were performed using IBM SPSS Statistics v23.0 (IBM Corp., Armonk, NY, USA).

Factors Associated With the Selection of On-Pump Beating Heart Technique for CABG

There were major clinical differences, at baseline, between patients in the ONBEAT versus ONSTOP groups. To adjust for this disparity, we performed propensity-score matching. But first, we determined the preoperative patient-factors independently associated with the selection of ONBEAT. This was a two-step process involving (1) univariate followed by (2) multivariable logistic regression analyses – both performed with ONBEAT (i.e. 'treatment' group) as the dependent variable. (1) Univariate outcomes with $p \leq 0.10$ were eligible for inclusion in multivariable logistic regression analyses. The effects of multi-collinearity between related variables were investigated, and significantly collinear variables were excluded, where appropriate, from subsequent multivariable analyses. (2) Multivariable logistic regression was performed in a backward-step elimination fashion to identify preoperative factors that were independently associated with ONBEAT.

Propensity-Score Matching

Postoperative outcomes before matching are shown in Supplementary Table 1. Propensity-score matching was performed for preoperative risk adjustment and to correct for treatment-selection bias. A propensity-score was generated for each patient using multivariable logistic regression, in the standard fashion, with treatment group (ONBEAT) as the dependent variable. Preoperative factors that had an independent influence on the risk of operative mortality were included as co-variates (Supplementary Table 2); as were any variables found to be independently associated with the selection of ONBEAT (Supplementary Table 3). The c-statistic was calculated to assess the discriminatory power of the propensity-score model with a cut-off of 0.70 being considered acceptable [20]. Patients in the ONBEAT group were then matched, in a 1:2 ratio, to ONSTOP controls. The matching sequence was performed without replacement, using the 'nearest-neighbourhood' matching method and a fixed caliper-width of 0.02. Matching was conducted in a 1:2 ratio, rather than the more commonly employed 1:1 method, due to the much larger pool of conventional CABG controls (5,774 ONSTOP vs. 77 ONBEAT patients) that were potential candidates for matching. Following propensity-score matching, the two groups were assessed for balance of baseline characteristics, using p-values and standardised difference scores, in the manner described by Austin [21]. A standardised difference of $\leq$ 15% was deemed satisfactory for inter-group balance (Table 1).

In the propensity-score matched groups, statistical methods that are suitable for 'one-to-many' matching were used to compare differences between ONBEAT and ONSTOP. Continuous variables were compared using one-way repeated measures analysis of variance (ANOVA), or the Kruskal-Wallis test for continuous data that did not follow a normal distribution [22]. Categorical variables were compared using Cochran's *Q* test [22]. To compare survival among matched triplets, the stratified log-rank test proposed by Klein and Moeschberger was used [21,23].

Results

Standardised difference scores and p-values show significant discordance between the two groups, at baseline, before propensity-score matching (Table 1). Patients who underwent ONBEAT were older (68.4 ± 10.1 vs. 65.4 ± 11.0 years, $p = 0.02$), had a greater number of co-morbidities and were much more likely to present for surgery in a critical preoperative state. Unsurprisingly, median logistic EuroSCORE I was significantly higher in the ONBEAT group (12.3% vs. 6.1%, $p < 0.001$). Patients who underwent ONBEAT had fewer diseased coronary systems requiring revascularisation. Before matching, patients who underwent ONBEAT had significantly higher rates of 30-day mortality (ONBEAT 9/77 (11.7%) vs. ONSTOP: 256/5774 (4.4%), $p < 0.001$), MACCE and non-elective return to theatre, and required longer periods of postoperative ventilation and ICU stay compared to ONSTOP (Supplementary Table 1).

Preoperative factors associated with early mortality and selection for ONBEAT are shown in Supplementary Tables 2 and 3. Univariate logistic regression yielded 27 co-variates with $p \leq 0.10$. After multivariable logistic regression, six variables remained as significant independent predictors of ONBEAT. These preoperative patient factors were: septuagenarian age, peripheral vascular disease, redo sternotomy, cardiogenic shock, emergency surgery and single-vessel disease.

Twenty-one (21) co-variates that were deemed independently associated with risk of early mortality (15 variables), or selection of ONBEAT for CABG (six variables), were used to generate the propensity-score (Supplementary Tables 2 and 3). The c-statistic of the propensity-score model was 0.76 (95% CI 0.70–0.82, $p \leq 0.001$). Matching by nearest neighbourhood propensity-score yielded 77 matched triplets (i.e. 77 ONBEAT vs. 154 ONSTOP patients). Baseline variables were well balanced after matching with appropriately similar standardised difference scores of $\leq$15% (Table 2). The exception was the number of patients with triple-vessel disease, which remained higher, only in terms of standardised difference, in the ONSTOP group (ONBEAT: 51/77 (66.2%) vs. ONSTOP: 116/154 (75.3%), $p = 0.18$, standardised difference = –20.1%).

Mean duration of CPB was similar between the two groups. Patients who underwent ONBEAT had significantly fewer distal anastomoses (2.5 ± 1.1 vs. 3.4 ± 1.2, $p < 0.001$) and were more likely to have incomplete revascularisation (ONBEAT: 15/77 (19.5%) vs. ONSTOP: 15/154 (9.7%), $p = 0.03$) (Table 3). In both groups, the left internal thoracic artery was the most common conduit. The radial artery (18/77 (23.4%) vs. 59/154 (38.4%), $p = 0.02$) and saphenous vein (52/77 (67.5%) vs. 126/154 (81.8%), $p = 0.02$) were both utilised less frequently as graft conduits in the ONBEAT group.

After propensity-score matching, there were no significant differences in early outcome between patients in the ONBEAT versus ONSTOP groups (Table 4). The rates of 30-day mortality were similar, ONBEAT: 9/77 (11.7%) vs. ONSTOP: 16/154 (10.4%), $p = 0.85$. Rates of MACCE were ONBEAT: 17/77 (22.1%) vs. ONSTOP: 38/154 (24.7%), $p = 0.84$. Risk-adjusted survival at 12 years was also comparable between the two matched groups (ONBEAT: 64.8% (95% CI 39.4-82.4%) vs. ONSTOP: 63.6% (95% CI 50.5-74.3%), $p = 0.89$) (Figure 1). The mean duration of follow-

Table 1 Preoperative profile of patients before propensity-score matching.

Variable	ONSTOP (n = 5,774)	ONBEAT (n = 77)	P-value	Standardised Difference
Age, years	65.4 ± 11.0	68.4 ± 10.1	0.02	28.4
Age <60	1,699 (29.4)	16 (20.8)	0.10	−20.0
Age 60–69	1,856 (32.1)	19 (24.7)	0.16	−16.6
Age 70–79	1,670 (28.9)	33 (42.9)	0.01	29.4
Age ≥ 80	549 (9.5)	9 (11.7)	0.52	7.1
Female	1,253 (21.7)	21 (27.3)	0.24	13.0
Hypertension	4,316 (74.8)	66 (85.7)	0.03	12
Diabetes requiring treatment	1,552 (26.9)	23 (29.9)	0.56	6.6
Arrhythmia	754 (13.1)	14 (18.2)	0.19	14.1
Cerebrovascular disease	501 (8.7)	13 (16.9)	0.01	24.8
Peripheral vascular disease	573 (9.9)	22 (28.6)	<0.001	48.7
Chronic lung disease	722 (12.5)	15 (19.5)	0.07	19.1
Congestive heart failure	882 (15.3)	19 (24.7)	0.02	23.7
Median creatinine, μmol.L^{-1}	87 (72, 102)	100 (81, 120)	<0.001‡	61.9
Baseline creatinine >150 μmol.L^{-1}	365 (6.3)	11 (14.3)	0.006	26.4
Dialysis	74 (1.3)	1 (1.3)	0.99	0.2
Previous PCI	713 (12.3)	14 (18.2)	0.12	16.3
Redo surgery	118 (2.0)	8 (10.4)	<0.001	35.1
CCS Class IV angina	2,337 (40.5)	31 (40.3)	0.97	−0.4
NYHA Class				
I–II	4,222 (73.1)	50 (64.9)	0.11	17.8
III	736 (12.7)	11 (14.3)	0.71	−4.5
IV	551 (9.5)	13 (16.9)	0.03	−21.8
Missing	265 (4.6)	3 (3.9)	0.77	3.4
LV-function impairment				
Normal or mild, EF >45%	3,896 (67.5)	47 (61.0)	0.23	−13.5
Moderate, EF 30–45%	1,298 (22.5)	20 (26.0)	0.47	8.2
Severe, EF <30%	471 (8.2)	9 (11.7)	0.26	11.8
Missing	109 (1.9)	1 (1.3)	0.71	−4.7
Status of surgery, n (%)				
Urgent	4,586 (79.4)	46 (59.7)	<0.001	−43.8
Emergency	1,126 (19.5)	27 (35.1)	0.001	35.5
Salvage	62 (1.1)	4 (5.2)	0.01†	23.8
Time from MI to surgery				
≤ 6 hours	358 (6.2)	7 (9.1)	0.30	10.9
6–24 hours	581 (10.1)	11 (14.3)	0.22	12.9
1–7 days	4,835 (83.7)	59 (76.6)	0.09	−17.9
ST-elevation MI	995 (17.2)	16 (20.8)	0.41	9.0
Direct catheter-lab to theatre	463 (8.0)	9 (11.7)	0.24	12.3
CPR before surgery	232 (4.0)	9 (11.7)	<0.004†	28.8
Cardiogenic shock	449 (7.8)	19 (24.7)	<0.001	47.1
Inotropes	340 (5.9)	15 (19.5)	<0.001†	41.7
Preoperative IABP	995 (17.2)	21 (27.3)	0.02	24.3
Median EuroSCORE I, logistic	6.1 (3.0, 13.9)	12.3 (7.3, 31.1)	<0.001‡	48.7
EuroSCORE I, additive	7.1 ± 3.6	9.6 ± 4.0	<0.001	65.7
1–5	2,225 (38.5)	14 (18.2)	<0.001	−46.4
6–9	2,550 (44.2)	31 (40.3)	0.49	−7.9
≥10	999 (17.3)	32 (41.6)	<0.001	55.2
No. diseased coronary systems				

Table 1. (continued).

Variable	ONSTOP (n = 5,774)	ONBEAT (n = 77)	P-value	Standardised Difference
1	155 (2.7)	6 (7.8)	0.02[†]	23.0
2	1,150 (20.0)	20 (26.0)	0.19	14.3
3	4,450 (77.3)	51 (66.2)	0.02	−24.8
Missing	4,450 (77.3)	0 (0.0)	>0.99	−8.1

Continuous data are mean ± SD. Categorical data are n (%), unless otherwise specified. † denotes Fisher's Exact Test. ‡ denotes Mann-Whitney U Test. Abbreviations: CABG, coronary artery bypass grafting; CCS, Canadian Cardiovascular Society; CPR, cardiopulmonary resuscitation; EF, ejection fraction; IABP, intra-aortic balloon pump; LV, left-ventricular; MI, myocardial infarction; NYHA, New York Heart Association Heart Failure Classification; ONBEAT, on-pump beating heart CABG; ONSTOP, conventional CABG; PCI, percutaneous coronary intervention.

up was 5.08 ± 3.5 years; with longest follow-up being 14.2 years.

Discussion

In this propensity-score matched study, we compared ONBEAT with ONSTOP for patients undergoing urgent, emergency or salvage CABG within 7 days of AMI. We found no significant difference in 30-day mortality or MACCE. Among patients undergoing ONBEAT, fewer grafts were performed and there was a higher rate of incomplete revascularisation compared to ONSTOP. Despite this, 12-year survival was similar between the two groups.

Following AMI, we have previously shown that, not only is there loss of functional myocardium in infarcted territories, but also acute changes in the remaining non-infarcted myocardium [3,4]. Glycogen, adenosine triphosphate and phosphocreatine are depleted, while oxygen consumption and lactate are increased [4,24]. These biochemical changes in the surviving myocardium denote an adaptive response to compensate for the acutely non-contractile, infarcted regions [25]. Consequently, if non-infarcted myocardium is subjected to further insults of ischaemia and reperfusion, by cardioplegic arrest and aortic cross-clamping, its metabolic status may be even more compromised leading to more profound impairment in myocardial function [4,25]. On-pump beating heart CABG, if conducted proficiently with adequate intracoronary perfusion pressure and by an experienced team, could theoretically minimise this double insult of global myocardial ischaemia and reperfusion injury, while maintaining the use of CPB [17,25,26].

On this pathophysiological premise, early adopters of ONBEAT utilised this hybrid technique for select high-risk candidates who were thought to poorly tolerated cardioplegic arrest, but were unsuitable for off-pump surgery due to haemodynamic instability [11,12,27]. Several single-centre studies comparing ONBEAT to ONSTOP in high-risk patients [7,8], or those with recent AMI [9], have reported significantly lower rates of early mortality favouring the ONBEAT approach. In these studies, in-hospital mortality ranged from 2.6 to 3.1% for ONBEAT, compared to 9.6% to 21.7% for ONSTOP. Other authors have identified lower rates of major complication following ONBEAT surgery including postoperative myocardial infarction, low output syndrome and acute renal failure [8,11,12,14].

Notably, studies that have shown the most favourable outcomes for ONBEAT [7–9] have arisen from single-centres where there may be existing technical expertise and/or a preference for the ONBEAT approach. Indeed, ONBEAT generally necessitates the use of a heart stabiliser, intra-coronary shunts to maintain blood-flow to distal territories during construction of grafts, modified techniques of CPB to maintain coronary perfusion pressure, and other technical nuances associated with operating on the beating-heart [13,26]. Our 15-year review of the ANZSCTS Database showed that only 1.3% (77 out of 5,851) of patients undergoing non-elective CABG, within 7 days of AMI, underwent the ONBEAT technique across Australia (range: 1-16 ONBEAT procedures per year). Consequently, any potential benefit afforded by the ONBEAT approach may well have been lost due to the relative unfamiliarity of the surgical team with the nuances of ONBEAT surgery. This notion is plausible and is supported by the higher rate of incomplete revascularisation, and relatively longer CPB time per graft, observed in the ONBEAT group compared to matched ONSTOP controls. By contrast, in Japan, the proportion of emergency CABG procedures performed with ONBEAT, ONSTOP and off-pump approaches in 2014 alone were 480 (24%), 420 (21%) and 1,086 (55%) cases, respectively [28]. These figures show that ONBEAT is utilised far more frequently in Japan, from which several early studies reporting positive results originate [7,9,11], than in Australia, and likely North America [29]. The relative experience and expertise of these authors [7–9,11], in performing ONBEAT surgery, may be a crucial factor in their success. Nevertheless, in our sample of patients from the ANZSCTS Database, the overall observed rate of early mortality was excellent and compared favourably to risk-adjusted benchmarks (median logistic EuroSCORE, 14.9% vs. actual observed mortality, 10.8%).

Another reason why we observed no difference in mortality or MACCE could be attributed to our small sample size and limited statistical power. One approach that may better evaluate whether ONBEAT offers clinical benefit and superior myocardial protection compared to ONSTOP, without the need for exceedingly large samples of patients, is a prospective randomised study with serial assessment of biochemical markers of myocardial injury. In a small trial of 50

Table 2 Preoperative profile of the patient sample after propensity-score matching.

Variable	ONSTOP (n = 154)	ONBEAT (n = 77)	P-value	Standardised Difference
Age, years	67.9 ± 10.2	68.4 ± 10.8	0.87	4.8
Age <60	31 (20.1)	16 (20.8)	0.45	1.6
Age 60–69	38 (24.7)	19 (24.7)	0.35	0.0
Age 70–79	72 (46.8)	33 (42.9)	0.42	−7.8
Age ≥80	13 (8.4)	9 (11.7)	0.14	10.8
Female	35 (22.7)	21 (27.3)	0.61	10.5
Hypertension	124 (80.5)	66 (85.7)	0.29	13.9
Diabetes requiring treatment	45 (29.2)	23 (29.9)	0.87	1.4
Arrhythmia	30 (19.5)	14 (18.2)	0.88	−3.3
Cerebrovascular disease	24 (15.6)	13 (16.9)	0.60	3.5
Peripheral vascular disease	48 (31.2)	22 (28.6)	0.80	−5.7
Chronic lung disease	36 (23.4)	15 (19.5)	0.70	−9.5
Congestive heart failure	44 (28.6)	19 (24.7)	0.55	−8.8
Median creatinine, μmol.L^{-1}	93 (72, 121)	100 (81, 120)	0.35[§]	14.8
Baseline creatinine > 150 μmol.L^{-1}	27 (17.5)	11 (14.3)	0.37	−8.9
Dialysis	3 (1.9)	1 (1.3)	0.78	−5.1
Previous PCI	28 (18.2)	14 (18.2)	0.38	0.0
Redo surgery	11 (7.1)	8 (10.4)	0.27	11.5
CCS Class IV Angina	57 (37.0)	31 (40.3)	0.85	6.7
NYHA Class				
I–II	97 (63.0)	50 (64.9)	0.79	4.1
III	28 (18.2)	11 (14.3)	0.46	−10.6
IV	23 (14.9)	13 (16.9)	0.88	5.3
Missing	6 (3.9)	3 (3.9)	>0.99	0.0
LV-function impairment				
Normal or mild, EF >45%	92 (59.7)	47 (61.0)	0.94	2.7
Moderate, EF 30–45%	37 (24.0)	20 (26.0)	0.59	4.5
Severe, EF <30%	20 (13.0)	9 (11.7)	0.83	−3.9
Missing	5 (3.2)	1 (1.3)	0.22	−13.9
Status of surgery, n (%)				
Urgent	92 (59.7)	46 (59.7)	0.70	0.0
Emergency	53 (34.4)	27 (35.1)	0.60	1.4
Salvage	9 (5.8)	4 (5.2)	0.92	−2.8
Time from MI to surgery				
≤ 6 hours	16 (10.4)	7 (9.1)	0.52	−4.4
6–24 hours	24 (15.6)	11 (14.3)	0.85	−3.6
1–7 days	114 (74.0)	59 (76.6)	0.83	6.0
ST-elevation MI	39 (25.3)	16 (20.8)	0.56	−10.8
Direct catheter-lab to theatre	22 (14.3)	9 (11.7)	0.73	−7.7
CPR before surgery	21 (13.6)	9 (11.7)	0.68	95.9
Cardiogenic shock	41 (26.6)	19 (24.7)	0.27	−4.5
Inotropes	29 (18.8)	15 (19.5)	0.96	1.7
IABP	47 (30.5)	21 (27.3)	0.36	−7.2
Median EuroSCORE I, logistic	14.9 (5.8, 28.2)	12.3 (7.4, 29.4)	0.98[§]	−13.5
EuroSCORE I, additive	9.6 ± 4.1	9.6 ± 4.0	0.99	1.1
1–5	27 (17.5)	14 (18.2)	0.93	1.7
6–9	62 (40.3)	31 (40.3)	0.83	0.0
≥10	65 (42.2)	32 (41.6)	0.88	−1.3

Table 2. (continued).

Variable	ONSTOP (n = 154)	ONBEAT (n = 77)	P-value	Standardised Difference
No. diseased coronary systems				
1	7 (4.5)	6 (7.8)	0.56	10.6
2	31 (20.1)	20 (26.0)	0.38	13.9
3	116 (75.3)	51 (66.2)	0.18	−20.1

Continuous data are mean ± SD and compared using one-way ANOVA unless otherwise specified. Categorical data are n (%) and compared using Cochran's *Q* Test. § denotes Kruskal-Wallis test for comparison of medians.

Abbreviations: CABG, coronary artery bypass grafting; CCS, Canadian Cardiovascular Society; CPR, cardiopulmonary resuscitation; EF, ejection fraction; IABP, intra-aortic balloon pump; LV, left-ventricular; MI, myocardial infarction; NYHA, New York Heart Association Heart Failure Classification; ONBEAT, on-pump beating heart CABG; ONSTOP, conventional CABG; PCI, percutaneous coronary intervention.

patients with moderately impaired left-ventricular function, undergoing non-emergency CABG (only 32% had a recent MI), Pegg et al. [17] assessed myocardial injury after ONBEAT versus ONSTOP surgery using troponin, creatine kinase-MB (CK-MB) and cardiac magnetic resonance imaging. Significantly, the authors reported higher rates of irreversible myocardial injury in the ONBEAT group. Proposed mechanisms for this unexpected finding were firstly, possible endothelial trauma and plaque disruption during insertion of intra-coronary shunts causing embolisation and downstream coronary occlusion. And secondly, low perfusion pressures during CPB (mean arterial pressure: 50–60 mmHg), resulting in likely inadequate native coronary artery blood-flow, especially to distal myocardial territories. In another trial of 81 low-risk patients undergoing elective CABG, Narayan et al. [15] identified a 34% higher release of troponin in the ONBEAT group compared to ONSTOP, although this difference did not reach statistical significance. Results from these two trials are in contrast to previous observational studies that have reported lower postoperative levels of troponin [14,27] and CK-MB [11] in high to very high-risk patients undergoing ONBEAT compared to ONSTOP. Perhaps due to the difficulties of conducting a randomised trial involving critically ill patients, both Pegg et al. and Narayan et al. excluded the highest risk patients such as those requiring emergency CABG [17] and with recent AMI [15]. These are the patients believed to gain most benefit from ONBEAT surgery. Given the retrospective nature of the present study, we did not collect data on biomarkers of myocardial injury.

Our findings for preoperative factors independently associated with the selection of ONBEAT by the treating surgical team were not unexpected. These were: septuagenarian age, peripheral vascular disease, redo surgery, cardiogenic shock, emergency surgery and single-vessel disease. In a single-institution analysis of records entered into the Society of Thoracic Surgeons Database, Edgerton and associates [29] highlighted a similar set of clinical features, with the addition of pre-existing renal failure and history of stroke as further risk factors. The combined evidence from our study and that of Edgerton et al. supports the notion that surgeons may have a preference to reserve the ONBEAT technique for only a select group of high risk, haemodynamically unstable patients who may only require fewer grafts, or grafts to more easily accessible targets.

Table 3 Intraoperative characteristics after propensity-score matching.

Variables	ONSTOP (n = 154)	ONBEAT (n = 77)	P-value
Cardiopulmonary bypass time, min	100.1 ± 40.6	94.8 ± 50.6	0.28
Cross-clamp time, min	68.4 ± 30.0	–	–
No. distal anastomoses	3.4 ± 1.2	2.5 ± 1.1	<0.001
LITA used	130 (84.4)	58 (75.3)	0.08
Radial artery used	59 (38.3)	18 (23.4)	0.02
Saphenous vein graft used	126 (81.8)	52 (67.5)	0.02
Incomplete revascularisation	15 (9.7)	15 (19.5)	0.03
Transfer to ICU with IABP	55/151 (36.4)	24/75 (32.0)	0.53
Transfer to ICU with ECMO or VAD	2/151 (1.3)	3/75 (4.0)	0.38

Continuous data are mean ± SD and compared using one-way ANOVA unless otherwise specified. Categorical data are n (%) and compared using Cochran's *Q* Test.

Abbreviations: CABG, coronary artery bypass grafting; ECMO, extra-corporeal membrane oxygenation; IABP, intra-aortic balloon pump; ICU, intensive care unit; LITA, left internal thoracic artery; ONBEAT, on-pump beating heart CABG; ONSTOP, conventional CABG; VAD, ventricular-assist device .

Table 4 Early postoperative outcomes of the propensity-score matched sample.

Outcomes	ONSTOP (n = 154)	ONBEAT (n = 77)	P-value
Deceased in operating theatre	3 (1.9)	2 (2.6)	0.82
30-day mortality	16 (10.4)	9 (11.7)	0.85
MACCE	38 (24.7)	17 (22.1)	0.84
Postoperative MI	6/151 (4.0)	1/75 (1.3)	0.47
Stroke, new permanent	8/151 (5.3)	1/75 (1.3)	0.17
Non-elective return to theatre	19/151 (12.6)	10/75 (13.3)	0.74
Graft occlusion	2 (1.3)	0 (0.0)	0.64
Bleeding	5 (3.3)	3 (4.0)	0.88
Deep sternal wound infection	3 (2.0)	1 (1.3)	0.78
Other cardiac	5 (3.3)	4 (5.3)	0.65
Other non-cardiac	4 (2.6)	2 (2.7)	0.86
Median ICU ventilation time, h	15 (8, 49)	19 (10, 47)	0.31§
Median ICU stay, h	65 (28, 117)	84 (47, 122)	0.20§
New renal failure	19/151 (12.6)	9/75 (12.0)	0.95
Median peak post-operative creatinine, μmol.L^{-1}	110 (80, 156)	112 (85, 176)	0.76§

Continuous data are mean ± SD and compared using one-way ANOVA unless otherwise specified. Categorical data are n (%) and compared using Cochran's *Q* Test. § denotes Kruskal-Wallis test for comparison of medians. MACCE = composite of 30-day mortality, postoperative MI, permanent stroke, or non-elective return to theatre.

Abbreviations: ICU, intensive care unit; MACCE, major adverse cardiac or cerebrovascular event; MI, myocardial infarction; ONBEAT, on-pump beating heart CABG; ONSTOP, conventional CABG.

Limitations

This study was retrospective and is thus subject to the unquantifiable factors that may result in hidden bias and confounding despite risk adjustment by propensity-score matching. Matching accounts only for observed (and observable) covariates and cannot account for unknown and latent factors that may affect assignment to treatment [30]. These unknown factors include clinicians' preference and judgement, patient frailty, and other patient co-morbidities which cannot be captured by database fields. Such biases can be controlled only through prospective randomised trials. Secondly, we were unable to analyse cases on an intention-to-treat basis. Instances of intraoperative conversion from one operative technique to another would likely be documented as the latter approach. The frequency of such events could not be quantified due to the lack of a dedicated data field for intraoperative conversion in the ANZSCTS Database. Lastly, despite our data arising from a large national cardiac surgery

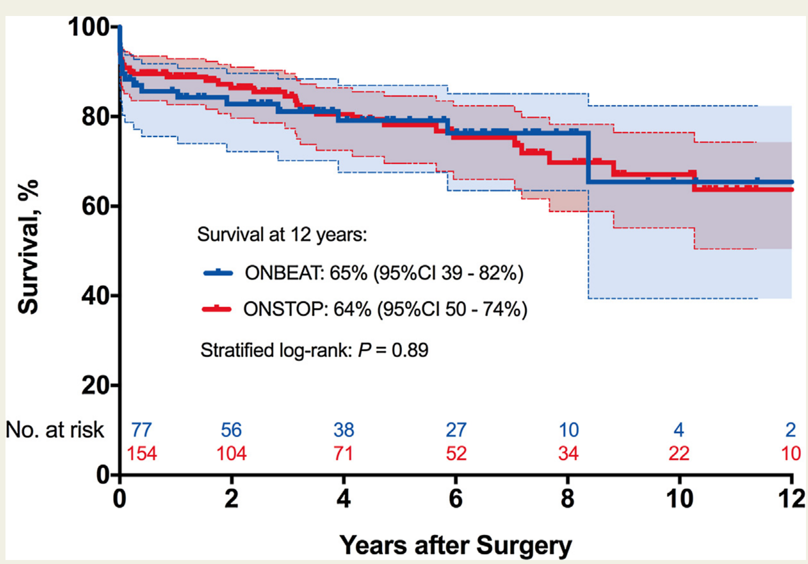

Figure 1 Long-term survival among propensity-score matched patients. Mean duration of follow-up was 5.08 ± 3.5 years; maximum follow-up was 14.2 years.

database, the relatively small number of patients meeting inclusion criteria over a 15-year period may have limited our ability to detect meaningful postoperative differences between ONBEAT and ONSTOP. Nevertheless, our sample of 77 patients who underwent urgent, emergency or salvage ONBEAT early after AMI is among one of the larger published studies comparing this subgroup of patients to conventional CABG [13,16]. Our study is also one of only a few that have reported long-term survival [10,12,15], and the only analysis to report survival beyond 8 years.

Conclusion

We have shown that ONBEAT can be performed safely in high-risk patients requiring coronary bypass early after AMI with similar short-term outcomes and long-term survival compared to conventional CABG. Nevertheless, the incidence of incomplete revascularisation was higher in the ONBEAT group. We conclude that on-pump beating heart CABG is an acceptable approach for patients who may poorly tolerate cardioplegic arrest and aortic cross-clamping, or when off-pump CABG may not be feasible due to haemodynamic instability.

Acknowledgements and Sources of Funding

The authors would like to thank the Australian and New Zealand Society of Cardiac and Thoracic Surgeons (ANZSCTS) National Cardiac Surgery Database Program. The ANZSCTS Database is funded by the Department of Health - Victoria, the Health Administration Corporation (GMCT) and Clinical Excellence Commission (CEC) - New South Wales, as well as individual funding from private and public hospitals. ANZSCTS Research activities are supported through a National Health and Medical Research Council Senior Research Fellowship and Program Grant awarded to C.M. Reid.

Disclosures

None.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.hlc.2018.06.1051.

References

[1] Windecker S, Kolh P, Alfonso F, Collet JP, Cremer J, Falk V, et al. 2014 ESC/EACTS Guidelines on myocardial revascularization. Eur Heart J 2014;35:2541–619.

[2] Hillis LD, Smith PK, Anderson JL, Bittl JA, Bridges CR, Byrne JG, et al. 2011 ACCF/AHA guidelines for coronary artery bypass graft surgery. Circulation 2011;124:e652–735.

[3] Munsch CM, Rosenfeldt FL, O'Halloran K, Langley LH, Conyers RA, Williams JF. The effect of orotic acid on the response of the recently infarcted rat heart to hypothermic cardioplegia. Eur J Cardiothorac Surg 1991;5:82–92. discussion 3.

[4] Newman MA, Chen XZ, Rabinov M, Williams JF, Rosenfeldt FL. Sensitivity of the recently infarcted heart to cardioplegic arrest: Beneficial effect of pretreatment with orotic acid. J Thorac Cardiovasc Surg 1989;97:593–604.

[5] Mukherjee D, Ashrafian H, Kourliouros A, Ahmed K, Darzi A, Athanasiou T. Intra-operative conversion is a cause of masked mortality in off-pump coronary artery bypass: a meta-analysis. Eur J Cardiothorac Surg 2012;41:291–9.

[6] Takagi H, Umemoto T. Worse long-term survival after off-pump than on-pump coronary artery bypass grafting. J Thorac Cardiovasc Surg 2014;148:1820–9.

[7] Mizutani S, Matsuura A, Miyahara K, Eda T, Kawamura A, Yoshioka T, et al. On-pump beating-heart coronary artery bypass: a propensity matched analysis. Ann Thorac Surg 2007;83:1368–73.

[8] Erkut B, Dag O, Kaygin MA, Senocak M, Limandal HK, Arslan U, et al. On-pump beating-heart versus conventional coronary artery bypass grafting for revascularization in patients with severe left ventricular dysfunction: early outcomes. Can J Surg 2013;56:398–404.

[9] Miyahara K, Matsuura A, Takemura H, Saito S, Sawaki S, Yoshioka T, et al. On-pump beating-heart coronary artery bypass grafting after acute myocardial infarction has lower mortality and morbidity. J Thorac Cardiovasc Surg 2008;135:521–6.

[10] Tsai YT, Lin FY, Lai CH, Lin YC, Lin CY, Tsai CS. On-pump beating-heart coronary artery bypass provides efficacious short- and long-term outcomes in hemodialysis patients. Nephrol Dial Transplant 2012;27:2059–65.

[11] Izumi Y, Magishi K, Ishikawa N, Kimura F. On-pump beating-heart coronary artery bypass grafting for acute myocardial infarction. Ann Thorac Surg 2006;81:573–6.

[12] Prifti E, Bonacchi M, Giunti G, Frati G, Proietti P, Leacche M, et al. Does on-pump/beating-heart coronary artery bypass grafting offer better outcome in end-stage coronary artery disease patients? J Card Surg 2000;15:403–10.

[13] Ueki C, Sakaguchi G, Akimoto T, Ohashi Y, Sato H. On-pump beating-heart technique is associated with lower morbidity and mortality following coronary artery bypass grafting: a meta-analysis. Eur J Cardiothorac Surg 2016. http://dx.doi.org/10.1093/ejcts/ezw129.

[14] Munos E, Calderon J, Pillois X, Lafitte S, Ouattara A, Labrousse L, et al. Beating-heart coronary artery bypass surgery with the help of mini extracorporeal circulation for very high-risk patients. Perfusion 2011;26:123–31.

[15] Narayan P, Rogers CA, Bayliss KM, Rahaman NC, Panayiotou N, Angelini GD, et al. On-pump coronary surgery with and without cardioplegic arrest: comparison of inflammation, myocardial, cerebral and renal injury and early and late health outcome in a single-centre randomised controlled trial. Eur J Cardiothorac Surg 2011;39:675–83.

[16] Chaudhry UA, Harling L, Sepehripour AH, Stavridis G, Kokotsakis J, Ashrafian H, et al. Beating-heart versus conventional on-pump coronary artery bypass grafting: a meta-analysis of clinical outcomes. Ann Thorac Surg 2015;100:2251–60.

[17] Pegg TJ, Selvanayagam JB, Francis JM, Karamitsos TD, Maunsell Z, Yu L-M, et al. A randomized control trial of on-pump beating heart and conventional cardiologic arrest in coronary artery bypass surgery patients with impaired left ventricular function using cardiac magnetic resonance imaging and biochemical markers. Circulation 2008;118:2130–8.

[18] Dinh DT, Lee GA, Billah B, Smith JA, Shardey GC, Reid CM. Trends in coronary artery bypass graft surgery in Victoria, 2001–2006: findings from the Australasian Society of Cardiac and Thoracic Surgeons database project. Med J Aust 2008;188:214–7.

[19] Australian and New Zealand Society of Cardiac and Thoracic Surgeons. ANZSCTS National Cardiac Surgery Database Program: Data Definitions Manual, v3. Melbourne, AUS: Dept. Epidemiology & Preventive Medicine, Monash University; 2011.

[20] Westreich D, Cole SR, Funk MJ, Brookhart MA, Stürmer T. The role of the c-statistic in variable selection for propensity score models. Pharmacoepidemiol Drug Saf 2011;20:317–20.

[21] Austin PC. Propensity-score matching in the cardiovascular surgery literature from 2004 to 2006: a systematic review and suggestions for improvement. J Thorac Cardiovasc Surg 2007;134:1128–35.

[22] Pett MA. Nonparametric statistics for healthcare research: statistics for small samples and unusual distributions, 1st ed. Thousand Oaks, CA, USA: SAGE Publications; 1997.

[23] Klein JP, Moeschberger ML. Survival analysis: techniques for censored and truncated data. New York: Springer-Verlag; 1997.

[24] Gudbjarnason S, Puri PS, Mathes P. Biochemical changes in non-infarcted heart muscle following myocardial infarction. J Mol Cell Cardiol 1971;2:253–76.

[25] Varatharajah K, Rosenfeldt FL. Changes in noninfarcted myocardium explain benefits of on-pump beating-heart coronary artery bypass grafting for acute myocardial infarction. J Thorac Cardiovasc Surg 2009;137:1575–1576.

[26] Mo A, Lin H. On-pump beating heart surgery. Heart Lung Circ 2011;20:295–304.

[27] Perrault LP, Menasche P, Peynet J, Faris B, Bel A, de Chaumaray T, et al. On-pump, beating-heart coronary artery operations in high-risk patients: an acceptable trade-off? Ann Thorac Surg 1997;64:1368–73.

[28] Masuda M, Okumura M, Doki Y, Endo S, Hirata Y, Kobayashi J, et al. Thoracic and cardiovascular surgery in Japan during 2014: Annual report by The Japanese Association for Thoracic Surgery. Gen Thorac Cardiovasc Surg 2016;64:665–97.

[29] Edgerton JR, Herbert MA, Jones KK, Prince SL, Acuff T, Carter D, et al. On-pump beating heart surgery offers an alternative for unstable patients undergoing coronary artery bypass grafting. Heart Surg Forum 2004;7:8–15.

[30] Garrido MM, Kelley AS, Paris J, Roza K, Meier DE, Morrison RS, et al. Methods for constructing and assessing propensity scores. Health Serv Res 2014;49:1701–20.