Emergency Coronary Artery Bypass Graft Surgery for Acute Coronary Syndrome

Beating Heart Versus Conventional Cardioplegic Cardiac Arrest Strategies

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Background**—**Aim of this study was to compare the outcome of beating heart versus conventional coronary artery bypass graft (CABG) strategies in acute coronary syndromes for emergency indications.

Methods and Results**—**638 consecutive patients with acute coronary syndrome (ACS) receiving emergency CABG surgery via midline sternotomy from January 2000 to September 2005 were evaluated. Propensity score analysis was used to predict the probability of undergoing beating heart (BH) (n=240) versus cardioplegic cardiac arrest (CA) (n=398) strategies. Patients presented with stable hemodynamics (n=531) or in cardiogenic shock (CS) (n=107). Hospital and follow-up outcome was compared by propensity score adjusted multiregression analysis. BH included 116 on-pump and 124 off-pump (OPCAB) procedures. There was a propensity to operate CS patients on the beating heart (multivariate odds ratio [OR], 3.8; $P=0.001$). Under stable hemodynamics significant predictors for BH selection were logEuroSCORE >20% (OR, 2.05), creatinine >1.8 mg/dL (OR, 4.12), complicated percutaneous coronary intervention (OR, 1.88), ejection fraction <30% (OR, 2.64), whereas left main disease (OR, 0.68), circumflex artery (OR, 0.32), and 3-vessel disease (OR, 0.67) indicated preference for cardioplegic arrest. Time from skin incision to culprit lesion revascularization was significantly reduced in BH patients. BH surgery led to a significant benefit in terms of less drainage loss, less transfusion requirement, less inotropic support, shorter ventilation time, lower stroke rate, and shorter intensive care unit stay. In CS, BH was associated with lower incidence of stroke, inotropic support, acute renal failure, new atrial fibrillation and sternal wound healing complications. In CS patients, hospital mortality rate was reduced when using beating heart strategies ($P=0.048$). Overall survival, major adverse cerebral and cardiovascular event rate, and repeated revascularization was comparable during a 5-year follow-up.

Conclusions**—**Beating heart strategies are associated with an improved hospital outcome and comparable long-term results for high-risk patients presenting acute coronary syndrome with or without CS. **(*Circulation*. 2006;114[suppl I]:I-477–I-485.)**

Key Words: acute coronary syndrome ■ beating heart surgery ■ cardioplegia ■ cardiopulmonary bypass ■ myocardial infarction

The use of beating heart (BH) versus conventional cardioplegic cardiac arrest (CA) strategies for myocardial revascularization is being intensively debated at present. There are varying results from different studies comparing beating and arrested heart coronary artery bypass graft (CABG) procedures. Results particularly depend on study design and number of patients included. Overall, routine patients may achieve an excellent outcome with either type of procedure,[1–8] whereas there are consistent laboratory findings of less myocardial enzyme and troponin release in BH surgery.[1,4,5,9] In recent years further efforts were made to identify high-risk subgroups that may benefit more from BH strategies. These included elective patients with poor left ventricular function, older age, renal or neurological dysfunction, and recent myocardial infarction (MI), but clinical results were also inconsistent.[10–13]

Patients with evolving acute coronary syndrome (ACS), defined as continuum from unstable angina (UA) to non–ST-segment elevation MI (NSTEMI) to ST-segment elevation MI (STEMI) display a high-risk entity in CABG surgery. Perioperative mortality is increased several fold compared with patients with stable angina and it may be advisable to delay surgical intervention whenever possible. However, in presence of refractory symptoms, hemodynamic alterations,

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or in STEMI patients, emergency surgical therapy within the first hours is indicated. Operative mortality for these patients using conventional arrested heart CABG techniques ranges from 1.6% to 32% and strongly depends on the preoperative hemodynamic condition.[14–20]

It can be speculated that preserving native coronary blood flow reduce reperfusion injury or "no reflow" phenomenon and advantages of BH surgery might be clinical significant just in emergency ACS patients. However, until now not much evidence exist on that issue and only few post hoc analyses have analyzed the impact on morbidity and mortality by using BH approaches in these patients.[21–24] Therefore, the aim of this study was to analyze our 5-year experience on patients with ACS and having an indication for emergency CABG surgery within the first 12 hours after onset of symptoms comparing BH and arrested heart CABG. Propensity score adjusted multiregression analysis was used to assess in-hospital and follow-up outcome on patients with or without preoperative cardiogenic shock (CS).

Patients and Methods

BH surgery was introduced as an alternative surgical strategy for emergency treatment of ACS at our institution in the year 2000. A total of 19.218 isolated CABG procedures were performed from January 2000 until September 2005; 638 (3.3%) of the patients with ACS and had an emergency indication (ie, within 12 hours after presentation) according to the current guidelines.[25] Also, 240 patients underwent BH operation and 398 received conventional CA; 107 patients were in acute CS. Only patients receiving conventional sternotomy and CABG surgery without any additional cardiac procedure were included in this evaluation. UA was present in 304 patients (47.7%), NSTEMI in 152 (23.8%), and STEMI in 182 (28.5%) patients, respectively. Indication for emergency operation (partly multiple) were (1) failed percutaneous coronary intervention (PCI) in STEMI patients (n=42); (2) ongoing ischemia despite optimal medical therapy in patients presenting primary CABG indication[25] (n=454); (3) ongoing ischemia despite successful or failed PCI (n =59); (4) eventful or complicated PCI (n =62); and (5) CS with complex coronary anatomy not suitable for PCI (n =107).

Diagnosis of AMI was made by conventional ECG in addition to enzyme or cardiac troponin criteria and confirmed by acute coronary angiography. Patients with ongoing angina without AMI character-

TABLE 1. Patient Characteristics According to Treatment of Emergency ACS

	Stable Hemodynamics				Cardiogenic Shock			
Characteristics	CA n=374	BH n=157	OR	*P*	CA n=24	BH n=83	OR	*P*
Demographics								
Age (y)	67±10	66±11	—	0.215	69±11	68±10	—	0.801
Age >70y (%)	43.9	39.5	0.84	0.387	50.0	48.2	0.93	0.536
Male (%)	75.1	73.9	0.94	0.833	70.8	69.9	0.96	0.570
BMI >30 (%)	24.9	21.7	0.84	0.504	16.7	21.7	1.40	0.776
Diabetes (%)	48.1	54.8	1.31	0.180	70.8	73.5	1.14	0.798
Hypertension (%)	90.9	87.3	0.69	0.211	91.7	88.0	0.66	0.466
Hyperlipidemia (%)	77.0	77.7	1.04	0.910	70.8	84.3	2.22	0.147
Renal insufficiency (%)	1.6	6.4	4.12	0.009	16.7	14.5	0.85	0.505
EuroSCORE log*	8.0	9.6	—	0.010	26.2	25.5	—	0.689
EuroSCORE log >20 (%)	13.9	24.8	2.05	0.004	70.8	66.3	0.81	0.807
Redo surgery (%)	2.4	5.1	2.18	0.113	4.2	4.8	1.16	0.688
Prior MI (%)	28.6	29.3	1.03	0.916	20.8	18.1	0.84	0.770
STEMI (%)	21.7	26.8	1.32	0.216	58.3	54.2	0.85	0.817
NSTEMI (%)	21.7	25.5	1.24	0.365	25.0	30.1	1.29	0.799
Complicated PCI (%)	7.2	12.7	1.88	0.046	4.2	16.9	4.67	0.100
Angiographic data								
Left main disease (%)	46.3	36.9	0.68	0.049	33.3	43.4	1.53	0.482
Circumflex disease (%)	93.0	80.9	0.32	<0.001	100.0	92.8	0.74	0.334
3-Vessel CAD (%)	69.5	60.5	0.67	0.045	95.8	80.7	0.182	0.108
Ejection fraction	54±14	49±16	—	0.002	34±15	40±16	—	0.100
Ejection fraction <30 (%)	6.7	15.9	2.64	0.002	54.2	34.9	0.45	0.092
Preoperative IABP (%)	2.4	5.7	2.47	0.066	33.3	47.0	1.77	0.254
Preoperative inotropic support (%)	9.1	15.9	1.89	0.033	87.5	90.4	1.14	0.707
Preoperative ventilation (%)	0	0	—	—	37.5	33.7	0.85	0.809
Preoperative thrombolysis (%)	4.5	7.6	1.74	0.207	12.5	13.3	1.07	0.615
CKMB fraction (U/l)*	17.7	23.0	—	0.070	45.3	41.3	—	0.589
CKMB >2-fold upper level (%)	23.5	29.3	1.35	0.189	45.8	45.8	1.00	0.997

BMI indicates body mass index.

*Data are given as median.

Odds ratios (ORs) are indicated as probability for operation on the beating heart related to cardioplegic cardiac arrest.

istics in ECG and normal enzymes at the beginning of the operation were considered to have UA. Preoperative CS was defined if the following criteria were present: systolic arterial hypotension <80 mm Hg for at least 30 minutes or the need for supportive measures (intra-aortic balloon pump [IABP], inotropes) to maintain a systolic blood pressure >80 mm Hg, end organ hypoperfusion (pH <7.3, lactate level >3.0 mmol/L, urine rate <0.5 mL/kg), acute pulmonary congestion mostly requiring preoperative ventilation, cardiac index <1.8 L/m^2 body surface area, and pulmonary capillary wedge pressure ≥20 mm Hg. Preoperative IABP and low-dose inotrops (dopamine <5 μg/kg per minute) were considered for CS if indicated for hemodynamic stabilization but not prophylactically to improve myocardial perfusion or to prevent hemodynamic instability. Diabetes was defined as hyperglycemia requiring insulin or noninsulin treatment, and chronic renal insufficiency was quoted for patients presenting creatinine plasma level >1.8 mg/dL.

The decision to perform CABG without cardiopulmonary bypass (off-pump coronary artery bypass [OPCAB]), on-pump BH (OnP-BH) or under CA was individually based on the preoperative assessment of the surgeon, including patients' preoperative hemodynamics, concomitant diseases, and extent of ACS. In the BH cohort 124 operations were planned as OPCAB and 116 as OnP-BH procedures. For CA crystalloid HTK (Bretschneider's) solution (54%) or blood cardioplegia (46%) with antegrade or retrograde application was applied. Operations were performed by a group of 10 senior surgeons with longstanding experience in both BH and CA CABG surgery.

Postoperative new onset of MI was defined when new q-wave or ST-segment elevation combined with new creatinine kinase MB fraction (CKMB) peak were present after initial enzyme drop. If it was considered, patients were immediately transferred for repeat angiography. Postoperative acute renal failure was defined as requirement for continuous veno-venous hemofiltration. Stroke was defined as transient or persisting postoperative hemiparesis or neurological dysfunction with morphological substrate confirmed by computer tomography or nuclear magnetic resonance imaging. Major adverse cerebral and cardiovascular events (MACCE) were assessed for all major cerebrovascular and cardiac events including death of all cause. Repeated revascularization was defined for all percutaneous coronary interventions irrespective of clinical symptoms. Indications were based on myocardial ischemia found during conventional diagnostic procedures, but not on the status of incomplete revascularization.

Surgical Technique

Routine sternotomy and internal mammary artery takedown were applied. BH surgery was performed using 2 pericardial traction sutures and a commercially available mechanical stabilizer. No preconditioning or intracoronary shunt insertions were performed. Proximal coronary snares were used when required. All anastomoses were performed using 7-0 or 8-0 monofilament sutures. The internal mammary artery (IMA) to the left anterior descending artery (LAD) was the first anastomosis in all patients, except that another culprit lesion was clearly identified. For LAD revascularization, IMA was used in all patients. In case of CS, patients first were connected to the cardiopulmonary bypass (CPB), followed by IMA harvesting. All patients received Aprotinin (Trasylol) at a dose of 2 million units. OPCAB patients received 150 IU/kg and on-pump patients 300 IU/kg of heparin. CPB was established by standard ascending aortic and right atrial cannulation. Moderate hypothermia of 32°C to 33°C was applied. At the end of the operation heparin was antagonized with protamine sulfate. A cell saver was used in OPCAB patients. Completeness of revascularization was expressed by the index for completeness of revascularization indicating the performed related to planned distal anastomoses. Full surgical revascularization was the aim in all patients and hybrid procedures were not primarily indicated.

Data Analysis

All data were prospectively recorded. Analyses were separately performed for patients with and without preoperative CS. Continuous variables were expressed as mean±standard deviation or median, categorical data were expressed as proportions. Comparisons were performed by using Student *t* test, Mann-Whitney *U* test, χ^2 test, or Fisher exact test as appropriate at a level of significance of $P<0.05$. Propensity analyses were carried out by using logistic regression models with stepwise backward procedure. To build the propensity score, 22 preoperative dichotomous variables indicated in Table 1 were used to compute the propensity score. Propensity score allowed for providing an estimate of probability to get into the BH or CA treatment group. The C-statistics for propensity score models were calculated. For analysis the logits of propensity score were used allowing a covariate adjusted outcome analysis.[26,27] To assess the impact of treatment strategy on outcome a propensity score adjusted logistic regression analysis was performed. Results are described as odds ratios (ORs) and 95% confidence intervals (CIs).

Overall survival and freedom from MACCE and repeated revascularization during a 5-year follow-up period were calculated by using Kaplan-Meier methods and log-rank-test. Cox regression models were adjusted for propensity score and multiple covariates that potentially affect postoperative outcome. Mid-term analyses were based on all patients including hospital deaths. $P<0.05$ were considered statistically significant. The statistical analyses were performed using 13.0 SPSS software package. The authors had full access to the data and take full responsibility for its integrity. All authors read and agree to the manuscript as written.

Results

CS was present in 24 of 380 patients in the CA (6.3%) and in 83 of 240 patients (34.6%) in the BH group. CS was associated with a significant propensity to receive BH surgery (univariate OR, 8.23; 95% CI, 5.0 to 13.5, $P<0.001$; multivariate OR, 3.8; 95% CI, 1.7 to 8.5, $P=0.001$). Demographics and preoperative hemodynamic status for BH versus CA in presence or absence of CS are given in Table 1.

TABLE 2. Intraoperative Data in Patients Presenting Stable Hemodynamics (n=531)

	CA Patients n=374	BH Patients n=157	*P*
Interval onset of symptoms/OP (h)	9.3±6.7	9.7±5.4	0.648
Interval catheter/OP (h)	6.5±3.2	6.1±2.9	0.539
Skin to skin time (min)	152±52	153±51	0.945
Skin to culprit lesion revascularization (min)	70±24	34±19	<0.001
CPB use (%)	100	38.2	—
CPB time (min)	73±32	94±37	<0.001
Cross-clamp time (min)	43±19	—	—
Distal anastomoses/patient	2.9±0.8	2.5±0.8	<0.001
Arterial grafts/patient	1.3±0.7	1.2±0.7	0.364
Venous grafts/patient	1.6±1.0	1.3±0.9	<0.001
LAD territory grafting (%)	99.2	95.5	0.009
Cx territory grafting (%)	74.7	25.3	<0.001
RCA territory grafting (%)	61.2	51.0	0.034
LIMA use (%)	99.2	98.7	0.865
Total arterial revascularization (%)	14.2	24.2	0.008
Incomplete revascularization (%)	10.7	17.8	0.032
Perioperative IABP (%)	12.6	17.8	0.133

CPB indicates cardiopulmonary bypass; Cx, circumflex artery; IABP, intraaortic balloon pump; LAD, left anterior descending artery; LIMA, left internal mammary artery; OP, start of the operation; RCA, right coronary artery.

TABLE 3. PS-Adjusted Outcome in Patients With Stable Hemodynamics

	CA Patients n=374	BH Patients n=157	OR	95% CI	PS-Adjusted *P*
No postoperative inotropic support (%)	47.9	63.7	2.26	1.50–3.43	<0.001
Low output syndrome (%)	11.0	9.6	0.58	0.30–1.15	0.119
Total IABP use (%)	15.0	23.6	1.10	0.66–1.84	0.708
Mean IABP support (h)*	16 (0–390)	22 (0–408)	—	—	0.137†
ECMO/VAD (%)	2.1	1.3	0.60	0.12–3.07	0.537
Drainage loss (mL)*	650	550	—	—	0.023†
Drainage loss >1000 mL (%)	29.1	19.7	0.54	0.33–0.87	0.012
Reexploration for bleeding (%)	4.8	0.6	0.09	0.01–0.68	0.020
Red blood cell units/patient*	2 (0–87)	1 (0–21)	—	—	0.020†
New myocardial infarction (%)	1.3	1.3	1.09	0.19–6.26	0.902
Postoperative reangiography (%)	5.1	5.7	1.22	0.51–2.89	0.660
Bypass dysfunction (%)	1.6	3.8	2.83	0.83–9.62	0.100
Total ventilation time (h)*	13.5 (5–904)	10.0 (3–580)	—	—	0.043†
Reintubation (%)	11.2	7.0	0.50	0.24–1.05	0.067
Postoperative atrial fibrillation (%)	30.2	29.3	0.85	0.55–1.31	0.463
Stroke (%)	6.7	2.5	0.30	0.10–0.92	0.035
Transitional syndrome (%)	16.8	16.6	0.97	0.57–1.66	0.919
Acute renal failure (%)	8.3	6.4	0.45	0.20–1.01	0.052
Gastrointestinal complications (%)	5.1	1.3	0.19	0.04–0.87	0.033
Sternal wound complications (%)	3.5	2.5	0.71	0.21–2.34	0.570
ICU stay (d)*	2.0 (1–46)	2.0 (1–35)	—	—	0.041†
Hospital stay (d)	12.6±8.2	10.4±6.8	—	—	0.015
Hospital mortality (%)	8.6	5.7	0.49	0.21–1.10	0.083

ECMO indicates extracorporeal membrane oxygenation; ICU, intensive care unit; PS, propensity score; VAD, ventricular assist device.

*Data are given as median and range.

†*P* by Mann-Whitney *U* test.

Patients With Stable Hemodynamics

As shown in Table 1, predictors for selection of a BH strategy were renal insufficiency (OR, 4.12; CI, 1.5 to 11.7), logistic EuroSCORE >20 (OR, 2.05; CI, 1.3 to 3.3), complicated PCI (OR, 1.88; CI, 1.12 to 3.46), ejection fraction <30% (OR, 2.64; CI, 1.5 to 4.8) and preoperative low-dose inotropic support (OR, 1.89; CI, 1.2 to 3.3). Factors discriminated against BH surgery were left main disease (OR, 0.68; CI, 0.5 to 0.9), significant circumflex artery disease (OR, 0.32; CI, 0.2 to 0.6), and 3-vessel coronary artery disease (OR, 0.32; CI, 0.5 to 0.9). The C-statistic for propensity score model was 86.4%.

Operative data are summerized in Table 2. In BH patients, time from skin incision to culprit lesion revascularization including IMA harvesting was significantly reduced. A total of 102 of 157 (65.0%) of the BH patients were planned for OPCAB procedure. In 5 patients (4.9%) conversion to OnP-BH was required because of inadequate visualization of the target vessel (n=1), deep intramyocardial course of the LAD (1) and hemodynamic compromise (3). In OnP-BH patients, CPB time was significantly prolonged compared with CA patients. In BH patients less distal anastomoses to LAD, right coronary artery, and circumflex artery territory were performed leading to a reduced completeness of revascularization (BH 82.2% versus CA 89.3%).

Propensity score-adjusted perioperative outcome is given in Table 3. A significantly lower number of BH patients required postoperative inotropic support; however, incidence of postoperative low output syndrome was similar between the groups. Mean blood loss was reduced associated with lower reexploration rate and transfusion requirement in BH patients. Clinical data concerning myocardial injury were comparable as no difference in new MI or atrial fibrillation was evident. However, bypass dysfunction revealed by postoperative reangiography was slightly higher in BH patients. Extracardiac morbidity (total ventilation time, stroke rate, and gastrointestinal complications) was lower leading to a reduced intensive care unit (ICU) and hospital stay in BH patients. Hospital mortality was lower in BH patients (BH 5.7% versus CA 8.6%) without reaching statistical significance. Multivariate analysis including 22 preoperative variables, completeness of revascularization, and all dichotomous outcome variables mentioned in Table 3 revealed age >70 (OR, 4.2; $P=0.03$), high postoperative inotropic support (OR, 45.3; $P<0.001$), reexploration (OR, 4.2; $P=0.01$), sternal wound complication (OR, 18.3; $P=0.03$),

TABLE 4. Intraoperative Data in Patients With Cardiogenic Shock (n=107)

	CA Patients n=24	BH Patients n=83	*P*
Interval onset of symptoms/OP (h)	4.2±2.1	3.8±2.6	0.745
Interval catheter/OP (h)	1.6±1.1	1.8±1.3	0.635
Skin to skin time (min)	155±47	167±51	0.325
Skin to culprit lesion revascularization (min)	78±27	39±25	<0.001
CPB use (%)	100	77.1	
CPB time (min)	88±34	98±38	0.224
Cross-clamp time (min)	45±21		
Distal anastomoses/patient	3.1±0.8	2.6±0.7	0.003
Arterial grafts/patient	1.0±0	1.0±0.62	0.851
Venous grafts/patient	2.1±0.8	1.6±0.9	0.006
LAD territory grafting (%)	100	98.8	0.591
Cx territory grafting (%)	91.7	77.6	0.089
RCA territory grafting (%)	75.0	69.6	0.799
LIMA use (%)	100	98.8	0.821
Total arterial revascularization (%)	0	9.6	0.194
Incomplete revascularization (%)	20.8	12.0	0.275
Perioperative IABP (%)	54.2	31.3	0.041

gastrointestinal complication (OR, 3.9; $P=0.02$), and postoperative acute renal failure (OR, 4.8; $P<0.001$) as independent risk factors for hospital mortality.

Patients With CS

Patient cohorts were comparable as indicated in Table 1. No significant selection bias for the one or the other treatment strategy could be identified. The C-statistic for propensity score model was 88.6%. Operative data for the CS subgroup are given in Table 4. Time interval from skin incision to culprit lesion revascularization was shorter in BH patients. Three of 22 (13.6%) patients planned for OPCAB procedure had to be converted to OnP-BH surgery because of hemodynamic instability during cardiac manipulation. CPB time and rate of revascularization of LAD, circumflex artery, and right coronary artery territories were comparable between the groups. In CA patients more distal anastomoses were performed; however, that did not significantly affect the completeness of revascularization (BH 88.0% versus CA 79.2%).

Propensity score-adjusted outcome analysis revealed a benefit of BH surgery concerning incidence of postoperative atrial fibrillation, acute renal failure, stroke rate, and sternal would complications, respectively (Table 5). Hospital mortality was also reduced in BH patients (BH 19.3% versus CA 33.3%; $P=0.048$). In multivariate analysis no independent predictor for hospital mortality could be identified.

Perioperative CKMB Release

Preoperative and early postoperative CKMB fractions for all ACS types are shown in Figure 1. In UA baseline levels were comparable. On postoperative day 1, CKMB increase was 4.5-times (CA) versus 2.7-times (BH) the baseline level ($P<0.001$). On postoperative day 2, CKMB level was also higher in CA patients ($P<0.001$), but without significant difference compared with postoperative day 1 levels. In NSTEMI patient baseline levels were significantly higher in BH patients ($P<0.001$). However, CKMB levels were comparable during the early postoperative course related to baseline level. For STEMI patients baseline as well as postoperative day 1 concentrations were comparable between BH and CA patients, with a trend to lower levels on postoperative day 2 for BH patients ($P=0.103$).

Follow-Up

Median follow-up among 573 hospital survivors was 2.78 years (range, 0.02 to 5.86 years). There were 62 deaths after hospital discharge. No patients received surgical coronary reintervention, 23 patients needed PCI during follow-up. Independent risk factors for follow-up mortality were age >70 years (relative risk [RR], 1.1; $P=0.002$), diabetes (RR, 2.4; $P=0.016$), postoperative dialysis (RR, 6.2; $P<0.001$), and preoperative cardiogenic shock (RR, 4.3; $P=0.001$). Excluding hospital deaths, follow-up survival was significantly worse in patients undergoing operation in progressive cardiogenic shock, with 1- and 4-year survival of 87.7% and 73.1% compared with 94.3% and 88.2% in patients presenting stable hemodynamics at the time of operation ($P<0.001$). Independent risk factors for follow-up MACCE were diabetes (RR, 2.6; $P<0.001$), STEMI at time of operation (RR, 1.73; $P=0.03$), and postoperative atrial fibrillation (RR, 1.94; $P=0.005$). Freedom from repeated revascularization was 95.0% for CA and 93.1% for BH patients ($P=0.74$). Independent risk factors for repeated revascularization were female gender (RR, 2.7; $P=0.05$) and diabetes (RR, 3.3; $P=0.04$). Neither cardiogenic shock nor incomplete revascularization could be identified as significant risk factors for MACCE or repeated revascularization.

For patients with stable hemodynamics, median follow-up was 3.3 years (95% CI, 3.1 to 3.5 years). Kaplan-Meier overall 4-year survival rate including hospital deaths was 84.1% (95% CI, 77.5 to 90.8%) for BH patients versus 82.1% (95% CI, 77.8% to 86.2%) for patients operated on the arrested heart. The MACCE-free 4-year survival rate was 78.2% for BH patients (95% CI, 69.4 to 87.0%) compared with 74.5% (95% CI, 69.6 to 79.5%) for cardioplegic arrested heart patients. As indicated in Figure 2a and 2b there were no significant differences between BH and CA patients.

For patients presenting cardiogenic shock at the time of operation, median follow-up was 2.5 years (95% CI, 2.3 to 2.7 years). Overall 4-year survival rate including hospital deaths was 60.3% (95% CI, 44.6% to 76.1%) for BH patients versus 44.5% (95% CI, 29.6% to 69.5%) for patients operated on the arrested heart. The MACCE-free 4-year survival rate was 56.4% for BH patients (95% CI, 41.5% to 71.7%) compared with 36.1% (95% CI, 14.9% to 57.2%) for cardioplegic arrested heart patients. As shown in Figure 2c and 2d, there were also no significant differences between BH and CA patients.

Discussion

Current indications for emergency CABG surgery in ACS patients are limited to those presenting with evolving myocardial ischemia refractory to optimal medical therapy, presence of left main stenosis and/or 3-vessel disease, ongoing

TABLE 5. PS-Adjusted Outcome in Patients Presenting Cardiogenic Shock

	CA Patients n=24	BH Patients n=83	OR	95% CI	PS-Adjusted *P*
High postoperative inotropic support (%)	87.5	65.1	0.26	0.06–0.99	0.049
Total IABP use (%)	87.5	78.3	0.49	0.12–1.94	0.308
IABP support (h)*	76 (0–262)	48 (0–860)	—	—	0.085†
ECMO/VAD (%)	4.2	2.4	0.16	0.01–3.37	0.238
Drainage loss (mL)*	975	700	—	—	0.233†
Drainage loss >1000 mL (%)	45.8	32.5	0.67	0.25–1.78	0.417
Reexploration for bleeding (%)	4.2	6.0	1.06	0.10–10.9	0.959
Red blood cell units/patient*	6.0 (0–46)	5.0 (0–42)	—	—	0.306†
New myocardial infarction (%)	8.3	1.2	0.11	0.01–1.70	0.114
Postoperative reangiography (%)	8.3	1.2	0.11	0.01–1.70	0.114
Bypass dysfunction (%)	2.1	1.2	0.38	0.02–5.01	0.472
Total ventilation time (h)*	70 (8–882)	66 (5–942)	—	—	0.908†
Reintubation (%)	20.8	18.1	0.86	0.27–2.70	0.681
Postoperative atrial fibrillation (%)	62.5	39.8	0.35	0.13–0.96	0.041
Stroke (%)	33.3	9.6	0.19	0.06–0.66	0.009
Transitional syndrome (%)	45.8	26.5	0.55	0.20–1.48	0.235
Acute renal failure (%)	50.0	31.3	0.41	0.08–0.97	0.046
Gastrointestinal complications (%)	20.8	8.4	0.57	0.15–2.19	0.411
Sternal wound complications (%)	12.5	2.4	0.09	0.01–0.85	0.036
ICU stay (d)*	9.0 (2–43)	6.0 (1–42)	—	—	0.767†
Hospital stay (d)*	18.5 (2–68)	14.0 (1–80)	—	—	0.292†
Hospital mortality (%)	33.3	19.3	0.44	0.10–0.98	0.048

*Data are given as median and range.
†*P* by Mann-Whitney *U* test.

ischemia despite successful or failed PCI, complicated PCI, or cardiogenic shock accompanied by complex coronary anatomy. Patients that meet these indications are relatively rare, representing only 3.3% of all stand-alone CABG procedures during the study period at our institution.

It can be speculated that maintaining native coronary blood and avoiding global myocardial ischemia is the optimal treatment strategy for ACS patients whenever CABG surgery is indicated. Based on the experience in high-risk patients,[10–13,21–24] we therefore extended our indication for BH surgery to emergency ACS patients as an alternative to conventional CABG. One interesting finding from our 5-year experience is that there was a significant bias to perform BH surgery in sicker patients and in presence of CS. This is in accordance with other studies that demonstrated a selection bias of sicker patients for on-pump BH techniques.[21] However, BH patients demonstrated less left main and circumflex artery disease. To perform appropriate statistical analysis, we therefore computed a propensity score for the individual patient according to the hemodynamic status at the beginning of the operation that allows a risk-adjusted evaluation.

In comparison to other studies focusing on AMI, we included all patients with ACS according to the current nomenclature.

Patients with Stable Hemodynamics

Perioperative mortality for emergency revascularization in AMI patients presenting under stable hemodynamic condition and using conventional CABG is varying. Creswell et al indicated a mortality rate of patients operated within 6 hours after onset of AMI symptoms of 9.1%.[17] In a multicenter analysis of 32 099 patients who underwent conventional CABG within 24 hours after AMI, hospital mortality was 14%.[19] Tomasco et al indicated a similar mortality rate of 13.4% for patients operated within 24 hours after AMI.[15] However, Sergeant et al found a remarkably lower mortality rate of 1.6% for this subset of patients.[16] Prospective or risk-adjusted analyses comparing BH and CA strategies for this subgroup are not available so far. In a retrospective analysis of 225 patients operated within <7 days after AMI, Locker reported a significantly reduced perioperative mortality for the OPCAB group.[22] The present analysis on a large number of patients revealed a trend toward a lower mortality in stable patients when operated by BH strategies. However, perioperative morbidity was significantly reduced as indicated by lower requirement for postoperative inotropic support, less blood loss, shorter ventilation time, less gastrointestinal complications, and lower stroke rate. This is in concordance to other studies that demonstrated lower neurological injury in off-pump surgery in elective patients.[28–30] 38% of our patients were operated with CPB support that did not significantly affect the postoperative neurological status. It remains speculative that preserved pulsatile blood flow plays a key role in preventing neurological injury.

BH patients received less grafts to all 3 coronary territories that in parts reflect the lower number of diseased vessels. The completeness of revascularization in BH patients was 82.2%

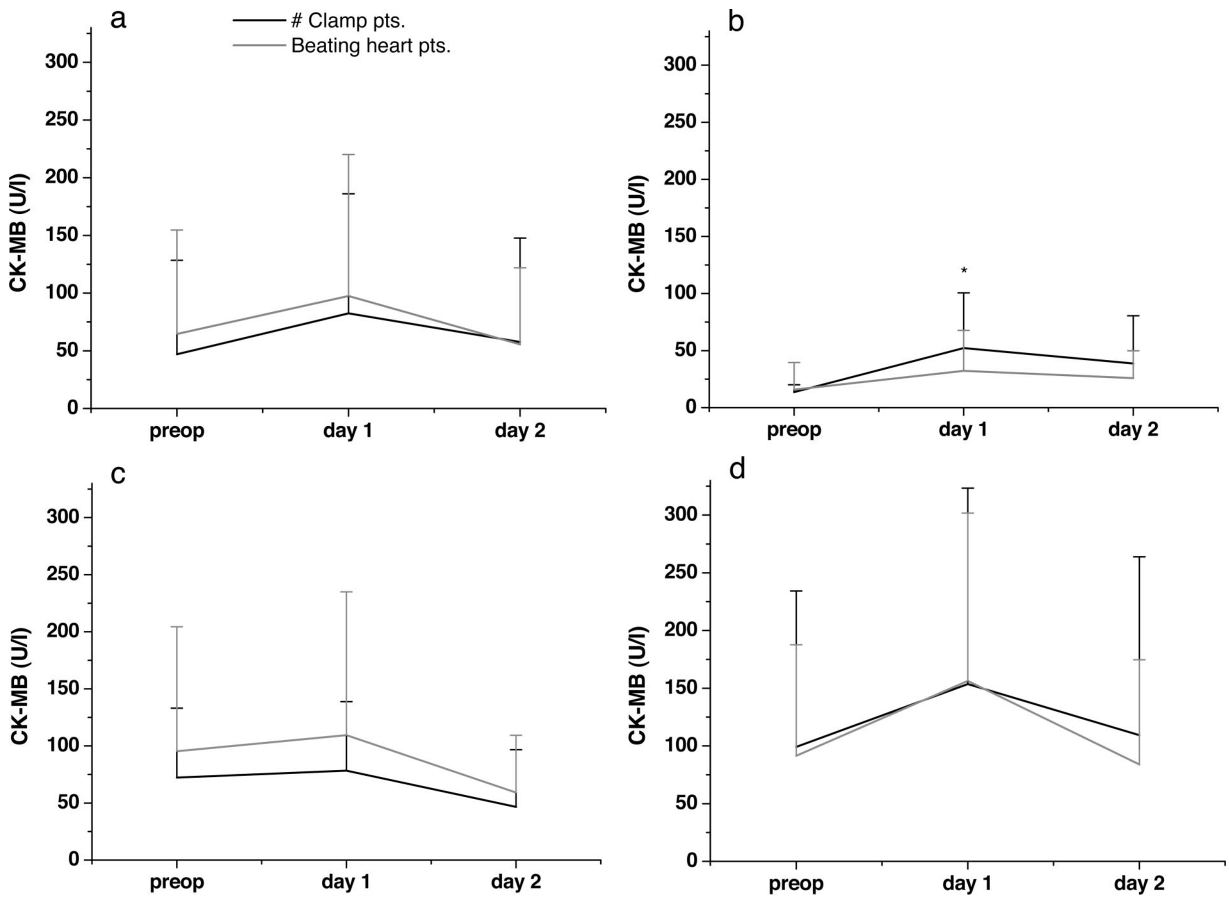

Figure 1. Preoperative CKMB fraction and on postoperative days 1 and 2 for (a) all patients, (b) patients presenting unstable angina, (c) non-ST segment elevation myocardial infarction, and (d) ST-segment elevation myocardial infarction. **P*<0.05, if significantly higher compared to previous day levels.

and significantly lower than in CA patients, but did not affect the LAD territory.

Postoperative inotropic support was reduced in BH patients. Nevertheless, we found a trend for more frequent IABP implantation in BH patients. This most likely reflects a bias for rather prophylactical IABP implantation in BH surgery to obtain better perioperative hemodynamics support.

Patients With Cardiogenic Shock

Patients with CS have a mortality rate ranging from 21.3% to 46.7%.[15,16,31] The data from the SHOCK trial particularly revealed a benefit of early revascularization strategies and also superiority of CABG compared with PCI. However, hospital mortality of CABG procedures in that trial was 39.6%.[31] Finding comparable preoperative risk factors in our study, hospital mortality was significantly reduced by using BH strategies including OnP-BH in 77.1%. By definition it is uncertain to idenitfy lingering perioperative MI in most of these patients, but we found less inotropic support, a lower rate of new MI, and a significantly lower rate of postoperative atrial fibrillation that might indicate less perioperative myocardial injury. The incidence of atrial fibrillation was high as occurred in 62.5% of CA patients compared with 39.8% in BH patients. Because we could no find a significant difference in atrial fibrillation between BH and CA strategies for stable patients, it can be speculated that the severity of preoperative myocardial damage triggers the development of atrial fibrillation and BH surgery might have an influence on that.[32] Stroke rate and the incidence of acute renal failure were also significantly reduced in BH patients, although most of the BH operations were performed with CPB support. It might be speculated that a faster postoperative cardiac recovery and preserved pulsatility have a protective potential. Thus, BH strategy is advantageous to reduce extracardiac complications in these high-risk patients, although a renoprotective effect of BH surgery in elective patients is controversially discussed.[33–35]

CKMB Enzyme Release

There is consistent evidence of reduced CKMB enzyme release in elective OPCAB surgery.[2,4,5,10] However, none of these studies could demonstrate clinical significance of these findings as the differences were rather small. We analyzed the CKMB levels separately for the different ACS types. For UA we could demonstrate a lower release of CKMB on postoperative day 1 in BH compared with CA patients. That is consistent to findings in elective patients.[2,4,5] In STEMI and in NSTEMI patients we did not find a significant difference in CKMB levels between cardioplegic and BH surgery on postoperative day 1 and postoperative day 2. It can be concluded that the extent of myocardial necrosis induced by cardioplegic CA is low compared with that caused by the AMI itself. For these patients other mechanisms like faster revascularization of the culprit lesion, attenuated "no reflow

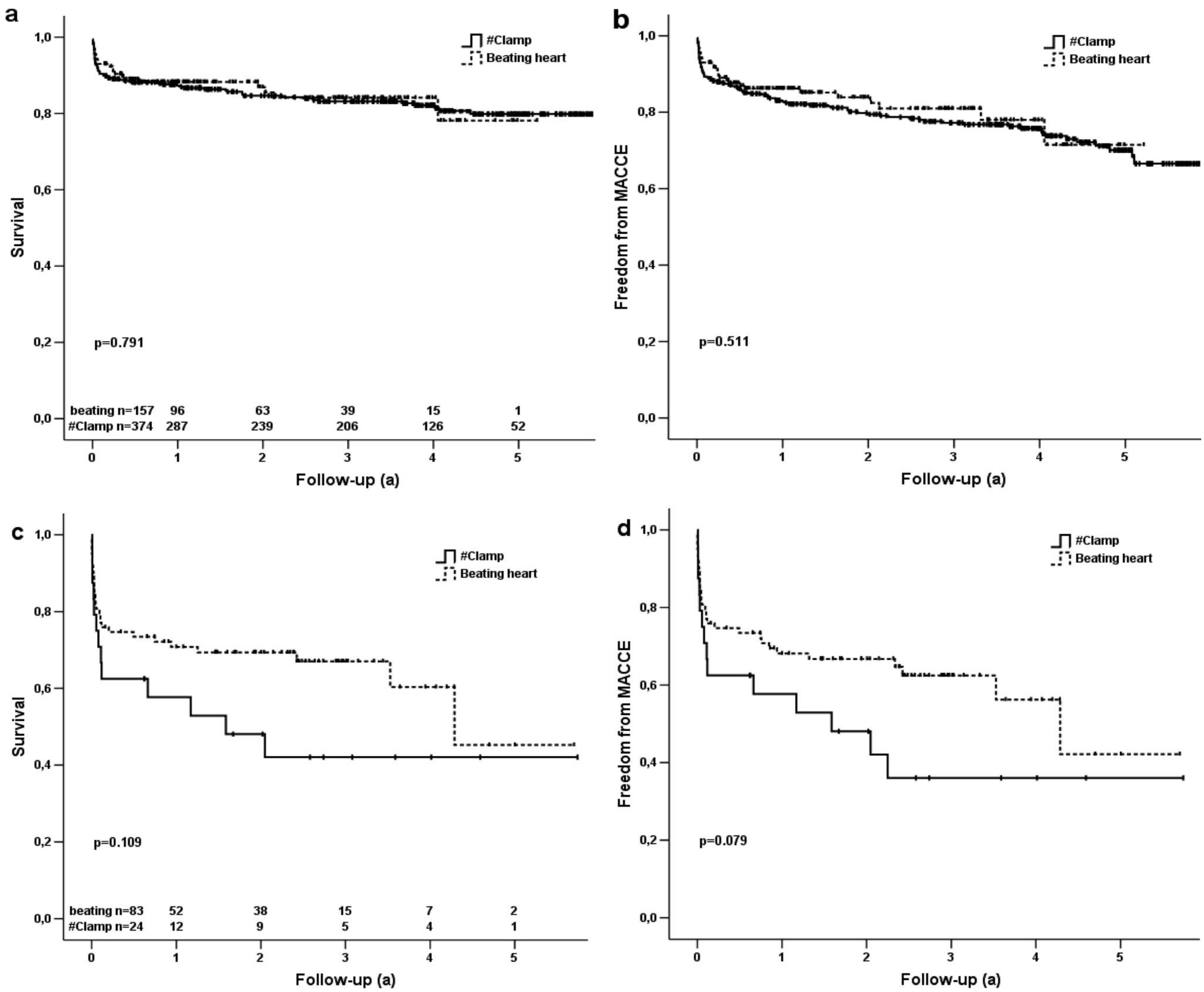

Figure 2. Propensity score adjusted long-term survival including hospital deaths in patients with stable hemodynamics (a) and in cardiogenic shock (c) according to the operative strategy. Additionally adjusted follow-up MACCE rate for hemodynamically stable (b) and cardiogenic shock (d) patients were given.

phenomenon," or reduced myocardial edema might lead to a better outcome when using BH strategies.

Follow-Up

BH and CA surgery late survival was comparable with significant worse survival in cardiogenic shock patients. Locker et al found a worse 5-year survival rate for OPCAB patients compared with CA patients.[22] One reason for these inconsistent findings might be the patient selection, because Locker included patients with AMI within 1 week and only few CS patients. Moreover, he considered OPCAB patients only, whereas our patients were operated both OPCAB and OnP-BH. However, we also found a reduced completeness of revascularization in the noncardiogenic shock patients when using BH surgery. Surprisingly, incompleteness of revascularization in our multivariate analysis was not a risk factor for late death, MACCE, or repeated revascularization. One reason might be that completeness of the LAD territory revascularization was similar between CA and BH patients. Diabetes could be identified as a major risk factor for late mortality and cardiac morbidity.

Limitations

There are some limitations of the present study. First of all it is nonrandomized. However, using specific statistical evaluations it allows for relatively precise risk and outcome assessment and comparison. The propensity score shares the limitations of all risk models and can only account for factors that are known.

Beside propensity score adjusted multivariate analysis used in this study propensity score can also serve for matching and stratification. Using propensity score–adjusted matching in acceptable variance, we could only include 26% of all patients for comparison excluding most of the high-risk patients. Using risk stratification by producing quintiles the patient numbers in 2 of the quintiles were too small to allow for comprehensive analysis. Therefore, in the current data analysis the propensity score was used as a covariate in traditional regression model producing more convincing results by considering the entire study population.[27]

The purpose of our study was to analyze the impact of preserved native coronary blood flow during emergency treatment for ACS. However, in the BH cohort patients were operated with or without extracorporeal circulation according to the surgeon's assessment and the clinical status of the patient. Within the arrested heart cohort the use of antegrade/retrograde blood and cristalloid cardioplegia was not standardized and decision was made on an individual basis. We could not totally exclude selection bias for blood versus cristalloid cardioplegic arrest that was not adjusted by propensity score analysis.

Disclosures

None.

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