A Randomized Trial of On-Pump Beating Heart and Conventional Cardioplegic Arrest in Coronary Artery Bypass Surgery Patients With Impaired Left Ventricular Function Using Cardiac Magnetic Resonance Imaging and Biochemical Markers

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Background—Beating heart coronary artery bypass grafting (CABG) improves early postoperative cardiac function in patients with normal ventricular function, but its effect in patients with impaired function is uncertain. We compared a novel hybrid technique of on-pump beating heart CABG (ONBEAT) with conventional on-pump CABG (ONSTOP) in patients with impaired ventricular function.

Methods and Results—In a single-center randomized trial, 50 patients with impaired ventricular function were randomly assigned to ONBEAT or ONSTOP. Patients underwent cardiac magnetic resonance imaging for function and delayed hyperenhancement early and later after surgery. Serial assessment of biochemical markers was also undertaken. Preoperative characteristics were well matched; cardiac index was 2.85 \pm 0.53 (ONBEAT) and 2.62 \pm 0.59 L \cdot min^{-1} \cdot m^{-2} (ONSTOP). Early after surgery, there was a trend toward a greater reduction in end-systolic volume index in ONSTOP patients versus ONBEAT (\(-9 \pm 8\) versus \(-4 \pm 11\) mL \cdot m^{-2}; P=0.06). The changes were sustained and significant at 6 months (\(-14 \pm 18\) versus \(-2 \pm 19\) mL \cdot m^{-2}; P=0.04). Furthermore, the incidence of new hyperenhancement at 6 days was higher in ONBEAT patients (P=0.05), with 6 of 17 (35%) sustaining 8.2 \pm 5.2 g of new hyperenhancement each versus 2 of 23 (9%) in the ONSTOP group, each with 9.8 \pm 9.0 g (P=0.86). Finally, median area under the curve for troponin was higher in ONBEAT at 461 (interquartile range, 226 to 1141) \mu g/L versus 160 (interquartile range, 98 to 357) \mu g/L for ONSTOP (P=0.002).

Conclusions—The incidence of new irreversible myocardial injury was significantly higher in ONBEAT than in ONSTOP patients. Furthermore, at 6 months, only ONSTOP patients demonstrated an improvement in ventricular geometry. The most likely mechanism is inadequate coronary perfusion to distal myocardial territories in patients with severe proximal coronary disease. (Circulation. 2008;118:2130-2138.)

Key Words: bypass ■ cardioplegia ■ grafting ■ heart failure ■ magnetic resonance imaging

Coronary artery disease is the most common cause of heart failure in the industrialized world.\(^1,2\) In selected patients with heart failure, coronary artery bypass grafting (CABG) improves both symptoms and prognosis\(^3\) but is associated with higher mortality, morbidity, and hospitalization costs compared with those with normal ventricular function.\(^9,10\)

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Conventional CABG uses cardiopulmonary bypass (CPB) and cardiac arrest to provide a stationary heart to facilitate surgery. This technique causes an obligate period of global myocardial ischemia that is attenuated by cardioplegic arrest of the heart. Currently, the optimal method for intraoperative
myocardial protection is blood cardioplegia, but this is still associated with low cardiac output syndrome in 10% of cases. Over the last decade, interest has reemerged in beating heart (“off-pump”) surgery, which avoids CPB, cardioplegic arrest, and consequently, the global “ischemic time.” In previous work by our group, it has been shown that in patients with normal left ventricular (LV) function, off-pump CABG is associated with improved early cardiac function compared with conventional CABG with the use of crystalloid cardioplegia. Although heart failure patients could potentially benefit from this improvement in early cardiac function, they may not be able to sustain an adequate intraoperative cardiac output during cardiac manipulations necessary for off-pump surgery. A hybrid procedure of beating heart surgery with the concomitant utilization of CPB (to provide mechanical support to the systemic circulation), but without cardioplegic arrest, might confer some of the advantages of the off-pump technique in these higher-risk patients.

In the study by Selvanayagam et al, the off-pump technique failed to show any benefit in terms of irreversible myocardial injury over conventional on-pump cardioplegic arrest; however, this study did not employ the use of intracoronary shunts. Coronary shunts are inserted into the native coronary artery during construction of the anastomoses; this is thought to improve distal perfusion and thereby reduce local ischemia during surgery. Cardiovascular magnetic resonance imaging (CMR) is accepted as the gold standard for the assessment of biventricular function. The technique allows serial cardiac assessment with excellent reproducibility, permitting a significant sample size reduction for heart failure trials. In addition, delayed enhancement CMR (DE-CMR) permits unprecedented quantification of myocardial necrosis, capable of detecting small foci of injury arising from percutaneous coronary intervention or CABG.

In this study, we compared a novel hybrid technique of on-pump beating heart surgery (ONBEAT) with the current gold standard for CABG, “on-pump with cold blood cardioplegic arrest” (ONSTOP), using CMR. Additionally, we measured serum markers of myocardial necrosis, namely, cardiac troponin I (cTn I) and creatine kinase–MB (CK-MB). Finally, we hypothesized that the ONBEAT technique using intracoronary shunts provided optimal intraoperative myocardial protection, lessening the extent of myocardial stunning and permanent myocardial injury compared with conventional CABG surgery.

**Methods**

Over 24 months between November 2005 and 2007, in a single-center randomized trial, all patients referred to a single surgeon (D.P.T.) for first-time isolated CABG were screened for inclusion. Patients were excluded if they required emergency CABG or had Canadian Classification Score class IVb angina, were enrolled in another clinical trial, had typical CMR contraindications, or had normal LV function defined by echocardiography, LV angiography, or nuclear scintigraphy. For safety reasons pertaining to proximity of CMR facilities to advanced resuscitation facilities, urgent patients (defined as requiring inpatient surgical revascularization for recent acute coronary syndrome or left main stem disease) were only approached for inclusion if they had been successfully medically stabilized (pain free for 72 hours).

Before March 2007, patients were included with a serum creatinine ≤170 µmol/L. However, subsequent to the US Food and Drug Administration warning on the use of gadodiamide-based contrast agents in patients with renal failure, only patients with an estimated glomerular filtration rate (GFR) ≥60 mL/min were recruited. Only patients with a measured ejection fraction (EF) <54% at CMR and who successfully completed the first CMR study were included in the study. Patients underwent their first CMR examination no more than 4 weeks before scheduled surgery, the second CMR scan as soon as feasible in the early postoperative stage, and the final scan after 6 months. Before recruitment, unique participant identifier numbers were randomly assigned to either surgical technique in blocks of 10 by a Web-based randomization program, the details of which were contained within sealed envelopes and held by 3 study investigators. Patients were ascribed their unique participant identifier the evening before surgery. The surgical team was only unblinded to the surgical procedure once the patient had been anesthetized. Fifty patients were accepted for inclusion; 25 were randomized to ONBEAT and 25 to ONSTOP.

**Ethics**

The study was approved by our local institutional research ethics committee (National Research Ethics Service No. 05/Q1603/42). Each patient gave written informed consent.

**Treatment and Procedures**

The aim of the surgery was to obtain complete revascularization utilizing the left internal mammary artery and saphenous vein grafts where possible. Postoperative deaths were recorded if they occurred within 30 days of surgery. Major adverse events included reoperation, cerebrovascular event causing >24 hours of neurological disability, reintubation for any cause, and hemofiltration for renal failure.

**Anesthesia**

All patients received a standard anesthetic protocol comprising scopolamine, fentanyl, pancuronium, etomidate, and propofol, and all patients were fully heparinized (3 mg/kg) to achieve an activated clotting time >400 seconds.

**Hemodynamic Parameters**

Invasive blood pressure monitoring was in situ throughout the surgical procedure, and measurements were charted every 15 minutes. All patients were placed on CPB, during which the mean arterial pressure was maintained between 50 and 60 mm Hg with pharmacological manipulation as necessary.

**ONSTOP and ONBEAT**

CPB was performed in a similar manner in both cohorts with the use of nonpulsatile flow and at a temperature of 34°C. A membrane oxygenator and alpha-stat control of acid base management were used.

**ONSTOP**

Myocardial protection was obtained with 1 L of cold blood cardioplegia delivered antegradely and repeated every 30 minutes as necessary.

**ONBEAT**

Circulatory support during surgery was provided with CPB. Commercially available stabilizers were used. Intracoronary artery shunts were used in all anastomoses where possible.

**CMR Protocol**

All CMR examinations were performed with the use of a 1.5-T MR scanner (Sonata, Siemens Medical Solutions, Erlangen, Germany), with prospective ECG gating and the patient in the supine position. After piloting with the use of localizers, steady-state free precession...
Delayed Hyperenhancement

DE-CMR was performed with a T1-weighted segmented inversion-recovery turbo fast low-angle shot sequence (echo time 4.8 ms, voxel size 1.4 × 2.4 × 7 mm, flip angle 20°) after a 5-minute delay after the administration of 0.1 mmol/kg contrast agent (gadodiamide; Omniscan, GE Healthcare). Images were acquired in 3 long-axis planes and in a short-axis stack covering the entire LV. The inversion time was meticulously adjusted throughout the acquisition to obtain optimal nulling of remote normal myocardium. The slice thickness at the apex was reduced to 5 mm to avoid partial volume effect. Areas of myocardial infarction were quantified by a computer-assisted planimetry program, MATLAB version 7.3.0.267 (Natick USA), by a single experienced observer blinded to surgical technique and supplementary data. With a specific gravity of 1.05 (Figure 1). Twenty-one patients were excluded after their first CMR scan for the following reasons: 15 patients had recovered normal LV function, 4 patients were unable to complete biochemical analysis. A probability of P<0.05 was considered statistically significant.

Power Calculation

Our primary end point was to detect a 10% difference in the mean change from baseline in ESVI after CABG (ONBEAT versus ONSTOP) as measured by the early postoperative CMR scan (ie, 6 days after operation). On the basis of the results observed in our other published trial assuming a change of similar magnitude,15 we expected the mean difference in ESVI for 1 patient between the groups with a significance level of 0.05 and a power of 80%.

The authors had full access to the data and take full responsibility for their integrity. All authors have read and agree to the manuscript as written.

Results

Between November 2005 and November 2007, 317 patients were referred for isolated CABG, of whom 71 (22%) were eligible for inclusion and gave written informed consent (Figure 1). Twenty-one patients were excluded after their first CMR scan for the following reasons: 15 patients had recovered normal LV function, 4 patients were unable to complete biochemical analysis. A probability of P<0.05 was considered statistically significant.

### Statistical Analysis

All data were analyzed on an intention-to-treat principle beginning immediately after randomization. Values were expressed as mean (±SD) or median (interquartile range, 25% to 75%) as appropriate. All end points were checked to see whether they followed a normal distribution. All normally distributed end points including change in LV volumes, measured at 6 days and 6 months, after both ONBEAT and ONSTOP procedures were compared with a mixed-effect model adjusting for the baseline measure. An additional sensitivity analysis was performed adjusting EuroSCORE and GFR at baseline because of an observed imbalance in these variables between the 2 groups. Dichotomous data were compared by the χ² statistic or Fisher exact test. Continuous variables that were not distributed normally were compared by the Mann-Whitney or Kruskal-Wallis test. No outliers were excluded from the main analysis, and women were excluded in a small subanalysis to ensure that the result was not gender specific. Patients who were excluded from the CMR comparisons were still included in the clinical/biochemical analysis. A probability of P<0.05 was considered statistically significant.

### Power Calculation

Our primary end point was to detect a 10% difference in the mean change from baseline in ESVI after CABG (ONBEAT versus ONSTOP) as measured by the early postoperative CMR scan (ie, 6 days after operation). On the basis of the results observed in our other published trial assuming a change of similar magnitude,15 we expected the mean difference in ESVI for 1 patient between the groups with a significance level of 0.05 and a power of 80%.
the CMR protocol because of claustrophobia, 1 patient had undiagnosed aortic stenosis necessitating concurrent aortic valve replacement, and 1 patient had a significant posterior LV aneurysm causing mitral valve insufficiency that required surgical repair.

Primary end point data were available for 45 patients (90%) (21 ONBEAT and 24 ONSTOP). Three deaths and 1 major adverse event occurred in the study group by 6 months (3 ONBEAT, 1 ONSTOP). One patient died within 30 days of surgery from multiple organ failure (ONBEAT). One patient had a tension pneumothorax resulting in prolonged cardiac arrest, from which the patient sustained a significant neurological deficit (ONBEAT). This patient later died from peritonitis on the 48th postoperative day after the surgical repair.

Other late deaths were excluded from further imaging because of retained epicardial pacing wires that precluded further assessment with CMR (ONBEAT). One of these patients died on the 34th postoperative day from bronchopneumonia. No other late deaths (up to 6 months) have been recorded. Three patients who were included at 6 days were unable to undergo further imaging at 6 months. One ONSTOP patient declined further imaging, 1 patient became claustrophobic (ONBEAT), and 1 had a new implantable cardiac defibrillator (ONBEAT).

The preoperative characteristics were similar between the 2 groups in terms of age, medications, and preoperative LV function (Table 1). More patients who were referred for urgent revascularization (for recent acute coronary syndrome or left main stem disease) were randomly assigned to the ONBEAT technique; furthermore, ONBEAT patients had a higher logistic EuroSCORE and lower GFR. Only 3 women were recruited into the study (3 of 50), and all were randomly assigned to the ONBEAT group (Table 1). All patients underwent surgery according to their randomization order.

### Surgical Characteristics

The operation time and number of distal anastomoses were similar between the 2 groups (Table 2). All patients received an internal mammary artery graft to the left anterior descending coronary artery. In total, 96 anastomoses were performed in the ONBEAT group (30 arterial) and 93 anastomoses in the ONSTOP group (31 arterial) ($P=0.86$). In addition to the first internal mammary artery, second arterial grafts were sited in 11 patients. Nine patients (4 ONBEAT, 5 ONSTOP) had 2 anastomoses involving the internal mammary artery, 1 patient had a right internal mammary artery graft (ONSTOP), and 1 patient had a radial artery graft (ONBEAT), all because of unsuitable venous conduits.

There was no difference in terms of death, major adverse event, duration of ventilation, intensive care, and hospital stay between the groups (Table 2). Fifteen patients from each group (60%) required moderate inotropic support with epinephrine (defined as stroke causing >24 hours of neurological disability, reoperation during hospital admission, or reintubation for any cause. Significant epinephrine requirement is defined as $>5 \mu g \cdot kg^{-1} \cdot min^{-1}$).

### Cine CMR

The median time between surgery and the second CMR scan was 7 (6 to 11.5) days for ONBEAT patients and 6 days (6 to 33 days) for ONSTOP patients. The median time between surgery and the second CMR scan was 7 (6 to 11.5) days for ONBEAT patients and 6 days (6 to 33 days) for ONSTOP patients.
Delayed Hyperenhancement

The preoperative DE-CMR scan showed significant preexisting myocardial damage (>2 g hyperenhancement) in all patients. The mean mass of preexisting hyperenhancement was 23.2±15.9 g in the ONBEAT group and 28.1±8.6 g in the ONSTOP group (P=0.19). Early after surgery, 40 patients (17 ONBEAT, 23 ONSTOP) had DE-CMR imaging. In addition to the aforementioned excluded patients, 4 patients (3 ONBEAT, 1 ONSTOP) did not tolerate the full CMR protocol (because of anxiety or breathlessness), and 1 patient (ONBEAT) had a pattern of hyperenhancement in noncoronary pattern precluding accurate quantification of DE mass. Of patients with DE-CMR data, 35% of ONBEAT patients (6 of 17) had evidence of new hyperenhancement, whereas only 9% of ONSTOP patients (2 of 23) had DE-CMR evidence of myocardial injury (P=0.05). Overall, for the 2 groups the median mass of new irreversible injury was 1.5 g (0 to 5) in the ONBEAT group and 1 (−2 to 2) in the ONSTOP group (P=0.1). In those patients with evidence of new myocardial injury, the mean mass of hyperenhancement per patient was 8.2±5.2 and 9.8±9.0 g, respectively (P=0.86).

Two distinct patterns of new myocardial injury appeared on DE-CMR imaging (Table 5). Three patients had a transmural pattern of myocardial injury, which followed a coronary artery distribution (2 ONBEAT, 1 ONSTOP); in these patients, median peak troponin was 48.2 µg/L (35.9 to 94.0). Two of these patients had new hyperenhancement in territories subtended by arterial grafts (Figure 2, panel ii), and the third patient had infarction corresponding to the site of a coronary artery endarterectomy. The second pattern of injury was associated with a slightly lower median peak troponin level of 23.3 µg/L (5.1 to 27.3); patients in this group had apical or subendocardial hyperenhancement in a pattern more suggestive of watershed infarction or embolization (Figure 2, panel i). Patients without evidence of new hyperenhancement had a median peak troponin of 4.7 µg/L (2.5 to 7.5); finally, patients without follow-up hyperenhancement data had a peak troponin of 10.9 µg/L (6.4 to 16.7) (P=0.005 for between groups comparison) (Table 5).

Serum Markers of Myocardial Injury

The median area under the curve for cTn I was significantly higher in the ONBEAT group (461 [226 to 1141] µg/L) than in the ONSTOP group (160 [98 to 357] µg/L) (P=0.002). Similar results were found for the area under the curve of

8.5) for ONSTOP patients (P=0.61). Preoperative cardiac function did not differ significantly between the 2 groups. After surgery, both groups sustained reductions in LV EF and stroke volume index, but cardiac index remained unchanged. A reduction in stroke volume index by 21% in both groups was compensated by an increase in heart rate; 22% in the ONBEAT group and 29% in the ONSTOP group (P=0.56) (Table 3).

ESVI was reduced in both groups early after surgery, but there was a trend toward a smaller reduction in ESVI in ONBEAT patients (Table 4). We also performed a post hoc sensitivity analysis for the change in EDVI and ESVI accounting for the baseline imbalance in the GFR and EuroSCORE between the 2 groups, and results were consistent with the findings without this adjustment (results not shown).

Table 3. Functional Data for Preoperative and Postoperative LV Function

<table>
<thead>
<tr>
<th>Variable</th>
<th>ONBEAT (n=21)</th>
<th>ONSTOP (n=24)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>EF, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preoperatively</td>
<td>40±11</td>
<td>39±11</td>
<td></td>
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<tr>
<td>6 Days</td>
<td>36±13</td>
<td>37±12</td>
<td></td>
</tr>
<tr>
<td>ΔEF</td>
<td>−4±8</td>
<td>−2±8</td>
<td>0.52</td>
</tr>
<tr>
<td>Cardiac index, L · m⁻² · mm⁻¹⁻¹</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preoperatively</td>
<td>2.85±0.53</td>
<td>2.62±0.59</td>
<td></td>
</tr>
<tr>
<td>6 Days</td>
<td>2.75±0.59</td>
<td>2.65±0.55</td>
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</tr>
<tr>
<td>ΔCardiac index</td>
<td>−0.09±0.72</td>
<td>+0.04±0.81</td>
<td>0.56</td>
</tr>
<tr>
<td>Stroke volume index, mL · mm⁻²⁻²</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Preoperatively</td>
<td>43±9</td>
<td>43±10</td>
<td></td>
</tr>
<tr>
<td>6 Days</td>
<td>34±8</td>
<td>34±8</td>
<td></td>
</tr>
<tr>
<td>ΔStroke volume index</td>
<td>−9±12</td>
<td>−9±12</td>
<td>0.86</td>
</tr>
<tr>
<td>ESVI, mL · mm⁻²⁻²</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Preoperatively</td>
<td>71±30</td>
<td>74±31</td>
<td></td>
</tr>
<tr>
<td>6 Days</td>
<td>67±32</td>
<td>65±30</td>
<td></td>
</tr>
<tr>
<td>ΔESVI</td>
<td>−4±11</td>
<td>−9±8</td>
<td>0.05</td>
</tr>
<tr>
<td>EDVI, mL · mm⁻²⁻²</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preoperatively</td>
<td>113±31</td>
<td>118±31</td>
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<tr>
<td>6 Days</td>
<td>101±30</td>
<td>99±32</td>
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<tr>
<td>ΔEDVI</td>
<td>−12±16</td>
<td>−19±14</td>
<td>0.17</td>
</tr>
<tr>
<td>Heart rate</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Preoperatively</td>
<td>67±10</td>
<td>62±10</td>
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<tr>
<td>6 Days</td>
<td>82±14</td>
<td>80±12</td>
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<tr>
<td>ΔHeart rate</td>
<td>15±18</td>
<td>18±10</td>
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Table 4. Summary of Results at 6 Days and 6 Months

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Mean (SD) Change From Baseline, n</th>
<th>Estimated Treatment Effect (95% CI)*</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESVI</td>
<td></td>
<td></td>
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<tr>
<td>6 Days</td>
<td>−3.8 (10.6), 21</td>
<td>5.4 (−0.2, 11.0)</td>
<td>0.06</td>
</tr>
<tr>
<td>6 Months</td>
<td>−2.0 (19.4), 19</td>
<td>11.6 (−0.8, 22.2)</td>
<td>0.04</td>
</tr>
<tr>
<td>EDVI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 Days</td>
<td>−12.4 (16.3), 21</td>
<td>5.8 (−3.2, 14.7)</td>
<td>0.20</td>
</tr>
<tr>
<td>6 Months</td>
<td>0.6 (21.3), 19</td>
<td>13.4 (1.1, 25.6)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

*Mixed effect model adjusted for baseline measure, ONBEAT vs ONSTOP.
CK-MB measurements (Table 5). All 3 women (ONBEAT) sustained a significant troponin/CK-MB rise (>75th percentile for the group); after women were excluded, the ONBEAT technique was still associated with significantly higher serum markers of myocardial injury (Table 5).

**Six-Month Follow-Up**

Forty-two patients had imaging at 6 months (19 ONBEAT, 23 ONSTOP). One patient had 2 intervening admissions to the hospital with pulmonary edema (ONSTOP); this patient had sustained significant postoperative myocardial injury with 16.1 g of new hyperenhancement. The remaining patients were well without further episodes of chest pain or hospital admission. Overall mean EF improved by 3.8% (ONBEAT) and by 5.6% (ONSTOP) (P=0.5). The early trend toward a difference in the ESVI between each group was sustained at 6 months (Figure 3, panel i); furthermore, similar changes were noted for EDVI at 6 months (Figure 3, panel ii). Three patients who had been unable to perform hyperenhancement imaging early after surgery had imaging at 6 months (2 ONBEAT, 1 ONSTOP). At 6 months, 7 of 19 ONBEAT patients (37%) had evidence of new myocardial injury after surgery compared with 2 of 24 ONSTOP patients (8%) (P=0.03).

**Discussion**

Heart failure patients represent a significant proportion of patients being referred for CABG, and early morbidity and mortality approach 4 times those of patients with normal ventricular function. Although our previous study suggested better preserved LV function with an off-pump technique, patients with impaired LV function may be unable to sustain an adequate intraoperative cardiac output during the beating heart technique; hence, the theoretical need exists for mechanical support from a CPB circuit. To the best of our knowledge, this is the first randomized trial to address the suitability of the beating heart technique in patients with impaired ventricular function. In addition, using our delayed
enhancement findings, we have provided further insights into the mechanisms of myocardial injury in patients after CABG.

**Overall LV Function**

The main finding of this study is that the ONBEAT technique is associated with poorer early and late cardiac remodeling compared with the ONSTOP technique, although both surgical techniques produce similar results in terms of overall LV function. Comparisons using ESVI are more useful than EF, stroke volume index, and cardiac index because ESVI is less dependent on loading conditions and therefore a better indicator of overall LV geometry. Furthermore, after surgery ESVI is an excellent predictor of long-term outcome.

Early after surgery, ESVI and EDVI were reduced in both surgical groups. Despite the significant increase in myocardial injury associated with the ONBEAT technique, there was only a minor difference in the early postoperative ESVI between the techniques. However, we believe that in patients with impaired LV function, short-term functional decline is an insensitive marker of procedure-related myocardial injury. Injury to hibernating segments may not produce significant volumetric change because preexisting dysfunction masks the loss of viable myocardium (Figure 4). Longer-term assessment would allow time for uninjured hibernating segments to recover function, thereby potentiating a difference. Our long-term follow-up data clearly demonstrate a sustained and significant difference in both EDVI and ESVI in the ONBEAT group, which is likely to be related to procedural injury from this technique.

**Irreversible Myocardial Injury**

Further supporting the volumetric data, we found a higher incidence of irreversible myocardial injury in the ONBEAT (35%) compared with the ONSTOP (9%) group. There was no difference in the magnitude of injury seen in patients from each respective group. With the exclusion of the 3 patients with transmural infarction, the injury in the ONBEAT group appeared to be the result of watershed infarction. We reported a similar observation in our previous study but assumed that this would be eliminated with the use of intracoronary shunts. The mean perfusion pressure during CPB is ~60 mm Hg but clearly may be much lower distal to significant proximal coronary stenoses. Therefore, distal shunts may be relatively ineffective. The present study suggests that the combination of bypass and intracoronary shunts may still not be adequate to perfuse the distal coronary territories, especially in the presence of significant proximal coronary disease. Furthermore, although 2 studies using intracoronary shunts have demonstrated improved intraoperative regional and global cardiac function during the insertion of a shunt, both studies examined only the short-term effect. Actual shunt insertion may cause endothelial trauma or plaque disruption in the native vessel, producing embolization of material and possible downstream myocardial injury. The full extent of this injury may take several hours to develop, much longer than the period covered by these studies.

**Other Insights From DE-CMR**

Three patients had significant transmural myocardial injury (2 ONBEAT, 1 ONSTOP) consistent with either native vessel (endarterectomy) or acute graft compromise (1 left internal artery).
mammary artery, 1 radial artery). Neither of these was confirmed by angiography because this was beyond the scope of this study.

**Serum Markers of Myocardial Injury**
Both DE-CMR and serum levels of cardiac biomarkers indicated evidence of increased myocardial injury associated with the ONBEAT compared with the ONSTOP technique. Historically, off-pump beating heart surgery has been associated with lower levels of cardiac enzyme release compared with on-pump surgery.\(^\text{15,26,27}\) The extent to which this is related to the ischemic period or to a systemic reaction from the CPB circuit remains unclear. Because both surgical groups in the present study were “on-pump,” differences in serum biomarker release can be attributed chiefly to ischemic myocardial injury, unlike in other trials of off-pump beating heart technique. In this study, ONBEAT was associated with higher median area under the curve for cTn I and CK-MB, and insights from DE-CMR suggest that in part this may be due to embolization or watershed infarction. Median cTn I measurements in patients without early DE-CMR data (8 ONBEAT, 2 ONSTOP) were significantly higher than those without new myocardial injury. These patients may have sustained complications from myocardial injury, which either precluded further assessment with CMR or diminished their ability to complete the DE-CMR protocol early after surgery. The inclusion of these patients, if it were possible, would only have served to compound the negative result of the study.

**Limitations**
The major limitation of our study was the sample size. Recruitment was often complicated by inability to lie flat, claustrophobia, or implantable cardiac devices. Furthermore, eligible heart failure patients were often excluded after completing the initial CMR assessment because the LV systolic dysfunction was not as severe as previous imaging indicated. Additionally, the unforeseen Food and Drug Administration warning on gadodiamide-based contrast agents in patients with renal dysfunction placed further restrictions on recruitment. Although gadodiamide can be administered to patients with mild to moderate renal disease, it is our unit policy not to administer contrast to research patients with a GFR <60 mL·min\(^{-1}\). Unfortunately, only 3 women were randomized in the study, and all to the ONBEAT technique, which may have had some impact on our results.

**Conclusions**
These findings are important because this is, to our knowledge, the first study of a hybrid technique of on-pump beating heart surgery versus the current gold standard of blood cardioplegia in patients with severe coronary disease and impaired LV function. The results of this study are counter-intuitive but clearly document higher levels of myocardial injury and poor cardiac remodeling in response to revascularization in ONBEAT patients. In part, the pattern of injury demonstrated by our hyperenhancement findings suggests either watershed infarction or distal embolization and highlights 2 areas that warrant further investigation: (1) the need for more information about antegrade coronary flow during the beating heart technique and the effect of low coronary perfusion pressures, especially in patients with severe proximal coronary disease; and (2) the need to investigate the longer-term consequences of coronary artery shunt placement. The ONBEAT technique is theoretically elegant in its conception; however, these issues need to be resolved before this hybrid technique is suitable for use in patients with impaired ventricular function.

**Sources of Funding**
This research was supported by a direct project grant from the British Heart Foundation (project grant No. PG05/037). Additional funding was provided by the Oxfordshire Health Services Research Committee and the Oxford Partnership Comprehensive Biomedical Research Centre with funding from the Department of Health’s National Institute for Health Research Biomedical Research Centre funding scheme.

**Disclosures**
None.

**References**


**CLINICAL PERSPECTIVE**

Although the financial burden of heart failure is growing in the United States, surgical research in this area is limited by difficult patient demographics. Coronary artery bypass grafting (CABG) affects both mortality and morbidity in heart failure patients; however, the benefits are balanced heavily by high operative risks. Beating heart CABG has benefits in terms of postoperative morbidity; however, the application of this technique in patients with impaired ventricular function remains untested. In a small randomized trial of patients with severe coronary artery disease and impaired ventricular function, a novel hybrid approach of on-pump beating heart surgery (ONBEAT) was compared with conventional cardioplegic arrest (ONSTOP). Left ventricular function and injury were assessed with cardiac magnetic resonance imaging before and 7 days after surgery with additional serial assessment of cardiac biochemical markers over the first 120 hours. Countercintuitively, the study clearly demonstrates a higher incidence of myocardial injury associated with the novel ONBEAT approach. We conclude that physiological coronary perfusion in patients with severe proximal coronary disease may not be sufficient to perfuse distal coronary beds, and in the absence of formal myocardial protection with cardioplegia, it renders these territories ischemic. Although this study is small, it has important implications for the application of beating heart techniques in patients with inadequate cardiac output and severe coronary artery disease.
A Randomized Trial of On-Pump Beating Heart and Conventional Cardioplegic Arrest in Coronary Artery Bypass Surgery Patients With Impaired Left Ventricular Function Using Cardiac Magnetic Resonance Imaging and Biochemical Markers

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_Circulation_. 2008;118:2130-2138; originally published online November 3, 2008;
doi: 10.1161/CIRCULATIONAHA.108.785105
_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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