Miniaturized Cardiopulmonary Bypass and Acute Kidney Injury in Coronary Artery Bypass Graft Surgery

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Background. Acute kidney injury (AKI) is one of the most important complications after on-pump coronary artery bypass graft surgery (CABG). Miniaturized cardiopulmonary bypass (mini-CPB) systems have been developed to allow the ease of on-pump surgery but tempering the disadvantages. Whether mini-CPB reduces the incidence of AKI remains to be determined.

Methods. Using a propensity score matched analysis, we investigated the occurrence of AKI among patients undergoing CABG on mini-CPB (n = 104) versus conventional CPB (n = 601). Acute kidney injury was defined according to the recent Acute Kidney Injury Network classification.

Results. Overall, acute kidney injury developed in 274 of 705 patients (38.8%). A total of 27 of 705 patients (3.8%) required renal replacement therapy. The median postoperative length of intensive care unit stay in survivors with AKI was 5.4 (3.9 to 6.8) days compared with 2.0 (1.0 to 3.0) days for patients without AKI (p = 0.0002). The overall incidence of AKI for patients undergoing mini-CPB was 30 of 104 (28.8%) compared with 244 of 601 (40.5%) for patients undergoing conventional CPB (p = 0.03). In the propensity score matched-pair statistical analysis, mini-CPB was independently associated with a decreased incidence of AKI (adjusted odds ratio [OR] 0.61; 95% confidence interval [CI]: 0.38 to 0.97). Other variables independently associated with AKI were preoperative glomerular filtration rate (OR 0.988 for 1 mL·min⁻¹·1.73 m⁻² increase; 95% CI: 0.98 to 0.99), postoperative red blood cell transfusion (OR 1.58; 95% CI: 1.12 to 2.23); CPB time (OR 1.005 for 1-minute increase; 95% CI: 1.0 to 1.009), and postoperative low output syndrome (OR 1.72; 95% CI: 1.23 to 2.41).

Conclusions. The present study showed that mini-CPB is associated with a lower incidence of AKI when compared with conventional CPB among patients undergoing CABG.

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Acute kidney injury (AKI) after coronary artery bypass grafting (CABG) remains a significant cause of perioperative morbidity and mortality [1]. The postoperative incidence of AKI has been assessed using a variety of definitions, with estimates ranging from 5% to 40% [2]. Despite extensive research in the prediction and treatment of this disease, there has been limited success in altering patient outcomes [2]. Acute kidney injury is mainly related to the adverse effects of cardiopulmonary bypass (CPB), which causes dramatic hemodynamic changes as well as activation of both innate and adaptive immune responses that can initiate or extend renal injury [2]. Off-pump CABG obviously avoids the deleterious effect of extracorporeal circulation. However, the beating-heart technique may be challenging, cumbersome, and may have inferior results with respect to long-term graft patency [3]. Therefore, CABG with CPB and cardioplegic arrest is still the standard method of choice in many institutes. Miniaturized cardiopulmonary bypass (mini-CPB) systems have been developed to allow the ease of on-pump surgery while tempering the disadvantages [4]. Major differences to conventional CPB are use of heparinized tubing and oxygenators, minimizing prime volume, use of a centrifugal pump, and elimination of cardiotomy suction and a venous reservoir. Mini-CPB reduces the hemodilution and the foreign surface area blood contact, thus attenuating the systemic inflammatory response syndrome.

Whether this better biological profile results in reduced AKI remains to be determined, however, with some discordant results reported [5, 6]. Such discordance...
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is available in the RHS, and it was used in this study. The

can offer blood flow from 1.0 to 6.0 L/min. A vent circuit
critical characteristics of vascular endothelium. The RHS
thromboresistance and biocompatibility by mimicking
Carmeda, Stockholm, Sweden) throughout to provide
this RHS are coated with heparin (BioActive Surface;

Gas exchange is 2.5 m². Primary blood contact surfaces of
this circuit is 600 mL, and the membrane surface area for
CPB system, offering minimal air and blood interface and
in patient risk profile between the two study groups.
Statistical Analysis
Continuous variables are shown as median with interquar-
tile range. All categorical data were displayed as percent-
geages. Comparisons were made with Mann-Whitney rank-
sum tests and χ² tests as appropriate. A post hoc χ² test
may be partially explained by the lack of a consensus
definition of AKI. There is increasing agreement that a
universal kidney injury definition is needed to facilitate
progress in the field of acute renal failure. Recently, the
Acute Kidney Injury Network has reached a consensus
on the definition of AKI [7], according to new data
showing that small changes in serum creatinine might be
associated with adverse outcomes. Therefore, we aimed
to evaluate whether mini-CPB decreases the occurrence
of AKI after CABG when compared with conventional
CPB, adopting the recently proposed AKI definition.

Patients and Methods
This study was reviewed and approved by the Institu-
tional Review Board of the University of Rome, and a
waiver of consent was granted. The authors have no
conflict of interest to disclose.

Patient Population
In the present study, we analyzed consecutive patients
undergoing isolated CABG at our institution between
May 2004 and January 2009 who met the following
criteria: (1) procedures on CPB; (2) no preoperative renal
failure requiring dialysis; and (3) no prior cardiac
surgery.
The study population consisted of 705 patients (median
age, 68 years; range, 59 to 73); 123 of the 705 were female.
The mini-CPB system (Resting Heart System [RHS];
Medtronic, Minneapolis, MN) was used in 104 patients
according to surgeon preference. In other cases (n = 601),
a conventional extracorporeal circulation system was
instituted.

Miniaturized CPB
The RHS is an integrated, low prime, semi-closed-loop
CPB system, offering minimal air and blood interface and
elimination of antifoam agents. The priming volume of
this circuit is 600 mL, and the membrane surface area for
gas exchange is 2.5 m². Primary blood contact surfaces of
this RHS are coated with heparin (BioActive Surface;
Carmeda, Stockholm, Sweden) throughout to provide
thromboresistance and biocompatibility by mimicking
critical characteristics of vascular endothelium. The RHS
can offer blood flow from 1.0 to 6.0 L/min. A vent circuit
is available in the RHS, and it was used in this study. The

blood from this vent is reinjected into the pump inflow.
The absence of cardiotomy reservoirs limits the artificial
surface-blood contact that occurs secondary to aspiration
of blood. Accordingly, an erythrocyte-scavenging device
is necessary when using the RHS. In addition, this system
has the technology to detect and remove small air bub-
bles in the circuit. If air is entrained from the right
atrium, visual and audible alarms alert the surgical team
to the condition so that it can be quickly remedied. Two
pairs of ultrasonic fluid sensors in the venous air removal
device detect air at the inlet of the device. When air
enters the device through the venous return line, air
bubbles are detected, and the device exerts evident visual
and audible indications while removing the venous air.
The air is automatically removed from the venous air
removal device until its sensors detect no remaining
air/blood mixture in the upper area of the device, and
then it returns to normal setting.

Conventional CPB
The priming volume amounted to 1,200 mL. The line was
coated with heparin (Medtronic). An oxygenator (Affinity
NT Oxygenator; Medtronic) and a standard roller pump
were included in the set. An arterial filter was used. The
intra pericardial suction device was used as usual.

Definition of AKI and Data Collection
Acute kidney injury was defined as an increase of serum
creatinine of 0.3 mg/dL or more (26.4 μmol/L) postoper-
atively according to the consensus definition proposed by
the Acute Kidney Injury Network [7] and stratified into
three classes: stage 1, increase of serum creatinine 150%
to 200% from baseline; stage 2, increase of serum creati-
nine of 200% to 300% from baseline; and stage 3, increase
of serum creatinine to more than 300% from baseline or
serum creatinine = 4.0 mg/dL. (354 μmol/L) after a rise of
at least 44 μmol/L or treatment with renal replacement
therapy. The four-variable Modified Diet and Renal Dis-
eease equation was used to estimate baseline glomerular
filtration rate (GFR) [8]. We did not use urine output in
defining AKI.

Data were prospectively collected and recorded in an
electronic database by physicians. Baseline serum creat-
inine value was defined as the value recorded just before
surgery. Serum creatinine values were taken after patient
admission to the intensive care unit and repeated at least
once every 24 hours. Based on these values, the difference
between the highest serum creatinine value and the
baseline value was calculated for each patient. Operative
mortality was defined as all deaths occurring within 30
days from surgery.

The European System for Cardiac Operative Risk Eval-
uation (EuroSCORE) [9] was derived to assess differences
in patient risk profile between the two study groups.

Statistical Analysis
Continuous variables are shown as median with interquar-
tile range. All categorical data were displayed as percent-
geages. Comparisons were made with Mann-Whitney rank-
sum tests and χ² tests as appropriate. A post hoc χ² test

Abbreviations and Acronyms
AKI = acute kidney injury
CABG = coronary artery bypass graft surgery
CI = confidence interval
CPB = cardiopulmonary bypass
Mini-CPB = miniaturized cardiopulmonary
      bypass
NYHA = New York Heart Association
OR = odds ratio
RHS = resting heart system

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to evaluate whether mini-CPB decreases the occurrence
of AKI after CABG when compared with conventional
CPB, adopting the recently proposed AKI definition.
analysis was performed to achieve the study power to detect significant differences for the outcome of interest. To investigate the effect of mini-CPB on the incidence of AKI, treatment selection bias was controlled for by constructing the propensity score to be operated on mini-CPB. Potential confounding factors considered in the analysis were selected on the basis of a literature review and clinical plausibility. These variables included (1) demographic characteristics such as age, sex, and body mass index (BMI); (2) clinical risk factors including preoperative GFR, diabetes mellitus, chronic obstructive pulmonary disease requiring treatment, hypertension, peripheral vascular disease, preoperative New York Heart Association (NYHA) class III–IV, left ventricular ejection fraction, prior percutaneous coronary intervention, myocardial infarction within 30 days, emergency surgery, preoperative medications including β-blockers, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, aspirin, and clopidogrel within 5 days from surgery; (3) procedural characteristics such as primary surgeon, number of grafts per patient, and CPB time; and (4) postoperative variables including red blood cell transfusion and the incidence of postoperative low cardiac output syndrome, defined as the need for postoperative intra-aortic balloon pump or inotropic support for longer than 30 minutes in the intensive care unit to maintain the systolic blood pressure at more than 90 mm Hg.

The propensity score was calculated for all 705 patients by means of a multivariate logistic regression analysis, including all significant variables listed in Table 1. To minimize the selection bias of the groups, three nonsignificant variables—age, primary surgeon, and the number of grafts per patient—were also used to construct a propensity score.

### Table 1. Patient Demographics, Clinical Data, and Procedural Characteristics

<table>
<thead>
<tr>
<th>Variables</th>
<th>Yes (n = 104)</th>
<th>No (n = 601)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age median (years), median [IQR]</td>
<td>68 [60.0–74.0]</td>
<td>67 [59.0–73.0]</td>
<td>0.3</td>
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<tr>
<td>Female, %</td>
<td>22.1</td>
<td>16.6</td>
<td>0.2</td>
</tr>
<tr>
<td>Body mass index (kg/m), median [IQR]</td>
<td>26.6 [24.4–29.4]</td>
<td>26.6 [24.7–29.0]</td>
<td>0.9</td>
</tr>
<tr>
<td>Clinical risk factors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preoperative GFR (mL·min⁻¹·1.73 m⁻²), median [IQR]</td>
<td>64 [49–78]</td>
<td>66 [54–80]</td>
<td>0.16</td>
</tr>
<tr>
<td>Diabetes mellitus, %</td>
<td>35.6</td>
<td>39.8</td>
<td>0.4</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease, %</td>
<td>7.6</td>
<td>15.6</td>
<td>0.04</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>95.2</td>
<td>92.5</td>
<td>0.4</td>
</tr>
<tr>
<td>Peripheral vascular disease, %</td>
<td>10.6</td>
<td>14.6</td>
<td>0.3</td>
</tr>
<tr>
<td>Preoperative NYHA functional class III–IV, %</td>
<td>8.6</td>
<td>17.2</td>
<td>0.04</td>
</tr>
<tr>
<td>Left ventricular ejection fraction, median [IQR]</td>
<td>55 [47.0–60.0]</td>
<td>55 [45.0–60.0]</td>
<td>0.6</td>
</tr>
<tr>
<td>Prior PCI, %</td>
<td>20.2</td>
<td>16</td>
<td>0.3</td>
</tr>
<tr>
<td>Myocardial infarction within 30 days, %</td>
<td>45.2</td>
<td>38.1</td>
<td>0.2</td>
</tr>
<tr>
<td>Emergency surgery, %</td>
<td>7.6</td>
<td>16.6</td>
<td>0.02</td>
</tr>
<tr>
<td>EuroSCORE, median [IQR]</td>
<td>5 [3.0–8.0]</td>
<td>6 [3.0–9.0]</td>
<td>0.3</td>
</tr>
<tr>
<td>Preoperative medications</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin within 3 days, %</td>
<td>52.9</td>
<td>43.9</td>
<td>0.1</td>
</tr>
<tr>
<td>Clopidogrel within 3 days, %</td>
<td>32.7</td>
<td>19.1</td>
<td>0.002</td>
</tr>
<tr>
<td>ACEI/ARB, %</td>
<td>63.5</td>
<td>62.4</td>
<td>0.9</td>
</tr>
<tr>
<td>β-blockers, %</td>
<td>64.4</td>
<td>56.4</td>
<td>0.1</td>
</tr>
<tr>
<td>Procedural characteristics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary surgeon, %</td>
<td>0.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1, % (n)</td>
<td>27.9 (29)</td>
<td>25.2 (151)</td>
<td></td>
</tr>
<tr>
<td>2, % (n)</td>
<td>21.1 (22)</td>
<td>21.2 (127)</td>
<td></td>
</tr>
<tr>
<td>3, % (n)</td>
<td>18.3 (19)</td>
<td>20.6 (124)</td>
<td></td>
</tr>
<tr>
<td>4, % (n)</td>
<td>20.2 (21)</td>
<td>19.5 (117)</td>
<td></td>
</tr>
<tr>
<td>5, % (n)</td>
<td>12.5 (13)</td>
<td>13.5 (81)</td>
<td></td>
</tr>
<tr>
<td>Number of grafts/patient, median [IQR]</td>
<td>3 [2.0–3.0]</td>
<td>3 [2.0–3.0]</td>
<td>0.1</td>
</tr>
<tr>
<td>CPB time (minutes), median [IQR]</td>
<td>104 [84.5–124.5]</td>
<td>103 [85.0–122.0]</td>
<td>0.7</td>
</tr>
<tr>
<td>Postoperative variables</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low cardiac output syndrome, %</td>
<td>8.2</td>
<td>12.5</td>
<td>0.2</td>
</tr>
<tr>
<td>Red blood cell transfusion rate, %</td>
<td>48.1</td>
<td>65.1</td>
<td>0.001</td>
</tr>
</tbody>
</table>

ACEI/ARB = angiotensin-converting enzyme inhibitors/angiotensin receptor blockers; CPB = cardiopulmonary bypass; GFR = glomerular filtration rate; IQR = interquartile range; NYHA = New York Heart Association; PCI = percutaneous coronary intervention.
Each mini-CPB patient was then closely matched with a conventional CPB patient having the same or nearest propensity score. In the matched cohort, a multivariate logistic stepwise regression was performed to identify factors independently associated with AKI, including all variables significantly associated to AKI at univariate analysis.

Models fit analysis was evaluated with the Hosmer-Lemeshow goodness-of-fit statistic. The C-statistic was used to assess the predictive power of propensity score. Odds ratios (OR) and their associated 95% confidence intervals (CI) were estimated. In all tests, values of \( p \) less than 0.05 were considered significant. The Statistical Package for the Social Sciences, version 11 (SPSS, Chicago, IL), and G*Power, version 3.0.5 for Windows (Erdfelder, Faul, & Buchner, 1996, Mannheim, Germany) were used for statistical analysis.

### Results

**Demographic, Clinical Data, and Perioperative Characteristics**

Demographic, clinical data, and perioperative characteristics are presented in Table 1 according to the use of mini-CPB. Age, sex distribution, and preoperative serum creatinine levels were similar between the two groups. Patients operated on with mini-CPB were more likely to receive clopidogrel within 5 days from surgery. Patients operated on with conventional CPB were more likely to have chronic obstructive pulmonary disease, preoperative NYHA class III/IV, and emergency surgery. Patient risk profile according to the EuroSCORE was similar between the two groups.

The distribution of primary surgeon did not differ...
between the two groups nor did the number of grafts per patient and cardiopulmonary bypass time. Conventional CPB was associated with an increased occurrence of red blood cell transfusion postoperatively.

Renal Outcomes
Baseline serum creatinine concentration was 1.1 mg/dL (0.9 to 1.3) versus 1.1 mg/dL (0.9 to 1.2) in the mini-CPB group versus conventional CPB group, respectively (p = 0.33). Postoperative peak serum creatinine concentration was achieved after 2 days (1 to 3), and it was 1.27 mg/dL (1.1 to 1.5) versus 1.37 mg/dL (1.1 to 1.7) in the mini-CPB and conventional CPB groups, respectively (p = 0.04). Overall, AKI developed in 27 of 705 patients (3.8%). The majority of patients had stage 1 AKI (n = 215), with few patients in stages 2 (n = 31) and 3 (n = 28). A total of 27 of 705 patients (3.8%) required renal replacement therapy. The median postoperative length of intensive care unit stay for survivors requiring AKI (p = 0.0002). The median postoperative length of intensive care unit stay for survivors requiring renal replacement therapy was 16.5 days (9 to 48) compared with 2.0 days (1.0 to 3.0) for patients without AKI (p < 0.0001). The incidence of renal replacement therapy was 1 of 104 (0.9%) and 26 of 601 (4.3%), respectively (p = 0.16).

Operative Mortality
Overall, the operative mortality rate was 2.5%. The operative mortality rate was 17 of 274 (6.2%) for patients with AKI compared with 1 of 431 (0.2%) for patients without AKI (p < 0.0001); and 10 of 27 (37%) for patients who required postoperative dialysis compared with 8 of 678 (1.1%) for patients who did not require postoperative dialysis (p < 0.0001). Operative mortality rate was 1 of 104 (0.9%) and 17 of 601 (2.8%) for patients undergoing mini-CPB versus conventional CPB, respectively (p = 0.49).

Propensity Score Matched Analysis for AKI
In the mini-CPB group, the median propensity score was 0.18 (interquartile range, 0.12 to 0.25); in the conventional CPB group, the median score was 0.12 (interquartile range, 0.17 to 0.24). The C-statistic for the propensity score model was 0.68 (95% CI: 0.65 to 0.72), indicating a good discrimination. Each of mini-CPB patients was successfully matched with a patient operated on with conventional CPB. Clinical patient characteristics for the mini-CPB group and the conventional CPB group after matching are listed in Table 2. All characteristics that differed significantly between two groups before matching became similar.

In the matched-pair statistical analysis, mini-CPB was found to be significantly associated with a decreased occurrence of AKI (28.8% versus 42.3%; unadjusted OR 0.55; 95% CI: 0.31 to 0.98; p = 0.04). Post hoc power analysis for χ² test showed that study was adequately powered to detect significant differences for the incidence of AKI (1–β: 0.89; critical χ²: 11; effect size w: 0.27) for an α value of 0.05.

After adjusting for other significant covariates, mini-CPB was independently associated with a decreased incidence of AKI (adjusted OR 0.61; 95% CI: 0.38 to 0.97). Other variables independently associated with AKI were preoperative glomerular filtration rate (OR 0.988 for 1 mL·min⁻¹·1.73 m²⁻¹ increase; 95% CI: 0.98 to 0.99), postoperative red blood cell transfusion (OR 1.58; 95% CI: 1.12 to 2.23), preoperative red blood cell transfusion (OR 1.005 for 1-minute increase; 95% CI: 1.0 to 1.009), and postoperative low cardiac output syndrome (OR 1.72; 95% CI: 1.23 to 2.41) (Table 3). The multivariate model significantly predicted the occurrence of AKI (model χ²: 33; p < 0.0001). The model was well calibrated among deciles of observed and expected risk (Hosmer-Lemeshow χ²: 12; p = 0.17).

Comment
The present study showed that in patients undergoing isolated CABG, mini-CPB is significantly associated with a decreased incidence of postoperative acute kidney injury when compared with conventional CPB.

Acute kidney injury is one of the most important complications after CABG [1, 2]. Consequences of AKI include an increase in mortality risk, which can exceed 60% among patients requiring dialysis. Even when serum creatinine values remain within the normal range, modest increases from baseline values are associated with increased odds of death as well as longer hospital stay [7, 10]. However, there have neither been any associated improvements in incidence nor in mortality, despite many recent advances in our understanding of the etiology and pathophysiology of AKI [2].

Table 3. Multivariate Logistic Regression Analysis for Risk Factors Associated With Acute Kidney Injury in the Propensity Score Matched Cohort

<table>
<thead>
<tr>
<th>Variables</th>
<th>Adjusted Odds Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative glomerular filtration rate⁵</td>
<td>0.988</td>
<td>0.98–0.99</td>
</tr>
<tr>
<td>Miniaturized cardiopulmonary bypass</td>
<td>0.61</td>
<td>0.38–0.97</td>
</tr>
<tr>
<td>Cardiopulmonary bypass time¹</td>
<td>1.005</td>
<td>1.0–1.009</td>
</tr>
<tr>
<td>Postoperative red blood cell transfusion</td>
<td>1.58</td>
<td>1.12–2.23</td>
</tr>
<tr>
<td>Postoperative low cardiac output syndrome</td>
<td>1.72</td>
<td>1.23–2.41</td>
</tr>
</tbody>
</table>

⁵ Model χ²: 33; p < 0.0001. ⁶ Hosmer-Lemeshow χ²: 12; p = 0.17. ⁵ For 1 mL·min⁻¹·1.73 m²⁻¹. ¹ Per 1-minute increase.
A major obstacle to finding successful management for AKI has been the conduct of trials adequately powered to show a benefit. Acute kidney injury requiring renal replacement therapy is relatively rare in postoperative cardiac surgical patients [11]. To power a study for an absolute reduction in renal replacement therapy requirement, the necessary sample size would be very large (n = 1,092, assuming an absolute reduction of 2%, a value = 0.01 and 1-β = 0.90). Such a study would require a large multicenter design and would be very costly. Alternatively, clinical endpoints could include surrogate outcomes showing consistent association with relevant clinical outcomes [7, 10]. In this regard, the inconsistencies in the current literature with respect to the definition of AKI need to be resolved so that future research can be meaningful, reproducible, and comparable.

The most promising classification today is based on the Acute Kidney Injury Network definition [7]. This definition had been strongly associated with adverse outcomes such as overall mortality and intensive care stay [12–14], and it should be routinely adopted in evaluating potential strategies for AKI. Mini-CPB has been shown to provide a better biological profile than conventional CPB, reducing the hemodilution and attenuating the systemic inflammatory response syndrome [4]. However, whether it may result in reduced AKI remains to be determined. The two largest randomized controlled trials reported discordant conclusions with regard to renal advantages of the mini-CPB system when compared with conventional CPB [5, 6]. It should be pointed out that neither study used AKI as the renal endpoint, and the number of patients with postoperative renal failure requiring renal replacement therapy was too low to reach a statistically significant difference. A potential role of mini-CPB in reducing AKI after CABG has been supported by studies that showed a decreased release of specific renal injury biomarkers such as N-acetyl-glucosaminidase and urinary interleukin-6 [4]. However, to draw definitive evidences from trials using changes in biomarker levels as surrogate outcome, biomarkers should be first demonstrate strong, independent, graded, and consistent associations with relevant clinical outcomes. In addition, the biomarker should have strong discriminatory characteristics that include a large difference between patients who present the clinical outcome of interest and those who do not.

In the present risk-adjusted analysis, we defined AKI according to the Acute Kidney Injury Network guidelines. We observed postoperative AKI in 40.5% of patients undergoing conventional CBP, and this result was quite similar to that recently reported by others [12]. In the propensity score matched cohort, minimized CPB was associated with an absolute reduction in AKI occurrence of 13.5%. As expected, stage 1 AKI developed in the majority of patients after surgery. However, it has been clearly shown that even this early stage of renal injury may negatively affect patient outcomes [10, 12–14], and mini-CPB should be expected to improve surgical results, reducing its occurrence.

Several mechanisms may contribute to reduce AKI in patients operated on using mini-CPB. The limited hemodilution provided by the miniaturized CPB system permits a reduction of postoperative red blood cell transfusion, which is a well-known risk factor for AKI [15]. In addition, the low hematocrit values during extracorporeal circulation have been shown to correlate significantly with high postoperative kidney proximal tubular damage assessed by N-acetylglucosaminidase and urinary interleukin-6 response [4]. A significant independent association was found between the lowest hematocrit during bypass and AKI [16], with significant benefits on renal function after reduction of the bypass prime volume. Moreover, mini-CPB has been shown to provide a better tissue perfusion, which accounts for better kidney protection. That might be, in part, the effect of the volume-constant perfusion featured in the closed-loop miniaturized CPB system, regularly resulting in an ele-
vated mean arterial pressure compared with conventional cardiopulmonary bypass. The increased perfusion pressure and the greater intravascular volume resulting from the removal of a venous reservoir may provide better capillary perfusion of all organs, including the kidney [17]. The impact of the inflammatory response induced by CPB within the kidney is not completely understood. It is interesting that animal models of renal ischemia-reperfusion injury have clearly demonstrated the pathologic role of interstitial inflammation and the elaboration of proinflammatory cytokines and reactive oxygen species in the production of tubular injury [18–21]. This local inflammatory response in experimental models is identical to that seen on a more global scale during CPB. Thus, it is likely that mini-CPB may additionally reduce kidney injury by attenuating such an inflammatory response.

This study has some limitations. It was retrospective in design, and the use of the mini-CPB system was not randomized; therefore, our results may be influenced by treatment bias. We performed statistical adjustment including the use of propensity scores in an attempt to account for the nonrandomized nature of the analysis. However, our propensity analysis was only modestly predictive, which is perhaps not surprising because of few baseline differences between the two groups.

Although we identified the association between mini-CPB CABG and a decreasing risk of AKI, causality cannot be proven. Further randomized controlled trials adequately powered are needed to confirm whether the mini-CPB system improves renal outcome after CABG. The present study confirmed that the recent AKI definition should be used as the renal endpoint in such trials. In fact, it strongly correlates with a patient's outcome, and at the same time, allows one to adequately power a study comparing mini-CPB versus conventional CPB CABG with a reasonable sample size (Fig 2).

References

INVITED COMMENTARY
Cardiopulmonary bypass (CPB) has been germane to the development of cardiac surgery. Although its use is often necessary, CPB is associated with the development of a well-described systemic inflammatory response. Benedetto and colleagues [1] examined the hypothesis that the Medtronic Resting Heart System mini-CPB cir-