On-pump beating-heart coronary artery bypass provides efficacious short- and long-term outcomes in hemodialysis patients

Yi-Ting Tsai1, Feng-Yen Lin2,3, Ching-Huang Lai4, Yi-Chang Lin1, Chih-Yuan Lin1 and Chien-Sung Tsai1

1Division of Cardiovascular Surgery, Department of Surgery, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan, 2Department of Internal Medicine, School of Medicine, Taipei Medical University, Taipei, Taiwan, 3Division of Cardiology, Department of Internal Medicine, Taipei Medical University Hospital, Taipei, Taiwan and 4Department of Public Health, National Defense Medical Center, Taipei, Taiwan

Correspondence and offprint requests to: Chien-Sung Tsai; E-mail: sung1500@ndmctsgh.edu.tw

Abstract

Background. On-pump beating-heart coronary artery bypass grafting surgery (CABG) is beneficial due to the elimination of cardioplegic arrest. However, there are few reports regarding its efficacy in chronic hemodialysis patients. This study investigated the potential benefits of on-pump beating-heart CABG in chronic hemodialysis patients.

Methods. From January 2002 to January 2010, 186 patients with chronic hemodialysis underwent CABG in our institution. In total, 82 patients underwent conventional CABG with cardioplegic arrest, 56 underwent off-pump CABG and 48 underwent on-pump beating-heart CABG. The early results and long-term outcomes were compared among these three groups.

Results. On-pump beating-heart CABG significantly reduced the duration of cardiopulmonary bypass (CPB) compared with conventional CABG. The post-operative pericardial drainage amount ($P < 0.01$), length of hospital stay ($P < 0.001$) and length of post-operative intensive care unit stay ($P < 0.001$) were significantly lower in the on-pump beating-heart and off-pump CABG groups than in the conventional CABG group. No significant difference was found regarding 30-day mortality and morbidity rates including stroke, pneumonia, arrhythmia, intestinal complication and low cardiac output syndrome. There were no statistical differences in the freedom from cardiac events ($P = 0.323$), but on-pump beating-heart CABG provided better long-term survival than conventional CABG ($P = 0.009$).

Conclusions. On-pump beating-heart CABG is a safe procedure that provides optimal operative exposure in chronic hemodialysis patients. The use of CPB and the elimination of cardioplegic arrest may be beneficial for the short- and long-term survival of chronic hemodialysis patients.

Keywords: beating heart; CABG; coronary artery disease; hemodialysis; uremia

Introduction

The surgical mortality and long-term survival of patients with end-stage renal disease (ESRD) after coronary artery bypass grafting surgery (CABG) are significantly worse than those of patients without ESRD [1–3]. However, CABG for hemodialysis-dependent patients with coronary artery disease could potentially improve their prognosis. Although conventional CABG with cardioplegic arrest made it possible for surgeons to perform coronary revascularization on a still bloodless heart, stopping the heart and temporarily replacing its functions with the heart–lung machine has associated risks. Off-pump CABG has become an established and feasible procedure and has been demonstrated to offer a greater benefit in hemodialysis-dependent patients [4, 5]. Nevertheless, ESRD patients are likely to develop three-vessel coronary artery disease associated with severe calcification and the possibility of hemodynamic collapse during off-pump CABG affects the technical ability and comfort level of the surgeon. Because of its hemodynamic stability, on-pump beating-heart CABG has been adopted in our institute for hemodialysis-dependent patients. The present work evaluates the early outcome and long-term survival of hemodialysis-dependent patients after this procedure in comparison with the conventional approach utilizing cardioplegic arrest and the off-pump approach.

Materials and methods

Patients

The Institutional Review Board approved this study and waived the requirement for individual consent because of its retrospective manner. From January 2002 to January 2010, 2176 patients underwent CABG at our institute. Of these, 186 experienced chronic renal failure with regular hemodialysis at least 6 months before CABG. Of these 186 consecutive patients, 82 underwent conventional CABG with cardioplegic arrest, 56 underwent off-pump CABG and 48 underwent on-pump beating-heart CABG.
CABG. All patients underwent an isolated CABG procedure; patients who underwent a simultaneous procedure (for example, valve surgery) or a previous a cardiac operation were excluded from this study. Data were collected retrospectively from patient charts and presented as the mean value and SD of the mean.

**Surgical technique**

Procedures were performed using cardiopulmonary bypass (CPB) in the conventional CABG and on-pump beating-heart CABG groups. CPB was established by aortic inflow cannulation and right atrium outflow cannula with a single two-stage cannula. Left ventricular (LV) venting was performed only in the conventional CABG group. In the conventional CABG group, all anastomoses were performed under cardiac arrest using tepid blood antegrade or retrograde cardioplegia or both. The CPB flow was maintained at ~2.5 L/min/m² during the cardiac arrest period. In the on-pump beating-heart CABG group, all coronary anastomoses were performed using a commercially available stabilizer and heart positioner. The CPB flow was maintained at 1.5–2.5 L/min/m² during coronary anastomosis, depending on the hemodynamic status. In the off-pump CABG group, all coronary anastomoses were performed using a commercially available stabilizer and heart positioner without the assistance of the heart–lung machine. All aortic-side anastomoses for the free graft in these three groups were performed with partial aortic clamping.

**Statistical analysis**

Data were expressed as means ± SD. The results for categorical variables were expressed as percentages. Statistical comparisons between groups were computed using Student’s t-test or the χ² test, according to the type of data. Survival rates were computed by Kaplan–Meier methods followed by a log-rank test. The Cox proportional hazard model was used to calculate the influence of pre-operative and operative factors on survival. We estimated the relationship between the mortality on different cut-point days and the determinants of interest by logistic regression analysis, after adjusting for confounders. For all statistical evaluations, differences in data with P-values of <0.05 were considered statistically significant. All analyses were performed with the SPSS 16 statistical package (SPSS Inc., Chicago, IL).

**Results**

**Pre-operative characteristics**

The pre-operative characteristics of the patients are listed in Table 1. The pre-operative characteristics of the three groups were similar regarding sex, body mass index values, mean pre-operative duration of hemodialysis, chronic obstructive pulmonary disease (COPD), diabetes mellitus, hypertension, peripheral arterial disease, cerebrovascular accident and hyperlipidemia. The rates at which patients had previously been hemodynamically unstable, suffered unstable angina or myocardial infarction or experienced a percutaneous coronary intervention (PCI), including percutaneous transluminal coronary angioplasty with or without stenting, did not differ among the groups. The on-pump beating-heart CABG patients were significantly older than the patients in the other two groups (mean age: conventional CABG, 63.6 ± 10.5 years; off-pump CABG, 62.7 ± 11.9 years; on-pump beating-heart CABG, 68.3 ± 12.0 years; P = 0.03). The conventional CABG and on-pump beating-heart CABG groups included significantly more patients designated as New York Heart Association (NYHA) classification III or IV (conventional CABG, n = 70, 85.4%; off-pump CABG, n = 36, 64.3%; on-pump beating-heart CABG, n = 40, 3.3%; P = 0.01) or diagnosed with impaired LV function (mean ejection fraction: conventional CABG, 45.1 ± 13.7%; off-pump CABG, 55.2 ± 12.6%; on-pump beating-heart CABG, 40.9 ± 9.9%; P < 0.001) or moderate or severe LV dilatation defined as left ventricular end-diastolic dimension (LVEDD) ≥60 mm (conventional CABG, n = 19, 23.2%; off-pump CABG, n = 6, 10.7%; on-pump beating-heart CABG, n = 15, 31.2%; P = 0.04). Otherwise, the off-pump CABG and on-pump beating-heart CABG groups included significantly more patients with aortic calcification (conventional CABG, n = 29, 35.4%; off-pump CABG, n = 37, 66.1%; on-pump beating-heart CABG, n = 35, 72.9%; P < 0.001). The European System for Cardiac Operative Risk Evaluation (EuroSCORE) was calculated for every patient and used as a predictor of peri-operative mortality. The on-pump beating-heart CABG group had the highest EuroSCORE among the three groups (conventional CABG, 9.9 ± 5.6; off-pump CABG, 8.4 ± 3.6; on-pump beating-heart CABG, 11.4 ± 5.0; P = 0.01).

**Peri-operative surgical characteristics**

Peri-operative and post-operative patient characteristics are shown in Table 2. The on-pump beating-heart CABG group experienced a shorter CPB duration than the conventional CABG group. Patients in the conventional CABG and on-pump beating-heart CABG groups had significantly more diseased coronary arteries and mean distal anastomoses, but no statistical difference for patients undergoing complete revascularization was observed. The incidence of complications including intra-operative or post-operative intra-aortic balloon pump (IABP) initiation, pneumonia, arrhythmia, stroke, intestinal complications, low cardiac output syndrome and sepsis did not differ among the three groups. The duration of intensive care unit stay was shorter in the off-pump CABG and on-pump beating-heart CABG groups (conventional CABG, 7.0 ± 4.9 days; off-pump CABG, 3.6 ± 3.2 days; on-pump beating-heart CABG, 3.8 ± 1.6 days; P < 0.001). Prolonged ventilation for >24 h was significantly less common in the off-pump CABG group (conventional CABG, n = 28, 58.3%; off-pump CABG, n = 7, 8.5%; on-pump beating-heart CABG, n = 3, 5.4%; P = 0.01). The duration of post-operative hospital stay was shorter in the off-pump CABG and on-pump beating-heart CABG groups (conventional CABG, 16.5 ± 8.5 days; off-pump CABG, 12.6 ± 4.2 days; on-pump beating-heart CABG, 13.1 ± 4.2 days; P < 0.001). The post-operative pericardial drainage amount was significantly lower in the off-pump CABG and on-pump beating-heart CABG groups (conventional CABG, 820.7 ± 511.4 mL; off-pump CABG, 620.7 ± 241.8 mL; on-pump beating-heart CABG, 652.3 ± 265.0 mL; P < 0.01). The 30-day mortality rate was lower in the off-pump CABG and on-pump beating-heart CABG groups, but no statistical difference was observed (conventional CABG, n = 7, 8.5%; off-pump CABG, n = 3, 5.4%; on-pump beating-heart CABG, n = 2, 4.2%; P = 0.57).

**Survival**

Figure 1 shows the survival curve. The survival analysis included hospital mortality. The 2-, 4-, 6- and 8-year survival rates in the conventional CABG group were 70.1
The values in the on-pump beating-heart CABG group were 93.7 ± 3.5, 87.0 ± 5.0, 87.0 ± 5.0 and 87.0 ± 5.0, respectively. Significant differences in survival were observed among the three groups (P = 0.023). In the Cox proportional hazard model analysis, three factors...
were found to be significant predictors of long-term death (Table 3), EuroSCORE, aorta calcification and conventional versus on-pump beating-heart CABG.

Freedom from cardiac events

The cardiac events included cardiac death, myocardial infarction, repeated CABG, repeated PCI and congestive heart failure. The freedom from cardiac events curve is shown in Figure 2.

The 2-, 4-, 6- and 8-year freedom from cardiac event rates were 87.1\% \pm 4.0, 80.5 \pm 4.9, 76.3 \pm 5.5 and 65.8 \pm 8.4\% in the conventional CABG group, 94.3 \pm 3.2, 81.9 \pm 5.5, 58.0 \pm 7.8 and 47.4 \pm 8.5\% in the off-pump CABG group and 95.7 \pm 3.0, 86.7 \pm 5.1, 80.0 \pm 7.9 and 80.0 \pm 7.9\% in the on-pump beating-heart CABG group. There were no statistical differences among the three groups (P = 0.323).

Discussion

ESRD is a strong risk factor for in-hospital and long-term mortality after CABG [2, 6, 7]. In the present study, we compared the outcomes from different surgical techniques, namely conventional CABG with cardioplegic arrest, off-pump CABG and on-pump beating-heart CABG, in ESRD patients with hemodialysis; more specifically, we examined whether on-pump beating-heart CABG improves patient short- and long-term outcomes.

Cardioplegic arrest and the use of CPB have led to tremendous progress in CABG, but the non-physiological nature of this technique may lead to mortality and morbidity. There are several potential reasons why myocardial injury is induced by CABG including surgical manipulation, cardioplegia, aortic cross-clamping resulting in global ischemia and reperfusion damage, hypothermia and the use of the CPB. Off-pump CABG has the potential to reduce the several adverse effects of conventional CABG. Many authors have reported the superiority of this procedure regarding early or midterm outcome compared with the conventional approach [4, 5, 8]. The difference between these

| Table 3. Cox proportional hazard model for death at the time of long-term follow-upa |
|---------------------------------|---------|----------|---------|------------------|
| Perioperative surgical characteristics | Hazard ratio | 95% CI   | P-value |
| Age                                      | 0.981   | 0.932–1.033 | 0.47    |
| Gender (male versus female)              | 1.121   | 0.530–2.370 | 0.77    |
| BMI                                      | 1.012   | 0.921–1.111 | 0.81    |
| Smoking                                  | 0.963   | 0.423–2.192 | 0.93    |
| COPD (yes versus no)                    | 0.740   | 0.330–1.658 | 0.46    |
| PAD                                      | 0.995   | 0.481–2.057 | 0.99    |
| Ejection fraction                       | 1.023   | 0.995–1.052 | 0.10    |
| Number of diseased vessels              | 0.651   | 0.370–1.434 | 0.14    |
| Aorta calcification                     | 3.980   | 1.851–8.558 | <0.01   |
| NYHA > III                              | 0.493   | 0.182–1.332 | 0.16    |
| EuroSCORE                                | 1.337   | 1.164–1.534 | <0.001  |
| Operative factors                       |         |           |         |
| Number of anastomoses per patient       | 1.348   | 0.852–2.132 | 0.20    |
| Ventilation >24 h                       | 2.087   | 0.911–4.782 | 0.08    |
| Postoperative periocardial drainage amount | 1.000 | 0.999–1.000 | 0.48    |
| Hospital days                           | 0.981   | 0.932–1.033 | 0.48    |
| Group 2 versus Group 1                  | 0.276   | 0.104–0.731 | 0.10    |
| Group 3 versus Group 1                  | 0.091   | 0.030–0.271 | <0.001  |

aGroup 1: conventional CABG; Group 2: off-pump CABG; Group 3: on-pump beating-heart CABG. BMI, body mass index; DM, diabetes mellitus; PAD, peripheral arterial disease.
two techniques involves two major components: CPB and cardioplegic arrest. Elimination of CPB may reduce the physiologic derangement caused by the systemic inflammatory response [9, 10] and the direct complication that stems from the use of CPB. The avoidance of cardioplegic arrest may attenuate the myocardial injury caused by the perturbation of ischemia/reperfusion injury [11, 12]. However, it is still not known which component is more important for a good surgical outcome after off-pump coronary revascularization. In addition, the technical difficulty and the possibility of hemodynamic collapse during off-pump CABG remain limitations of this procedure. Therefore, beating-heart CABG with CPB provides optimal operative exposure without the impact of cardioplegic arrest for coronary revascularization.

Patients with ESRD who depend on hemodialysis generally have an increased risk of death due to cardiovascular and non-cardiovascular causes [13]. At the time of dialysis initiation, 19% of patients have severe LV hypertrophy. Only 23% of patients with ESRD exhibit regular cardiac function as determined by echocardiography [14]. In addition, a uremic environment is cardiotoxic and causes LV dysfunction [15]. Another important factor is hyperparathyroidism secondary to renal failure that has been demonstrated to be associated with accelerated atherosclerosis and the calcification of cardiac structures [16]. Therefore, ESRD patients have a 3- to 4-fold higher risk of death than other patients after CABG [2]. Limited clinical data revealed a benefit of CPB-supported beating-heart CABG in selected high-risk patients [17] by means of preserving native coronary blood flow, unloading the heart and guaranteeing adequate organ perfusion. Therefore, the present study was designed to assess the effects of beating-heart CABG with CPB in hemodialysis patients in comparison with off-pump CABG and conventional CABG with cardioplegic arrest. On-pump beating-heart CABG can eliminate the effect of cardioplegic arrest, and an acceptable trade-off has been reported between conventional CABG and off-pump CABG [18]. Although the indication for off-pump CABG differed between patients, off-pump procedures were performed in relatively safe cases, taking into account lesions, target vessels and pre-operative hemodynamic stability. In the report by Van Dijk et al. [19], only 25% of patients had triple-vessel disease; in contrast, 78% of patients had normal LV function, and the number of distal anastomoses per patient in the off-pump CABG group was remarkably lower than that in the conventional CABG group. The reason why patients in the off-pump CABG group received fewer grafts than patients in the conventional CABG group was that it was difficult to obtain satisfactory exposure of the lateral and posterior parts of the heart, leading to difficulties in off-pump CABG surgery [20, 21]. In patients in whom hemodynamic collapse was expected during anastomosis, such as those with lower LV ejection fraction, severe LV dilatation, multiple vessel disease and higher EuroSCOREs, off-pump CABG was rarely indicated in our institute. In contrast, in patients in which ascending aortic calcification was noted during operation, conventional CABG with cross-clamp of the aorta is avoided when possible. As shown in Table 1, the off-pump CABG patients had significantly lower EuroSCOREs, better LV ejection fraction and less severe LV dilatation. The conventional CABG patients exhibited significantly less aortic calcification.

Various authors have reported that the off-pump technique for CABG significantly reduces the incidence of perioperative myocardial infarction, hospital mortality, stroke and respiratory failure in some subgroups as compared with cardioplegic arrest [4, 22, 23]; our data presented here did not reveal significant differences regarding post-operative morbidity, including the incidence of pneumonia, arrhythmia, stroke, intestinal complications, sepsis, low cardiac output and additional intra-operative or post-operative IABP initiation in ESRD patients. The 30-day mortality rate was lower in the on-pump beating-heart CABG (4.2%) and off-pump CABG groups (5.4%) than in the conventional CABG group (8.5%), but no statistical difference was observed (P = 0.57).

Although various reports have suggested that the avoidance of CPB is superior for some subgroups regarding early mortality and morbidity, only a few reports discussing the impact of CPB on prolonged ventilation are available [24, 25]. Rothenburger et al. [25] demonstrated that cardiac surgery and CPB induce both pro- and anti-inflammatory immune responses. The imbalance of pro-inflammatory and anti-inflammatory mediators is of crucial importance for the post-operative systemic inflammatory response syndrome that is believed to prolong mechanical ventilation. Cislaghi et al. [24] analyzed 3269 CABG patients and found that a CPB time >91 min was an independent predictor of prolonged mechanical ventilation. In our data, the on-pump beating-heart CABG group had a lower CPB time than the conventional CABG group (106.8 ± 33.2 min for on-pump beating-heart CABG versus 145.4 ± 53.8 min for conventional CABG), and it was believed to contribute to the benefit regarding the time to extubation. However, the on-pump beating-heart CABG group did not exhibit a benefit regarding reduced prolonged ventilation for ESRD patients compared with the conventional group (P = 0.32).

The use of homologous blood products has been linked to increased neurological dysfunction, wound infection and long-term morbidity and mortality [26]. Therefore, reducing blood loss and transfusion is an important priority. The less common requirement of post-operative pericardial drainage and blood transfusion in the off-pump CABG group relative to the conventional CABG group has been described in the majority of previous reports [19–21]. The difference has been linked to hemodilution [27], the air–blood interface, hypothermia and the use of CPB [28, 29]. In our study, the amount of post-operative pericardial drainage in the on-pump beating-heart CABG group was approximately equal to that in the off-pump CABG group but was less than that in the conventional CABG group (P < 0.01). Our results revealed that the on-pump beating-heart technique did not significantly increase the amount of post-operative pericardial drainage compared to the off-pump technique. The elimination of hypothermia and decreased CPB time for the on-pump beating-heart technique resulted in less post-operative pericardial drainage than observed for conventional CABG with standard CPB.

The length of hospital stay after CABG is a function of numerous factors related to patient demographics,
comorbid conditions, the severity of coronary heart disease and post-operative morbidity [32]. The off-pump technique has demonstrated advantages in reducing the length of hospital stay. In our study, the length of post-operative hospital stay in the on-pump beating-heart group was similar to that in the off-pump CABG group but lower than that in the conventional CABG group (P = 0.001), although there were more confounding comorbid conditions, including older age, higher EuroSCORE, impaired LV function and more frequent aortic calcifications in the on-pump beating-heart group. The advantage of on-pump beating-heart CABG is that it provides optimal exposure of the coronary arteries and guarantees hemodynamic stability during operation.

The benefits of the off-pump technique have been affirmed in some studies of men, women, patients with compromised ejection fractions and elderly patients as well as patients with other comorbid factors, such as diabetes mellitus, renal insufficiency, COPD and a history of cerebrovascular disease [23, 33, 34]. Despite its widespread use and short-term efficacy, substantial uncertainty remains about the long-term outcomes of off-pump CABG, especially in ESRD patients. In the studies by Hu et al. [33] and Shroyer et al. [36], off-pump CABG is associated with small short-term gains but increased long-term risks of repeat revascularization and major vascular events, especially among high-risk patients. There are concerns about the accuracy and patency of the anastomosis [21, 37]. In a long-term 8-year observation, we found that the long-term risks of freedom from cardiac events were better for the on-pump beating-heart CABG patients than for off-pump CABG patients, although no statistical difference was observed. In contrast, the long-term survival was significantly better in the on-pump beating-heart CABG group than the other two groups, especially for the conventional CABG group (P = 0.009). As shown in Figure 1, the survival advantage of on-pump beating-heart CABG appears in the first post-operative year compared with conventional CABG and in the third post-operative year compared with off-pump CABG. Good evidence is available that incomplete revascularization at CABG can lead to poor long-term prognosis [36, 37]. Although the completeness of revascularization among the three groups was not significantly different, the tendency was toward a lower number of diseased coronary arteries in the off-pump CABG group (P < 0.001). In addition, the off-pump CABG group included fewer patients designated as NYHA classification III or IV or with impaired LV function, moderate or severe LV dilatation defined as LVD >60 mm and higher EuroSCOREs, which are believed to influence the surgical outcome. In the current study, Cox proportional hazard model analysis demonstrated the superiority of the on-pump beating-heart technique, but not for off-pump, compared to conventional CABG. Based on these experiences, we believe that the on-pump beating-heart technique provides optimal operative exposure and a more stable operative environment than the off-pump approach, and it reduces the reluctance of surgeons to graft small, multiple diseased and calcified coronary vessels. This technique combines the advantages of off-pump CABG with the better exposure provided by CPB to facilitate complete revascularization in hemodialysis patients with multiple vessel coronary disease.

Study limitation

There are a few limitations to this study. The lack of an objective means of graft function assessment is considered a limitation of this study in comparing the three techniques in terms of the patency of anastomosis. Indeed, the study is limited by its retrospective non-randomized nature, and it involves too many confounding factors to reveal any clear advantage of the on-pump beating-heart technique. In addition, due to the long observation period, the patient groups are not only representative for differential surgical approaches but also for different treatment period (Supplementary data). It would be ideal to have a prospective randomized study design for hemodialysis patients, restricted only to surgeons who are adequately experienced in all techniques.

Conclusion

In conclusion, the present study revealed that the operative strategy of using the on-pump beating-heart technique provides superior results for patients receiving hemodialysis regarding both short- and long-term outcomes.

Supplementary data

Supplementary data are available online at http://ndt.oxfordjournals.org/.

Acknowledgements. This work was supported by Tri-Service General Hospital (TSGH-C99-013-S02), National Defense Medical Center, Taiwan.

Conflict of interest statement. None declared.

References

On-pump beating-heart CABG in hemodialysis patients

the Society of Thoracic Surgeons National Adult Cardiac Database. Circulation 2006; 113: 1063–1070


Received for publication: 2.1.11; Accepted in revised form: 11.8.11