Outcome of Coronary Artery Bypass Grafting in End Stage Renal Disease Patients

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SUMMARY

Introduction: End stage renal disease (ESRD) patients have a much higher rate of cardiac disease and cardiac mortality as compared with the general population. Revascularisation such as coronary artery bypass grafting (CABG) may also carry a higher rate of complications and morbidity. We compared our ESRD patients who underwent CABG with the general population and ESRD population.

Methods: This is an observational study of ESRD patients who underwent CABG in our centre from 2003-2009 with case-control matching comparison with non-ESRD patients for ICU and hospital stay; and ESRD patients without CABG for survival. Patients with concomitant valvular operation were excluded. The primary outcomes were peri-operative complications and survival.

Results: Eleven patients with mean age of 57.5±8.5 were included. All except 1 were diabetics. One patient had excessive haemorrhage requiring immediate re-thoracotomy, and this was complicated with thrombosed AVF. Four patients experienced intradialytic hypotension post-operatively but all resolved within 1 week. Both ESRD and non-ESRD patients had equal number of ICU stay (3.1 versus 3.2 days, p=0.906) and hospital stay (7.6 versus 6.9 days, p=0.538). With average of 3.3 years follow-up (range from 1 to 7 years), 4 deaths were observed but only one from cardiac cause. Both ESRD cohorts with or without CABG have compatible left ventricular mass: 295 ± 86 vs 343 ± 113 g (p=0.226) and left ventricular mass: 174 ± 54 vs 206 ± 63 g/m2 (p=0.157). The outcome of CABG ESRD patients was comparable to matched ESRD patients without CABG with 90.9 % versus 91.9% 1 year survival, 95.5% versus 77.7% 2 year survival, 71.4% versus 70.3% 3 year and 40.0% versus 40.3% at 5 year survival (p=0.627, 0.386, 0.659 and 0.683 respectively).

Conclusion: CABG in ESRD patients carries an acceptable peri-operative complication rate. They have acceptable ICU and hospitalization duration in comparison to non-ESRD patients. Their long term survival was at least as good as matched ESRD patients without CABG.

KEY WORDS:
Coronary Artery Bypass Grafting, End Stage Renal Disease, Clinical Outcome

INTRODUCTION

ESRD patients have a much increased cardiovascular morbidity and mortality compared to age matched control. Mortality rate from cardiovascular disease (CVD) in ESRD patients has been reported to be approximately double to more than 10 times that of the general population and thus they should be considered the "highest risk group" when considering CVD risk factor intervention [1]. In the general population, CABG when compared to medical therapy, has been shown to reduce the risk of subsequent MI and improve survival in high risk patients which included those with left main stem disease, triple vessel disease, and those with reduced LV function [2,3].

The perioperative mortality of ESRD patients who underwent CABG has been reported to be approximately three times that of non-ESRD patients [4,5,6,7,8]. Recent nested case-control studies has shown that dialysis patients have longer duration of hospital stay after CABG in comparison to the matched non-ESRD control [9, 10]. The long term survival after CABG in this ESRD patients have also been reported to be lower than the non-ESRD patients [11, 12]. Many studies have utilized the CABG registry and perform logistic analysis or other relevant multivariate analysis in order to estimate the risk of complication and mortality with CABG and compared between ESRD and non-ESRD patients [4,5]. However, there are currently very few studies utilizing head-to-head matching of demographic profile to compare the clinical outcome between ESRD patients who have undergone CABG and those who have not.

We thus aim to compare outcome of our ESRD patients who have undergone CABG with ESRD population who have not, as well as the post-CABG non ESRD patients. We hope this will give us a clearer picture as to the actual outcome of CABG in ESRD population.

MATERIALS AND METHODS

Study design and population

This is an observational study of ESRD patients who underwent CABG in our centre from 2003 to 2009. The cases were retrospectively surveyed prior to year 2007 while prospectively surveyed from 2007 onwards. Patients with concomitant valvular operation were excluded. All ESRD CABG patients were recorded without exception. Their names

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were listed in Operational Theatre Book of cardiothoracic surgery for Kuching Hospital. We have performed CABG without valvular surgery for 6 ESRD patients prior to year 2007 and 5 patients after year 2007.

The primary outcomes were peri-operative complications and survival. The intensive care unit (ICU) and hospital stay were compared between the ESRD and non-ESRD patients. The survival of ESRD patients who underwent CABG was compared with matched non ESRD CABG population from the CABG registry of our hospital, as well as the ESRD patients without CABG from the ESRD registry of our hospital. We matched them according to age, gender, diabetes and hypertension status, as well as year of commencing dialysis, dialysis duration and dialysis modality to the historical controls.

All CABG patients and ESRD patients were followed-up from the day of CABG or the commencement of haemodialysis. Duration of follow-up ranged from 1 to 7 years with an average of 3.3 years. The great majority of our patients have undergone off-pump CABG.

Left Ventricular Assessment
We defined left ventricular mass with:
$LVM = 1.04((LVIDd+IVSd+LVPWd)^3 – LVIDd^3) -13.6$.
LVM index = LVM/ body surface area.

Whereby
- LVDd: left ventricular diameter at the end of diastole,
- IVSd: interventricular septum thickness at the end of diastole,
- LVPWd: posterior wall thickness of left ventricle at the end of diastole.

Left ventricular hypertrophy, LVH will be defined as LVMI >= 134 g/m^2 for male patients and LVMI >= 110 g/m^2 for female patients [13].

Statistical Methods
The statistical data were analyzed using Microsoft excel and SPSS (Statistical package for Social Science. SPSS Inc. 233 South Wacker Drive, 11th Floor, Chicago, Illinois 60606-6307).

Kolmogorov Smirnov test was initially used to determine whether the data is in statistical normal distribution. Basic demographic profile of the CABG ESRD cohort and their matched control subjects were documented in table I. Mean ± standard deviation was shown. Geometric transformation was performed with natural log in duration of hospital stay to achieve the Gaussian distribution. This was followed by appropriate parametric or non-parametric test. Univariate analysis was performed with parametric test (e.g., paired student t-test for ejection fraction pre and post-operation, independent samples t-tests for other purposes).

In view of varying surveillance duration of the subjects in all cohorts, Cox regression hazard ratio analysis, rather than log rank test, was performed to compare the survival of ESRD patients and matched ESRD patients without CABG.

RESULTS

Clinical profile of ESRD CABG Cohort
There were a total of 11 ESRD patients who underwent CABG in our centre during this period of time. All were on hemodialysis (HD) with mean and median of prior dialysis duration of 10 months and 6 months respectively. There were 9 males and 2 females and their age ranged from 44 to 73 years old. All were diabetic except one who had unknown cause of ESRD.

Indication for CABG based on coronary angiogram, could be classified as triple vessels disease (7 patients), double vessels disease (DVD) with left anterior descending (LAD) conorary artery involvement (3 patients) and DVD plus left main stem and LAD involvement (1 patient).

Patients also have symptoms such as, intradialytic hypotension (4 patients), unstable angina (4 patients), chest pain during HD (1 patient), and non-specific cardiac symptoms with echocardiogram finding of regional wall dysmotility (2 patients).

Previous comorbidities of these ESRD cohort included ischaemic stroke for two patients, a case of previous myocardial infarction and a case of chronic atrial fibrillation on warfarin. There was an incidental case of dextrocardia. All patients had haemoglobin level of ≥ 10 g/dL and their nutrition was reasonable with albumin ≥ 35 g/L before the CABG.

Perioperative complication
One patient had excessive haemorrhage post op requiring immediate re-thoracotomy, and this was complicated by thrombosis of AVF. The other patients' vascular access did not have any problem. Four patients experienced intradialytic hypotension post-operatively but all resolved within 1 week. All patients were able to continue hemodialysis post operatively and none needed continuous renal replacement therapy.

Changes in Left Ventricular Contractility
Nine out of the eleven patients have ventricular regional wall dysmotility on pre-operative echocardiogram involving either apical, anterior, septal and/or inferior cardiac wall while the other 2 patients have no regional wall dysmotility.

Among these 9 patients with regional wall dysmotility, 3 improved with CABG and maintained good regional wall motility for at least 3 months; 1 improved transiently (noted on intra-op transoesophageal echocardiogram) but not sustained (as shown on post-op transthoracic echocardiogram); 5 had no significant changes with CABG.

Modified Simpson's Method was used primarily to assess changes of ejection fraction on echocardiogram. Pre-operative ejection fraction was 46 ±12%, and EF was 45% +/- 12 % one week post-operation and 51% ± 10% one to two months post operatively. Four patients have greater than 10% improvement in ejection fraction ; six patients have no significant changes in ejection fraction while 1 patient have greater than 10 % reduction in ejection fraction post CABG. All survived patients have good effort tolerance as well as haemodialysis tolerance.

Table I: Basic Demographic Profile of ESRD CABG patients, Matched non-ESRD CABG patients and Matched ESRD patients without CABG

		ESRD CABG patients	ESRD patients without CABG	p-value
Age on initiation of dialysis	year	56.7 ± 8.8	56.2 ± 9.5	0.852
Left ventricular mass	g	295 ± 86	343 ± 113	0.226
Left ventricular mass index	g/m^2	174 ± 54	206 ± 63	0.157
Ejection Fraction*	%	48.7 ± 11.0	58.1 ± 14.4	0.044

*Baseline Ejection Fractions were derived from average of Modified Simpson's Method and Teich Method.

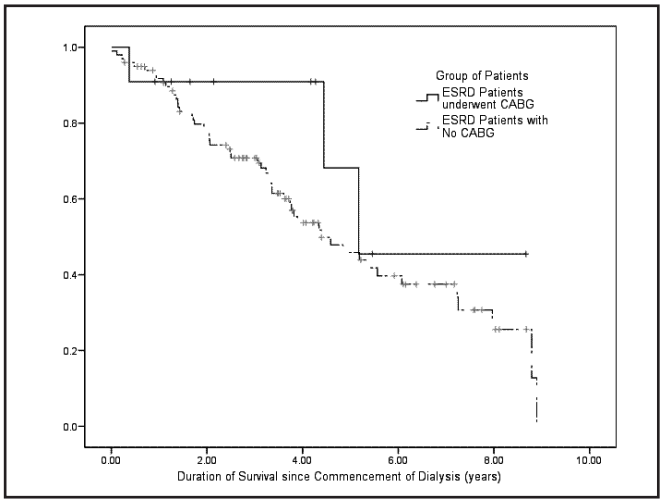

Fig. 1: Kaplan Meier Survival curve for all cause mortality in ESRD CABG patients versus ESRD patients without CABG Kaplan-Meier estimates of survival were plotted. Cox regression survival analysis showed hazard ratio of 0.71 (Confidence interval: 0.22 - 2.29, p=0.567) in ESRD CABG patients versus ESRD patients without CABG.

Survival

There were 4 deaths (36% out of 11 patients) but only one from cardiac cause, i.e., biventricular heart failure, deceased 3 months after CABG. Besides, two deaths were due to brain stem haemorrhage, hyperkalaemia, occurring 4.5 and 6.8 years after CABG. There is another fatal case with cervical vertebral fracture as a result of motor vehicle accident.

The average number of CICU (Coronary Intensive Care Unit) stay was 3.1 days and hospital stay was 7.6 days. The one-year, two-year, three-year, four-year and five-year survivals for the ESRD CABG cohort were 90.9%, 88.9%, 71.4%, 66.7% and 40.0% respectively.

Comparison with Non ESRD CABG Cohort in duration of CICU and hospital stay

There were a total of 198 non-ESRD patients who underwent CABG at our centre during this period of time. The mean age for both groups was 58 years and both groups have male predominance, 82% (Male:female (M:F) = 9:2) and 87% (M:F = 172:26) respectively (p=0.645). However, ESRD cohort has a markedly higher prevalence of diabetes mellitus (DM), i.e., 91% (10 out of 11 patients) vs 42% (84 out of 198 patients) compared to the non ESRD cohort (p=0.002).

In view of the high prevalence of diabetes mellitus among ESRD patients who underwent CABG, diabetes status was matched in our outcome analysis together with other factors. Every ESRD CABG patient was matched to 2 non-ESRD CABG patients based on age, gender, diabetes, hypertension status and time (year) of CABG. Twenty-two best matched controls were identified.

Both ESRD patients and non-ESRD patients have equal number of CICU 3.1 ± 1.1 days versus 3.2 ± 3.7 days (p=0.906) and hospital stay 7.6 versus 6.9 days (geometric mean, p=0.538).

Comparison with matched ESRD patients without CABG in survival

Every ESRD CABG patient was matched to 9 ESRD haemodialysis patients as control based on age, gender, diabetes, hypertension status, year of commencing dialysis and duration of dialysis. 11 x 9 = 99 best matched controls were identified. Therefore, Diabetes: non-diabetes patients number was 90:9 in ESRD control while ESRD CABG patients was 10:1. Gender ratio of male:female patients number was 81:18 in ESRD control while ESRD CABG patients was 9:2. Their clinical profiles were presented in table I with significantly lower EF in ESRD CABG patients in comparison to ESRD patients who did not have CABG. Among the patients with detail echocardiogram measurements, 8 out of 9 ESRD CABG patients have left ventricular hypertrophy (LVH) in comparison to 55 out of 58 ESRD patients without CABG (88.9 vs 94.8%, p=0.446). Besides, regional wall dysmotily was recorded as 4 out of 9 in ESRD CABG patients while 12 out of 63 in ESRD patients who did not have CABG (p=0.086).

The survival curves are comparable between the two groups as shown in figure 1. The ESRD patients without CABG have a recorded 91.9% 1 year survival, 77.7% 2 year survival, 70.3% 3 year survival, 52.4% 4 year survival and 40.3% (p=0.118) 5 year survival (with comparative p-value 0.627, 0.386, 0.659, 0.406 and 0.683 respectively).

DISCUSSION

ESRD patients have a high risk of cardiovascular disease and mortality. Outcome of interventions such as CABG is unclear and could be associated with significant perioperative complications and mortality.

Powell KL *et al* has shown that the hospitalization duration was longer in 28 ESRD patients during CABG compared to the non-ESRD 84 matched control subjects with 1:3 matching [11]. In a retrospective study of non-dialysis patients and dialysis patients undergoing CABG in 2001, dialysis patients had a markedly increased risk of in-hospital mortality (11.1% versus 3.4%, odds ratio 3.38, confidence interval: 2.54 - 4.50) [5]. The long term survival of ESRD patients undergoing CABG was also reported to be poor previously, i.e., 56% 2 year survival[14].

In our study, among ESRD patients undergoing CABG, the perioperative complication rate was low and the number of ICU and hospital stay was comparable to non-ESRD matched population (3.1 versus 3.2 days, p=0.906 and 7.6 versus 6.9 days, p=0.538 respectively). We did not record any peri-operative fatality in our small ESRD CABG cohort, and the long term survival was also acceptable.

The differences in outcome could be due to various reasons. The great majority of CABG in our hospital was done off pump which has been reported to be associated with lower morbidity and mortality. Analysis of United States Renal Data System has also shown that Off-pump CABG was associated with significantly reduced all-cause mortality compared with on-pump coronary artery bypass surgery (hazard ratio 0.92, p = 0.02) [15] in ESRD patients. Our patients also have good Hb and albumin before the CABG. Careful selection and diligent optimization of patients may also contribute to the good result. Hence, the better reported outcome in our study is likely due to overall better management of the ESRD patients undergoing CABG in this current era. One recent study also showed substantial improvement of perioperative mortality rate among ESRD patients from 31% to 5.4% (versus 4.7% to 1.8% among non-ESRD) over a 5 years period [4]. The median length of in-hospital stay dropped in half from 25 to 13 days (versus 14 to 10 days among non-ESRD) [4].

In our study, we compare the long term survival of our ESRD patients undergoing CABD and that of ESRD patients without CABG. This, to our knowledge, has not been reported before. Our result showed that the survival of our ESRD patients undergoing CABG is comparable to those ESRD patients without CABG albeit not in statistical significance. This might be due to the potential bias in the selection of candidate for CABG, whereby CABG surgery might only be performed in patients who were clinically fit. Anyway, the ejection fractions were significantly lower in CABG patients and incidence of regional wall dysmotility higher, while their left ventricular mass indexes were compatible.

Our study showed that CABG can be done safely in ESRD patients with acceptable perioperative complications. The length of CICU and hospital stay and first 2 year survival was also comparable to those non ESRD patients undergoing CABG. When compared with other matched ESRD patients without CABG, their short and long term survival was comparable.

Analysis of the Nationwide Inpatient Sample database of United State showed that, annual rates of CABG among ESRD patients doubled from 2.5 to 5 per 1000 patient-years from 1988 to 2003 [4]. Meanwhile, patients with greater co-morbidities such as diabetes and hypertension are increasingly undergoing CABG [4]. Our study serves as a reassurance that CABG can be done safely in appropriate ESRD patients with acceptable short and long term outcome.

One limitation of our study is the small number of ESRD patients with CABG. As this is a retrospective study, it also has its in-built designing defect which should be rectified with larger prospective study. We suggest clinical status and co-morbidity matching as a tool for constructing appropriate control in a larger cohort to further analyse the outcome of CABG in ESRD patients in the future. This might potentially aid in the development of current clinical practice guidelines in management of cardiovascular disease in dialysis patients [16].

Finally, based on our result, we should not be hesitant to recommend ESRD patients for CABG if indicated as they have acceptable perioperative complication rate, length of ICU and hospital stay and acceptable short and long term survival.

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