ARTIGO ORIGINAL ORIGINAL ARTICLE

CARDIAC SURGERY IN PATIENTS WITH DIALYSIS-DEPENDENT END STAGE RENAL FAILURE: SINGLE CENTRE EXPERIENCE

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Abstract

Background: Patients under dialysis have a high cardiovascular risk and they are at increased risk when submitted to cardiac surgery.

Aim of the study: to evaluate morbidity, early and late mortality, and predictive factors of mortality in patients under dialysis who underwent cardiac surgery.

Methods: A retrospective observational study was performed including all dialysis dependent patients who underwent cardiac surgery (coronary, valvular or combined procedures) in our institution between 2007 and 2014. A population of 95 consecutive patients was obtained (no exclusions). Perioperative variables and predictors of mortality were analysed and the endpoints were early and late mortality. Propensity score matching, with a control group of patients with creatinine clearance >90mL/min, was performed by logistic regression, with a 1:1 matching. Kaplan Meier curves were performed for late mortality.

Results: Early mortality was 9.4% (EuroSCORE II 4.1%). In univariate analysis, mean time of cardiopulmonary bypass (CPB) ($p=0.016$) and EuroSCORE II ($p=0.02$) were related with early mortality. In a multivariate analysis model, combined procedures (OR 138.09; CI95% 1.82-10498.4; $p=0.03$) and CCS (Canadian Cardiovascular Society) 3-4 (OR 70.951; CI 95% 1.32-3810.11; $p=0.037$) were predictors of mortality. In multivariable analysis, CPB time >152 min was a predictor of early mortality ($p=0.001$). After propensity score matching, 30 day, one year and late mortality were higher in the dialysis group.

Conclusions: Early and late mortality were significantly higher in dialysis dependent patients. Predictive factors of mortality were CPB time and EuroSCORE II in univariable analysis, and CCS 3-4 and combined procedures in multivariable analysis.

INTRODUCTION

The incidence and prevalence of patients with renal failure who need kidney replacement therapy is increasing. In Portugal there were 11738 patients (1135 patients per million population) undergoing hemodialysis in 2016.[1] Dialysis dependent patients develop coronary and valvular disease earlier and more frequently than the general population. In 2016, dialysis patients global mortality was 13.09% and death due to cardiovascular disease was 24.6%.[1]

Accounting for this cardiovascular burden, non-specific and specific risk factors are identified, including vascular and valvular calcifications and left ventricular hypertrophy. Consequently, surgical risk is greater.[2] However, studies have been conflicting regarding mortality and its predictors in dialysis patients. Thus, it continues to be unclear which patients benefit from surgery and when is surgical risk prohibitive.

The purpose of this study was to characterize end stage renal disease (ESRD) patients under dialysis who underwent cardiac surgery in one institution, to evaluate morbidity, early and late mortality, time to discharge and determine predictive factors for these outcomes.

MATERIALS AND METHODS

A retrospective observational study was performed including all ESRD-dialysis dependent patients who

underwent cardiac surgery in one institution between 2007 and 2014. No exclusion factor was applied. The population was characterized regarding perioperative variables, including EuroSCORE I and II and the endpoints were early (≤30days after surgery) and late mortality (mortality during follow up). Mortality was obtained from consultation of a national register, with a follow up rate of 100%. Mean follow-up was 3.6 ±2 years.

Patients

A population of 95 ESRD-dialysis dependent patients was obtained (96% haemodialysis; 4% peritoneal dialysis). Mean age was 65±11 years (range 33 to 88 years), 81% were male. Preoperatively, 33% had previous history of acute myocardial infarction; 35% had an ejection fraction <50%. (Table 1)

Table 1 **Cardiovascular risk factors and other preoperative characteristics. Extracardiac vascular disease: Cerebrovascular disease, peripheral vascular disease, claudication.**
(CCS: Canadian Cardiovascular Society; NHYA: New York Heart Association)

Male gender	77	81%
Diabetes mellitus	35	36.8
Dyslipidaemia	43	45.3
Smoking	25	26.3
Overweight/obesity	48	50.5
Hypertension	79	83.2
Extracardiac vascular disease	32	33.7
Cerebrovascular disease	18	18.9
Poor ejection fraction (<30%)	3	3.2
NYHA III/IV	23	24.2
CCS 3/4	22	23.2
Urgent/emergent operation	17	18%

Patient management protocol

Dialysis patients are always referred to the Nephrology service on admission so that a pre-operative dialysis session can be performed. Post-operative surveillance is maintained by the nephrology team. This ensures optimal hydroelectrolytic and metabolic status at the time of surgery and adequate management in the perioperative period.

Statistical analysis

Statistical analysis, including univariable and multivariable analysis (logistic regression) to identify predictors of early mortality were performed using SPSS v. 20. A p value of 0.05 or less was considered significant. A propensity score matching model was performed by logistic regression, including all variables statistically and clinically relevant (age, sex, comorbidities, preoperative status, type and characteristics of surgical procedure and mortality) with a 1:1 matching. The control group included all patients submitted to cardiac surgery during the same time frame with estimated creatinine clearance >90mL/min based on Cockcroft Gault equation (n=2144). Kaplan Meier curves were performed for late mortality.

RESULTS

Regarding timing of surgery, 77 were elective and 17 were urgent/emergent. Reoperations accounted for 8.5% of total of surgeries. Procedures performed are presented in Table 2.

Table 2 **Procedures performed**

Main procedures	N =95	%
Coronary artery bypass graft	42	44%
Valvular surgery Isolated aortic valve Multiple valve	33 22 11	35% 23% 12%
Combined valvular and coronary surgery	11	12%
Other procedures	9	9%

Cardiopulmonary bypass (CPB) was used in 63.2% of surgeries. Mean time of CPB was 110 ± 50 minutes (minimum 20 minutes, maximum 256 minutes).

Revascularization included 2.3±0.96 grafts/patient, arterial grafts in 92.7% and complete revascularization in 74.1%. Among coronary artery bypass graft (CABG) surgeries, 71.4% (30 cases) were performed off pump.

Valvular surgery involved 48 prosthetic valves (44% of which were mechanical) and 11 valve repairs. Two aortic valve replacements were performed off pump (transapical approach).

Early mortality was 9.4% (EuroSCORE 9.5%, EuroSCORE II 4.1%) (Table 3). The median time of in-hospital stay after surgery was 8 days. One-year mortality was 18.9%. Mortality at the end of follow-up (3.6 ±2 years) was 33.7%.

Table 3 **EuroSCORE I and II and early mortality.**
(CABG: coronary artery bypass graft)

	CABG (n=42)	Valvular surgery (n=33)	All patients (n=95)
EuroSCORE I (mean)	7.5%	10.7%	9.5%
EuroSCORE II (mean)	3.4%	5.3%	4.1%
Early mortality (%)	4.8%	9.1%	9.4%

Regarding CABG, early mortality was 0% (0 out of 30) in off pump surgery and 14% when on pump (1 death out of 7 patients). In univariate analysis, mean time of CPB ($p=0.016$) and EuroSCORE II ($p=0.02$) were related with early mortality (Table 4).

Table 4 **Univariable analysis of early mortality**
(CCS: Canadian Cardiovascular Society; CPB: cardiopulmonary bypass; NHYA: New York Heart Association)

	p
Diabetes mellitus	0.282
Dyslipidaemia	0.694
Hypertension	1.000
Extracardiac arteriopathy	0.713
Low ejection fraction (<30%)	1.000
NYHA III/IV	0.035
CCS 3/4	0.428
Mean time of CPB	0.016
EuroSCORE II	0.02

In a multivariate analysis model, combined procedures and CCS 3-4 were predictors of mortality with an OR 138.09 (CI95% 1.82-10498.4; $p=0.03$) and OR 70.951 (CI 95% 1.32-3810.11; $p=0.037$) respectively (Table 5).

With ROC curves analysis, CPB time >152 minutes was the cut-off value for increased risk of early mortality. In multivariable analysis, CPB time >152 min was a predictor of early mortality ($p=0.001$).

Propensity score matching

In order to compare mortality in this population with a control group with normal renal function (estimated creatinine clearance > 90ml/min), propensity score matching 1:1 was performed. The characteristics of the control (normal renal function) group are presented in table 6.

Table 6 **Normal renal function (control) group.**
(CCS: Canadian Cardiovascular Society; CPB: cardiopulmonary bypass; NHYA: New York Heart Association)

Male gender	77	81%
Diabetes mellitus	44	46%
Smoking	11	12%
Overweight/obesity	52	55%
Hypertension	64	67%
Extracardiac arteriopathy	10	11%
Cerebrovascular disease	17	18%
Poor ejection fraction (<30%)	2	2%
NYHA III/IV	23	24%
CCS 3/4	16	17%
Urgent/emergent operation	14	15%
Age (mean)	62 years	
EuroSCORE II (mean)	2.1%	
CBP time (mean)	95 minutes	

After propensity score matching, 30 day and 1 year mortality were significantly higher in the dialysis group comparing with the control group. (Table 7) Analysis of

Table 5 **Multivariable analysis of early mortality.**
(BMI: body mass index; CI: confidence interval; CCS: Canadian Cardiovascular Society; CPB: cardiopulmonary bypass; NHYA: New York Heart Association; OR: odds ratio)

Variables	OR	95% CI	*p*
CPB	1.586	0.07-34.32	0.77
Urgent/emergent	1.135	0.14-9.35	0.91
Combined procedures	138.090	1.82-10498.4	0.03
CCS 3-4	70.951	1.32-3810.11	0.04
Diabetes mellitus	1.757	0.23-13.68	0.59
Extracardiac arteriopathy	0.164	0.01-2.63	0.20
NHYA III/IV	5.817	0.61-55.77	0.13
Ejection fraction	0.000	0-0	1.00
BMI	1.166	0.94-1.45	0.16
Age	1.028	0.92-1.14	0.61
Female	0.221	0.01-3.8	0.30
Cerebrovascular disease	0.806	0.01-43.97	0.92
Pulmonary disease	2.177	0.1-49.19	0.62
Coronary disease	1.392	0.04-43.47	0.85

Table 7 **Comparison of early and one year mortality in the dialysis *vs.* the control (normal renal function) group.**

	Dialysis group	Control group	*p*
Early mortality (≤30days)	9.4%	0%	<0.001
1-year mortality	18.9%	3.2%	<0.001

late mortality using Kaplan Meier curves also demonstrated a higher mortality of the dialysis group (figure 1).

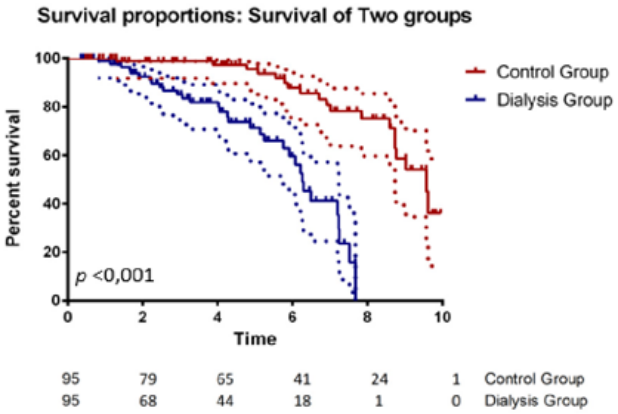

Figure 1 *Kaplan Meier curves for survival of control (normal renal function) and dialysis groups after propensity score matching (time in years).*

DISCUSSION

Overall mortality due to cardiovascular disease is more frequent in dialysis-dependent patients (30% to 50%) than in an age-corrected control population (less than 15%).[3,4]

Coronary heart disease affects 30%–60% of patients with ESRD.[5] This high incidence is related with predisposing factors such as hyperlipidaemia, hypertension, anaemia, fluid overload, platelet dysfunction and disturbances of calcium phosphate metabolism.[6] ESRD patients usually present multivessel disease, and present with proximal lesions, extensive calcifications, or diffuse disease.[5]

Due to the coexisting noncardiac morbidities, the deleterious consequences of renal disease and dialysis, perioperative results and long term mortality of cardiac surgery have been worse in dialysis patients.[3] Furthermore, indications and referral for operation may often be delayed in patients with ESRD and this may also contribute to the high perioperative mortality.[7] However, although perioperative risk of dialysis-dependent patients is higher, it is not prohibitive, and good candidates for surgery can be identified.[8]

According to Ko *et al.*, the overall operative mortality of dialysis patients reported in the literature was 9% in 1993. In isolated CABG procedures it was 9%, 12% in valvular operations and 13% in combined CABG with valvular operations.[9]

Horst *et al.* reviewed available literature in 2000 obtaining 863 patients over 30 years and described a perioperative mortality rate for isolated CABG, isolated cardiac valve operation, and combined procedures of 8.9%, 19.3%, and 39.5%, respectively. Overall perioperative mortality rate was 12.5% combining all cardiac surgical procedures with CPB.[10]

More recently, Nicolini et. al. revised 18 reports with a total of 1725 dialysis patients submitted to heart surgery and presented a mean perioperative mortality rate of 13.3% (range 0 to 36.7%).[11]

Takami *et al.* reported an in-hospital mortality of 9.8% in a group of 245 haemodialysis dependent patients.[12] In a study with 45 patients, thirty-day mortality was 13.3% and late mortality was 46.6%.[13]

Yamauchi *et al.* compared 1,300 HD-dependent chronic renal failure patients with 18,387 non-HD patients submitted to isolated CABG and described a 30-day mortality of 4.8% *vs.* 1.4% in the HD and non-HD groups, respectively.[14] Operative mortality and major complications were also more frequent in the HD group (23.1% *vs.* 13.7%).[14]

In a study including 5308 patients who underwent valve surgery, including 224 dialysis dependent patients, the in-hospital mortality rate for the entire cohort was 5.7% (n = 304) and it was significantly higher for those under dialysis before surgery (18.3% *vs* 5.2%; $p < .0001$).[15]

Deutsch *et al.* obtained a 30-day mortality of 17.6% in a group of 204 patients. The highest mortality rates occurred in patients undergoing combined procedures.[2]

Rahmanian *et al.* in a series of 245 patients with end-stage kidney failure requiring dialysis stratified mortality by procedure and obtained the highest mortality rate in patients undergoing single/multiple valve procedures (17.1%), followed by combined valve/CABG (12.8%), isolated CABG (10.3%), and aortic (9.1%) procedures. Overall hospital mortality was 12.7% and the EuroSCORE was 18%.[16]

Yamamura studied 76 dialysis patients and reported an overall in-hospital mortality rate of 17.1%. In patients undergoing CABG the hospital mortality rate was 13.8%, in aortic valve replacements (AVR) it was 12.5% and in AVR plus CABG 33.3%.[17]

Therefore early mortality in our centre (9.4%) is comparable to that reported in literature and to EuroSCORE. Mortality according to procedure (4.8% for isolated CABG and 9.1% for isolated valvular surgery) is favourable compared to other reports in literature.

Rahmanian *et al.* also described 1-year, 3-year, and 5-year survival of 72.3%± 3.3%, 53.3%± 4.0%, and 39.0% ± 4.5% respectively in a series of 214 discharged patients.[16]

Yamamura obtained a 5-year overall survival rate of 39% ±8%.[17] The 1-year survival rate for isolated CABG

was 77.0% ± 0.7 %; for isolated AVR was 79.0% ±0.8% and for concomitant surgery was 21% ±18%. In this last group, survival was significantly poorer.[17]

One year (18.9%) and late mortality in our series (21.9%) is in the range of that reported by other authors.

Regarding predictors of mortality, many have been pointed out in different studies. In the study by Yamauchi *et al.*, age, chronic obstructive pulmonary disease, peripheral artery disease, congestive heart failure, arrhythmia, preoperative inotropic agent requirement, New York Heart Association class IV, urgent or emergent operation, poor left ventricular function, aortic valve regurgitation (>2), and mitral valve regurgitation (>3) were indicated as preoperative predictors of operative mortality in the dialysis group.[14]

Horst et. al. described duration of dialysis equal to or longer than 60 months, and NYHA class IV as being associated with substantially increased relative risk for perioperative death.[10]

Yamamura *et al.* showed that age higher than 70 years, low-output and concomitant surgery were significant risk factors for mortality in a univariate logistic analysis. The multivariate logistic analysis described concomitant surgery (odds ratio 4.37, $p<0.007$) as the only significant risk factor for mortality.[17] Horst *et al.* also reported combined procedures as a risk factor for mortality based on a univariate logistic analysis.[10] Rahmanian *et al.* identified peripheral vascular disease as an independent predictor for mortality.[16]

NYHA class IV and emergent operation were appointed as risk factors for mortality by Ko *et al.* based on a univariate logistic analysis.[9] Takami *et al.* identified only diabetes mellitus as an independent predictor of hospital mortality with an odds ratio of 2.74.[12]

Age, blood product usage and postoperative pulmonary complications have also been described as significant predictors of 30 day mortality and late death.[13]

In the current study, only CCS 3-4 and combined procedures were statistically significant predictors of mortality.

Regarding higher risk compared to general population, Rahmanian *et al.* adjusted for potential confounding factors, and concluded that end-stage kidney failure requiring dialysis was a predictor of hospital mortality (odds ratio, 3.1; $p<0.001$).[16] Propensity score matching found in literature was only used to compare CABG vs PCI or included preoperative non-dialytic renal disease.[18]

After matching our study and control groups, we concluded that 30 day, one year and late mortality were significantly higher in the dialysis group, which did not come as an unexpected result.

Limitations to this study are related to its retrospective and single-centre study and the relatively small number of patients.

CONCLUSIONS

Patients submitted to cardiac surgery who are under dialysis are known to be at higher risk of morbidity and mortality. In our study, early and late mortality was significantly higher in dialysis dependent patients comparing with patients with normal renal function. CPB time and EuroSCORE II were predictive factors of mortality in univariable analysis, whereas CCS 3-4 and combined procedures were related with higher mortality in multivariable analysis. However, EuroSCORE II may underestimate the true risk of this group of patients. This study has limitations due to its retrospective, single-centre and small-sampled methods. A study with a larger number of patients, multicentric and prospective would be the ideal methodology to analyse this population and optimize care according to their specific characteristics.

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