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Adverse Cardiovascular Events in Post-Renal Transplant Patients, a Retrospective Study of Five Hundred Cases Over Twenty-Two Years

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Abstract

Background Renal transplant recipients (RTRs) remain at an increased risk of fatal and non-fatal cardiovascular (CV) events compared to the general population. Death is most commonly due to cardiovascular diseases.

Purpose The primary outcome of this work is the determination of adverse CV events and their risk factors in the RTR population and their effect on mortality.

Methods A retrospective analysis has been performed on data from 500 patients at the Cairo Kidney Center, Cairo, Egypt, who underwent kidney transplantation with a graft from a living donor. Data was collected for RTR starting from 1992 till 2014.

Results The mean age of patients was 41.90 ± 9.67 years. 63.8% of them were males. CV complications (stable angina pectoris, acute coronary syndrome, new left ventricular hypertrophy (LVH), positive myocardial perfusion scan, elevated cardiac enzymes, and invasive coronary angiography) occurred in (22.6%, 2.4%, 49.8%, 13.6%, 1.8%, and 7.6%) of patients, respectively. Other CV complications occurred in (24.0%, 11.2%, and 40.8%), including Congestive Heart Failure (CHF), cardiomyopathy, and arrhythmias.The main causes of mortality were CV diseases, infections, cancer, surgical complications, and liver disease (19.0%, 13.4%, 1.6%, 1.4%, and 1.2%), respectively.

Conclusion RTR are at an extremely high risk of adverse CV events. CV complications (CHF, ischemic heart diseases, LVH, and arrhythmias) are the leading causes of death in RTR.

Keywords Cardiovascular disease · Hypertension · Dyslipidemia · Cardiomyopathy · Arrhythmia · Cerebrovascular accidents

Introduction

Kidney transplantation is undertaken to improve the quality and length of life of individuals with end-stage kidney disease. Studies have shown that although transplantation improves life expectancy compared with dialysis, survival remains well below general population estimates [1]. Approximately 50% of patients die with a functioning transplant, with approximately 50% of these deaths from cardiovascular disease or stroke [2]. Patients with chronic kidney disease (CKD) and those on dialysis, in particular, have an elevated CV risk compared to the general population [2]. Patients have a high burden of CV disease before receiving a transplant [3]. Determining the incidence of CV events after a kidney transplant and the associated risk factors is therefore important in order to inform physicians of the need for CV disease screening and prevention as part of the transplant evaluation [4]. Transplantation has been shown to reduce CV events [5].

CV diseases are still the major known cause of death in kidney transplant patients [2]. CV diseases are an umbrella term which covers congestive heart failure (CHF), coronary artery disease (CAD), cerebrovascular disease, and peripheral vascular disease. In addition to the conventional CV disease risk factors (such as obesity, smoking habits, diabetes, hypertension, or dyslipidemia), several other factors seem to influence the high incidence of cardiovascular events in

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renal transplant patients. These include the duration of prior dialysis, graft function after transplantation, hyper-homocysteinemia, elevated inflammatory markers, proteinuria, acute rejection episodes, post-transplant diabetes mellitus, and the toxic effects of immunosuppressant medications and other drugs [6].

Aim of the Work

The primary outcome for this study is the determination of the cardiovascular events in the presence of other competitive events in renal transplant patients. Secondary outcome parameters are estimation of risk factors for cardiovascular complications in renal transplant recipients and the incidence of mortality related to cardiovascular events.

Methods

We conducted a single-center retrospective study on five hundred patients admitted to the Cairo kidney center over a period of twenty-two years starting from 1992 to 2014. All patients included underwent primary or repeated renal transplantation from a living donor. All the patients were assessed preoperatively for age and gender, body weight, height, body mass index, the primary cause of renal failure, dialysis protocol, and whether there were any repeated transplants. Cardiovascular risk factors and complications were collected and followed for five years, including peripheral vascular diseases and cerebrovascular diseases. Postoperative phase assessment: either acute rejection or infections were collected. Biochemical parameters and vital signs were collected in the first week, second week, first month, third month, sixth month, and yearly thereafter. Renal function is estimated using the Cockcroft-Gault formula and the modified Modification of Diet in Renal Disease (MDRDeGFR) equation.

Post-transplant cardiovascular events including:

1. Ischemic heart diseases (stable angina pectoris, acute coronary syndrome, and invasive coronary intervention; positive stress electrocardiogram; positive myocardial perfusion scan; elevated cardiac enzymes).
2. Congestive heart failure is confirmed by complete transthoracic echocardiography examination and measuring Ejection fraction (EF) using M-mode & Simpson's formula to determine the left ventricular end-diastolic volume and the end systolic volume from the apical two and four chamber views; systolic heart failure is confirmed if EF is below 45% and assessment of left ventricular hypertrophy.
3. Electrocardiograms or Holter monitors are used to detect arrhythmia.
4. Cerebral vascular events (stroke and transient ischemic attacks) were confirmed by CT brain and carotid duplex.

Statistical Analysis

Data were collected, revised, coded, and entered into the IBM SPSS version 23 Statistical Package for Social Science. When the data was parametric, it was presented as mean, standard deviations, and ranges; when non-parametric, it was presented as median, inter-quartile range (IQR). Qualitative variables were presented as numbers and percentages. The comparison regarding qualitative data was done by using the chi-square test and/or Fisher exact test when the expected count in any cell was found to be less than 5. The comparison between the two groups regarding quantitative data and parametric distribution was done by using an Independent t-test, while with non-parametric distribution it was done by using the Mann–Whitney test. The comparison between more than two paired groups regarding quantitative data and parametric distribution was done by using the Repeated Measures ANOVA test, while with non-parametric distribution it was done by using the Friedman test. The confidence interval was set to 95% and the margin of error accepted was set to 5%.

Results

This retrospective study analyzed data from five hundred patients who received renal transplants. Focusing on cardiovascular risk factors and complications for five-year follow-up. We will discuss our results under four headings. a) Demographic and patient data for renal transplant patients regarding age, sex, race, weight, height, body mass index, cause of renal failure, risk factors, laboratory investigations, hemodialysis duration, and operative details. b) Cardiovascular complications, which include congestive heart failure, ischemic heart disease, arrhythmias, left ventricular hypertrophy, hypertension, central nervous system (TIAs, cerebrovascular stroke, cerebrovascular hemorrhage), and peripheral vascular disease c) Non-cardiovascular complications, such as intraoperative complications, graft dysfunction, proteinuria, graft rejection, post-transplant diabetes, infections, and immunosuppressive medication complications. d) Deaths and risk factors.

Demographic and Patients' Data

As shown in Table 1 for demographic and patient data prior to renal transplantation, the mean age of patients was

Table 1 Demographic and patient data prior to transplantation

Items	Number of patients (Total = 500)	Mean ± SD
Age in years	500 (100%)	41.90 ± 9.67
Weight (kg)	500 (100%)	79.49 ± 12.53
Height (meter)	500 (100%)	1.69 ± 0.08
BMI	500 (100%)	28.08 ± 5.06
Age < 10 yrs	1 (0.2%)	
Age (10–18) yrs	11 (2.2%)	
Age (19–30) yrs	52 (10.4%)	
Age (31–40) yrs	131 (26.2%)	
Age (41–50) yrs	220 (44.0%)	
Age > 50 yrs	85 (17.0%)	
Male	319 (63.8%)	
Female	181 (36.2%)	
BMI < 25	133 (26.6%)	
BMI (> 25—< 30)	221 (44.2%)	
BMI (> 30—< 35)	97 (19.4%)	
BMI (> 35—< 40)	38 (7.6%)	
BMI > 40	11 (2.2%)	
Smoking	112 (22.4%)	
Hereditary nephropathy	22 (4.4%)	
Hypertensive nephropathy	200 (40.0%)	
Diabetic nephropathy	174 (34.8%)	
primary glomerulopathy	68 (13.6%)	
Glomerulopathy associated with systemic disease	15 (3.0%)	
Idiopathic nephropathy	59 (11.8%)	
Chronic tubulointerstitial nephritis	37 (7.4%)	
Renal macrovascular (vasculopathy)	5 (1.0%)	
Obstructive uropathy	15 (3.0%)	
Diabetes	175 (35.0%)	
Hypertension	207 (41.4%)	
Dyslipidemia	408 (81.6%)	
Alcoholic	1 (0.2%)	
Left ventricular hypertrophy (LVH)	408 (81.6%)	
History of arrhythmias	390 (78.0%)	
History of angina	225 (45.0%)	
History of MI	69 (13.8%)	
History of CHF	178 (35.6%)	
History of previous coronary angiography	227 (45.4%)	
Dialysis duration < 5 yrs	74 (17.1%)	
Dialysis duration > 5 yrs	360 (82.9%)	
Patients on hemodialysis	438 (87.6%)	
Patients not on hemodialysis	62 (12.4%)	
Repeated renal transplantation	13 (2.6%)	

41.90 ± 9.67 years, 61% of the recipient patients' age was over 41 years, 63.8% of them were males, Regarding BMI for all transplant recipients, it was 28.08 5.06; the majority was between 25 and 35 (63%); 112 patients out of 500 were originally smokers before transplantation (23%), Hypertensive nephrosclerosis was the leading cause of renal failure in our study participants (40%), followed by diabetic nephropathy (34.8%), glomerulonephritis (13.6%), idiopathic kidney disease (11.8%), chronic tubulointerstitial nephritis (7.4%), and congenital renal disease (4.4%). As expected, the majority (97.4%) of the patients had their first kidney transplant and only (2.6%) had a repeat transplant.

Regarding risk factors prior to transplantation, 35% of patients were diabetics and 42% were hypertensive, 81.6% had dyslipidemia and 81.6% had left ventricular hypertrophy (LVH), 78.0% had a history of previous arrhythmias, 45% mentioned a history of angina, and 45.5% confirmed diagnostic coronary angiography procedure, 35.6% had a history of congestive heart failure (CHF), and 82.9% had more than 5 years of dialysis. Hemodialysis was done in 87.6%, while 12.4% were not on scheduled regular hemodialysis.

Cardiovascular Complications

Regarding cardiovascular complications after renal transplantation, as seen in Table 2, stable angina pectoris occurred in 22.6% of patients, attacks of acute coronary syndrome occurred in 2.4% of patients. Development of new LVH happened in 49.8% of patients. Positive myocardial perfusion scan was done in 13.6% of patients. Elevated cardiac enzymes were seen in 1.8% of patients, and 7.6% were subjected to invasive coronary angiography. Other cardiovascular complications include CHF in 24% of patients, cardiomyopathy in 11.2%, and all types of arrhythmias in 40.8% of patients, with atrial and ventricular arrhythmias occurring in 6.0% and 30.2% of patients, respectively. Bradycardias which lead to permanent pacemaker implantation were seen in 4.6% of patients. Newly developed hypertension and dyslipidemia were seen in 43.4% and 11.6% of patients, respectively. Regarding vascular complications, peripheral vascular disease was recorded in 10.4% of patients, cerebral vascular stroke in 4.4% of patients.

Table 2 General cardiovascular complications in recipients of renal transplantation

Items	Number of patients (Total = 500)
Stable angina pectoris	113 (22.6%)
Acute Coronary Syndrome	12 (2.4%)
Development of LVH after transplantation	249 (49.8%)
Positive myocardial perfusion scan	68 (13.6%)
Elevated cardiac enzymes	9 (1.8%)
Need invasive coronary artery angiography	38 (7.6%)
CHF	120 (24.0%)
Cardiomyopathy (EF < 45%)	56 (11.2%)
Arrhythmias	204 (40.8%)
Atrial arrhythmias	30 (6.0%)
Ventricular arrhythmias	151 (30.2%)
Need for pacemaker for bradycardias	23 (4.6%)
Developed hypertension	217 (43.4%)
Developed new Dyslipidemia	58 (11.6%)
Transient ischemic attacks	19 (3.8%)
Cerebrovascular stroke	22 (4.4%)
Cerebrovascular Hemorrghic insult	6 (1.2%)
Peripheral vascular disease	52 (10.4%)

Table 3 showed risk factors affecting the incidence of ischemic heart disease in post renal transplantation patients. There was a highly statistically significant difference in age, gender, BMI, smoking, development of left ventricular hypertrophy, and proteinuria as they were much higher in the ischemic heart disease group. while hypertension and post-transplantation diabetes mellitus (PTDM) were not statistically significant.

Regarding the newly developed congestive heart failure group versus the non-congestive heart failure group, as seen in Table 4, there was a statistically significant difference regarding higher age, obesity, systemic hypertension, PTDM, smoking, development of left ventricular hypertrophy, and proteinuria. On the other hand, there was no statistically significant difference regarding gender. Table 5 showed that the mean age at time of renal transplantation was 43.02 ± 8.46 in the LVH group, which was significantly higher than the non-LVH group at 40.79 ± 10.65 with p value = 0.01. Also, there was a highly statistically significant difference regarding obesity, proteinuria, hypertension, and PTDM as they were much higher in the LVH group. While smoking doesn't show a statistically significant risk factor for the development of LVH.

Table 6 showed a comparison between the arrhythmia group and the non-arrhythmia group post renal transplantation. There was statistical significance between the arrhythmias group and the non-arrhythmias group regarding higher age, male gender, systemic hypertension, PTDM, smoking, proteinuria, and obesity. However, it was puzzling that there was no statistically significant difference in the development of left ventricular hypertrophy.

Table 7 showed there was a high statistically significant difference with older age, male gender, smoking, development of left ventricular hypertrophy and proteinuria in cerebrovascular disease group. On other hand no statistically significant difference was found between both group regarding hypertension and PTDM.

Non cardiovascular Complications

4-Mortality and Risk Factors

Upon comparing hypertension, diabetes mellitus and Ischemic heart disease incidence before and after renal transplantation we found significant increase in number of hypertensive patients and decrease in ischemic heart disease patients while number of diabetic patients did not change before and after renal transplantation Table 8.

The main causes of mortality were cardiovascular diseases, infections, cancer, surgical complications, and liver

Table 3 Factors correlating with the incidence of post-transplant ischemic heart disease

		Non IHD No. = 381	IHD No. = 119	P-value
Age (year) at time of TX	Mean ± SD	40.55 ± 9.67	49.42 ± 5.22	< 0.001*
Sex	Female	169 (39.9%)	12 (15.8%)	< 0.001*
	Male	255 (60.1%)	64 (84.2%)	
BMI	Mean ± SD	27.56 ± 4.86	30.97 ± 5.16	< 0.001*
Obesity	BMI < 25	123 (29.0%)	10 (13.2%)	< 0.001*
	BMI (> 25—< 30)	197 (46.5%)	24 (31.6%)	
	BMI (> 30—< 35)	71 (16.7%)	26 (34.2%)	
	BMI (> 35—< 40)	25 (5.9%)	13 (17.1%)	
	BMI > 40	8 (1.9%)	3 (3.9%)	
Hypertension	No	254 (59.9%)	46 (60.5%)	0.919
	Yes	170 (40.1%)	30 (39.5%)	
Smoking	No	367 (86.6%)	21 (27.6%)	< 0.001*
	Yes	57 (13.4%)	55 (72.4%)	
Post Transplantation DM	No	304 (71.7%)	47 (61.8%)	0.084
	Yes	120 (28.3%)	29 (38.2%)	
Development of LVH	No	238 (56.1%)	13 (17.1%)	< 0.001*
	Yes	186 (43.9%)	63 (82.9%)	
Proteinuria	No proteinuria	193 (45.5%)	16 (21.1%)	< 0.001*
	Non-significant proteinuria ≤ 0.5 g/day	92 (21.7%)	10 (13.2%)	
	Significant proteinuria > 0.5 g/day	139 (32.8%)	50 (65.8%)	

Table 4 Factors correlating with the incidence of post-transplant congestive heart failure

		No CHF No. = 380	CHF No. = 120	P-value
Age (year) at time of TX	Mean ± SD	40.17 ± 9.63	47.38 ± 7.58	< 0.001*
Sex	Female	142 (37.4%)	39 (32.5%)	0.333
	Male	238 (62.6%)	81 (67.5%)	
Obesity	BMI < 25	124 (32.6%)	9 (7.5%)	< 0.001*
	BMI (> 25—< 30)	182 (47.9%)	39 (32.5%)	
	BMI (> 30—< 35)	47 (12.4%)	50 (41.7%)	
	BMI (> 35—< 40)	20 (5.3%)	18 (15.0%)	
	BMI > 40	7 (1.8%)	4 (3.3%)	
Hypertension	No	197 (51.8%)	103 (85.8%)	< 0.001*
	Yes	183 (48.2%)	17 (14.2%)	
PTDM (NODAT)	No	286 (75.3%)	65 (54.2%)	< 0.001*
	Yes	94 (24.7%)	55 (45.8%)	
Smoking	No	318 (83.7%)	70 (58.3%)	< 0.001*
	Yes	62 (16.3%)	50 (41.7%)	
Development of LT VH	No	233 (61.3%)	18 (15.0%)	< 0.001*
	Yes	147 (38.7%)	102 (85.0%)	
Proteinuria	No proteinuria	185 (48.7%)	24 (20.0%)	< 0.001*
	Non-significant < = 0.5 g/day	85 (22.4%)	17 (14.2%)	
	Significant proteinuria > 0.5 g/day	110 (28.9%)	79 (65.8%)	

disease (19.0%, 13.4%, 1.6%, 1.4%, and 1.2%), respectively. There was much overlap in causes of death as most patients died with more than one single cause, such as ischemic heart disease and arrhythmias or cancer and congestive heart failure. Cardiovascular related death occurred in 19% of the entire transplant cohort and accounted for 64% (95/151) of all deaths, making this the leading cause of post-transplant mortality Fig. 1.

Table 5 Factors correlating with the development of post-transplant left ventricular hypertrophy

		Development of LVH		P-value
		No	Yes	
		No. = 251	No. = 249	
Age (year) at time of TX	Mean ± SD	40.79 ± 10.65	43.02 ± 8.46	0.01*
Sex	Female	94 (37.5%)	87 (34.9%)	0.559
	Male	157 (62.5%)	162 (65.1%)	
Obesity	BMI < 25	127 (50.6%)	6 (2.4%)	< 0.001*
	BMI (> 25—< 30)	122 (48.6%)	99 (39.8%)	
	BMI (> 30—< 35)	0 (0.0%)	97 (39.0%)	
	BMI (> 35—< 40)	1 (0.4%)	37 (14.9%)	
	BMI > 40	1 (0.4%)	10 (4.0%)	
Hypertension	No	132 (52.6%)	168 (67.5%)	< 0.001*
	Yes	119 (47.4%)	81 (32.5%)	
PTDM	No	225 (89.6%)	126 (50.6%)	< 0.001*
	Yes	26 (10.4%)	123 (49.4%)	
Smoking	No	202 (80.5%)	186 (74.7%)	0.121
	Yes	49 (19.5%)	63 (25.3%)	
Proteinuria	No proteinuria	119 (47.4%)	90 (36.1%)	0.006*
	Non-significant < = 0.5 g/day	54 (21.5%)	48 (19.3%)	
	Significant proteinuria > 0.5 g/day	78 (31.1%)	111 (44.6%)	

Table 6 Factors correlating with post-transplant arrhythmias

		No arrhythmia	Arrhythmia	P-value
		No. = 296	No. = 204	
Age (year) at time of TX	Mean ± SD	39.00 ± 9.90	47.96 ± 5.53	< 0.001*
Sex	Female	172 (50.9%)	9 (5.6%)	< 0.001*
	Male	166 (49.1%)	153 (94.4%)	
Hypertension	No	219 (64.8%)	81 (50.0%)	0.002*
	Yes	119 (35.2%)	81 (50.0%)	
PTDM	No	252 (74.6%)	99 (61.1%)	0.002*
	Yes	86 (25.4%)	63 (38.9%)	
Smoking	No	321 (95.0%)	67 (41.4%)	< 0.001*
	Yes	17 (5.0%)	95 (58.6%)	
Development of LVH	No	172 (50.9%)	79 (48.8%)	0.657
	Yes	166 (49.1%)	83 (51.2%)	
Proteinuria	No proteinuria	177 (52.4%)	32 (19.8%)	< 0.001*
	Non-significant < = 0.5 g/day	84 (24.9%)	18 (11.1%)	
	Significant proteinuria > 0.5 g/day	77 (22.8%)	112 (69.1%)	
Obesity	BMI < 25	103 (30.5%)	30 (18.5%)	0.021*
	BMI (> 25—< 30)	148 (43.8%)	73 (45.1%)	
	BMI (> 30—< 35)	56 (16.6%)	41 (25.3%)	
	BMI (> 35—< 40)	23 (6.8%)	15 (9.3%)	
	BMI > 40	8 (2.4%)	3 (1.9%)	

Discussion

Cardiovascular disease (CVD) is the leading cause of mortality in the general population as well as in renal transplant recipients (RTR). The risk of cardiovascular events (CVEs) is significantly reduced months after transplantation when compared to those with end-stage renal disease (ESRD) on the waiting list. Although the

Table 7 Factors correlating with post-transplant cerebrovascular disease

		No Cerebrovascular Disease	Cerebrovascular Disease	P-value
		No. = 459	No. = 41	
Age (year) at time of transplantation	Mean ± SD	40.99 ± 9.47	52.07 ± 4.96	< 0.001*
Sex	Female	178 (38.8%)	3 (7.3%)	< 0.001*
	Male	281 (61.2%)	38 (92.7%)	
BMI	Mean ± SD	27.92 ± 4.98	29.90 ± 5.59	0.016*
Hypertension	No	270 (58.8%)	30 (73.2%)	0.072
	Yes	189 (41.2%)	11 (26.8%)	
Smoking	No	381 (83.0%)	7 (17.1%)	< 0.001*
	Yes	78 (17.0%)	34 (82.9%)	
PTDM	No	322 (70.2%)	29 (70.7%)	0.938
	Yes	137 (29.8%)	12 (29.3%)	
Development of LVH	No	241 (52.5%)	10 (24.4%)	0.001*
	Yes	218 (47.5%)	31 (75.6%)	
Proteinuria	No proteinuria	207 (45.1%)	2 (4.9%)	< 0.001*
	Non-significant < = 0.5 g/day	99 (21.6%)	3 (7.3%)	
	Significant proteinuria > 0.5 g/day	153 (33.3%)	36 (87.8%)	

Table 8 The incidence of hypertension, diabetes mellitus and ischemic heart disease before and after renal transplantation

		Before RTx No. = 500	After RTx No. = 500	P-value
Hypertension	No	293 (58.6%)	76 (15.2%)	0.001*
	Yes	207 (41.4%)	424 (84.8%)	
Diabetes mellitus	No	326 (65.2%)	351 (70.2%)	0.091
	Yes	174 (34.8%)	149 (29.8%)	
Ischemic heart disease	No	269 (53.8%)	424 (84.8%)	< 0.001*
	Yes	231 (46.2%)	76 (15.2%)	

mortality is lower than those on the waiting list, certain implicated factors particular to RTRs collectively keep this risk from reaching that of the general population [7]. Regarding the demographic and patient data in the current study, the mean age of patients who received a renal transplant was 41.90 ± 9.67 years, and this age is reasonable as currently the majority of patients developing ESRD who are eligible for kidney transplantation are between 45 and 65 years of age [8]. Men made up 63.8% of our participants, while women made up only 36.2%, which is consistent with many data findings in Europe, where 38% of incident RRT patients in 2015 were women [9], and 42% were women in 2016 [10].

The main etiology of renal failure in our participants was hypertension (40%), followed by diabetic nephropathy (34.8%), and then glomerulonephritis (13.6%). in concordance with a recent study done in Egypt [11]. Hypertension, diabetes, dyslipidemia, and obesity are highly prevalent in patients with ESRD. These risk factors persist following organ transplantation and are often exacerbated by the drugs used for immune-suppression in organ transplantation. Additional transplant-specific factors such as poor graft function and proteinuria are also associated with increased cardiovascular risk in renal transplanted patients [12]. In the current study, 81.6% of our patients had dyslipidemia,we agree with Devine et al., 2019 as dyslipidemia is a common problem peri-transplantation, with over 60% of RTR

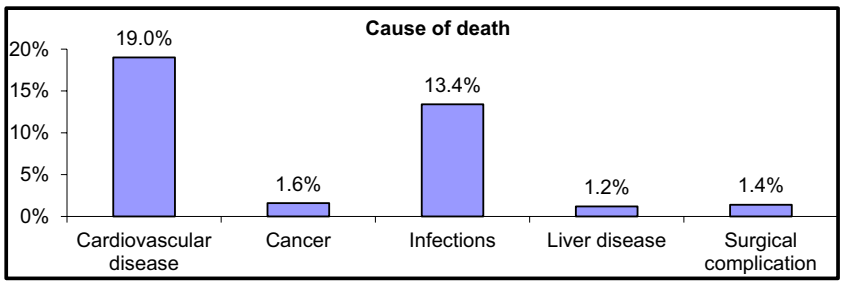

Fig. 1 Incidence of post-transplant mortality stratified by cause

affected [12]. Other risk factors such as hypertension: in the current study, 41.4% of participants had hypertension before renal transplantation, which had a little difference with Devine, who found hypertension was already present in over 60% of patients prior to transplantation [12]. The present study found that 35.0% of all transplanted patients had diabetes mellitus and only 22% were smokers. Our data were in concordance with a study published by Kasiske and Klinger in 2000 reported that 25% of recipients were smokers at the time of transplantation. The smoking prevalence in the RTR actually mirrored the prevalence in the general population. This study demonstrated that smoking was an independent risk factor for graft loss, cardiovascular disease, and death [13].

Pre-transplant cardiac evaluation should identify existing cardiac conditions that can be risk-modified and exclude patients with a low chance of survival in the near future.A critical goal of preoperative evaluation is to determine whether an active cardiac condition is present, such as unstable angina, recent myocardial infarction (MI), decompensated congestive heart failure (CHF), significant arrhythmia, or valvular heart disease. The presence of one or more of these conditions is associated with high perioperative cardiovascular morbidity and mortality [14]. In the current study, 49.8% of patients developed LVH, 23.8% developed IHD, 22.6% developed stable angina pectoris, and 2.4% developed Acute Coronary Syndrome (ACS). Other cardiovascular complications were mentioned as CHF in (24.0%) of patients, EF below 45% in (11.2%), and arrhythmias in (40.8%). There was also a highly statistically significant difference regarding obesity, proteinuria, hypertension, and PTDM as they were higher in the LVH group, but no statistically significant difference was found between both groups regarding smoking.

In our study, there was a decrease in LVH post-transplantation than pre-transplantation, in line with many studies that concluded that renal transplantation improves cardiac functions, including LV systolic function [15]. These results came in concordance with K Slubowska et al., who found LVH (mainly concentric) was found in 51.2% of the patients in the early period and in 50% of the patients at 1 year. In 30% of the patients with baseline LVH, it regressed at 1 year and in another 30%, LVH developed de novo. In the early period, LV mass was influenced by age, sex, BMI, estimated glomerular filtration rate (eGFR), and a history of cardiovascular disorders during dialysis therapy, whereas at 1 year after transplantation it was influenced by age, sex, BMI, 24-h systolic blood pressure, a history of hypertension during dialysis therapy, and an abnormal 24-h blood pressure profile. Weight gain interfered with LVH regression during the 1st year after transplantation, whereas no improvement in blood pressure control contributed to the de novo development of LVH [16]. The improvement in LVEF in patients in the absence of any significant change in LV volume is more consistent with the hypothesis that transplantation leads to clearance of toxins, which have been associated with the development of uremic cardiomyopathy [17].

Regarding IHD, we found highly statistically significant differences between patients with IHD and those who did not have IHD as higher age, more males, smokers, proteinuria, and development of LVH as they were present in the IHD group. Our findings are in concordance with many studies as the incidence of acute MI is high in patients with ESRD, occurring in up to 30% and 52% of patients by the end of the first and second years on dialysis, respectively. At present, MI is associated with a poor long-term prognosis in the general dialysis population, with mortality estimated to be 60% at 12 months [18]. A retrospective study based upon the United States Renal Data System (USRDS) evaluated the clinical correlates of post-transplant MI. Among nearly 36,000 patients, the incidence of MI at 6, 12, and 36 months was 4.3, 5.2, and 11.1%, respectively. Increased age, receiving kidneys from older donors and deceased donors, delayed allograft function, and the presence of pre-transplant comorbidities such as diabetes, angina, peripheral vascular disease, and MI were the main risk factors.The diagnosis of post-transplant diabetes and the development of allograft failure were also significantly associated with the development of an MI [3].

In a retrospective analysis of the placebo arm of the Assessment of LESCOL in Renal Transplantation (ALERT) study, the independent risk factors for nonfatal MI by multivariate analysis were preexisting coronary heart disease, total cholesterol level, and prior acute rejection. Age, diabetes, ST-T changes, and elevated serum creatinine levels were independent risk factors for cardiac death [19]. The international multicenter PORT study (Patient Outcomes in Renal Transplantation), published in 2010, reported specific risk factors for MI after RT in 23,575 patients: acute rejection, pre-transplantation duration of dialysis, and diabetes [20]. The Didier et al. study, identifying 94,340 MI patients over a 5-year follow up period from a baseline population of 3,306,383 patients, showed relevant findings: a 45% higher risk of acute myocardial infarction in RT patients after multivariate adjustment,specific profiles of MI with kidney transplantation,and a 15% higher risk of all-cause mortality among RT patients after MI [21].

Congestive Heart Failure is 12–36 times more prevalent in patients with ESRD compared with the general population. In dialysis patients, the 3-year mortality after diagnosis of congestive heart failure is 50%. Multiple factors predispose to congestive heart failure in patients with ESRD. Hypertension, diabetes, anemia, volume overload, arteriovenous fistulae, increased catecholamine levels, hyperparathyroidism, ischemic heart disease, and malnutrition are common in this population and all have been associated with

LV dysfunction [12]. In our study, congestive heart failure was diagnosed in 24.0% of patients, and cardiomyopathy in 11.2%. There was a highly statistically significant difference regarding age, smoking, proteinuria, and the development of LVH. Also, a highly statistically significant difference was found between both groups regarding hypertension and PTDM. Studies have shown that cardiomyopathy, either with or without clinical heart failure, is common among kidney transplant recipients. As an example a retrospective analysis of data derived from the USRDS showed that the cumulative incidence of new-onset heart failure (HF) was 10.2% and 18.3% at 12 and 36 months, respectively [3]. In a retrospective study of 638 consecutive kidney transplant recipients who were free of cardiac disease at one year, new-onset HF occurred as frequently as new-onset ischemic heart disease (1.26 versus 1.22 events per 100 patient-years, respectively) [22]. Independent risk factors for new-onset HF after transplantation include age, diabetes, anemia, and hypertension. Studies of USRDS data have identified obesity, donor factors that may predict suboptimal graft function, and graft loss as risk factors for HF [23]. Obesity and smoking are associated with an increased risk of HF [23].

Regarding our results, arrhythmia was found in 40.8%, atrial arrhythmias, ventricular arrhythmias, and bradycardias in (6.0%, 30.2%, and 4.6%), respectively. The arrhythmia group had a highly statistically significant association with age and male gender. There was a highly statistically significant difference regarding smoking, hypertension, PTDM, and proteinuria as they were higher in the arrhythmia group. On the other hand, no statistically significant difference was found between both groups regarding the development of LVH. In concordance to a study that showed the incidence of AF is higher in the peri-transplant period, probably associated with surgical stress, anesthesia, and excess catecholamine production [24]. Following renal transplantation (after approximately 17 months), AF declines below the prevalence recorded in ESRD patients on the transplant waiting list [25]. A possible explanation may be the regression of left ventricular hypertrophy over the first 2 years after transplantation. In the study of Delville et al., a 12-month follow-up was available for all 244 patients. Overall, 38 (15.5%) renal transplant recipients had a cardiovascular event during the first year post-transplantation, with AF reported in 13 (5.3%) of them [26].

Regarding cerebrovascular diseases, they occurred in 8.2% of all patients in the current study. There was a highly statistically significant association regarding age and male gender in the cerebrovascular disease group. There was also a highly statistically significant association regarding obesity, smoking, proteinuria, and development of LVH as they were higher in the cerebrovascular disease group. In the ALERT trial, Abedini et al. sought to uncover the incidence and risk factors of cerebrovascular disease (ischemic and hemorrhagic strokes). Diabetes, previous cerebrovascular events, age, and renal function proved to be risk factors for ischemic strokes, while diabetes, polycystic kidney disease, LVH, and systolic blood pressure were associated with risks for hemorrhagic strokes. The prevalence of cerebrovascular disease, over an average follow-up period of 6.7 years in this study, was 8.6%, with an approximate incidence of 1.3% yearly [27]. These rates were similar when compared to other cohorts [28].

Postoperative complications such as PTDM have been shown to increase the risk of morbidity and mortality among these patients. In fact, PTDM is now considered to be a major determinant of loss of renal allograft, development of infections, and increased risk of cardiovascular morbidity and mortality, and thus it can significantly affect the clinical outcome of transplant recipients. PTDM is defined as the development of diabetes for the first time after transplantation in previously non-diabetic transplant recipients [29]. The prevalence of PTDM can range between 2 and 53% [30]. In the present study, PTDM occurred in 29.8%, higher than a recent study that found the prevalence of PTDM in renal transplant recipients was 17.2% [30]. The moderately high prevalence of PTDM in our study could be attributable to the fact that almost all kidney transplant recipients received steroids as part of their immunosuppressive regimen.

In most nephropathies, proteinuria is a biological marker of renal abnormality and an important risk factor for progressive renal damage and subsequent renal function decline in most nephropathies [31]. In addition, proteinuria after renal transplantation has been associated with poor implant outcome for years. Early proteinuria (persistence of urine protein excretion > 0.5–1.0 g/24 h during one- and three-months) is an independent and powerful predictor of graft loss, cardiovascular morbidity, and mortality, and short-term reduction of proteinuria is associated with improved long-term graft survival [32]. In our study, significant protein > 0.5 was found in 37.8% of participants. There were some factors closely related to graft lesions which occurred during the transplant procedure or after, such as long cold ischemia time,graft function recovery time and the effect of m-TOR drugs.

Regarding post-transplantation mortality, 30.2% of patients died 15 years post-renal transplantation. The main causes of mortality were cardiovascular complications followed by infections, cancer, surgical complications, and liver disease (19.0%, 13.4%, 1.6%, 1.4%, and 1.2%), respectively. The causes of death among transplant recipients have changed over time and vary with age. In a single-center study, for example, cardiac disease, cancer, and stroke as causes of death increased from 9.6%, 1.2%, and 2.4%, respectively, for the period 1970 to 1979 to 30.3%, 13.2%, and 8% for 1990 to 1999 [33]. Furthermore, death from cardiovascular disease is much less common in younger people than in older people [34]. Among prevalent

transplant patients from 1994 to 1996, the following was the percentage of deaths due to the most significant life-threatening disorders: For those aged 0 to 19, (20 to 44), and 45 to 64), all cardiac causes accounted for 18, 33, and 37 percent of deaths, respectively. Infection accounted for 25, 17, and 19% of the total. Malignancy accounted for 16 percent, 8 percent, and 11 percent, respectively. Recent trends reported that among the 210,327 RT patients, 3.2% died within one year, mainly with CV death (24.7%) [35].

Congestive Heart Failure is associated with increased mortality after transplantation [36]. In our study, 11.6% of renal transplanted patients died with CHF, which comes in concordance with another single-center study who assessed left ventricular systolic dysfunction, defined as left ventricular ejection fraction less than or equal to 45% by gated single photon emission computed tomography at the time of transplantation, was associated with 4.8 times the risk of cardiac death, 2 times the risk of all-cause mortality, and 1.8 times the risk of cardiac complications, compared with normal cardiac function [36]. A study of USRDS data identified the clinical diagnosis of new-onset heart failure after transplant as a potent predictor of subsequent death [3].

Conclusion

Renal transplant recipients are at an extremely high risk of adverse cardiovascular events. Cardiovascular complications (congestive heart failure, ischemic heart diseases, left ventricular hypertrophy, arrhythmias, and cerebral accidents) are the leading cause of death in renal transplant recipients (19%). Transplant recipients were at high risk because of advanced age, smoking, previous long-term dialysis, diabetes, and proteinuria. The main cause of renal failure in our participant patients was hypertensive nephrosclerosis (40%), followed by diabetic nephropathy (34.8%). Other complications, such as chest infections, UTI, gastroenteritis, and wound infection, occurred early in the postoperative period.

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Declarations

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