Predictors and Prognostic Implications of Major Adverse Cardiovascular Events after Renal Transplant: 10 Years Outcomes in 321 Patients

Waqas Aftab, MD¹ Padmini Varadarajan, MD¹ Shuja Rasool, MD¹ Ramdas G. Pai, MD¹

¹ Division of Cardiology, Loma Linda University Medical Center, Loma Linda, California

Address for correspondence Ramdas G. Pai, MD, Division of Cardiovascular Medicine, 11234 Anderson Street, Room 4414, Loma Linda, CA 92354 (e-mail: ramdaspai@yahoo.com).

Int J Angiol 2014;23:131–138.

Abstract

Renal transplantation is the treatment of choice in patients with end-stage renal disease. Major adverse cardiac events (MACE) are common after renal transplant, especially in the perioperative period, leading to excess morbidity and mortality. The predictors and long-term prognostic implications of MACE are poorly understood. We analyzed predictors and implications of MACE in a cohort of 321 consecutive adult patients, who received renal allograft transplantation between 1995 and 2003 at our institution. The characteristics of 321 patients were: age at transplant 44 ± 13 years, 60% male, 36% diabetes mellitus (DM), left ventricular ejection fraction (LVEF) $60 \pm 16\%$. MACE occurred in 21 patients with cumulative rate of 6.5% over 3 years after renal transplant, 57% occurring within 30 days, 67% within 90 days, and 86% within 180 days. MACE was not predicted by any clinical or pharmacological variables including age, gender, hypertension, DM, prior myocardial infarction, smoking, duration of dialysis, LVEF, or therapy with β -blockers (BB), angiotensin converting enzyme inhibitors, or calcium channel blockers. However, a clinical decision to perform a stress test or a coronary angiogram was predictive of higher MACE rate. MACE, irrespective of type, was independently associated with higher mortality over a period up to 15 years and this seemed to be blunted by BB therapy. MACE rate after renal transplantation decreases over time, most occurring in the first 90 days and is not predicted by any of the traditional risk factors or drug therapies. It is associated with higher long-term mortality.

Keywords

- end-stage renal disease
- survival
- major adverse cardiac events

Renal transplantation is the preferred treatment for patients with end-stage renal disease (ESRD) because of the survival benefit it confers.¹ However, mortality even after transplant remains high compared with age-matched control groups.² Major adverse cardiovascular events (MACE) are common after renal transplant and these remain the leading cause of death in the long term as well.² Their incidence remains high despite very aggressive preoperative cardiac evaluation protocols. The aim of our study was to study the predictors of

MACE in a large cohort of patient, evaluate their long-term implications, and gain insights into their prevention.

Patients and Methods

Study Design and Patient Population

This is a retrospective cohort study from a single large academic center. The study was approved by the institutional review board which waived the need for consent. Medical

records of 321 consecutive adult patients who received renal allograft transplantation between 1993 and 2003 were reviewed. This population has been described in an earlier report.³

Data Collection

Details on cardiac risk factors, medications, stress test results, coronary angiogram, and coronary intervention were collected from chart review by medical residents and related to MACE. All electrocardiograms, echocardiograms, stress tests, and angiograms were interpreted by one of the cardiology attending. Hypertension was defined as blood pressure greater than 140/90 mm Hg or a history of hypertension and being on antihypertensive medications. Diabetes mellitus (DM) was defined as fasting blood sugar greater than 125 mg/dL or being on a regimen of antidiabetic therapy. Coronary artery disease (CAD) was deemed to be present if any of the following were present: a history of angina pectoris, myocardial infarction (MI), a positive stress test, angiographic evidence of CAD, coronary intervention, coronary artery bypass surgery, or presence of significant wall motion abnormalities on the echocardiogram. Pharmacological data were collected as a single point posttransplant use of aspirin, β blockers (BB), calcium channel blocker (CCB) and angiotensin converting enzyme inhibitor or angiotensin receptor blocker (AB). The therapies were broadly categorized and details of different agents or their doses were not collected.

Definition of Major Adverse Cardiac Events

MACE was defined as one of these events: as sudden cardiac death, fatal or nonfatal MI, unstable angina requiring coronary revascularization, direct current cardioversion therapy, or atrial or ventricular arrhythmias or pulmonary edema requiring prolonged or recurrent ventilator support. MI was defined as typical rise and fall of cardiac enzymes (troponin or creatine kinase myocardial) in the setting of chest pain with or without ST depression or elevation. Data on MACE were collected from renal transplant to 3 years postoperatively. Mortality data were obtained from Social Security Death Index.

Statistical Analysis

Analysis was performed using Stat View 5.01 (SAS Institute Inc, Cary, NC). Characteristics of patients with and without MACE were compared using the student *t*-test for continuous variables and chi-squared test for categorical variables. Univariate logistic regression was used to determine the predictors of MACE. Statistical tools used for survival analysis included the Kaplan–Meier method and Cox regression model. A *p* value of < 0.05 was considered significant.

Results

Baseline Patient Characteristics

These are shown in ► **Table 1**. The mean age of the recipients was 44 ± 13 years (range 15–78 years) at the time of transplant, males 60%, DM in 36%, hypertension in 89%, dyslipidemia in 23%, CAD in 20%, and left ventricular ejection

Table 1 Baseline patient characteristics

Age	44 $\pm$ 13 y
Male	60%
Smoking	13%
Diabetes mellitus	36%
Hypertension	89%
Dyslipidemia	23%
Diabetes and hypertension	35%
Hemodialysis duration	
1–5 y	77%
5–10 y	18%
> 10 y	3%
New York Heart Association class	
Class I	1%
Class II	91%
Class III	5%
Class IV	None
Arrhythmias	6%
Abnormal electrocardiograms	11%
Left ventricular EF	60 $\pm$ 16%
EF $\geq$ 40%	89%
EF < 40%	11%
Stress test performed	62%
Positive stress of those performed	33%
Coronary angiograms performed	28%
Positive angiogram of those performed	27%
Any significant coronary artery disease	18%
Revascularization performed	6%
Percutaneous coronary intervention	2%
Coronary artery bypass graft surgery	4%
Aspirin use	10%
BB use	27%
AB use	31%
CCB use	56%
BB and AB	11%
BB and CCB use	18%
AB and CCB use	18%

Abbreviations: AB, angiotensin receptor blocker; BB, beta-blocker; CCB, calcium channel blocker; EF, ejection fraction.

fraction was $60 \pm 16\%$. A total of 77% of patients who received transplant had been on dialysis for 1 to 5 years, 18% for 6 to 10 years, and 5% for more than 10 years. A total of 86 patients were on a BB, 98 on an AB, 181 on a CCB, and 32 on aspirin. Patients who were younger than the age of 30 years were mostly risk stratified by a 12 lead electrocardiogram (ECG) and in older patients, an echocardiogram was also performed in addition to 12 lead ECG. A total of 198 (62%) patients

Table 2 Patient characteristics in different stress test subgroups

Variable	Patients with no stress test (n = 123)	Patients with stress tests (n = 198)	Patients with positive stress tests (n = 65)	Patients with negative stress tests (n = 133)
Age (y), mean $\pm$ SD	48 $\pm$ 11	58 $\pm$ 11	60 $\pm$ 11	57 $\pm$ 12
Male (%)	56	62	72	57
Hypertension (%)	83	92	95	91
Smoking (%)	15	12	11	12
Diabetes mellitus (%)	11	52	51	53
Dyslipidemia (%)	12	29	25	32
Prior myocardial infarction (%)	2	9	11	7
LVEF (%)	59 $\pm$ 13	61 $\pm$ 12	61 $\pm$ 12	61 $\pm$ 12
MACE (%)	4	8	12	6
Deaths (n)	29	90	35	55

Abbreviations: LVEF, left ventricular ejection fraction; MACE, major adverse cardiac events; SD, standard deviation.

underwent one or more forms of stress testing and of these, those 65 (33% of those with stress tests) had positive results. Patients who underwent stress test were older in age than those who did not. Of 321 patients, 91 (28%) patients underwent coronary angiography and of these 25 (27% of angiographic cohort) patients were positive for significant disease defined as $> 70\%$ luminal diameter narrowing in one or more main coronary arteries. Of the patients who had positive stress test (n = 65), 54 (82%) underwent coronary angiography and only 15 had significant CAD leading to a positive predictive value of 29%, whereas in patients with negative stress test (n = 133), 24 underwent coronary angiogram. In this group, nine had a positive angiogram. In patients who did not undergo any stress test (n = 123), 11% (n = 13) were directly referred for angiogram and in this group, only one patient had a positive angiogram. The odds ratios (OR) for performing coronary angiography by multivariate logistic

regression analysis were as follows: history of prior MI (OR, 3.35; 95% confidence interval [CI], 1.22–9.22; $p = 0.02$), DM (OR, 2.86; 95% CI, 1.60–5.13; $p = 0.001$) and a positive stress test (OR, 3.29; $p = 0.0007$). The likelihood ratio for a positive angiogram was significant for male gender (hazard ratio [HR], 4.2; $p = 0.04$), hyperlipidemia (HR, 11.7; $p = 0.0006$), decision to perform stress testing (HR, 3.6; $p = 0.05$) and marginally significant for baseline abnormal electrocardiogram (HR, 3.4; $p = 0.06$). Characteristics of patients undergoing stress and angiographic testing along with subgroups based on test results are listed on ► **Tables 2 and 3**.

Frequency, Types, and Time Course of Major Adverse Cardiac Event

► **Table 4** summarizes the baseline characteristics of patients with MACE and compares it to those without. There were a total of 21 events of MACE recorded over a period of 3 years.

Table 3 Patient characteristics in different angiographic subgroups

Variable	Patients with no coronary angiogram (n = 230)	Patients with coronary angiogram (n = 91)	Patients with positive coronary angiogram (n = 25)	Patients with negative coronary angiogram (n = 66)
Age (y)	52 $\pm$ 12	59 $\pm$ 11	61 $\pm$ 12	58 $\pm$ 11
Male (%)	58	63	80	58
HTN (%)	87	93	96	92
Smoking (%)	15	9	8	9
DM (%)	30	59	68	56
Dyslipidemia (%)	20	29	56	18
Prior MI (%)	3	13	24	9
LVEF	61 $\pm$ 12	59 $\pm$ 14	63 $\pm$ 11	57 $\pm$ 14
MACE (%)	5	11	8	12
Deaths (n)	71	48	13	35

Abbreviations: DM, diabetes mellitus; HTN, hypertension; LVEF, left ventricular ejection fraction; MACE, major adverse cardiac events; MI, myocardial infarction.

Table 4 Correlates of major cardiac adverse events

Variable	MACE (<i>n</i> = 21)	No MACE (<i>n</i> = 300)	<i>p</i> Value
Age (y)	49 ± 13	44 ± 13	0.07
Male	67	59	0.49
Smoking (%)	20	13	0.35
Hypertension (%)	90	89	0.80
Diabetes mellitus (%)	45	36	0.40
Hyperlipidemia (%)	10.0	24	0.16
Prior myocardial infarction (%)	5.0	6	0.80
Abnormal electrocardiogram (%)	0	10	0.14
LVEF (%)	66 ± 7	60 ± 12	0.12
Stress testing done (%)	76	60	0.15
Positive stress test of those performed (%)	50	31	0.12
Coronary angiogram (%)	48	28	0.04
Positive angiograms of those performed (%)	10	25	0.60
Revascularization performed (%)	7	11	0.66

Abbreviations: LVEF, left ventricular ejection fraction.

Patients in this subgroup had average age of 49 ± 12 years at time of transplant, 20% were smoker, 91% were hypertensive, 45% were diabetic, 10% had dyslipidemia, and 5% had prior history of MI. Of 21 patients, 76% (*n* = 16) had undergone one form or the other of a stress test before transplant, with a positive rate of 50% (*n* = 8). Of these eight patients with positive stress test, seven (88%) underwent coronary angiogram with a positive rate of 13%. In other patients (*n* = 3) who had negative stress test or were either directly referred for angiogram or had the procedure done in the setting of acute cardiac event, only one patient (33%) had significant stenosis of coronary arteries and was later referred to coronary artery bypass grafting (CABG). ►**Fig. 1** shows the distribution and time line of MACE after transplant. There were nine (43%)

cases of non-ST segment elevation myocardial infarction (NSTEMI) or unstable coronary syndrome, four (19%) cases of cardiac arrest, five (24%) cases of pulmonary edema, one case of postoperative ventricular tachycardia (5%), and two (10%) cases of atrial flutter. Approximately 21% of the events occurred in the first 24 hours, 57% in first 30 days, 67% in 90 days, and 86% in 180 days postoperatively.

Predictors of Major Adverse Cardiac Event

MACE was predicted only by a decision to perform coronary angiogram and not by any other demographic, clinical, or pharmacological variables (►**Table 5**). The findings of stress test or coronary angiogram did not predict MACE as well. Group comparison of patients based on presence or absence

Fig. 1 Figure showing frequency of different types of major adverse cardiac events (MACE) and their timeline. MI, myocardial infarction.

Table 5 Univariate predictors of MACE

Variable	Hazard ratio	95% confidence interval	p Value
Age (y)	1.03	0.97–1.07	0.07
Female	0.72	0.28–1.83	0.49
Smoking	1.71	0.54–5.49	0.35
Hypertension	1.21	0.27–5.44	0.80
Diabetes mellitus	1.47	0.59–3.67	0.40
Hyperlipidemia	0.36	0.082–1.591	0.18
Prior myocardial infarction	0.77	0.10–6.06	0.80
Stress test performed	2.14	0.75–5.89	0.16
Positive stress test	2.13	0.78–6.13	0.13
Coronary angiogram performed	2.45	1.01–6.01	0.05
Positive coronary angiogram	0.63	0.12–3.19	0.56
LV ejection fraction < 40%	1.05	0.98–1.12	0.12

Abbreviations: LV, left ventricular.

of certain clinical and demographic characteristics showed decision to perform stress testing or coronary angiography to be predictors of higher rates of MACE (►Table 6).

Impact of Major Adverse Cardiac Event on Long-Term Survival

Over a mean period of 10 ± 4 years, there were 119 events of death. On univariate analysis, MACE following transplant was a significant predictor of higher mortality (HR, 2.9; 95% CI, 1.7–5.1; $p = 0.002$). This remained significant after adjusting for other univariate predictors of mortality such as age, DM, prior MI, and use of BB or AB (HR, 2.7; 95% CI, 1.5–4.8; $p = 0.001$; ►Fig. 2). In patients with MACE, smoking had a significant detrimental impact on survival ($p < 0.0001$, ►Fig. 3) and treatment with BB offered mar-

ginal protection against mortality ($p = 0.06$, ►Fig. 4). Different types of MACE, including pulmonary edema and arrhythmic events, had similar impact on survival as MI (►Fig. 5).

Discussion

Our study provides an interesting insight into patient characteristics of transplant recipients who suffer from MACE and impact of MACE on long-term survival. Unstable coronary syndromes were most frequent event, followed by pulmonary edema, cardiac arrest, and arrhythmias. The rate of MACE was highest in first few weeks after transplant surgery which is also the time of high catecholamine levels and overall hypercoagulable state.^{4,5} This is conceivable, as the serious positive

Table 6 MACE rates in different clinical subgroups

Variable	MACE rate	p Value
Female vs. male	5.4 vs. 7.3%	0.49
Smoking vs. no smoking	9.5 vs. 5.8%	0.34
Hypertensive vs. normotensive	6.6 vs. 5.6%	0.80
Diabetes vs. no diabetics	7.8 vs. 5.4%	0.41
Hyperlipidemia vs. normal lipids	2.7 vs. 7.3%	0.15
Prior MI vs. no MI	5.0 vs. 6.4%	0.80
Stress testing vs. no testing	8.0 vs. 4.1%	0.15
Poststress vs. no test	12.3 vs. 4.1%	0.03
Coronary angiogram vs. no angiogram	11.0 vs. 4.8%	0.04
Positive angiogram vs. normal study	8.0 vs. 12.1%	0.57
Revascularization vs. medical therapy	5.6 vs. 8.6%	0.66
BB vs. no BB	8.0 vs. 6.0%	0.50
AB vs. no AB	6.1 vs. 6.7%	0.84

Abbreviations: AB, angiotensin receptor blockers; BB, beta-blocker; MACE, major adverse cardiac events.

Fig. 2 Adjusted Kaplan-Meier survival curves of patients with and without MACE. Cum. survival, cumulative survival; MACE, major adverse cardiac events.

Fig. 3 Effect of smoking on survival in patients with MACE. Cum. survival = cumulative survival.

Fig. 4 Effect of β -blocker therapy on survival in patients with MACE. BB, beta blocker, Cum. survival, cumulative survival.

Fig. 5 Adjusted Kaplan-Meier survival curves of patients with ischemic versus nonischemic MACE. Cum. survival, cumulative survival; MI, myocardial infarction.

biological impact of the transplanted kidney takes few weeks to set in, when an eventual improved biological and vascular environment reduces the rate of MACE. High catecholamine tone in immediate postoperative period would possibly also explain the marginal benefit of BB treatment, known to reduce sympathetic activity, on survival in these patients.

In our study, clinical characteristics or demographics of the MACE patients were not much different from the patients without MACE except that patients with MACE tend to be of slightly higher age than patients without MACE. MACE rates were not predicted by traditional risk factors, but only by a decision to perform stress test or coronary angiogram and not even by their findings. Surprisingly, the rate of significant obstructive CAD on angiogram was only 10% in all patients with MACE and only 29% in patients with NSEMI. Of seven patients with MI, four (57%) had undergone coronary angiograms before the transplant with one patient having significant CAD and one patient underwent coronary angiogram after the transplant showing three vessel disease requiring posttransplant bypass grafting. This low rate was not just limited to patients with MACE but in all 321 patients. In the whole cohort ($n = 321$), a total of 91 coronary angiograms were performed including patients with MACE with overall positive rate of only 25%. Our observation thus supports the observations of De Lima et al who have shown correlation of coronary angiography with MACE with < 50% positive studies.⁶ However, this is in contrast to the findings of other studies of stress imaging and coronary angiography which have shown to correlate the findings of their studies with MACE.⁷ We believe that this mismatch observed in our study points toward predominance of type II MI (mismatch between supply and demand) in postoperative period or other clinical scenarios rather than classic type of type I MI resulting from rupture of coronary artery plaque.⁸ It could also reflect presence of other cardiac risk factors such as high oxidative stress, presence of underlying cardiomyopathy and abnormal microcirculation in ESRD patients resulting in cardiac enzyme elevation and MACE^{9,10} factors which are constantly being debated and need further investigational studies.

The poor correlation between positive angiograms and survival in our study also presents as an apparent contrast with the studies done on ESRD patients on transplant waiting list or posttransplant patients.¹¹ It can be explained by the positive impact of kidney transplant on patient survival even in high risk groups such as those with CAD, low number of patients in our study, and long-term nature of it. The above discussion however opens room of debate for predictive role of preoperative stress test or coronary angiogram widely employed as part of screening programs and risk stratification strategies in the United States and Europe on patient survival and occurrence of MACE. In our study, though stress test was predictive of MACE and was also significant predictor of survival on univariate cox proportional HR analysis, it lacked the same power on multivariate regression analysis and could not independently predict survival. On the contrary, coronary angiogram predicted MACE as well as survival not only in univariate model but also in multivariate model. This observation thus extends the observations of other studies done by De Lima et al⁶ and Enkiri et al¹² who have argued for the superiority of the coronary angiogram in predicting survival or events over stress imaging. However, the low rate of angiographic positivity in our study makes us suggest that careful risk stratification using clinical judgment is the primary tool of prediction for MACE. Thus, our observations highlight the interesting yet underappreciated role of the clinicians and their clinical judgment that often plays a role in high risk patient identification, not merely by traditional risk factors but also by accounting for the unmeasured clinical risk factors and underappreciated historical factors such as poor activity level, prior episodes of noncardiac chest pain, frequent hospitalizations, and prior noncardiac complications with general anesthesia.

In terms of traditional risk factors such as DM and age at transplant, high mortality was observed for every 5 years increase in age till 65 year in the whole cohort of 321 patients but not in patients with MACE or subgroup with NSTEMI. Similarly, DM appeared to be a very strong predictor of poor long-term survival in the whole cohort but not in patients with MACE or subgroup of MACE patients with NSTEMI ($p = 0.61$). Smoking or history of smoking did not predict survival in the whole cohort but was a strong predictor of poor survival in patients with MACE ($p < 0.0001$). These interesting findings can possibly be explained by the dramatic changes in life style of the patients after renal transplant and overall improved physical activity level obtunding the impact of age and reducing overall CV risk. In the case of diabetes, renal transplant recipients continue to exhibit poor survival possibly because of poor allograft renal function and recurrence of diabetic nephropathy,¹³ worsening hyperglycemia, dyslipidemia, or infections¹⁴ but at the same time, also undergo marked reduction in proatherogenic status and overall inflammation,¹⁵ decrease in oxidative stress and in end products of glycosylation¹⁶ which may explain no impact of diabetes on survival in MACE group or MACE with NSTEMI group. The role of diabetes as a risk factor for MI in posttransplant setting is a matter of active debate. Kasiske et al in their study of more than 50,000 medicare patients on deceased

donor waiting list between 1995 and 2002 have shown decreased risk¹⁷ in early time period as well late after transplant in patients with diabetes. On the contrary, Lentine et al, in their study of more than 35,000 patients from United States Renal Data system with Medicare being the primary payer, have implicated diabetes as the main risk factors for posttransplant MI.¹⁸ Despite these differences in these major studies, there appears to be a general consensus of increased MI risk compared with general population or similar posttransplant patients without diabetes and decreased risk compared with similar patients on transplant waiting list.

Our study highlights that though smoking or history of smoking did not predict MACE, it did contribute significantly toward poor survival in this subgroup. It has previously been shown that smoking before transplant or incidentally afterward is associated with high mortality and graft loss.¹⁹ The rate of MI in posttransplant patients has been shown to decrease long after quitting. Though the numbers in our study are very small and it is hard to draw firm conclusions from this observation, yet it does show a trend in survival and an addressable target in ESRD population as has been advocated by others.

This study also extends the observations of other studies which have shown that besides MI, poor survival in posttransplant patients is also contributed by new onset CHF, atrial fibrillation and other arrhythmias.^{20,21} Despite small numbers, we were able to compare survival rates between NSTEMI group and non-STEMI group showing no difference between them. When inter- and intra-group survival analysis was done for patients with MACE, without MACE, those with MACE because of MI and those without MI using Kaplan-Meier survival curves and log-rank test, the survival in non-MI group was not different from the group with MI and was significantly worse than patients without MACE.

Conclusions

In summary, our study shows increased rate of MACE in the first 4 weeks after the transplant surgery and poor long-term survival with it. MACE was predicted by decision to perform stress test and coronary angiogram and not by any of the conventional risk factors. However, the decision to perform preoperative stress testing or coronary angiogram depended upon measured and unmeasured clinical factors including older age, presence of diabetes, prior MI, hyperlipidemia, and abnormal ECG. Patients who were denied transplantation in the presence of positive stress tests, positive coronary angiograms, or other severe comorbidities were not part of this study and hence their outcome, had they received the transplant remains unknown. It is thus conceivable to think that patients with multiple cardiovascular (CV) risk factors and in particular those with diabetes pose special challenge for preoperative risk stratification. No single diagnostic or risk assessment strategy is satisfactory. Hence, these patients should be carefully assessed and in appropriate clinical settings, selected ones should be referred for a stress test or coronary angiogram. Furthermore, as, majority of the events occur within first 3 months of the transplantation, these

patients should probably continue to receive risk reduction therapies and individualized management of risk factors in this period of high vulnerability.

Limitations

Our study has several limitations. First, it is a retrospective, observational study and the findings are mostly descriptive in nature. Second, we did not have transplant specific information and data on use of immunosuppression that may have potentially changed the outcomes. Also, our study is limited by the fact that this was based upon follow-up visits and hospital admissions to our own institute. We may have missed some events in patients who lost follow-up or had events that were treated at places other than our institute.

Financial Disclosures

None.

Conflict of Interest

None.

References

- Suthanthiran M, Strom TB. Renal transplantation. *N Engl J Med* 1994;331(6):365–376
- Ojo AO, Hanson JA, Wolfe RA, Leichtman AB, Agodoa LY, Port FK. Long-term survival in renal transplant recipients with graft function. *Kidney Int* 2000;57(1):307–313
- Aftab W, Varadarajan P, Rasool S, Kore A, Pai RG. Beta and angiotensin blockades are associated with improved 10-year survival in renal transplant recipients. *J Am Heart Assoc* 2013;2(1):e000091
- Mangano DT. Perioperative cardiac morbidity. *Anesthesiology* 1990;72(1):153–184
- Schouten O, Boersma E, Hoeks SE, et al; Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echocardiography Study Group. Fluvastatin and perioperative events in patients undergoing vascular surgery. *N Engl J Med* 2009;361(10):980–989
- De Lima JJ, Sabbaga E, Vieira ML, et al. Coronary angiography is the best predictor of events in renal transplant candidates compared with noninvasive testing. *Hypertension* 2003;42(3):263–268
- Cai Q, Serrano R, Kalyanasundaram A, Shirani J. A preoperative echocardiographic predictive model for assessment of cardiovascular outcome after renal transplantation. *J Am Soc Echocardiogr* 2010;23(5):560–566
- Thygesen K, Alpert JS, White HD; Joint ESC/ACCF/AHA/WHF Task Force for the Redefinition of Myocardial Infarction. Universal definition of myocardial infarction. *J Am Coll Cardiol* 2007;50(22):2173–2195
- Sharma R, Pellerin D, Brecker SJ. Cardiovascular disease in end stage renal disease. *Minerva Urol Nefrol* 2006;58(2):117–131
- Bejan-Angoulvant T, Bergerot C, Juillard L, et al. Myocardial microvascular disease and major adverse cardiovascular events in patients with end-stage renal disease: rationale and design of the MICROCARD study. *Nephrol Dial Transplant* 2012;27(7):2886–2891
- Fabbian F, Cacici G, De Biase V, et al. Relationship between major adverse cardiac events and angiographic findings in dialysis patients. *Int Urol Nephrol* 2011;43(4):1171–1178
- Enkiri SA, Taylor AM, Keeley EC, Lipson LC, Gimple LW, Ragosta M. Coronary angiography is a better predictor of mortality than noninvasive testing in patients evaluated for renal transplantation. *Catheter Cardiovasc Interv* 2010;76(6):795–801
- Meier-Kriesche HU, Baliga R, Kaplan B. Decreased renal function is a strong risk factor for cardiovascular death after renal transplantation. *Transplantation* 2003;75(8):1291–1295
- Miles AM, Sumrani N, Horowitz R, et al. Diabetes mellitus after renal transplantation: as deleterious as non-transplant-associated diabetes? *Transplantation* 1998;65(3):380–384
- Cueto-Manzano AM, Morales-Buenrostro LE, González-Espinoza L, et al. Markers of inflammation before and after renal transplantation. *Transplantation* 2005;80(1):47–51
- Makita Z, Bucala R, Rayfield EJ, et al. Reactive glycosylation end-products in diabetic uraemia and treatment of renal failure. *Lancet* 1994;343(8912):1519–1522
- Kasiske BL, Maclean JR, Snyder JJ. Acute myocardial infarction and kidney transplantation. *J Am Soc Nephrol* 2006;17(3):900–907
- Lentine KL, Brennan DC, Schnitzler MA. Incidence and predictors of myocardial infarction after kidney transplantation. *J Am Soc Nephrol* 2005;16(2):496–506
- Hurst FP, Altieri M, Patel PP, et al. Effect of smoking on kidney transplant outcomes: analysis of the United States Renal Data System. *Transplantation* 2011;92(10):1101–1107
- Abbott KC, Hypolite IO, Hsieh P, Cruess D, Taylor AJ, Agodoa LY. Hospitalized congestive heart failure after renal transplantation in the United States. *Ann Epidemiol* 2002;12(2):115–122
- Herzog CA, Strief JW, Collins AJ, Gilbertson DT. Cause-specific mortality of dialysis patients after coronary revascularization: why don't dialysis patients have better survival after coronary intervention? *Nephrol Dial Transplant* 2008;23(8):2629–2633