# The Revised Cardiac Risk Index (RCRI) is a Useful Tool for Evaluation of Perioperative Cardiac Morbidity in Kidney Transplant Recipients

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**Abbreviations:**

| | |
|---|---|
| CAD, | coronary artery disease |
| CHF, | congestive heart failure |
| CVA, | cerebrovascular disease |
| ESRD, | end-stage renal disease |
| IDDM, | insulin-dependent diabetes mellitus |
| RCRI, | revised cardiac risk index |
| ROC, | receiver operator characteristic |

Abstract

Background: We evaluated a published Revised Cardiac Risk Index (RCRI) to determine if this preoperative cardiovascular risk stratification tool would be useful in the kidney transplant recipient population.

Methods: We identified all kidney transplants from 2005 to 2009 (n=1652) at our institution. We performed a detailed retrospective chart review of: 1) all recipients who underwent preoperative coronary angiography (n=169), and 2) an age and transplant year matched group who did not undergo coronary angiography (n=156). Charts were reviewed for the presence of specific preoperative cardiovascular risk factors and perioperative cardiovascular complications (as defined by RCRI plus elevation of troponin) from time of surgery to hospital discharge. The total number of risk factors for each patient was compared with the occurrence of postoperative cardiac complications to identify a possible association.

Results: The number of risk factors was highly predictive of cardiovascular complications (ROC area 0.77, $p<0.0001$). History of coronary artery disease (CAD) was most strongly associated (odds ratio 20.59, CI 4.73 - 89.53, $p=0.0001$) and history of congestive heart failure (CHF) was also significantly associated with cardiac complications (odds ratio 2.95, CI 1.01 - 8.59, $p=0.0475$).

Conclusion: The RCRI is a useful tool for cardiac risk stratification in kidney transplantation and could be used to develop protocols for intra- and post-operative care to minimize complications.

## Introduction

Cardiovascular disease is a major cause of morbidity and mortality in adult patients with end-stage renal disease (ESRD) on dialysis and the most common cause of death in the first few months following transplantation (1-3). Kidney transplant recipients are therefore evaluated for risks of cardiovascular complications. However, this task is becoming increasingly onerous as the age of recipients continues to increase and the waiting time to receive a deceased donor organ becomes prolonged and less predictable (4). The “Guidelines on Perioperative Cardiovascular Evaluation and Care for Noncardiac Surgery” published by the American College of Cardiology (ACC) and the American Heart Association (AHA) were not felt to be adequate for patients with ESRD due to limited symptoms in many of these patients with cardiovascular disease (4,5). Since the cardiovascular screening and treatment practices of many transplant programs were highly variable and inconsistent with published guidelines, the ACC/AHA worked with representatives of the American Society of Transplant Surgeons (ASTS), American Society of Transplantation (AST), and National Kidney Foundation (NKF) to develop a consensus document regarding “Cardiac Disease Evaluation and Management Among Kidney and Liver Transplantation Candidates” (6).

These guidelines suggest that preoperative cardiac testing is justified because it is difficult to quantify cardiovascular risk based on patient history alone. Although risk stratification indices have been published, few have been tested on this unique patient population (7). One such stratification tool, the “Revised Cardiac Risk Index (RCRI)” (8), is a commonly used, well validated, simple and practical stratification tool. Evidence based risk stratification of renal transplant patients could help guide perioperative medical management, potentially improving safety and reducing cost. This study aims to determine whether the RCRI can predict major cardiovascular morbidity in the renal transplant patients, and to determine which of the RCRI preoperative risk factors are most strongly associated with adverse cardiac events.

## Results

Baseline patient characteristics are presented in Table 1. The total incidence of cardiac complications in the study population was 7.1% (23/325). All of these patients were on dialysis at the time of transplant. The cardiac safety endpoints included death, myocardial infarction, congestive heart failure, complete heart block, ventricular fibrillation, and elevated troponin. Of the 23 patients who had an adverse cardiac event, three died; one patient died from coronary in-stent thrombosis, and two patients died from a myocardial infarction in the setting of overwhelming sepsis. The remaining 20 patients with cardiac complications had either a non-ST elevation myocardial infarction, congestive heart failure, or an isolated elevated troponin (n=5), with only 3 requiring any postoperative invasive coronary intervention (Table 2).

An increasing number of RCRI preoperative risk factors was significantly associated with higher rates of perioperative cardiac complications (ROC area 0.77, $p<0.0001$). When stratified by patient age, this significant association was again seen for patients age ≥ 50y (ROC area 0.77, $p<0.0001$), but not for patients <50y in whom only 2 complications occurred (Figure 1).

History of CAD was most strongly associated with cardiac complications (odds ratio 20.59, CL 4.73-89.53, $p=0.0001$) and history of CHF was also significantly associated with cardiac complications (odds ratio 2.95, CL 1.01-8.59, $p=0.0475$). IDDM history strongly but non-significantly trended with cardiac complications (odds ratio 2.29, CL 0.96-5.43, $p=0.061$), and history of CVA showed no such trend. Patient gender and organ graft type were only weakly and not significantly associated with cardiac complications, and this association weakened further after adjustment for the number of RCRI risk factors.

## Discussion

The RCRI was shown to be an effective tool for predicting perioperative cardiovascular complications with kidney transplantation. A strong association was found between the number of RCRI risk factors and the incidence of cardiovascular morbidity. The ROC area in our analysis was 0.77, similar to the ROC area reported by Lee et. al. (0.76 derivation cohort and 0.81 validation cohort) in their landmark paper which defined the RCRI (8). But while in Lee's study of vascular surgery patients each risk factor contributed to the prediction of cardiovascular morbidity with roughly equal weight, such

was not the case in our kidney transplant population. CAD was most strongly associated with cardiovascular morbidity, as would be expected. Unexpectedly, CHF came in a distant second, perhaps because pulmonary edema was more a function of fluid overload in a dialysis patient rather than secondary to acute myocardial ischemia or dysfunction. IDDM did not significantly predict excess risk, but a strong trend suggested that the study might have been underpowered to detect the association. Gender and age, two historical risk factors for developing cardiovascular disease, were also evaluated for their predictive effects in the kidney transplant population (9). Too few cardiovascular complications occurred in patients <50yrs of age to determine any meaningful association between risk factors and cardiovascular morbidity. The results of this study do however suggest that younger patients without a history of CAD or CHF are unlikely to suffer from cardiovascular complications. Interestingly, although men had more cardiovascular complications than women, once the confounding effects of other RCRI risk factors (such as CAD and CHF) were factored out, no statistical differences were seen between the sexes.

This study has several important limitations due to its retrospective design. First, it was not always apparent whether the preoperative diagnosis of CAD was made purely through history and physical exam or whether cardiac diagnostic testing played a role. Second, patient selection criteria for cardiac testing were not standardized, and specific reasons for choosing to test were not always documented. Our institution follows the guidelines developed by the American Society of Transplantation (10) whereby all patients with potential cardiac symptoms or abnormal cardiac diagnostic tests are

referred for evaluation by a transplant cardiologist, who then decides whether further cardiac testing is indicated. However, as a regional referral center our institution transplants patients from other institutions, which may utilize different algorithms to work up their patients preoperatively. Given this lack of standardization, it is possible that in some patients, cardiac diagnostic tests uncovered previously unknown CAD that would have been missed by risk factor evaluation alone. Furthermore, postoperative management and surveillance of cardiac complications were also not standardized. Since electrocardiograms, serum troponin levels, and chest radiographs were not routinely ordered, silent myocardial ischemia might have been underreported. Given these limitations, we cannot recommend abandoning diagnostic testing on asymptomatic patients deemed at risk for coronary ischemia. Larger prospective trials would be needed to further develop perioperative best practice guidelines in the kidney transplant patient population.

Another limitation was that we did not analyze the coronary angiography results and correlate them to perioperative cardiac morbidity. However, our study was not designed to evaluate the perioperative ischemic risk of a specific coronary anatomy, as has previously been done (11). Rather, its goal was to evaluate the utility of the RCRI in the kidney transplant population. We therefore set out to select a patient population with enough presumed high-risk subjects (and therefore anticipated cardiac complications) to enable a meaningful statistical analysis; the coronary angiography subgroup in retrospect met these goals. Nevertheless, our total number of complications, while not

insignificant, was too low to perform a multivariate logistic regression, and therefore the effects of confounding variables could not be excluded.

Given these limitations, we cannot recommend that the RCRI be used to replace cardiac testing or determine organ allocation. Nevertheless, accurate risk stratification can help medical personnel identify high-risk patients that may benefit from increased perioperative monitoring combined with goal-directed cardiovascular therapy (12). With careful titration of fluid balance and watchful monitoring of cardiac function, cardiac morbidity may be reduced. Further research needs to be conducted to determine the best perioperative management strategy for kidney transplant candidates with heart disease. Given that the number-one cause of patient death with a functioning transplant is cardiovascular disease (13), even a small reduction in cardiovascular morbidity can have a significant impact.

## Materials and Methods

After obtaining Institutional Review Board approval for this retrospective study (IRB# 10-000577, 9/28/09) we reviewed the electronic records of 1652 kidney transplant operations performed at UCLA medical center between 2005-2009. Based on a sample size calculation aimed at achieving 80% power to detect a correlation of at least 0.15 or higher between the number of RCRI risk factors and cardiac complications at a $p<0.05$ level of significance, we determined that we needed a study population of 325 patients. Our study group included all patients (n=169) who underwent preoperative coronary angiography and an age and transplant year matched group (n=156), which did not

undergo coronary angiography. Indications for coronary angiography included: 1) evidence of myocardial ischemia on non-invasive stress testing, 2) clinical suspicion based upon patient symptoms and/or multiple cardiovascular risk factors. The detailed chart review of each of these 325 cases focused on the pertinent preoperative history, intraoperative events, and postoperative course, as described below.

After collecting preoperative baseline characteristics we applied the previously published RCRI (8) to the entire study group, identifying the following six preoperative risk factors: coronary artery disease (CAD), congestive heart failure (CHF), cerebrovascular disease (CVA), insulin-dependent diabetes mellitus (IDDM), serum creatinine> 2mg/dL, and high risk (suprainguinal vascular abdominal) surgery. The perioperative record was reviewed for the development of the following cardiovascular complications, as defined in the RCRI study: myocardial infarction, cardiac arrest, congestive heart failure, complete heart block, and ventricular fibrillation. Myocardial infarction was defined as the development of pathologic Q waves (≥30 msec in duration and ≥0.1 mV in depth) in two or more contiguous precordial leads or two or more adjacent limb leads, or an elevation of creatine kinase MB isoenzyme levels (or total creatine kinase if measures of creatine kinase MB were not available) to at least two times the upper limit of the normal range (14). Congestive heart failure was diagnosed as the presence of pulmonary rales, pulmonary congestion on chest radiograph, or the presence of a third heart sound. Complete heart block was defined as loss of atrioventricular conduction. Troponin levels were obtained at the discretion of the treating physician. Isolated perioperative elevated troponin (>0.04mg/dL) was also

captured as a complication given its association with poor cardiovascular outcome (15,16). The perioperative course and 30 day outcome of the patients who had an adverse cardiac event was then investigated and described.

The total number of risk factors for each patient was compared with the occurrence of postoperative cardiac complications to identify a possible association. This comparison was also stratified by age (≥50y vs. <50y) to determine that variable's impact on this association. The bivariate relationship between each individual RCRI risk factor and the incidence of cardiac complication was then assessed. Finally, graft type (living vs. deceased donor) and patient gender were analyzed as potential predictive factors in addition to those defined by the RCRI.

*Statistical methods*

The association between the number of risk factors and the occurrence of complications was assessed using Spearman correlation to test for trend. Prediction accuracy of using the RCRI for predicting the risk of cardiac complications was evaluated using the area under the receiver operator characteristic (ROC) curve. The bivariate relationship between each individual component of the RCRI and the odds of having a complication was assessed using logistic regression. In addition, the relationship between gender and graft type versus the odds of having a complication was assessed before and after adjusting for the number of risk factors using logistic regression. These results are reported as odds ratios with corresponding 95% confidence intervals under the above logistic models.

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**Table and Figure Legends**

**Table 1**. Patient Characteristics with Revised Cardiac Risk Index (RCRI) factors

**Table 2.** Detailed Description of Patients with Cardiovascular Complications

**Table 2 legend**

Afib – atrial fibrillation, AICD – automatic implanted cardiac defibrulator, CABG – coronary artery bypass graft, CAD – coronary artery disease, CHF – congestive heart failure, CXR – chest x-ray, DD – deceased donor, ECG - elctrocardiogram
EF – ejection fraction, LAD – left anterior descending coronary artery, LBBB – left bundle branch block, LR – living related donor, LU – living unrelated donor,
MI – myocardial infarction, NSTEMI – non ST elevation myocardial infarction,
OHT – orthotopic heart transplant, PCI – percutaneous coronary intervention,
POD – post operative day, Pulm – pulmonary, RCA – right coronary artery, Trop – troponin elevation

**Figure 1**.  Cardiac Complications (%)

**Figure 1. legend**

The incidence of perioperative cardiac complications is plotted against the number of Revised Cardiac Risk Index (RCRI) risk factors.  Dark bars represent all patients; light bars represent patients older than age 50 years.  Exact percent values appear above each bar.

**Table 1**. Patient characteristics with Revised Cardiac Risk Index (RCRI) factors

| | |
|---|---|
| General characteristics (n=325) | |
| Age (yr) | 54 (range 31-82) |
| Male sex (%) | 62 |
| Age ≥ 50 years (%) | 65 |
| | |
| RCRI risk factors (%) | |
| Coronary artery disease | 38 |
| Insulin-dep. diabetes mellitus | 26 |
| Congestive heart failure | 10 |
| Cerebrovascular accident | 6 |
| Creatinine > 2mg/dL | 100 |
| Abdominal vascular surgery | 100 |
| | |
| Number of RCRI risk factors (%) | |
| 2 risk factors | 46 |
| 3 risk factors | 34 |
| 4 risk factors | 14 |
| ≥5 risk factors | 6 |

**Table 2.** Detailed Description of Patients with Cardiovascular Complications

| | AGE | SEX | DONOR TYPE | RCRI | Complications | Comment |
|---|---|---|---|---|---|---|
| 1 | 67 | M | DD | 5 | MI, Death | CABG 5 yrs prior, stress thallium (-) pre-op. Post-op E Coli sepsi |
| 2 | 54 | M | DD | 5 | MI, CHF | LAD stent 4y pre-op. NSTEMI, reintubated POD1 for CHF. PCI+ |
| 3 | 54 | M | DD | 5 | MI, CHF | Pre-op ischemic cardiomyopathy, EF 35%, AICD placed empirica |
| 4 | 63 | M | DD | 5 | MI, CHF | Pulmonary edema, ST depressions on ECG, NSTEMI medically |
| 5 | 64 | M | LR | 5 | CHF | OHT 11y pre-op secondary to ischemic CM. Post-op CHF requiri |
| 6 | 64 | F | DD | 4 | MI, Death | RCA angioplasty 4 years prior to surgery, pre-op perfusion scan NSTEMI, death POD #20 from sepsis-multi organ systems failure |
| 7 | 63 | F | DD | 4 | MI, CHF | Coronary angiogram 2 years pre-op showed non-obstructive CA hypoxemic, severe hypotension. NSTEMI treated with medicatio |
| 8 | 61 | M | DD | 4 | MI | Pre-op coronary stent. NSTEMI post-op, PCI shows restenosis, |
| 9 | 52 | M | LU | 4 | CHF | CABG 4y pre-op, PCI w/stents 3y pre-op. Stress test (-) for ische + positive troponin, treated with diuretics |
| 10 | 58 | M | LR | 4 | Trop | Multiple pre-op PCI with stenting. Pre-op stress test (-). Post-op |
| 11 | 51 | M | DD | 4 | Trop | Pre-op coronary angiogram showed non-obstructive CAD. Intra- transplant. Post-operative stress test (-) |
| 12 | 63 | M | LR | 3 | MI, Death | CABG 12y pre-op, distal LAD stent 6y pre-op, (-)myoview pre-op surgery. Cardiac arrest and death POD 9. Autopsy showed in ste |
| 13 | 69 | F | DD | 3 | MI, CHF | CABG 2 years pre-op, (-)adenosine stress test 1 year pre-op. Po coronary stents placed POD 14. |
| 14 | 57 | M | DD | 3 | MI | CABG 11y pre-op, stress thallium mild (+) in RCA territory. Post- |
| 15 | 57 | F | DD | 3 | MI | CABG 1yr pre-op, stress thallium mild (+). Post-op Afib w/ rapid v |
| 16 | 61 | M | DD | 3 | MI | History of MI 6yrs pre-op. Post-op NSTEMI s/p hypotension and |
| 17 | 62 | M | DD | 3 | MI | CABG 1 year pre-op. NSTEMI post-op, Medically treated. |
| 18 | 58 | M | LU | 3 | CHF | CABG 6y pre-op, EF 40%. Mild pulmonary edema POD# 1 treate |
| 19 | 66 | M | DD | 3 | CHF | CABG 6y pre-op, AVR, PCI, AICD for v-tach 1y pre-op. Mild post treated with diuretics |
| 20 | 67 | F | DD | 3 | Trop | Pre-op MI treated with PCI + stent. Post-op Afib with rapid ventri |
| 21 | 66 | M | DD | 3 | Trop | PCI with stent 1y pre-op. Routine troponin (+) post-op, otherwise |
| 22 | 47 | F | LU | 3 | Trop | Post-op Afib with rapid ventricular rate, medically treated |
| 23 | 45 | F | DD | 2 | MI | Adenosine thallium 4 months pre-op (-). Post-op hypotension, NS |