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# Similar risk profiles for post-transplant renal dysfunction and long-term graft failure: UNOS/OPTN database analysis

**NAUMAN SIDDIQI, MAUREEN A. MCBRIDE, and SUNDARAM HARIHARAN**

*Division of Nephrology, Medical College of Wisconsin, Milwaukee, Wisconsin; and United Network for Organ Sharing, Richmond, Virginia*

**Similar risk profiles for post-transplant renal dysfunction and long-term graft failure: UNOS/OPTN database analysis.**

*Background.* Renal dysfunction measured by serum creatinine (>1.5 mg/dL) at 1 year post-transplant correlates with long-term kidney graft survival. The purpose of this study was to compare the risk factors for elevated serum creatinine (SCr) >1.5 mg/dL at 1 year post-transplantation, and for long-term graft failure.

*Methods.* Between 1988 and 1999, 117,501 adult kidney transplants were reported to Organ Procurement and Transplantation Network/United Network for Organ Sharing (OPTN/UNOS). Of these, 96,091 were functioning at 1 year and SCr was available on 85,135 transplants. Donor and recipient demographics (age, sex, and race), transplant [living vs. cadaveric, previous transplantation, panel reactive antibody (PRA), human leukoocyte antigen (HLA) mismatch, cold ischemic time (CIT) and post-transplant delayed graft function (DGF), use of azathioprone vs. mycophenolate mofetil (MMF), cyclosporine A (CsA) vs. tacrolimus (Tac)], induction antibody, acute rejection within 1 year variables were used in the logistic regression model to estimate odds ratio (OR) for elevated 1 year serum creatinine (SCr). A Cox proportional hazard model was used to estimate the relative risk (RR) for long-term kidney graft failure with and without censoring for death with a functioning graft.

*Results.* Five-year actuarial graft survival for living donor transplant with SCr >1.5 and ≤1.5 mg/dL at 1 year post-transplant was 83% and 88.6% ($P < 0.001$). The corresponding values for cadaveric transplant grafts were 66.5% and 77.9% ($P < 0.001$). The overall prevalence of renal dysfunction at 1 year post-transplant (SCr >1.5 mg/dL) declined from 54.5% in 1988 to 42.3% in 1999. There was a strong concordance between the key variables, such as cadaveric transplant, increasing CIT, HLA mismatch, DGF, and acute rejection, recipient race (black), younger age, and nondiabetics status; and donor race (black) and older age for elevated SCr and long-term graft failure.

*Conclusion.* Donor (age), race (black), recipient race (black), immunologic variables (HLA mismatch, DGF, acute rejection) were identified as important risk factors for elevated SCr at 1 year post-transplantation and long-term graft failure. Elevated SCr should be used as a short-term marker for predicting long-term transplant survival.

**Key words:** risk factors, post-transplant renal dysfunction, long-term graft failure.

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Renal transplant success is measured by evaluating short-term end points such as acute rejection rates and 1-year graft survival [1]. Newer immunosuppressive agents such as mycophenolate mofetil (MMF), tacrolimus (Tac), and sirolimus have been shown to reduce short-term acute rejection rates in clinical trials without impacting short-term survival rates [2–7]. Improvements in short- and long-term graft survival rates after renal transplantation have been noted in a large database analysis [8]. Short-term survival improvements coupled with reduced acute rejection rates have lessened our ability to measure alternative newer therapies that can further optimize graft survival. This dilemma has prompted investigators to evaluate alternative short-term markers that can predict long-term survival. Post-transplant renal function is one such surrogate marker considered for predicting long-term survival [1, 9].

Post-transplant renal function within the first year has been correlated with long-term survival in single-center series, as well as in large database analysis [9, 10]. In a recent United Network for Organ Sharing (UNOS)/Organ Procurement and Transplantation Network (OPTN) analysis, post-transplant serum creatinine >1.5 mg/dL was shown to be associated with poor long-term survival [9]. This prompted us to compare factors for short-term renal dysfunction and long-term graft failure. The present study compares the risk factors for elevated serum creatinine (SCr) >1.5 mg /dL at 1 year with risk factors for long-term graft failure using the UNOS/OPTN database.

## METHODS

All adult renal transplant recipients reported to the UNOS/OPTN database between 1988 and 1999 that were

alive with a functioning graft at 1 year post-transplant were included in the study. Patients that received multiorgan transplants such as simultaneous kidney and pancreas grafts were excluded from the analysis. Post-transplant renal dysfunction at 1 year was defined by elevated SCr >1.5 mg /dL. Long-term graft failure was defined as resumption of permanent dialysis therapy, repeat transplantation, or death. Long-term graft failure was also examined after censoring for death with a functioning graft.

Potential risk factors for renal dysfunction at 1 year and long-term graft failure were divided into four groups: donor, recipient, transplant, and post-transplant factors. These variables included the following characteristics: donor (age, sex, and race), recipient [age, sex, race, cause of end-stage renal disease (ESRD)], pretransplant maintenance dialysis therapy, previous transplantation], transplant [living vs. cadaveric, human leukocyte antigen (HLA) mismatch, elevated plasma renin activity (PRA) >80% vs. ≤80%, cold ischemia time (CIT) in hours, and transplant year] and post-transplant [delayed graft function (DFG), clinical acute rejection within 1 year post-transplant, use of antibody induction, and discharge immunosuppression, including use of mycophenolate mofetil (MMF) vs. azathioprine (Aza), Cyclosporine A (CsA) vs. tacrolimus (Tac)].

The Kaplan-Meier method was used to estimate post 1-year actuarial graft survival [11]. A maximum likelihood estimate of the projected half-life (median value) was calculated assuming exponentially distributed graft survival times. The analysis did not account for reporting bias associated with early notification of critical events (graft failure) and delayed notification for continued survival. In order to account for differences in characteristics among patient groups, the odds ratio (OR) for developing renal dysfunction at 1 year was estimated using a logistic regression model, and the relative hazard (RH) for long-term graft failure was estimated using a Cox proportional hazards model. $P$ values of $< 0.05$ were considered significant. All statistical analyses were performed using SAS version 8.2 (SAS Institute, Cary, NC).

## RESULTS

Between 1988 and 1999, a total of 117,501 adult renal transplants were reported to UNOS/OPTN. Among these, 96,091 renal grafts were functioning at 1-year post-transplantation, and SCr was available for 85,135 grafts. Thus, a total of 85,135 transplants were included in this study. There were 24,701 (29%) living donor transplants and 60,434 (71%) cadaveric transplants. Of these, 11,283 (13.3%) were repeats, and the remaining 73,852 (86.7%) were primary grafts. Among these, 41,299 (48.5%) recipients had elevated SCr >1.5 mg/dL at 1 year post-transplantation. A total of 23,570 (28%) grafts failed; 8394 (36%) of these failed because of patient death.

**Table 1.** Donor and recipient demographics and characteristics for all renal transplants with 1-year serum creatinine >1.5 and ≤1.5 mg/dL, *N* (%)

| | Creatinine ≤1.5 mg/dL | Creatinine >1.5 mg/dL | *P* value |
|---|---|---|---|
| *N* | 43,836 (51.5%) | 41,299 (48.5%) | |
| Donor type | | | <0.001 |
| LD Tx | 13,937 (31.8%) | 10,764 (26.1%) | |
| CD Tx | 29,899 (68.2%) | 30,535 (73.9%) | |
| Donor age >50 years | 4,593 (10.6%) | 11,398 (27.8%) | <0.001 |
| Donor race | | | <0.001 |
| White | 34,005 (78.1%) | 32,196 (78.0%) | |
| Black | 4,050 (9.3%) | 4,821 (11.7%) | |
| Other | 5,473 (12.6%) | 4,042 (9.8%) | |
| Donor sex | | | <0.001 |
| Male | 26,688 (60.9%) | 21,412 (51.8%) | |
| Female | 17,145 (39.1%) | 19,885 (48.2%) | |
| Recipient age | | | <0.001 |
| 18–34 years | 11,283 (25.7%) | 12,369 (29.9%) | |
| 35–49 years | 16,623 (37.9%) | 16,720 (40.5%) | |
| ≥50 years | 15,930 (36.3%) | 12,210 (29.6%) | |
| Recipient race | | | <0.001 |
| White | 28,961 (66.1%) | 25,330 (61.4%) | |
| Black | 7,226 (16.5%) | 10,894 (26.4%) | |
| Other | 7,619 (17.4%) | 5,056 (12.2%) | |
| Recipient sex | | | <0.001 |
| Male | 21,056 (47.9%) | 29,911 (72.4%) | |
| Female | 22,780 (51.9%) | 11,388 (27.6%) | |
| Pre-tx dialysis | | | <0.001 |
| Yes | 37,698 (85.8%) | 36,058 (87.3%) | |
| No | 3,269 (7.4%) | 2,353 (5.2%) | |
| PRA >80% | 918 (2.2%) | 747 (1.9%) | <0.001 |
| Prior transplantation | 5,617 (12.8%) | 5,666 (13.7%) | <0.001 |
| HLA mismatch | | | <0.001 |
| 0–2 | 16,245 (37.8%) | 12,976 (32.0%) | |
| 3–4 | 19,266 (44.8%) | 19,571 (48.2%) | |
| 5–6 | 7,506 (17.5%) | 8,049 (19.8%) | |
| CIT >24 hours | 9,815 (25.4%) | 11,269 (30.24%) | <0.001 |
| DGF Yes | 5,264 (12.2%) | 8,719 (21.4%) | <0.001 |
| AR within 1-year post-tx Yes | 12,103 (30.0%) | 18,044 (47.8%) | <0.001 |

Abbreviations are: LD, living donor transplant; CD, cadaver donor transplant; TX, transplant; DGF, delayed graft function; CIT, cold ischemia time in hours; AR, acute rejection; HLA, human leukocyte antigen; PRA, panel reactive antibody.

Table 1 illustrates differences in the demographic, transplant, and post-transplant variables for recipients with 1 year SCr >1.5 and ≤1.5 mg/dL. Those with elevated SCr at 1 year were more likely to be male, black, and have had a previous transplant. They were less likely to have the diagnosis of diabetes than recipients with SCr ≤1.5 mg/dL at 1 year. Donor factors were also different. Those with elevated SCr were more likely to have received kidney from a female donor, black donor, or an older donor. Recipients with SCr >1.5 mg/dL at 1 year were also more likely to have CIT >24 hours, DGF, acute rejection within one year, and were less likely to have received a well-matched kidney.

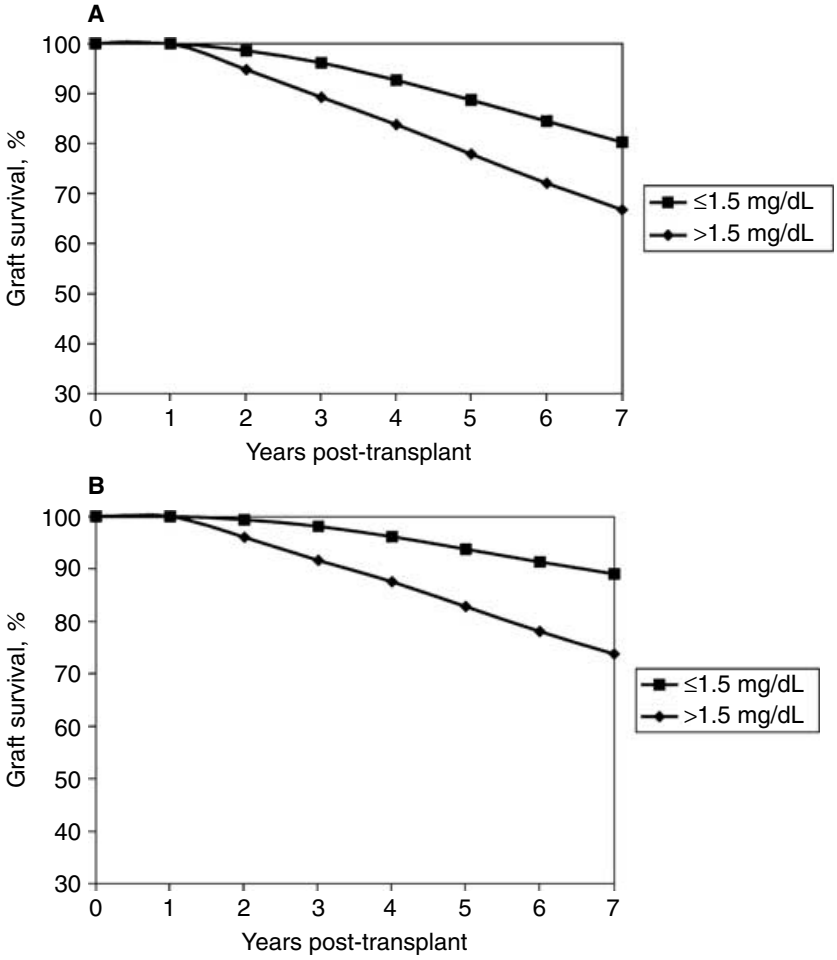


**Fig. 1. Post 1-year actuarial kidney graft survival for living donor grafts without (*A*) and with (*B*) censoring for death with a functioning graft according to 1 year serum creatinine (≤1.5 mg/dL and >1.5 mg/dL).**

Figures 1 and 2A and B show the post 1-year actuarial kidney transplant graft survival for living and cadaveric recipients with 1-year SCr ≤ and >1.5 mg/dL. Lower long-term survival was noted in both living ($P < 0.001$) and cadaveric ($P < 0.001$) donor recipients with 1 year SCr >1.5 mg/dL. The 5-year actuarial graft survival for living donor recipients with SCr >1.5 and ≤1.5 mg/dL at 1-year post-transplant were 83% and 88.6%, respectively. The corresponding values for cadaveric grafts were 66.5% and 77.9%, respectively. The differences between graft survival after living and cadaveric transplantation with SCr ≤ and >1.5 at 5 years were 5.6 and 11.4 percentage points, respectively. The projected median half-life for grafts from living and cadaveric recipients with SCr ≤ and >1.5 mg/dL are shown in Figures 3A and B. The half-lives were approximately halved in recipients with elevated SCr in both living and cadaveric donor grafts, compared with those with SCr ≤1.5 mg /dL. The kidney graft half-lives for living and cadaveric grafts with SCr ≤1.5 mg/dL was 24.9 and 15.8 years, respectively. The corresponding values for graft with SCr >1.5 mg/dL were 13 and 8.3 years, respectively. When censored for death with a functioning graft the difference in pr ojected half-lives persisted, however, to a lesser degree between SCr ≤ and >1.5 mg/dL. Kidney graft half-lives for living donor kidney grafts with SCr ≤ and >1.5 mg/dL were 44.5 and 17.4 years, respectively. The corresponding values for cadaveric donor grafts were 31.2 and 11.7 years, respectively. The difference in graft half-life with elevated SCr for living and cadaveric donor grafts were 29.8% and 32.7%, respectively.

Table 2 shows the results of the logistic regression analysis for elevated SCr at 1 year. The parameter estimate, OR, 95% CI, and *P* value are shown for recipient, donor, transplant, and post-transplant variables. Significant variables associated with increased risk of renal dysfunction included were: recipient (younger age, black race), donor (older age, female sex, black race), transplant variables (DGF), and post-transplant variables (acute rejection within 1 year).

Table 3 shows the result of the proportionate hazard analysis for long-term graft failure with and without censoring for death. The RH values were significantly higher for long-term graft failure for variables such as recipient

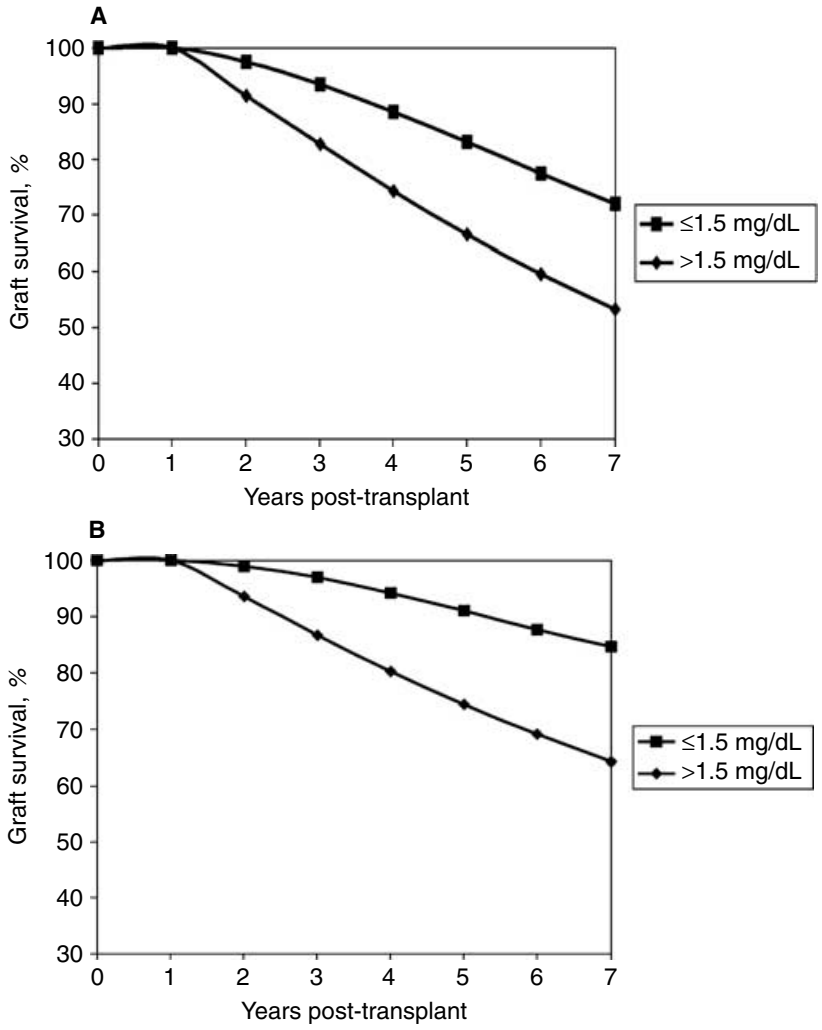


**Fig. 2. Post 1-year actuarial kidney graft survival for cadaver donor grafts without (*A*) and with (*B*) censoring for death with a functioning graft according to 1 year serum creatinine (≤1.5 mg/dL and >1.5 mg/dL).**

(older age, black race, diabetes), donor (older age, black race), transplant (previous transplant, elevated PRA, cadaveric recipient, DGF) and post-transplant (acute rejection within 1 year). The RH values for long-term graft failure when censored for death were similar except for recipient age and diabetes, where the risk of graft failure was less when death was excluded as a graft failure (Table 3).

The odds of developing post-transplant renal dysfunction were higher with the following risk variables: recipient age (34 vs. 44 years), 20%; race (black vs. other), 68%; donor age (44 vs. 34 years), 54%; race (black vs. other), 36%; DGF, 44%; and acute rejection, 98% ($P < 0.0001$). The RH values for long-term graft failure were: recipient age (34 vs. 44 years), 3%; race (black vs. other), 55%; donor age (44 vs. 34 years), 12%; race (black vs. other), 22%; DGF, 21%; and acute rejection, 34% ($P < 0.0001$). The RH values for long-term graft failure when censored for death were: recipient age (34 vs. 44 years), 25%; race (black vs. other), 86%; donor age (44 vs. 34 years), 17%; race (black vs. other), 28%; DGF, 20%; and acute rejection, 50% ($P < 0.0001$).

Table 4 shows the OR and RH for selected risk variables for post-transplant renal dysfunction at 1 year (*a*), long-term graft failure including death (*b*), and long-term graft failure censoring for death (*c*). The increased OR and RH values were similar in magnitude and direction for many variables, such as recipient (race), donor (age, race), and transplant (cadaver grafts, CIT, HLA mismatch, DGF, acute rejection within 1 year), for predicting post-transplant elevated SCr and long-term graft failure are shown in Tables 2, 3, and 4. The OR for elevated SCr and RH values for long-term graft failure were dissimilar for older recipients, female recipients, and for those who had diabetes (Tables 2, 3, and 4). However, the RH values for long-term graft failure decreased when long-term graft failure was censored for death with a functioning graft. For example, the RH decreased from 1.48 to 1.08

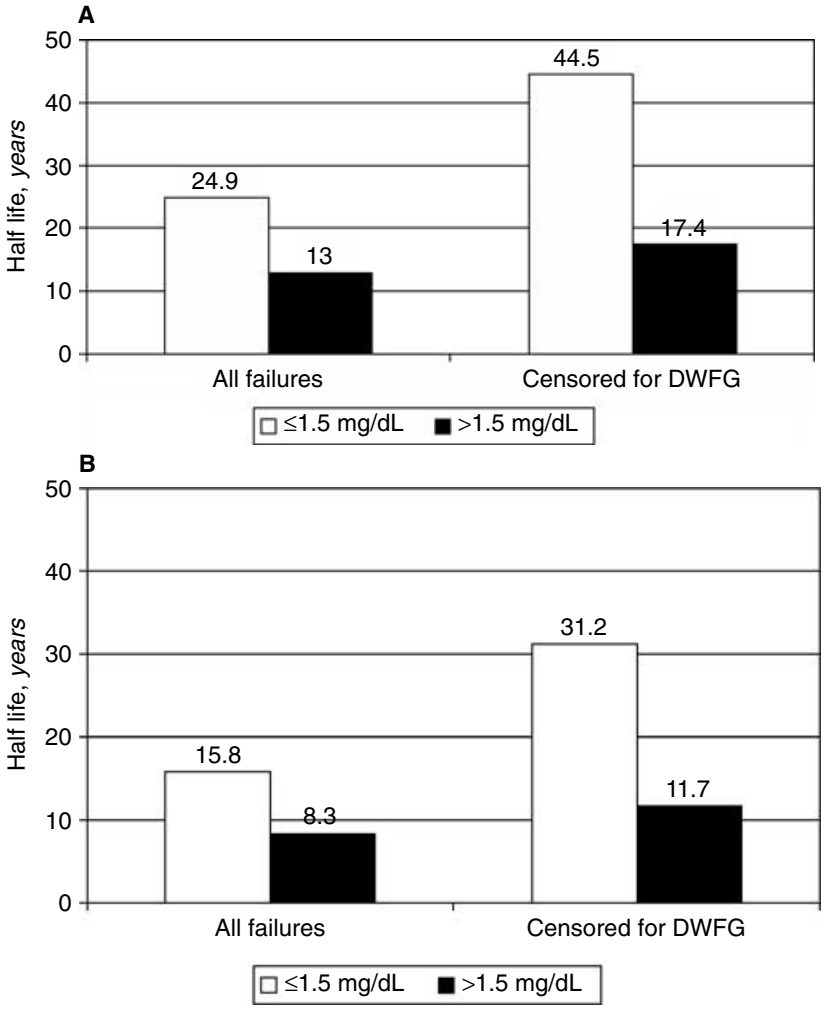


**Fig. 3. Projected median kidney graft half-life in years, for living donor (*A*) and cadaver donor (*B*) kidney grafts according to 1-year serum creatinine (≤1.5 mg/dL and >1.5 mg/dL) with and without censoring for death with a functioning graft.**

for diabetic recipient, and 1.42 to 0.76 for recipient age (64 vs. 44 years). Thus, older recipients and those who had diabetes had higher risk of graft failure because of death with a functioning graft rather than isolated graft failure.

## DISCUSSION

Improvements in short-term graft survival and lower acute rejection rates have impeded our ability to assess further advances [1]. Long-term graft survival is an ideal marker for evaluating future transplant outcome, but impractical because of the longer follow-up and large cohort of patients that are required to estimate such an outcome. Hence, it is important to consider short-term markers, which can predict long-term survival [1], such as post-transplant renal function [9]. The current study quantifies the degree of risk profiles for short-term graft dysfunction and long-term survival.

Post-transplant SCr as a marker is limited, as it varies by age, sex, race, and body weight. Thus, SCr may correlate with long-term graft failure without adequate predictive values. The present study was undertaken to compare the risk factors for elevated SCr and long-term graft failure after correcting for various donor, recipient, transplant, and post-transplant variables. The proportion of recipients with certain demographics, transplant, and post-transplant variables were different in those recipients who had SCr >1.5 mg /dL in this study (Table 1). Appropriately, these recipient, donor transplant, and post-transplant variables were included in the logistic regression and proportional hazard models. Thus, the OR and RH estimations derived in this study were adjusted for various key risk variables between the groups.

The odds of developing post-transplant renal dysfunction at 1 year were higher with certain variables, such as recipient (younger age, male sex, and black race), donor (older age, female sex, and black race), transplant (cadaveric grafts, DGF, HLA mismatch), and post-transplant variables (acute rejection) (Table 2). These

**Table 2.** Logistic regression model for predicting elevated serum creatinine >1.5 mg/dL at 1-year post-transplantation

| Variable | Parameter estimate | RH | 95% CI | *P* value |
|---|---|---|---|---|
| Recipient | | | | |
| Age—Linear | −0.2056 | | | <0.0001 |
| Age—Quadratic | −0.0231 | | | <0.0001 |
| 34 vs. 44 | | 1.20 | (1.18, 1.23) | |
| 54 vs. 44 | | 0.80 | (0.78, 0.81) | |
| 64 vs. 44 | | 0.60 | (0.58, 0.63) | |
| Female vs. male | −1.2179 | 0.30 | (0.29, 0.31) | <0.0001 |
| Black vs. other | 0.5200 | 1.69 | (1.61, 1.76) | <0.0001 |
| Diabetic vs. other | −0.2867 | 0.76 | (0.72, 0.78) | <0.0001 |
| HTN nephrosclerosis vs. other | −0.0603 | 0.94 | (0.90, 0.99) | 0.0150 |
| Donor | | | | |
| Age 44 vs. 34 years | 0.4366 | 1.55 | (1.53, 1.57) | <0.0001 |
| Female vs. male | 0.3068 | 1.36 | (1.32, 1.40) | <0.0001 |
| Black vs. other | 0.3066 | 1.36 | (1.29, 1.44) | <0.0001 |
| Transplant | | | | |
| HLA mismatch | 0.0390 | 1.04 | (1.03, 1.05) | <0.0001 |
| CIT 26 vs. 16 hours | 0.0782 | 1.08 | (1.06, 1.10) | <0.0001 |
| DGF vs. no DGF | 0.3638 | 1.44 | (1.38, 1.50) | <0.0001 |
| LD vs. CD | −0.0597 | 0.94 | (0.91, 0.98) | 0.0033 |
| Post-transplant variables | | | | |
| Antibody induction | 0.0629 | 1.07 | (1.03, 1.10) | 0.0002 |
| Acute rejection within 1-year | 0.6831 | 1.98 | (1.92, 2.05) | <0.0001 |
| MMF vs. other | −0.1527 | 0.86 | (0.82, 0.90) | <0.0001 |
| TAC vs. CsA | −0.2813 | 0.76 | (0.71, 0.80) | <0.0001 |

Abbreviations are: LD, living donor transplant; CD, cadaver donor transplant; TX, transplant; DGF, delayed graft function; CIT, cold ischemia time in hours; AR, acute rejection; HLA, human leukocyte antigen; PRA, panel reactive antibody; MMF, mycophenolate mofetil; TAC, tacrolimus; CsA, cyclosporine.

are well known variables that are known to impact long-term graft survival [12–16]. Thus, the present study clearly identifies these risk factors when SCr was used as an end point instead of long-term survival.

The impact on long-term graft survival was estimated in the present study by actuarial survival analysis, as well as projected median graft half-lives. There was a substantial impact on long-term graft survival with elevated SCr at 1 year for both living and cadaver grafts (Figs. 1 and 2). Substantial impact on graft survival cannot be attributed to death, as similar trends were observed when grafts were censored for death with a functioning graft. It is possible that this may be caused by a higher proportion of black recipients, or those who had repeat transplants, DGF, and increasing degree of HLA mismatches, who were included in the elevated SCr group. To correct this bias, these risk factors were included in the Cox model to control their impact on long-term survival. The present study detected various well-known risk variables that impact on long-term graft failure (Tables 3 and 4), including recipient (age, sex, race), donor (age, sex, race), transplant (DGF), and post-transplant (acute rejection).

The present study is the first one to compare the risk factors between a short-term end point—SCr >1.5 mg /dL—and long-term graft failure. It is interesting that not only the risk factors identified, but also the degree of risk, were similar when estimated by OR and RH methods (Table 4). The degree of risk profiles for elevated SCr and long-term graft failure were similar for demographic and immunologic variables such as black recipients (1.68 vs. 1.55), black donors (1.35 vs. 1.22), HLA mismatch (1.04 vs. 1.05), and acute rejection (1.98 vs. 1.34). Variables such as recipient age and presence of diabetes revealed differential magnitude of OR and RH (Table 2); however, these two risk factors were reduced when long-term graft failures were censored for death with a functioning graft (Table 4). These two risk variables are known to impact long-term survival caused by increased recipient mortality.

The present study is limited as a result of lack of other donor and recipient variables such as proteinuria, body weight, or body mass index (BMI), donor creatinine, and donor renal histology. Proteinuria remains a hallmark of renal disease progression and should be included in predicting renal dysfunction as well as long-term graft failure. However, this information was not available in the UNOS/OPTN database. Short- and long-term outcome of renal transplantation is also dependent on the quality of the donor kidney. This can be assessed by the donor's SCr and or renal histology. Donor histology is a better marker over SCr because of limitations previously mentioned. Transplant outcome is also dependent on donor body weight, which determines daily creatinine production. Induction antibody therapy as a variable was not included in this analysis. Preserving renal function through preventing acute rejection may be achieved with induction of antibody therapy. In this analysis, acute rejection was used as variable over induction antibody treatment. Despite these limitations, our analysis is important as it compares the risk profiles between short-term end points such as renal function to long-term graft failure as a gold standard end point of transplant outcome.

The purpose of this study was to compare the risk factors for renal dysfunction and long-term graft failure. The risk characters identified and degree of elevation were similar. In addition, lower risk profiles identified with recipient age and diabetes were reduced when censored for death. The present study is limited because it does not address the positive and negative predictive values of elevated SCr and long-term graft failure. Despite the limitations in considering elevated SCr as a short-term marker for predicting long-term graft outcome, the current study clearly illustrates the similarity in risk variables for elevated SCr and long-term graft failure, and corroborates that elevated SCr at 1 year post-transplantation is a valid surrogate marker for long-term graft failure. Elevated SCr at 1 year post-transplantation is a biochemical marker which is widely available and easily reproducible,

**Table 3.** Risk factors for long-term graft failure (post 1-year) with and without censoring for death with a functioning kidney using Cox regression model

| | Without censoring for death | | | | Censoring for death | | | |
|---|---|---|---|---|---|---|---|---|
| Variable | Parameter estimate | RH | 95% CI | *P* value | Parameter estimate | RH | 95% CI | *P* value |
| Recipient | | | | | | | | |
| Age—Linear | 0.0411 | | | <0.0001 | −0.1949 | | | <0.0001 |
| Age—Quadratic | 0.0673 | | | <0.0001 | 0.0275 | | | <.0001 |
| 34 vs. 44 years | | 1.03 | (1.01, 1.04) | | | 1.25 | (1.23, 1.27) | |
| 54 vs. 44 years | | 1.11 | (1.10, 1.13) | | | 0.85 | (0.83, 0.86) | |
| 64 vs. 44 years | | 1.42 | (1.37, 1.47) | | | 0.76 | (0.72, 0.80) | |
| Female vs. male | −0.0308 | 0.97 | (0.94, 1.00) | 0.0224 | 0.0476 | 1.05 | (1.02, 1.08) | 0.0043 |
| Black vs. other | 0.4355 | 1.55 | (1.50, 1.60) | <0.0001 | 0.6205 | 1.86 | (1.79, 1.94) | <0.0001 |
| Diabetes vs. other | 0.3939 | 1.48 | (1.43, 1.53) | <0.0001 | 0.0750 | 1.08 | (1.03, 1.13) | 0.0009 |
| Nephrosclerosis vs. other | 0.1943 | 1.21 | (1.17, 1.26) | <0.0001 | 0.1790 | 1.20 | (1.14, 1.25) | <0.0001 |
| Donor | | | | | | | | |
| Age 44 vs. 34 years | 0.1090 | 1.12 | (1.10, 1.13) | <0.0001 | 0.1530 | 1.17 | (1.15, 1.18) | <0.0001 |
| Black vs. other | 0.1957 | 1.22 | (1.17, 1.27) | <0.0001 | 0.2503 | 1.28 | (1.22, 1.35) | <0.0001 |
| Transplant | | | | | | | | |
| Previous transplant | 0.2894 | 1.34 | (1.29, 1.38) | <0.0001 | 0.3551 | 1.43 | (1.37, 1.49) | <0.0001 |
| HLA Mismatch | 0.0471 | 1.05 | (1.04, 1.06) | <0.0001 | 0.0628 | 1.06 | (1.05, 1.08) | <0.0001 |
| PRA % (>80 vs. <80) | 1.1725 | 1.19 | (1.09, 1.29) | <0.0001 | 0.1297 | 1.14 | (1.03, 1.26) | 0.0140 |
| CIT (31 vs. 21) | | | | | 0.0223 | 1.02 | (1.00, 1.04) | 0.0130 |
| LD vs. CD | 0.2943 | 0.75 | (0.72, 0.77) | <0.0001 | −0.1902 | 0.83 | (0.79, 0.86) | <0.0001 |
| DGF | 0.1905 | 1.21 | (1.17, 1.25) | <0.0001 | 0.1844 | 1.20 | (1.16, 1.25) | <0.0001 |
| Post-transplant | | | | | | | | |
| Acute rejection within 1 year | 0.2925 | 1.34 | (1.31, 1.38) | <0.0001 | 0.4068 | 1.50 | (1.45, 1.55) | <0.0001 |
| TAC vs. CsA | 0.0685 | 1.07 | (1.00, 1.15) | 0.0452 | 0.1438 | 1.15 | (1.07, 1.25) | 0.0004 |
| MMF vs. other | −0.0778 | 0.93 | (0.88, 0.98) | 0.0038 | −0.1259 | 0.88 | (0.83, 0.94) | <0.0001 |

Abbreviations are: DGF, delayed graft function; CIT, cold ischemia time in hours; HLA, human leukocyte antigen; LD, living donor; CD, cadaver donor; MMF, mycophenolate mofetil; CsA, cyclosporine; TAC, tacrolimus.

**Table 4.** Comparable risk factors for 1-year elevated SCr and long-term graft failure (post 1-year) with and without censoring for death with a functioning kidney

| Variables | OR (95% CI) | *P* value |
|---|---|---|
| Risk for elevated SCr at 1 year | | |
| Donor age (44 vs. 34 years) | 1.55 (1.53, 1.57) | <0.0001 |
| Donor—Black vs other | 1.36 (1.29, 1.44) | <0.0001 |
| Recipient—age (34 vs. 44 years) | 1.20 (1.18, 1.23) | <0.0001 |
| Recipient—Black vs. other | 1.69 (1.61, 1.76) | <0.0001 |
| Recipient—Female vs. male | 0.30 (0.29, 0.31) | <0.0001 |
| Recipient—Diabetes vs. no diabetes | 0.76 (0.72, 0.78) | <0.0001 |
| DGF vs. no DGF | 1.44 (1.38, 1.50) | <0.0001 |
| HLA mismatch | 1.04 (1.03, 1.05) | <0.0001 |
| Acute rejection within 1 year | 1.98 (1.92, 2.05) | <0.0001 |
| Risk for all long-term (post-1 year) graft failure | | |
| Donor age (44 vs. 34 years) | 1.12 (1.10, 1.13) | <0.0001 |
| Donor—Black vs. other | 1.22 (1.17, 1.27) | <0.0001 |
| Recipient—age (34 vs. 44 years) | 1.03 (1.01, 1.04) | <0.0001 |
| Recipient—Black vs. other | 1.55 (1.50, 1.60) | <0.0001 |
| Recipient—Female vs. male | 0.97 (0.94, 1.00) | 0.0224 |
| Recipient—Diabetes vs. no diabetes | 1.48 (1.43, 1.53) | <0.0001 |
| DGF vs. no DGF | 1.21 (1.17, 1.25) | <0.0001 |
| HLA mismatch | 1.05 (1.04, 1.06) | <0.0001 |
| Acute rejection within 1 year | 1.34 (1.31, 1.38) | 0.0038 |
| Risk for long-term (post-1 year) graft failure after censoring for death | | |
| Donor age (44 vs. 34 years) | 1.17 (1.15, 1.18) | <0.0001 |
| Donor—Black vs. other | 1.28 (1.22, 1.35) | <0.0001 |
| Recipient—age (34 vs. 44 years) | 1.25 (1.23, 1.27) | 0.0043 |
| Recipient—Black vs. other | 1.86 (1.79, 1.94) | <0.0001 |
| Recipient—Female vs. male | 1.05 (1.02, 1.08) | NS |
| Recipient—Diabetes vs. no diabetes | 1.08 (1.03, 1.13) | 0.0009 |
| DGF vs. no DGF | 1.20 (1.16, 1.25) | <0.0001 |
| HLA mismatch | 1.06 (1.05, 1.08) | <0.0001 |
| Acute rejection within 1 year | 1.50 (1.45, 1.55) | <0.0001 |

Abbreviations are: DGF, delayed graft function; HLA, human leukocyte antigen.

making it a convenient marker for evaluating transplant outcome.

## CONCLUSION

Short-term post-transplant renal dysfunction is associated with long-term graft failure. Characteristics associated with elevated SCr at 1 year are similar to those associated with long-term graft failure. Elevated SCr at 1 year is a reasonable surrogate marker for evaluating transplant outcome.

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*Reprint requests to Sundaram Hariharan, M.D., Division of Nephrology, 9200 West Wisconsin Avenue, Milwaukee, WI 53226.*
*E-mail: hari@mcw.edu*

## REFERENCES

1. Hariharan S, McBride MA, Cohen EP: Evolution of endpoints for renal transplant outcome. *Am J Transplantation* 3:933–941, 2003
2. Sollinger HW: Mycophenolate mofetil for the prevention of acute rejection in primary cadaveric renal allograft recipients. *Transplantation* 60:225–232, 1995
3. European Mycophenolate Mofetil Cooperative Study Group: Placebo-controlled study of mycophenolate mofetil combined with cyclosporine and corticosteroids for prevention of acute rejection. *Lancet* 345:1321–1325, 1995
4. The Tricontinental Mycophenolate Mofetil Renal Transplantation Study Group: A blinded, randomized clinical trial of

mycophenolate mofetil for the prevention of acute rejection in cadaveric renal transplantation. *Transplantation* 61:1029–1037, 1995
5. Pirsch JD, Miller J, Deierhoi MH, Vincenti F, Filo RS: A comparison of tacrolimus (FK506) and cyclosporine for immunosuppression after cadaveric renal transplantation. *Transplantation* 63:977–983, 1997
6. Kahan BD: Efficacy of sirolimus compared with azathioprine for reduction of acute renal allograft rejection: A randomized multicentre study. The Rapamune US study group. *Lancet* 356:194–202, 2000
7. McDonald AS: A worldwide, phase III, randomized, controlled safety and efficacy study of a sirolimus/cyclosporine regimen for the prevention of acute rejection in recipients of primary mismatched renal allografts. *Transplantation* 71:271–280, 2001
8. Hariharan S, Johnson CP, Bresnahan BA, *et al*: Improved graft survival after renal transplantations in recipient in the United States, 1988 to 1996. *N Engl J Med* 342:605–612, 2000
9. Hariharan S, McBride MA, Cherikh WS, *et al*: Post transplant renal function in the first year predicts long-term kidney transplant survival. *Kidney Int* 62:311–318, 2002
10. Giral M, Taddei C, Nguyen JM, *et al*: Single center analysis of 468 first cadaveric kidney allograft with uniform ATG-CsA sequential therapy, in *Clinical Transplants*, edited by Cecka MJ, Terasaki PI, Los Angeles, UCLA Tissue Typing Laboratory, 1996, pp 257–264
11. Kaplan EL, Meier JP: Nonparametric estimation from incomplete observations. *J Am Stat Assoc* 53:457–481, 1958
12. Cecka MJ: The UNOS Scientific Renal Transplant Registry, in *Clinical Transplants*, edited by Cecka MJ, Terasaki PI, Los Angeles, UCLA Tissue Typing Laboratory, 1998, pp 1–16
13. Hariharan S, McBride M, Bennett L, Cohen EP: Risk factors for renal allograft survival from older cadaver donors. *Transplantation* 64:1748–1754, 1997
14. Hariharan S, Schroeder TJ, First MR: Effect of race on renal transplant outcome. *Clin Transplant* 7:235–239 1993
15. Takemoto SK, Terasaki PI, Gjertson DW, Cecka JM: Twelve year's experience with national sharing of HLA-matched cadaveric kidneys for transplantation. *N Engl J Med* 343:1078–1084, 2000
16. Hariharan S: Long-term kidney transplant survival. *Am J Kidney Dis* 38:S44–S50, 2001