Predicting the Ideal Serum Creatinine of Kidney Transplant Recipients by a Simple Formula Based on the Balance Between Metabolic Demands of Recipients and Renal Mass Supply From Donors

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ABSTRACT

Serum creatinine (Scr) is the most frequently used test to estimate graft function after kidney transplantation. Our previous study demonstrated that the independent predictors of recipient posttransplantation Scr included the ratio of graft weight to recipient body weight, the ratio of graft weight to recipient body surface area (BSA), and the ratio of graft weight to recipient body mass index (BMI). A prospective analysis about the impact of the balance between metabolic demands and renal supply on posttransplantation Scr of recipients was previously reported. We plotted the scatter graph using the X-axis as the independent predictors of Scr by linear regression and the Y-axis as the recipient Scr. To generate the predictive formula of Scr, we calculated a fit of the line of plotted cases using a linear regression method with 2 regression lines for prediction of the upper and lower 95% confidence intervals. Each line was converted into a predictive formula: Scr = −0.0033*(Graft weight(g)/Recipient BSA(m²))+1.75. Under 95% confidence, the Scr ranges from −0.0033*(Graft weight(g)/Recipient BSA(m²))+1.07 to −0.0033*(Graft weight(g)/Recipient BSA (m²))+2.44. Scr = −0.1049*(Graft weight(g)/Recipient body weight(kg))+1.72, which ranges from −0.1049*(Graft weight(g)/Recipient body weight(kg))+1.06 to −0.1049*(Graft weight(g)/Recipient body weight(kg))+2.37. Scr = −0.0158*(Graft weight(g)/Recipient BMI(kg/m²))+1.56, which ranges from −0.0158*(Graft weight(g)/Recipient BMI(kg/m²))+0.75 to −0.0158*(Graft weight(g)/Recipient BMI(kg/m²))+2.26. Prediction of posttransplantation Scr may be achieved by measuring graft weight as well as recipient weight and height. When recipient Scr is significantly higher than that predicted by the formula, a clinician should suspect an underlying graft injury.

Graft function after kidney transplantation is influenced by many factors which interact in complex fashion. In clinical practice, serum creatinine (Scr) is the most frequently used laboratory test to estimate graft function. Moreover, Scr levels may be used to screen for changes in renal function, because their measurement is simple and inexpensive. The Scr level is also a valuable prognostic marker of subsequent graft function at all times after transplantation.

Creatinine is a metabolic product of creatine and phosphocreatine, which are both found almost exclusively in muscle. Thus, creatinine is constantly produced from muscle; its production is proportional to muscle mass. Production of creatinine can change over long periods if there are alterations in muscle mass. Age- and gender-related differences in creatinine production are also largely attributable to differences in muscle mass. Although dietary creatinine or creatine from ingested meat is another source of variability in Scr levels, it normally accounts for only a small proportion of overall creatinine production.

Creatinine is continuously excreted by the kidneys into the urine. Creatinine is freely filtered by the renal glomerulus because it is small and does not bind to plasma.
proteins; in addition, it is actively secreted by renal tubules.\(^5\) Therefore, determination of the Scr concentration is widely used to follow renal function in clinical practice, even after kidney transplantation. For kidney recipients, initial graft function to excrete creatinine should be determined by the nephron mass provided by a transplanted kidney.

Posttransplantation Scr level in kidney recipients is determined by the balance between the metabolic demands of recipients (the amount of creatinine production) and renal functional supply from the donor (the capacity for creatinine excretion). Our previous study demonstrated that independent predictors of recipient posttransplantation Scr included the ratio of graft weight to recipient body weight, the ratio of graft weight to recipient body surface area (BSA), and the ratio of graft weight to recipient body mass index (BMI).\(^6\) Prediction of posttransplantation Scr of recipients should be possible purely based on the balance between the metabolic demands of recipients and the renal mass supplies from the donor. However, it can be influenced by many insults, such as ischemia/reperfusion damages, rejection episodes, nephrotoxic immunosuppressants, diabetes, hypertension, infection, and other complications, especially in the early period posttransplantation. When the Scr of the recipient after kidney transplantation is much higher than the ideal value by the predictive formula, the clinician should suspect an underlying source of graft injury.

PATIENTS AND METHODS

We performed a prospective analysis of the effect of renal allograft mass and recipient metabolic demand on the posttransplantation Scr after living donor kidney transplantation. We attempted to specifically analyze the impact of the balance between metabolic demands and renal supply on the posttransplantation Scr. In order to limit other factors that might affect renal function, the study population was restricted to living donor transplants that demonstrated immediate function. To eliminate the possible impact of immunologic or nonimmunologic factors on graft function, we excluded recipients with pre- or posttransplantation diabetes, cadaveric donor transplants, posttransplantation ischemic injuries to the graft, rejection episodes, drug toxicities, systemic or local infections, or complications such as vascular or urologic adverse events which may result in a functional decrease in the kidney graft.

The donated kidney was weighed just after the cold flush during the operative procedures. The recipient Scr was measured on a daily basis postoperatively. We defined the baseline level of creatinine as the nadir which increased less than 20% over 3 consecutive days. The recipients were also weighed on a daily basis posttransplantation. The dry weight of the recipients was used as a parameter of metabolic demands. Dry weight was defined as the recipient’s body weight within a month posttransplantation when the Scr had reached baseline. The body weight of the recipient was stable at the nadir, and the recipient was not on diuretics. We recorded the heights of both donors and recipients. The BSA was calculated with the DuBois\(^7\) formula, as well as the lean body weight (LBW) and the BMI.

We plotted the scatter graph using the X-axis as the independent predictors of Scr by linear regression and the Y-axis as the recipient Scr. Furthermore, we calculated a fit of the line of plotted cases using a linear regression method with lines for the upper and lower 95% confidence intervals (CI). Each line was converted into the predictive formula. Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) version 10.0 (SPSS Inc, Chicago, Ill, United States).

RESULTS

During the study period, 195 kidney transplantations were performed that met the study criteria. The average age, weight, and height of donors were 38.7 ± 10.3 years, 63.0 ± 10.4 kg, and 165.2 ± 8.2 cm, respectively. Their calculated BSA, LBW, and BMI were 1.7 ± 0.2 m\(^2\), 48.3 ± 8.0 kg, and 23.0 ± 2.8 kg/m\(^2\), respectively. Donated kidneys weighed 215.5 ± 40.5 g (range, 108.9–335.0 g). The average age, weight, and height of recipients were 37.2 ± 10.2 years, 57.0 ± 9.8 kg, and 166.8 ± 8.8 cm, respectively. Their calculated BSA, LBW, and BMI were 1.6 ± 0.2 m\(^2\), 46.4 ± 7.7 kg, and 20.4 ± 2.7 kg/m\(^2\), respectively.

Linear regression demonstrated that the independent predictors of recipient posttransplantation Scr included the ratio of graft weight to recipient body weight, the ratio of graft weight to recipient BSA, and the ratio of graft weight to recipient BMI, as previously reported.\(^6\) Among the ratios, the absolute value of the beta-coefficient (\(P = .024\), beta-coefficient = –11.501, 95% CI = –0.253–0.018) of the ratio of graft weight to recipient BSA was the highest, implicating that the ratio would be most predictive for the Scr after transplantation.

As per the findings that the ratio of graft weight to recipient BSA was an independent predictor of recipient Scr, the scatter graph by X-axis of the ratio of graft weight to recipient BSA and Y-axis of recipient Scr is displayed in Fig 1. A fit line of the plotted cases with 2 95% CI regression lines were calculated using linear regression.
Each line was converted into a predictive formula: \( \text{Scr} = -0.0033 \times (\text{Graft weight} / \text{Recipient BSA}^2) + 1.75 \). Under 95% confidence, the Scr ranges from \( -0.0033 \times (\text{Graft weight} / \text{Recipient BSA}^2) + 1.07 \) to \( -0.0033 \times (\text{Graft weight} / \text{Recipient BSA}^2) + 2.44 \). As per the findings that the ratio of graft weight to recipient BMI was also an independent predictor of recipient Scr, the scatter graph with a statistical fit line and 2 regression lines for prediction of the upper and lower 95% CI by X-axis of the ratio of graft weight to recipient BMI and Y-axis of recipient Scr is displayed in Fig 2. Each line was converted into the predictive formula: \( \text{Scr} = -0.0158 \times (\text{Graft weight} / \text{Recipient BMI}^2) + 1.56 \). Under 95% confidence, the Scr ranges from \( -0.0158 \times (\text{Graft weight} / \text{Recipient BMI}^2) + 0.75 \) to \( -0.0158 \times (\text{Graft weight} / \text{Recipient BMI}^2) + 2.26 \).

DISCUSSION

Estimating the impact of any one factor after kidney transplantation is difficult due to the complex interactions on outcomes. Theoretically, the lowest or ideal Scr after kidney transplantation cannot be predicted purely on a basis of the metabolic demand and renal mass supply even though the study populations are strictly controlled, because there are subclinical damages to the kidney graft due to ischemia/reperfusion injury, cyclosporine or tacrolimus nephrotoxicity, and other factors. However, if the recipient’s Scr after kidney transplantation is higher than the value predicted by our formula, the clinician should suspect underlying graft damage and consider diagnostic plans such as ultrasonography with Doppler, radioisotope scan, or kidney graft biopsy.

Most surgeons do not routinely weigh the kidney graft during transplant surgery. However, by using the predictive formula with graft weight and recipient BSA calculated with estimated dry weight and height of recipient, the clinician could simply predict the lowest or ideal Scr after kidney transplantation. Measurement of graft weight should be recommended because it may provide a helpful guide for the postoperative diagnostic plans without risk or time consumption during the operative procedures.

In conclusion, prediction of posttransplantation Scr based on the balance between the demand and supply is important to evaluate recipient kidney graft function. It may be determined easily and risk free by weighing the graft during the transplantation procedure and measuring the weight and height of the recipient. If a kidney recipient has a significantly higher Scr than the Scr predicted by the formula in the posttransplantation period, the clinician should suspect possible underlying graft injuries and make further diagnostic plans to determine the cause of graft dysfunction.

REFERENCES


![Fig 2. The scatter plots and the statistical fit lines by the ratio of graft weight to recipient body mass index versus recipient serum creatinine after transplantation. Lines indicate the fit line of plotted cases using a linear regression method (middle line), with 2 regression lines for prediction of the upper (upper line) and lower (lower line) 95% confidence intervals.](image-url)