Pretransplant Malnutrition Risk Score: A Simple and Useful Tool for Predicting Kidney Transplant Outcomes

Marina Santos  
Faculty of Medical Sciences

Evaldo Nascimento  
Faculty of Medical Sciences

Marcus Lasmar  
University Hospital of the Faculty of Medical Science

Raquel Fabreti-Oliveira  (✉ raquel.fabreti@cienciasmedicasmg.edu.br)  
Faculty of Medical Sciences

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Abstract

Background: The prevalence of malnourished patients before transplantation and the influence of malnutrition on graft and patient outcomes remain underestimated, despite being associated with higher postoperative morbidity and mortality. This study aimed to develop an easy nutritional screening tool and evaluate the impact of the nutritional status on clinical outcome, graft survival and mortality risk in kidney transplant (KT) patients.

Methods: In this retrospective cohort study including 451 KT patients, we developed a score by using anthropometric, clinical, and laboratory measures performed in the pretransplant evaluation. The sum of all its components ranged from 0 to 12 points. The patients were stratified into 3 groups: G1 (0 or 1 point)=low risk, G2 (2 to 4 points)=moderate risk, and G3 (>5 points)=high risk of malnutrition.

Results: Stratifying the patients, G1, G2, and G3 were composed of 90, 292, and 69 patients, respectively. Patients from G1 maintained the lowest serum creatinine levels at hospital discharge when compared with others (p=0.012). The incidence of infection in the patients from G3 had was higher than patients from G1 and G2 (p=0.030). G3 recipients showed worse GS than G1 patients (p=0.044). G3 patients showed almost threefold higher risk for graft loss (HR 2.94, 95% CI 1.084-7.996).

Conclusions: KT patients with higher malnutrition risk score was associated with worse outcomes and graft survival. The nutritional screening tool is easy to be used in clinical practice to evaluate the patient in preparation for KT.

Background

Chronic kidney disease (CKD) is considered a worldwide public health problem with an increasing incidence and prevalence each year.\(^1,2\) Annual costs for the treatment of CKD and end-stage renal disease (ESRD), including disease diagnosis and renal replacement therapy (RRT), and treatment of associated diseases are very high.\(^3\) In patients with ESRD, malnutrition can occur in a large proportion, ranging from 18–75\%,\(^4\) as a consequence of several factors, and such patients usually present increased catabolism with reduction in lean body mass and fat.\(^5,6,7,8,9\) In addition, a concomitant malnutrition-inflammation complex syndrome, an important risk factor for cardiovascular disease and mortality, can occur.\(^10\) The nutritional status of these patients cannot be overlooked, being an important determinant of clinical outcomes in patients with CKD and one of the main predictor factors for morbidity and mortality in dialysis patients.\(^11\) The best method for malnutrition diagnosis in these patients is still a matter of great discussion. Although the foregoing measures of nutritional status have practical value, each of these methods has limitations.\(^12,13,14\)

In the last decades, graft and patient survival have improved; however, post-transplant complications remain high\(^15,16,17\) and the demand for KT far exceeds the supply of available organs, causing a persistent increase in the number of patients on the waiting list with a parallel increase in the waiting time
for cadaveric kidney transplant. Increasing long-term graft survival and reducing the need for a new transplant are paramount for improving patient outcomes and for those awaiting a graft. Patients on the waiting list or preparing for kidney transplantation often have significant nutritional changes and may become malnourished due to organ failure and associated symptoms. Following a successful kidney transplant, improved intake and gradual enhancement of adequate nutritional status are expected on these patients.

The malnutrition in KT is associated with higher postoperative morbidity and mortality. Some studies showed a prevalence of 15–23% of recipients with body mass index (BMI) less than 21. In addition to post-treatment complications, such as rejections and infections, nutritional status may be an important determinant of clinical outcomes in transplant patients. Little is known about the role of malnutrition in KT recipient. Moreover, the prevalence of malnourished patients before and after transplantation and the influence of malnutrition on outcomes after the procedure are still underestimated. Many of the nutritional assessment scores are capable of detecting the deleterious effects of malnutrition. However, these scoring systems often require specific subjective assessments, so they are time consuming and not practical in everyday routine of dialysis services or due to require an evaluation of an expert, such as nutritionists and/or nutrologist physicians.

The aim of this investigation was to develop an easy and rapid nutritional screening tool, based only on routine objective measurements, capable of identifying the nutritional risk and evaluate its impact on the clinical outcome, graft survival and mortality risk in KT patients.

Subjects And Methods

Patients and study design

This retrospective cohort study, consisting of a convenience sample with adequate sample size to meet the aim of the study composed by 451 kidney recipients (292 males and 159 females) transplanted with kidney from deceased or living donors. These patients were selected from a total of 618 KT recipients based on the inclusion criteria aged > 18 and < 65 years, who underwent clinical and laboratory evaluation and direct measurement of weight and height before the surgery. Patients with incomplete medical records and those involved in other clinical studies were excluded. The transplants period was between 2008 and 2018 in the Transplantation Center of the University Hospital of the Faculty of Medical Sciences (UHFMS), Belo Horizonte, Minas Gerais, Brazil. In order to avoid bias in data collection, all patient information necessary for the study was collected from the medical records by only two trained people. This study was approved by the ethics committee of the Faculty of Medical Sciences (permit n° 2.122.409) and conducted based on principles of the Declaration of Istanbul. Informed consent has been obtained from the subjects and the procedures followed were in accordance with the Helsinki Declaration of 1975, as revised in 2013.

Immunosuppression therapy
Induction immunosuppressive therapy with thymoglobulin (rATG) (Genzyme, Mississauga, Canada) was used in retransplanted, hypersensitized, and sensitized patients with donor-specific anti-human leukocyte antigen antibodies (DSA). For the maintenance therapy, a three-drug regimen that included tacrolimus (Libbs Laboratory, São Paulo, Brazil) or cyclosporine A (Biosintética, São Paulo, Brazil), corticosteroid prednisone (Eurofarm, São Paulo, Brazil), and mycophenolic sodium (Novartis, Basel, Switzerland) was used. This maintenance immunosuppressive protocol was adjusted for patients who had adverse effects of calcineurin inhibitors proved by biopsy, diarrhea and abdominal pain, weight loss, or skin cancer or when virus reinfection by cytomegalovirus, polyomavirus, or human papilloma virus was detected. The graft function was evaluated based on measured using serum creatinine levels.

Patients follow-up

The patients were monitored after the KT weekly in the first month, every 15 days in the second month, every 30 days from the third month to the first year, every 2 months during the second year, and every 3 months after the second year of transplantation. Patients were evaluated by a nephrologist and laboratory tests were performed to monitor kidney function, blood counts, electrolytes, glucose level, liver function, drug levels etc. Other tests were also ordered whenever necessary, such as other laboratory tests, ultrasound, immunologic tests and kidney biopsy.

Nutrition score

We developed a practical and objective score using pretransplant available data, based on the Malnutrition Inflammation Score (MIS), described in prospective studies. The score proposed in this study is a simplification of the validated MIS score. The scores for pretransplant malnutrition risk (PTMR) were calculated using anthropometric data, laboratory tests, and clinical conditions (Table 1) available in all pretransplant kidney patient’s medical records.
Table 1
Pretransplant malnutrition risk score based on anthropometric, laboratory, and clinical data.

| Anthropometric data | Laboratory data | Clinical data |
|---------------------|-----------------|---------------|
| **BMI (kg/m²)**     | **Albumin**     | **Dialysis time (in years)** |
| BMI ≥ 22            | ≥ 3.8 mg/dL     | In dialysis for less than 1 year or preemptive transplant |
| □ 0 point           | □ 0 point       | □ 0 point |
| BMI 20-21.99        | 3.4–3.79 mg/dL  | In dialysis for over 1 year and less than 2 years |
| □ 1 point           | □ 1 point       | □ 1 point |
| BMI < 20            | < 3.4 mg/dL     | In dialysis for over 2 years |
| □ 2 points          | □ 2 points      | □ 2 points |

| **Serum cholesterol** | **Serum cholesterol** | **Comorbidities** |
|-----------------------|-----------------------|-------------------|
| BMI ≥ 120 mg/dL       | BMI ≥ 120 mg/dL       | No major comorbidities (not included in group I*) and non-diabetic |
| □ 0 point             | □ 0 point             | □ 0 point |
| BMI 100-119.99 mg/dL  | BMI 100-119.99 mg/dL  | Diabetes mellitus with up to one target organ injury other than nephropathy |
| □ 1 point             | □ 1 point             | □ 1 point |
| BMI < 100 mg/dL       | BMI < 100 mg/dL       | At least one comorbidity of group I* |
| □ 2 points            | □ 2 points            | □ 2 points |

| **Lymphocyte total count** | **Lymphocyte total count** | **Score 0–1 point: low risk (G1); 2–4 points: moderate risk (G2); score ≥ 5 points: high malnutrition risk (G3).** |
|---------------------------|---------------------------|--------------------------------------------------|
| BMI ≥ 1500 mg/dL          | BMI ≥ 1500 mg/dL          | Score 0–1 point: low risk (G1); 2–4 points: moderate risk (G2); score ≥ 5 points: high malnutrition risk (G3). |
| □ 0 point                 | □ 0 point                 | □ 0 point |
| BMI 800–1499 mg/dL        | BMI 800–1499 mg/dL        | □ 1 point |
| □ 1 point                 | □ 1 point                 | □ 2 points |

| **Clinical data** | **Clinical data** | **Clinical data** |
|-------------------|-------------------|-------------------|
| **Dialysis time (in years)** | **Dialysis time (in years)** | **Comorbidities** |
| In dialysis for less than 1 year or preemptive transplant | In dialysis for over 1 year and less than 2 years | No major comorbidities (not included in group I*) and non-diabetic |
| □ 0 point | □ 0 point | □ 0 point |
| In dialysis for over 2 years | | Diabetes mellitus with up to one target organ injury other than nephropathy |
| □ 2 points | | □ 2 points |
| At least one comorbidity of group I* | | At least one comorbidity of group I* |
| □ 2 points | | □ 2 points |

Anthropometric data were assessed using BMI (ratio of dry weight in kilograms (kg)/height in meters squared (weight [kg]/height² [m])). BMI may be used to assess malnutrition, specially when it is less than 23Kg/m². The laboratory tests included serum albumin, cholesterol levels, and total lymphocyte count, which are nutritional markers used in patients with CKD and can be considered efficient markers of nutritional status and associated with CKD patients prognosis. These tests were performed by the UHFMS laboratory before transplant procedure.

Clinical data included preexisting comorbid conditions and time of patient on dialysis. Each component was classified according to its severity, from 0 to 2 points. The sum of all components of PTMR score ranged from 0 to 12 points. The patients were evaluated and stratified into three groups: group 1 (G1): 0
or 1 point, group 2 (G2): 2 to 4 points, and group 3 (G3): 5 or more points. A higher score showed a more severe pretransplant risk of malnutrition and inflammation.

Based on these clustering criteria, the G1, G2, and G3 were composed of 90, 292, and 69 patients, respectively. The median time on RRT used as clinical data for grouping the patients was 9.0 (0 to 11), 20.5 (12 to 23), and 48.0 (24 to 73) months in G1, G2, and G3, respectively. The distribution of RRT type for G1, G2, and G3 respectively, was hemodialysis (75.56%, 94.48%, 89.86%), peritoneal dialysis (7.78%, 5.52%, 10.14%), and preemptive transplant (16.67%, 0.0%, 0.0%). The main causes of ESRD for patients from G1, G2, and G3 were, respectively, undetermined (47.78%, 46.05%, 49.28%), chronic glomerulonephritis (26.67%, 15.12%, 11.59%), diabetes mellitus (0.0%, 17.87%, 13.04%), autosomal polycystic kidney disease (11.11%, 6.19%, 7.25%), hypertensive nephropathy (5.56%, 9.62%, 11.59%), and others (8.89%, 5.15%, 7.25%).

Statistical analysis

Statistical analysis was performed using anthropometric, clinical, laboratory and immunogenetic information of recipients and their donors from databases with the SPSS analysis program for Windows version 18.0 (Chicago, IL, US). Differences were considered statistically significant if p value < 0.05. The continuous numerical variables were submitted to normal distribution analysis by the Kolmogorov-Smirnov test. The comparison of means was performed using F test by one-way analysis of variance (ANOVA) with Tukey’s post hoc test. For variables with non-normal distribution, the comparison was made using the Kruskal-Wallis test. For the comparison of categorical variables, the chi-square test was used. Graft and patient survival analyses were performed using the Kaplan-Meyer method, and the comparison among the three groups was made by log-rank test. Cox multivariate model of proportional risks (hazard ratio – HR) was used to define predictive factors for the risk of graft failure. For the Cox regression analysis, the dependent variable was the time between the date of transplant to the last date of follow-up or occurrence of graft loss. The independent variables were demographic characteristics, clinical and laboratory data, and outcome. The significant independent variables (p > 0.25) were used into the model by the hierarchical method. The HR (95% confidence interval) values were used to identify the effects of independent variables on the risk of graft loss. The importance of each variable in the model was assessed using the Wald test, and the assumption of proportionality of risk was assessed by analyzing the Schoenfeld residuals.

Results

Demographic characteristics and clinical data

We developed a score for the assessment of nutritional risk in pretransplant patients based on anthropometric, laboratory, and clinical data (Table 1). The demographic characteristics and clinical data of the patients are shown in Table 2. No statistical difference was found in the proportion of men and women in the three groups (Table 2). The mean age at the date of the transplant was 40.73, 44.85, and 45.71 for G1, G2, and G3, respectively. The patients from G2 and G3 had a mean age greater than those
from G1 \((p = 0.013)\) (Table 2). In G1, the majority of patients (84.4\%) received kidney from living donors, and in G3, most of the patients (63.77\%) received kidney from deceased donors \((p < 0.001)\) (Table 2).
Table 2
Demographic characteristics and clinical data of 451 kidney transplant patients according to score for nutritional status.

| Variable                        | G1                  | G2                  | G3                  | p value |
|---------------------------------|---------------------|---------------------|---------------------|---------|
| Number of patients              | 90 (19.96%)         | 292 (64.74%)        | 69 (15.30%)         |         |
| **RECIPIENT**                   |                     |                     |                     |         |
| Sex                             |                     |                     |                     |         |
| Male                            | 65 (72.22%)         | 179 (61.30%)        | 48 (69.57%)         | 0.109   |
| Female                          | 25 (27.78%)         | 113 (38.70%)        | 21 (30.43%)         |         |
| Receptor age (year) ± SD        | 40.73 ± 12.432      | 44.85 ± 12.396      | 45.71 ± 12.884      | 0.013   |
| ABO blood group (n = 449)       |                     |                     |                     |         |
| O                               | 43 (47.78%)         | 133 (45.86%)        | 37 (53.62%)         | 0.849   |
| A                               | 35 (38.89%)         | 111 (38.28%)        | 24 (34.78%)         |         |
| B                               | 7 (7.78%)           | 33 (11.38%)         | 5 (7.25%)           |         |
| AB                              | 5 (5.56%)           | 13 (4.48%)          | 3 (4.35%)           |         |
| Retransplantation               | 2 (2.22%)           | 11 (3.77%)          | 6 (8.70%)           | 0.145   |
| Risk of antibody-mediated rejection (n = 450) | | | | |
| No sensitized                   | 61 (68.54%)         | 174 (59.59%)        | 37 (53.62%)         | 0.379   |
| Sensitized without DSA          | 23 (25.84%)         | 100 (34.25%)        | 26 (37.68%)         |         |
| Sensitized with DSA             | 5 (5.62%)           | 18 (6.16%)          | 6 (8.70%)           |         |
| Mean % PRA Class I              | 8.00 ± 20.78        | 9.93 ± 21.82        | 10.90 ± 22.83       | 0.678   |
| Mean % PRA Class II             | 4.95 ± 15.13        | 6.43 ± 19.13        | 7.13 ± 18.85        | 0.732   |
| **DONOR**                       |                     |                     |                     |         |
| Donor age (year) ± SD           | 39.67 ± 10.949      | 43.29 ± 12.649      | 42.52 ± 13.734      | 0.056   |
| Donor type                      |                     |                     |                     |         |
| Living                          | 76 (84.44%)         | 134 (45.89%)        | 25 (36.23%)         | < 0.001 |
| Deceased                        | 14 (15.56%)         | 158 (54.11%)        | 44 (63.77%)         |         |

G: group; SD: standard deviation; DSA: donor-specific antibody. p values < 0.05 are indicated in bold.
For deceased donor (n = 216)

| Variable                        | G1            | G2            | G3            | p value |
|---------------------------------|---------------|---------------|---------------|---------|
| Cold ischemia time (h) ± SD     | 14.185 ± 8.1407 | 16.989 ± 6.5732 | 16.565 ± 5.9264 | 0.332   |
| Expanded criteria               | 5 (35.71%)    | 36 (22.78%)   | 12 (27.27%)   | 0.520   |

HLA-A, -B, -DRB1 mismatching (n = 449)

|                     | G1            | G2            | G3            | p value |
|---------------------|---------------|---------------|---------------|---------|
| 0                   | 19 (21.35%)   | 21 (7.22%)    | 5 (7.25%)     | **0.003** |
| 1 to 3              | 43 (48.31%)   | 161 (55.33%)  | 40 (57.97%)   |         |
| 4 to 6              | 27 (30.34%)   | 109 (37.46%)  | 24 (34.78%)   |         |
| rATG immunotherapy induction | 12 (13,33%) | 56 (19,18%) | 17 (24,64%) | 0.190   |

No statistical difference was found among the three groups for the variables donor age, ABO blood group, retransplantation, and risk for antibody mediated-rejection (Table 2). For patients who received kidney from a deceased donor, no statistical differences were found among the three groups for cold ischemia time and transplantation with donor with expanded criteria (Table 2). Considering the HLA-A, -B, and -DRB1 compatibility, based on the number of HLA mismatching (0 to 6), patients from G1 had better HLA compatibility with their donors than patients from G2 and G3 (p = 0.003) (Table 2).

**Outcomes associated with Nutrition score**

No statistical difference was observed in patients with delayed graft function (DGF) incidence for those recipients that received kidney from a deceased donor (Table 3). The proportion of infection episodes by cytomegalovirus, urinary tract infection by any etiologic agent, and polyomavirus was not statistically different among the three groups (Table 3). However, when the incidence of infection and the immunotherapy induction was analyzed at the same time, patients from G3 had a higher proportion of infections (35.1%) when compared to the other patients from G1 (14.6%) and G2 (20.3%) (p = 0.030). The rejection proportions in the first year were not statistically different among the groups, despite the trend toward higher proportions observed in G2 and G3 than in G1 (Table 3). However, patients in G3 lost their grafts more than those in G2 and G1, mainly due to immune cause or infection (p = 0.038) (Table 3).
Table 3
Outcomes in transplanted patients with different nutritional profiles before transplantation.

| Variable                              | G1 (n = 90) | G2 (n = 292) | G3 (n = 69) | p value |
|---------------------------------------|-------------|--------------|-------------|---------|
| **DGF for deceased donor (n = 216)**  | 7 (50.00%)  | 94 (59.49%)  | 31 (70.45%) | 0.284   |
| **Main infections**                   | 48 (53.33%) | 182 (62.33%) | 37 (53.62%) | 0.188   |
| Cytomegalovirus                       | 10 (20.83%) | 37 (20.33%)  | 6 (16.22%)  | NA      |
| UTI                                   | 28 (58.33%) | 89 (48.90%)  | 16 (43.24%) |         |
| Polyomavirus                          | 0 (0%)      | 6 (3.30%)    | 2 (5.41%)   |         |
| **Rejection episodes in the first year** | 19 (21.11%) | 76 (26.03%)  | 19 (27.54%) | 0.577   |
| TCMR                                  | 13 (68.42%) | 65 (85.53%)  | 14 (73.68%) | NA      |
| AMR                                   | 6 (31.58%)  | 8 (10.53%)   | 5 (26.32%)  |         |
| TCMR + AMR                            | 0 (0.00%)   | 3 (3.95%)    | 0 (0.00%)   |         |
| **Graft loss caused by**              | 17 (18.89%) | 77 (26.37%)  | 23 (33.33%) | 0.038   |
| Immune cause*                         | 1 (5.88%)   | 17 (22.08%)  | 8 (34.78%)  | NA      |
| Infection                             | 5 (29.41%)  | 20 (25.97%)  | 9 (39.13%)  |         |
| Other**                               | 10 (58.82%) | 35 (45.45%)  | 5 (21.74%)  |         |
| Missing data                          | 1 (5.88%)   | 5 (6.49%)    | 1 (4.35%)   |         |

DGF: delayed graft function; UTI: urinary tract infection; NA: not analyzed; TCMR: T cell-mediated rejection; AMR: antibody-mediated rejection; NA: not analyzed.

*Immune cause: TCMR, AMR, and IFTA (interstitial fibrosis and tubular atrophy). **Other: delayed graft function, vascular thrombosis, and cardiovascular disease. p values < 0.05 is indicated in bold.

In recipients who did not lose their graft, patients from G1 were able to maintain lower serum creatinine levels when compared with patients from G2 and G3 at hospital discharge (p = 0.012). More similar kidney functions were observed mainly in the first year after transplantation in patients of the three groups (Fig. 1). Kaplan-Meier survival curves (Fig. 2) showed that GS was statistically different among the groups in over comparison analysis (p = 0.046). Patients from G1 had better GS than those from G3 (p = 0.044). The estimated means in months for graft survival time were 100.56 ± 46.49, 94.64 ± 54.34, and 77.76 ± 49.01 for G1, G2, and G3, respectively. Although the differences in mortality risk over ten years were not statistically significant, a trend of a lower mortality risk in G1 patients than in G2 and G3 patients was observed (p = 0.775) (Fig. 3).

In univariate Cox regression analysis of the association between graft loss and covariates, a significant relationship was found with donor age, retransplant, patients from G3, sensitized patients without DSA who did not receive rATG immunotherapy, those who received kidney from deceased donor, patients with DGF, patients who received an immunosuppressive drug other than TAC or CSA therapy, and those who
had T cell-mediated rejection (TCMR) or antibody-mediated rejection (AMR) (Table 4). Of these, the following significant predictors remained on multivariate analysis: patients from G3 with high malnutrition risk, sensitized patients without DSA, those who have had DGF, and patients who have had TCMR or AMR rejection episodes (Table 4). With regard to the risk for graft loss, G3 showed almost threefold higher risk (hazard ratio [HR] 2.94; 95% confidence interval [CI] 1.084–7.996), and sensitized patients without DSA who did not receive rATG immunotherapy and patients with DGF had almost twofold higher risk (HR 1.904, 95% CI 1.168–3.105; HR 1.921, 95% CI 1.238–2.980). Patients with TCMR or AMR rejection had a 2.18-fold higher risk (HR 2.180, 95% CI 1.251–3.798) (Table 4).
Table 4
Predictive factors associated with the occurrence of graft loss.

| Variable                              | HR    | 95% CI for HR | p value | HR    | 95% CI for HR | p value |
|---------------------------------------|-------|---------------|---------|-------|---------------|---------|
| **Univariate analysis**               |       |               |         |       |               |         |
| Receptor age                          | 1.006 | 0.991         | 1.021   | 0.418 |               |         |
| Donor age                             | 1.022 | 1.006         | 1.037   | 0.005 |               |         |
| Male                                  | 1.005 | 0.689         | 1.466   | 0.979 |               |         |
| Retransplantation                     | 1.555 | 0.757         | 3.193   | 0.229 |               |         |
| HLA-A,-B,-DRB1 MM                     | 1.388 | 0.692         | 2.786   | 0.356 |               |         |
| 0 MM                                  | Reference |            |         |       |               |         |
| 1 to 3                                | 1.387 | 0.675         | 2.849   | 0.374 |               |         |
| 4 to 6                                | 1.387 | 0.675         | 2.849   | 0.374 |               |         |
| Pretransplant malnutrition risk score |       |               |         |       |               |         |
| G1 - Score 0–1                        | Reference |            |         |       |               |         |
| G2 - Score 2–4                        | 1.43  | 0.845         | 2.418   | 0.183 | 1.506         | 0.613   | 3.696   | 0.372 |
| G3 - Score &ge; 5                     | 1.881 | 1.005         | 3.522   | 0.048 | 2.944         | 1.084   | 7.996   | **0.034** |
| Risk of AMR                           |       |               |         |       |               |         |
| Non sensitized                        | Reference |            |         |       |               |         |
| Sensitized without DSA                | 1.343 | 0.917         | 1.967   | 0.13  | 1.904         | 1.168   | 3.105   | **0.010** |
| Sensitized with DSA                   | 1.38  | 0.685         | 2.779   | 0.368 | 1.045         | 0.434   | 2.520   | 0.921 |
| Deceased donor (vs living donor)      | 2.081 | 1.43          | 3.028   | 0.051 |               |         |         |         |
| Expanded criteria                     | 1.309 | 0.782         | 2.191   | 0.305 |               |         |         |         |
| Cold ischemia time                    | 1.008 | 0.971         | 1.047   | 0.678 |               |         |         |         |
| Delayed graft function                | 2.583 | 1.789         | 3.729   | < 0.001 | 1.921 | 1.238   | 2.980   | **0.004** |
| **Multivariate analysis**             |       |               |         |       |               |         |         |         |
| HR: hazard ratio; MM: mismatch; TAC: tacrolimus; CSA: cyclosporine A; CP: corticosteroid prednisone; TCMR: T cell-mediated rejection; AMR: antibody-mediated rejection. |

Variables with p ≤ 0.25 in univariate analysis were used to construct the Cox multivariate analysis. p values < 0.05 are indicated in bold.
### Univariate analysis

|                      | Reference | TAC + MYF + CP | CSA + MYF + CP | Other | Induction therapy | TCMR or AMR rejection | Infection episode |
|----------------------|-----------|---------------|---------------|-------|------------------|-----------------------|------------------|
|                      |           | 0.83          | 0.455         | 1.511 | 0.542            | < 0.001               | 0.991            |
|                      |           | 1.654         | 0.722         | 3.786 | 0.234            | 1.047                 | 0.658            |
|                      |           |               |               |       |                  |                       | 0.684            |
|                      |           |               |               |       |                  |                       | 1.437            |
|                      |           |               |               |       |                  |                       | 0.963            |
|                      |           |               |               |       |                  |                       |                 |

HR: hazard ratio; MM: mismatch; TAC: tacrolimus; CSA: cyclosporine A; CP: corticosteroid prednisone; TCMR: T cell-mediated rejection; AMR: antibody-mediated rejection.

Variables with p ≤ 0.25 in univariate analysis were used to construct the Cox multivariate analysis. p values < 0.05 are indicated in bold.

### Discussion

In this retrospective cohort study, 451 KT recipients were followed up for 10 years. We developed a PMR score for these patients and found that almost 80% of the kidney recipients were classified as moderate to high risk of malnutrition. Malnutrition is highly prevalent in ESRD patients on hemodialysis treatment, and it is associated with hospitalization and death. However, data regarding the actual prevalence and incidence in transplant patients, especially during the first post-transplant year, and their relationship with graft and patient outcomes are underestimated. The immediate post-transplant period is considered the critical phase because the patient is recovering from the surgical procedure and taking high doses of immunosuppressant medications. The body needs to treat protein catabolism, promote wound healing, and treat electrolyte abnormalities. Malnutrition at this time is associated with impaired surgical wound healing and higher risk of infection.

About 85% of the patients from G1 received kidney from living donor compared with 46% and 36% of the patients from G2 and G3, respectively. Thus, patients from G1 had less time on hemodialysis and were transplanted younger than patients from G2 and G3, thereby reducing the risk of becoming malnourished. In addition, patients from G1 transplanted with a living donor had better HLA compatibility with their donors than patients from G1 and G3. Immunotherapy induction using rATG in malnourished patients from group 3 increased the incidence of post-transplant infections by cytomegalovirus, urinary tract infection, and polyomavirus.

Patients with higher risk of malnutrition in this study were associated with higher incidence of infections when the patient was induced with rATG. This treatment strategy is effective to reduce acute cellular rejection and possibly humoral rejection in patients with immunological risk. However, it is associated
with infectious complications. Malnutrition affects immunity, through a variety of mechanisms, increasing the risk of infection and infection itself contributes to malnutrition.\(^{33}\)

In our study, we also found that patients with higher risk of malnutrition were associated with lower allograft survival. Our findings are consistent with previous studies.\(^{34,35,36}\) Improving allograft function is essential to decrease the risk of graft failure and to enhance patient's survival. The ability to predict short- and long-term outcomes in KT can be extremely useful for improving long-term results and for reducing the number of re-transplants.

Evaluation of the nutritional risk, one of the strongest predictors of morbidity and mortality in CKD patients, is a difficult and frequently forgotten process.\(^{37}\) Serum albumin, serum cholesterol level, and total lymphocyte counts are considered markers for nutrition status, and their low levels are associated with increased risk of mortality in ESRD.\(^{6,38,39}\) Hypoalbuminemia has been linked to poor clinical outcomes in all stages of CKD with higher hospitalization indices and mortality. Therefore, serum albumin is considered a reliable marker of nutritional and clinical status.\(^{13,40,41}\) Anthropometry may be used as a confirmatory tool; BMI is the most commonly used, and it is also a predictor for increased risk of mortality in patients undergoing regular dialysis.\(^{28,42}\) Extreme BMI values can be related to higher mortality of kidney recipients.\(^{43}\) Several nutritional scores have been developed over the years to help nephrologists, but none of them can be applied on every patient. Kalantar-Zadeh et al. developed the MIS for evaluation of the severity of malnutrition-inflammation complex syndrome on maintenance dialysis therapy.\(^{28}\) This system was already used to evaluate malnutrition in different stages of CKD and showed an association with mortality in those patients, including KT patients.\(^{35,40}\) However, the regular assessment of complete clinical parameters is time consuming, it can be expensive and not practical in the routine pretransplant evaluation. Therefore, the use of a simple nutrition screening can be very helpful. A tool that can also be used without a nutrition expert evaluation, such as anthropometric, laboratory, and clinical data are already available in the patients' medical records. In our experience, this study appears to be the first to evaluate the predictive power of poor nutritional status on graft and patient outcomes by using a simple score based on routine objective measurements.

This study has several strengths, including its design and the relatively notable size of kidney transplant patients with 10 years of follow up. Our study has some limitations. It is a single center study. Information bias could not be dismissed, as the data were obtained from medical records. Despite this, the sample size was adequate and a robust statistical analysis was applied in order to give this study external validity and reproducibility. This study has the potential to be of great importance and application for the pretransplant evaluation of recipients.

In conclusion, patients with higher malnutrition risk score were associated with worse outcomes and poor allograft survival. This study highlights the importance of nutrition screening to identify malnutrition as early as possible in pretransplant patients. Predicting short-term outcomes in KT can be useful to foresee long-term results and reduce the need for retransplantation. Future studies are necessary to better
elucidate the metabolic changes and special nutrient demands in this period and to further explore the benefits of nutrition intervention on pre- and post-transplant outcomes.

**Abbreviations**

AMR: antibody-mediated rejection; BMI: body mass index; CKD: chronic kidney disease; CSA: cyclosporine A; DGF: delayed graft function; DSA: donor-specific anti-human leukocyte antigen antibodies; ESRD: end-stage renal disease; GS: graft survival; KT: kidney transplant; MIS: malnutrition inflammation score; PTMR: pretransplant malnutrition risk; rATG: thymoglobulin; RRT: renal replacement therapy; TCMR: T cell-mediated rejection; TAC: tacrolimus; UHFMS: University Hospital of the Faculty of Medical Sciences; UTI: urinary tract infection.

**Declarations**

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**Authors’ contributions**

Marina Ribeiro de Oliveira Santos participated in research design, collected the data, writing the paper and in the performance of the research. Evaldo Nascimento participated in research design and revised the manuscript. Marcus Faria Lasmar participated in research design and in the final approval of the version to be published. Raquel Aparecida Fabreti-Oliveira participated in research design, writing the paper, in the performance of the research and in data analysis.

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**Availability of data and materials**

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

**Ethical approval and consent to participate**
Ethics approval for this study was granted by the ethics committee for human research of the Faculty of Medical Sciences of Minas Gerais, MG state, Brazil, under permit #2.122.409, and was conducted in accordance with the principles of the Helsinki and Istanbul Declarations. Informed consent was signed by all the patients.

Consent for publication

Not applicable.

Conflict of interests

The authors declare no conflicts of interest regarding the publication of this paper.

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