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Renal transplantation: better fat than thin

Hsiang Chung, MS,[a,c] *Vincent W.T. Lam, MS,*[a,c] *Lawrence P.K. Yuen, MBBS,*[a] *Brendan J. Ryan, MBBS,*[a] *Philip J. O'Connell, MD, PhD,*[b] *Jeremy R. Chapman, MD,*[b] *Wayne J. Hawthorne, MD, PhD,*[a,c] *and Henry C. Pleass, MD*[a,c,*]

[a] *Department of Surgery, Westmead Hospital, Westmead, New South Wales, Australia*
[b] *Department of Renal Medicine, Westmead Hospital, Westmead, New South Wales, Australia*
[c] *Discipline of Surgery, Sydney Medical School, The University of Sydney New South Wales, Australia*

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ABSTRACT

Background: Obesity has been a relative contraindication for renal transplantation. This study evaluates the impact of pretransplant body mass index (BMI) on renal transplant outcomes in a single institution in the era of modern immunosuppression.

Materials and methods: A 10-y retrospective analysis was undertaken of 454 consecutive patients who received a renal transplant at Westmead Hospital from January 1, 2001 to December 31, 2010. The role of pretransplant BMI on patient survival, graft survival, surgical complications, and postoperative complications was studied.

Results: The mean age of transplant of this study population was 45.4 ± 13.0 y. Live donation rate was 53.5%, and 60.6% were male. The median preoperative BMI was 25.6 (range, 14.3–51.4). One-year and 5-y patient survival were 97.4% and 86.6%, respectively, whereas 1-y and 5-y death-censored graft survival were 97.1% and 91.9%, respectively. Patients with BMI >30 did not exhibit any significant difference in survival or graft failure but had higher surgical wound infection rates (hazard ratio 3.95, $P < 0.01$). Patients with preoperative BMI <18.5 were associated with a six-fold increase in both death and death-censored graft failure ($P < 0.01$).

Conclusions: Pretransplant obesity increases wound infection but is not a contraindication to renal transplantation. Future prospective studies are required to further define the impact of low preoperative BMI <18.5.

1. Introduction

In Australia, 25% of adults are obese, defined by a body mass index (BMI) of >30. Another 37% are overweight [1]. This is not dissimilar to the United States where 65% of the population is either overweight or obese [2]. These proportions are reflected in renal transplant recipients with 60% being either overweight or obese [3], and up to 80% of diabetic renal transplant recipients being obese [4].

Obesity is a significant health risk in the general population because of its strong association with cardiovascular death and other cardiovascular risk factors including hypertension, hyperlipidemia, insulin resistance, proteinuria, and glomerulopathy [5–7] as well as being an independent risk factor for

* *Corresponding author*. Department of Surgery, Westmead Hospital, Cnr Hawkesbury and Darcy Roads, Westmead, NSW 2145, Australia. Tel.: +61 29 845 7365; fax: +61 29 893 7440.
E-mail address: Henry_Pleass@wsahs.nsw.gov.au (H.C. Pleass).
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reduced life expectancy. From a surgical point of view, operating on obese patients is also associated with increased perioperative complications including wound infections, myocardial infarction, and urinary tract infections [8].

There is no consensus on whether obesity defined by BMI should be an exclusion criterion for renal transplantation. Obesity is not listed as a contraindication on a number of official clinical guidelines for renal transplantation [9–12]. However, BMI remains a selection criterion for renal transplantation in many centers throughout the world [13]. The effect of obesity on renal transplant recipients has been previously studied with conflicting results [14–27]. Yet, few of these studies include only patients from the tacrolimus-based era of modern immunosuppression [18,21,27–31]. In our Australian population, we have found that patients referred for renal transplantation are becoming increasingly more obese. This study aims to investigate the effects of pretransplant obesity on renal transplant outcomes over the past 10 y using tacrolimus-based immunosuppression.

2. Materials and methods

A retrospective analysis was performed of 454 consecutive adult patients who underwent renal transplantation at Westmead hospital between January 2001 and December 2010. Multiple organ transplant recipients were excluded from this analysis. Baseline recipient and donor characteristics were collected including age, sex, history of previous smoking, chronic obstructive pulmonary disease, coronary artery disease (CAD), peripheral vascular disease (PVD), cerebrovascular disease, diabetes mellitus, hypertension, length of time on dialysis pretransplant, type of dialysis, donor age, cerebrovascular cause of donor death, living donors, donation after cardiac death (DCD), extended criteria donors (ECDs), prior grafts, cold ischemic time, second warm ischemic time, human leukocyte antigen (HLA) mismatches (A, B, and DR), peak and pretransplant panel reactive antibodies (PRA). Pretransplant BMI was calculated based on the patients' height and dry weight. The recipients were then divided based on their pretransplant BMI into four groups: underweight (BMI <18.5), normal weight (BMI between 18.5 and 25), overweight (BMI between 25 and 30), and obese (BMI >30) based on the World Health Organization classification [32].

The outcome measures analyzed included patient survival, graft survival, death-censored graft survival, delayed graft function (DGF), acute rejection, and postoperative complications. Graft failure was defined as the date when permanent dialysis was commenced or on patient death. In death-censored graft failure, patients who die with functioning grafts were instead censored on the date of death. DGF was defined by the need for dialysis in the week after transplantation. A postoperative infectious complication was defined as any infection, which occurred within 30 d of transplantation. All patients were followed up until death or the end of the study (February 15, 2012).

Eligibility criteria for kidney transplantation were according to the Transplantation Society of Australia and New Zealand guidelines [10]. In brief, these included actual or impending requirement for renal dialysis and anticipated 5-y survival $>80\%$. Exclusion criteria included untreated infections, recent active malignancies, current cigarette smoking, and significant untreated CAD.

Before being accepted onto the waiting list for transplantation, all patients were reviewed by a transplant surgeon and physician independently. Preoperative assessment included clinical evaluation, comprehensive biochemical studies, cardiac stress tests, age appropriate population-based malignancy screening, and dental checkups. While on the waiting list, patients are subjected to annual clinical reviews by both transplant physicians and surgeons. Allocation of cadaveric renal allografts was centrally directed and occurred strictly on the basis of computerized algorithm, ranking potential recipients by both HLA compatibility and waiting time.

2.1. Immunosuppression

Standard immunosuppression was based on the patient's perceived immunologic risk from HLA mismatch, current PRA, and prior grafts. Low risk patients were given low-dose tacrolimus (trough levels: 3–7 ng/mL), mycophenolate mofetil, prednisolone, and induction of interleukin 2 (IL-2) receptor antibodies. In moderate risk patients, the tacrolimus was given at normal dose (trough levels: 10–14 ng/mL first month and 5–10 ng/mL after) and in high-risk patients, antithymocyte globulin replaced IL-2 receptor induction therapies. All patients received perioperative intravenous cefazolin and postoperative sulphamethoxazole, trimethoprim and valganciclovir for 6 mo.

2.2. Statistical analysis

Continuous variables were compared using the one-way analysis of variance test. Differences in proportion were evaluated using the χ^2 test or Fisher exact test as appropriate. Multivariate analysis of categorical outcome variables was performed using logistic regression. Survival curves for patient survival, graft survival, and death-censored graft survival were generated using the Kaplan–Meier method. Differences in survival curves between two groups were evaluated *via* the log-rank test. Survival times were analyzed using Cox proportional hazard models. Multivariate analysis was performed *via* backward stepwise elimination, with $P = 0.1$ as the elimination threshold for potential confounders. Statistical analysis was performed using IBM SPSS statistics version 20.0 (Armonk, NY). P values of <0.05 were considered statistically significant. All estimates are presented with 95% confidence intervals (CIs).

3. Results

3.1. Patient demographics

A total of 454 patients underwent renal transplantation during this 10-y period. The baseline characteristics for the pretransplant BMI groups are included in Table 1. Live donor renal transplantation occurred in 53.5% of the patients, none of which were ABO incompatible. 5.9% of patients received DCD kidney and 17.4% received an ECD kidney. The underweight group had a significantly lower mean age and fewer