

# Body Mass Index Impact on the Long-Term Outcome after Kidney Transplantation in Japanese Patients

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## Abstract

**Objective:** While high BMI has negative impact on patients with acute or chronic kidney disease, low BMI is related to mal-nutrition and poor survival in patients on dialysis. On the other hand, pretransplant medical policy recommends recipients to improve their overweight status in order to prevent postoperative surgical complications. We investigated how pretransplant BMI influence postoperative course in Japanese end-stage renal disease patients.

**Patients and methods:** We reviewed 219 patients who underwent kidney transplantation between 1986 and 2014 at our institution. Pediatric recipients (age<20) were excluded. We divided the recipients into 4 groups by BMI (under 18.5, 18.5-21.9, 22.0-24.9, over 25.0). Postoperative complications (wound related and infectious adverse events), allograft rejection, and allograft survival were investigated among the BMI groups.

**Results:** Post-transplant infectious disease was more frequent (5 in 27 cases: 18.5%) in over 25.0 group than any of other BMI groups (0 to 2.1%,  $p=0.006$ ). Ten year allograft survival rate of over 25.0 group was inferior to that of under 18.5 group ( $p=0.037$ ). Meanwhile, BMI over 25.0 did not impair graft survival compared to other factors (age, preemptive transplantation, ABO blood type incompatibility and mycophenolate mofetil utilization) in Cox proportional hazards analysis.

**Conclusion:** Overweight (BMI>25.0) in Japanese kidney recipients might affect post-transplant infectious disease occurrence; however, it is not a deteriorating factor for long-term allograft survival.

**Keywords:** Chronic kidney disease; Dialysis; Transplantation; BMI

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## Introduction

The obesity adversely affects the condition of a patient with AKI and CKD. On the other hand, it is a fact that BMI relates to the survival rate positively in the patients on dialysis, since a drop of the muscle quantity drives malnutrition as the cause of poor patients survival. When such an end-stage renal disease (ESRD) patient is going to receive a renal transplantation, weight loss is instructed in many institutes because of a consideration for complications after the transplant. It has not been well answered whether or not and how much we have to improve obesity before renal transplantation for an altitude obesity patient [1]. In order to prevent complications after transplant, it is necessary

to lose weight without reducing quantity of muscle [2]. Since there are some differences in frequency and gravity of obesity by a country and the race, it is difficult to make a constant standard. The difference of patient survival rate between any BMI groups is reported to be negligible compared with dialysis patients who had not been transplanted. Besides post-transplant short-term problems; operation time, wound infection, hospital stay and delayed graft function, high BMI does not affect the long-term patient survival [3]. Pretransplant BMI criteria of our institute had been changed fewer than 25 at 2011, as marginal line of Japanese overweight definition. We reviewed the medical records and estimated the justification of our BMI criteria.

## Patients and Methods

We reviewed medical records of 285 patients who underwent kidney transplantation between 1986 and 2014 at our institution. Pediatric recipients (age at transplantation <20) were excluded. There were residual 219 patients (123 male and 96 female). We divided them into 4 groups by BMI at the transplantation. There were 27 cases of overweight recipients (BMI over 25.0), 57 cases with BMI 22.0-24.9 (high average), 94 cases with BMI 18.5-21.9 (low average), and 41 cases of emaciated (BMI under 18.5). Mean BMI in total recipients was 21.0 (**Figure 1**). Postoperative complications (wound related and infectious adverse events), allograft rejection, and allograft survival were investigated among the BMI groups.

This retrospective study was approved by Hokkaido University Hospital Committee of Clinical Research Guideline (#014-0372).

Statistical analyses were performed with JMP Clinical for JMP Academic Suite 32/64-bit (SAS Institute Japan). One-way ANOVA was used to compare normally distributed continuous variables and the Kruskal-Wallis H test was used to evaluate skewed or discrete ordinal variables. The chi-square test was used to compare nominal scale variables. Survival curves were estimated with the Kaplan-Meier method using the log-rank test. In order to evaluate the influences of BMI, the Cox proportional hazards model was employed. Proportional hazards assumption was confirmed by  $\ln[-\ln(\text{survival function})]$ . Two-tailed  $P < 0.05$  was considered statistically significant.

## Results

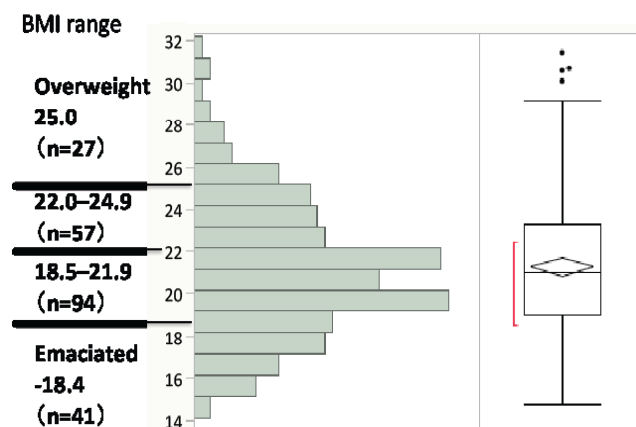
Post-transplant infectious disease (needed hospital stay) was

more frequent (5 in 27 cases: 18.5%) in overweight (BMI >25.0) group than any of other BMI groups (0 to 2.1%,  $p = 0.006$ ). Ten years allograft survival of overweight group was inferior to that of emaciated (BMI <18.5) group (45 vs. 88%,  $p = 0.037$ ). There were no significant difference of surgical wound related complications, allograft rejection rate, and the frequency of allograft loss among the BMI groups (**Table 1**).

Allograft survival curve in overweight group was inferior to that of emaciated group ( $p = 0.037$ , Kaplan-Meier method, **Figure 2**).

Since these four BMI groups presented different baseline components as a patients' clinical cohort, we examined each differences as **Table 2**. For baseline factors of the recipient, evaluation period was longer in emaciated group and overweight group, recipient age was younger in emaciated group, male recipient rate was high in higher BMI groups, dialysis period was short in overweight group. For donor, male rate was high in emaciated group; there were some differences in HLA mismatches, DCD rate, ABO incompatibility among the groups. Furthermore, induction rate of some immunosuppressant was different in overweight group (**Table 2**).

In order to adjust these confounding factors in baseline cohort among the groups, Cox proportional hazards analysis was performed. Univariate analysis revealed that recipient age (>60), polycystic kidney disease as an original disease, preemptive transplantation, immunosuppressant (basiliximab, rituximab, tacrolimus, MMF) were related to risk factors (**Table 3**). We selected 5 exposure factors including BMI as outcome events/total cohort number (39/219) and tested by multivariate analysis. BMI (>25.0) did not impair long-term graft survival compared to other



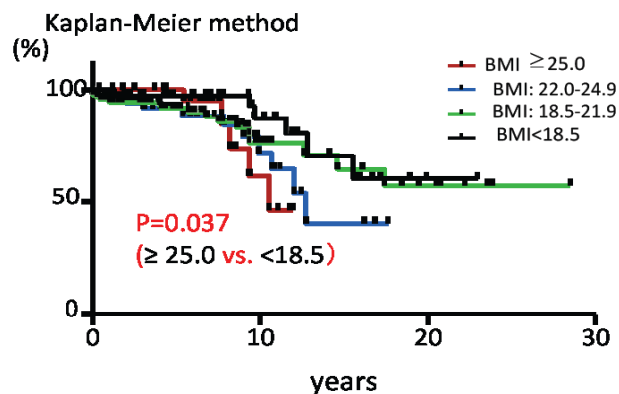
**Figure 1** BMI distribution at the time of kidney transplantation in this study (n=219). Median BMI was 21.03 (ranged 14.7-31.4). Mean BMI was 21.26 (SD: 3.21).

**Table 1** Adverse effects and survival.

BMI Group (n)	Wound related	Infection	Acute rejection	Allograft loss	10 year graft survival
<18.5 (41)	2 (4.9%)	0 (0.0%)	7 (17.1%)	7 (17.1%)	88%
18.5-21.9 (94)	4 (4.3%)	2 (2.1%)	11 (11.7%)	16 (17.0%)	76%
22.0-24.9 (57)	4 (7.0%)	1 (1.8%)	4 (7.0%)	11 (19.3%)	65%
25.0 (<27)	3 (11.1%)	5* (18.5%)	4 (14.8%)	5 (18.5%)	45%**

\*  $P = 0.006$

\*\*  $P = 0.037$



**Figure 2** Allograft survival curves of the four groups. Survival curve in overweight group was inferior to that of emaciated group ( $p=0.037$ , Kaplan-Meier method).

**Table 2** Baseline cohort differences among BMI groups.

	BMI group	Emaciated ~18.4	Low ave. 18.5~21.9	High ave. 22.0~24.9	Overweight 25.0~
Recipient	FU period (years)	9.4 0-23	6.6 0-28	5.2 0-18	<b>7.1</b> <b>0-12</b>
	Age (years)	<b>35</b> <b>20-67</b>	42 21-67	45 20-69	44 25-63
	Male (%)	<b>6 (14.6)</b>	52 (55.3)	43 (75.4)	22 (81.4)
	Dialysis (years)	2.5 0-31.4	2.0 0-30	2.7 0-22.3	<b>1.3</b> <b>0-13</b>
Original disease	Diabetes	3 (7.3)	13 (13.8)	11 (19.2)	4 (14.8)
	IgAN	10 (24.4)	20 (21.3)	9 (15.8)	7 (25.9)
	polycystic	1 (2.4)	7 (7.4)	7 (12.3)	2 (7.4)
Donor	Age (years)	55 21-78	55 13-74	57 24-75	<b>57</b> <b>39-69</b>
	Male (%)	<b>21 (51.2)</b>	37 (39.4)	22 (38.6)	8 (29.6)
	HLA mismatches	3 0-5	3 0-6	<b>2</b> <b>0-6</b>	3 0-5
	Deceased	9 (22.0)	22 (23.4)	9 (15.8)	<b>3 (11.1)</b>
	ABO incompatible	8 (19.5)	16 (17.0)	<b>18 (31.6)</b>	5 (18.5)
	aHLA sensitized	3 (7.3)	5 (5.3)	2 (3.5)	1 (3.7)
IS	Basiliximab	35 (85.4)	82 (87.2)	50 (87.7)	22 (81.5)
	Rituximab	10 (24.4)	21 (22.3)	18 (31.6)	<b>3 (11.1)</b>
	Tacrolimus	32 (78.0)	64 (68.1)	35 (61.4)	23 (85.2)
	MMF	33 (80.5)	74 (78.7)	46 (80.7)	<b>26 (96.3)</b>

significant factors (recipient age, preemptive transplantation, ABO blood type incompatibility and mycophenolate mofetil induction) (**Table 4**).

## Discussion

Our data could not clarify the effect of higher BMI for long-term post-transplant allograft survival. It might be due to the fact that there are no recipients with morbidly obese which was seen in other foreign reports [2]. Additionally, such severe obesity may cause short-term events (delayed graft function, wound infection, longer operation time, long hospital stay and new onset diabetes after transplantation), which did not reach any disadvantage for the long-term period [3].

Obesity control guideline in Japan (2006) recommended that

overweight case should diet intake restriction (25 kcal/kg/day) along with standard body weight [4]. But well-controlled CKD patients have been restricted in protein intake (0.6 g/kg/day). Calorie restriction in CKD patients may result in mal-nutrition and Nitrate unbalance with simple weight loss for BMI control. Pretransplant high BMI and high muscle volume was reported not to be surgical and immunological risk because of low mortality and graft failure ratio [5]. We have to adjust each recipient's nutrition status (serum albumin, protein intake) in order to prevent the trap of 'obesity paradox' [6].

We must pay much attention for low muscle mass with high BMI patient as a true high risk recipient (sarcopenia obesity) which is independent risk factor of post-transplant morbidity and mortality [7,8]. For the future, we will test the body cell mass analysis for CVD, fat obesity risk criteria using impedance

**Table 3** Cox proportional hazards analysis (Univariate).

	HR	95% CI	P
Male recipient	1.03	[0.76, 1.38]	0.85
Recipient age>60 *	2.79	[1.74, 4.28]	0.00
BMI ≥ 25	0.84	[0.55, 1.36]	0.46
Diabetes *	0.57	[0.39, 0.88]	0.01
IgA Nephropathy	0.84	[0.60, 1.21]	0.35
Polycystic kidney dis. *	0.51	[0.31, 0.90]	0.02
Preemptive *	0.46	[0.32, 0.68]	0.00
Deceased	0.97	[0.67, 1.44]	0.87
Donor age>60	1.26	[0.91, 1.72]	0.16
Male donor	0.80	[0.59,1.08]	0.14
ABO incompatible	0.97	[0.67, 1.44]	0.87
aHLA sensitized	0.71	[0.38, 1.50]	0.34
Basiliximab *	0.15	[0.07, 0.30]	0.00
Rituximab *	0.28	[0.19, 0.40]	0.00
Tacrolimus *	0.44	[0.29, 0.67]	0.00
MMF *	0.00	[0.02, 0.02]	0.00

**Table 4** Cox proportional hazards analysis (multivariate).

	HR	95% CI	P
<b>Recipient age&gt;60 *</b>	1.81	[1.12, 2.84]	0.017
<b>Preemptive *</b>	0.67	[0.46, 0.99]	0.045
<b>ABO incompatible</b>	1.44	[0.99, 2.04]	0.052
<b>MMF *</b>	0.00	[0.00, 53.8]	0.000
<b>BMI ≥ 25</b>	1.25	[0.73, 1.95]	0.769

(Total number: 219/outcome events: 39=5.62)

evaluation other than BMI [9,10]. Our data was small in patient number and there are some limitations existed in our study. Overweight patient population was different from other western countries, our retrospective cohort study could not reveal the significance of BMI in outcome of kidney transplantation and background patient cohort of our data was different among the 4 groups in some clinical patient's characters.

## Conclusion

Overweight (BMI>25.0) in Japanese kidney recipients might affect post-transplant infectious disease occurrence; however, it is not a deteriorating factor for long-term allograft survival.

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