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Body composition and outcomes in dialysis patients and renal transplant recipients

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ABSTRACT

Overweight (body mass index [BMI] = 25 - 30 kg/m^2) and obesity (BMI ≥ 30 kg/m^2) have become mass phenomena with a pronounced upward trend in prevalence in most countries throughout the world and are associated with increased cardiovascular risk and poor survival. In patients with end stage renal disease (ESRD) undergoing maintenance hemodialysis an 'obesity paradox' has been consistently reported, i.e., a high BMI is incrementally associated with better survival. Whereas this 'reverse epidemiology' of obesity is relatively consistent in maintenance hemodialysis patients, studies in peritoneal dialysis patients have yielded mixed results. Moreover, the effect of pre- and post-transplant obesity in kidney transplanted patients on long-term graft and patient survival has not been well established. However, BMI is unable to differentiate between adiposity and muscle mass and may not be an acceptable metric to assess the body composition of ESRD patients. Assessing lean body mass, in particular skeletal muscle, and fat mass separately are needed in ESRD patients using gold standard techniques such as imaging techniques. Alternatively, inexpensive and routinely measured surrogate markers such as serum creatinine, waist and hip circumference or mid-arm muscle circumference can be used. We have reviewed and summarized salient recent data pertaining to body composition and clinical outcomes about the association of survival and body composition in maintenance dialysis patients and kidney transplanted recipients.

Implication for health policy/practice/research/medical education:

BMI is not adequate to assess the obesity or body composition in ESRD, and higher BMI is not necessarily associated with poor outcomes in dialysis or kidney transplanted patients.

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1. Background

Individuals with advanced (Stage 5) chronic kidney disease (CKD), also known as end-stage renal disease (ESRD), usually require renal replacement therapy to survive, either in form of maintenance dialysis treatment or kidney transplantation. Those who undergo maintenance dialysis treatment have a high annual mortality of approximately 20% to 23% in the United States and 15% to 20% in Europe, apparently mostly due to cardiovascular or infectious diseases (1). Despite decades of ongoing efforts towards correcting such conventional risk factors as obesity, hypertension, or hypercholesterolemia or

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other potential risk factors such as dialysis dose, anemia or hyperhomocysteinemia, dialysis patient survival has not improved substantially (1). Several recent randomized controlled trials in CKD patients have failed to show any survival benefit of increasing dialysis dose, lowering serum cholesterol, correcting hyperhomocysteinemia or improving anemia (2).

Whereas obesity is a risk factor for the development of CKD per se (3), many epidemiologic studies have indicated inverse associations between obesity or other cardiovascular risk factors and mortality in CKD and cardiac patients (4, 5). A higher death rate has been observed in CKD patients who have a low, rather than a high, body mass index (BMI) (6), blood pressure (7) or serum concentrations of cholesterol (8) or homocysteine (9); whereas high values of these risk factors are associated with improved survival. Other patients populations including those with heart failure (10), coronary artery disease (5, 11), or elderly individuals (12) also exhibit this so-called "obesity paradox". However, most studies have not examined the relative contribution of fat vs. muscle mass or their changes over time to survival benefits of larger body size. Assessing muscle mass or lean body mass (LBM) is particularly difficult in large epidemiologic studies and require such elaborate tests of body composition as dual energy X-ray absorptiometry (DEXA) (13). Among biochemical markers of muscle mass, serum creatinine is most routinely measured, but its association with kidney function has hampered its utility as such (14). Nevertheless, in long-term dialysis patients with minimal or no residual renal function who undergo a stable dialysis treatment regimen, time-averaged serum creatinine concentration appear to be a more likely surrogate of muscle mass, and its changes over time may represent parallel changes in skeletal muscle mass (15, 16). Here, we summarized the salient findings of selected recent studies about the association of survival and body composition in ESRD patients on maintenance dialysis or kidney transplant recipients.

2. Body composition and survival in patients on maintenance dialysis

Measures of superior nutritional status, such as a high BMI in combination with normal or high muscle mass, are usually associated with greater survival in maintenance dialysis patients (17-22). In a study of incident peritoneal dialysis patients, the best survival was observed in those with high BMI and normal or high muscle mass (17). Unlike the general population, some, but not all, studies have shown that being overweight (perhaps a surrogate for "overnutrition") may enhance survival among hemodialysis patients (18, 23-29). Given the consistency of the observations, there may be conditions in these and other chronic disease populations which render them more resistant to hardship and poor outcomes at higher BMI values. Several explanations have been suggested (30, 31). including a more stable hemodynamic status in obese individuals (32), higher concentration of tumor necrosis factor alpha receptors in obesity (33), neurohormonal alterations of obesity (34), endotoxin-lipoprotein interaction (35), differences in bone and mineral and vitamin D (36, 37), reverse causation (38), survival bias (39), time discrepancies among competitive risk factors (over- vs. under-nutrition) (39), and the overwhelming effect of malnutrition inflammation complex on traditional cardiovascular risks (40, 41). Since the almost 2/3 of maintenance hemodialysis patients in the US die within 5 years of commencing dialysis treatment (42), the long-term effects of conventional risk factors on future mortality may be overwhelmed by their potential short-term benefits or by other risk factors intrinsic to dialysis populations, such as under-nutrition and inflammation. Indeed, it may be that dialysis patients do not live long enough to die of the consequences of over-nutrition, since they die much faster from other health conditions such as protein-energy wasting (43-46). Hence, obesity, by providing more nutritional reserve, may protect them against early death (47).

We have summarized pertinent data of several leading studies in the field *(Table 1)*. Hemodialysis patients appear to have a lower BMI than age- and sex-matched control subjects from the general population (48). In a recent matched analyses that compared the lipid profiles of 285 hemodialysis patients with those of 285 non-ESRD outpatients evaluated in the same medical center, matched one-to-one on age (± 5 years), sex, race, and diabetes mellitus status, the BMI was found to be significantly lower in the hemodialysis patients than in the non-ESRD control subjects (26.2 ± 6.0 compared with 31.5 ± 7.8; $P < 0.001$) (49). The Diaphane collaborative study group in France (50) was one of the first to report on the paradoxical observation of a lack of increase in mortality with high BMI in dialysis patients. This study included a cohort of 1453 younger, mostly non-diabetic, French hemodialysis patients followed between 1972 and 1978 in 33 French dialysis centers (50). Leavey *et al.* (24), while assessing the influence of many commonly used clinical variables on dialysis survival, confirmed the above lack of association between higher BMI values and increased mortality risk in a national sample of 3607 hemodialysis patients in the United States Renal Data System (USRDS). The mean BMI was 24.4 ± 5.3 in this study. In hazard regression models, low BMI was independently and significantly predictive of increased mortality. Kopple *et al.* evaluated 12965 hemodialysis patients and found that those patients with greater weight-for-height percentiles had lower mortality rates (47). After adjustment for clinical characteristics and laboratory measurements, the inverse relation between mortality rates and weight-for-height percentiles was still highly significant, particularly for patients in the lower 50th percentile of body weight-for-height (47). These findings suggest that not only BMI, but other measures of body size also correlate inversely with mortality in maintenance dialysis patients, independently of case-mix factors and comorbid conditions.

Recently, we studied a contemporary cohort of 121,762 thrice-weekly treated hemodialysis patients in a single large dialysis organization for up to 5 years and found that higher BMI, up to 45 kg/m^2, and higher serum creatinine, a likely surrogate of larger muscle mass, are each independently and incrementally associated with greater survival even after extensive multivariate adjustment for available surrogates of nutritional status and inflammation (22). Loss or gain in dry weight over time exhibited a graded association with greater mortality or survival, respectively, and so did changes in serum creatinine over time as a surrogate of changes in muscle mass. The concordant combination of the changes in these two body composition surrogates, if in the same direction, maintained the same graded death-predictability. However, among hemodialysis patients with a discordant combination; those who lost weight but gained muscle mass, represented by a parallel increase in serum creatinine, had a greater survival than those who gained weight but lost muscle, shown by a decrease in serum creatinine level over the same period of time. These associations were relatively robust and consistent across different demographic groups of hemodialysis patients (22).

Supporting to this observation, Noori *et al.* recently showed that higher mid-arm muscle circumference (MAMC) is a surrogate of larger lean body mass (LBM) and an independent predictor of better mental health and greater survival in hemodialysis patients (51). Adjusted death HRs were 1.00, 0.86, 0.69, and 0.63 for the first to fourth MAMC quartiles, respectively (51). Moreover, she examined 742 patients using near-infrared interactance-measured to assess the LBM and fat mass (FM) (40). After adjustment for important co-variables, the highest quartiles of FM and LBM were associated with greater survival in women: HRs of 0.38 (95% CI: 0.20, 0.71) and 0.34 (95% CI: 0.17, 0.67), respectively (reference: first quartile). In men, the highest quartiles of FM and percentage FM but not of LBM were associated with greater survival: HRs of 0.51 (95% CI: 0.27, 0.96), 0.45 (95% CI: 0.23, 0.88), and 1.17 (95% CI: 0.60, 2.27), respectively (40). By comparison, obesity may be associated with worse survival outcomes among peritoneal dialysis patients (26, 52). However, opposite results were found when the body composition was taken into account. In a study of incident peritoneal dialysis patients, the best survival was observed in those with high BMI and normal or high muscle mass (17). More-

Table 1. Summary of studies with large sample sizes (>1000 subjects) indicating a reverse epidemiology of obesity in maintenance hemodialysis (MHD) patients

Reference	Sample size	Follow-up period (yr)	Findings and source of data
Degoulet *et al.* (1982) (50)	1453	5	Higher death rate with lower BMI. Younger, mostly nondiabetic, French MHD patients.
Leavey *et al.* (1998) (100)	3607	5	Higher mortality with lower BMI. USRDS data.
Fleischmann *et al.* (1999) (23)	1346	1	Better survival with overweight and obesity. Mostly African American MHD patients. Mississippi patients only.
Kopple *et al.* (1999) (47)	12965	1	Lower mortality with progressively higher weight-for-height; lowest mortality rates in overweight MHD patients. Data from Fresenius Medical Care.
Wolfe *et al.* (2000) (101)	9165	2	Better survival in overweight and obese MHD patients. USRDS data.
Leavey *et al.* (2001) (24)	9417	4	Mortality risk decreased with increasing BMI in both US and European MHD patients in the DOPPS, independent of the degree of sickness.
Port *et al.* (2002) (102)	45967	2	The highest BMI tertile had the lowest mortality risk. Data from the US Federal billing records
Lowrie *et al.* (2002) (103)	43334	1	The log of risk decreased linearly for weight, weight-for-height, and BSA and was reverse J-shaped for weight/height and BMI. Data from Fresenius Medical Care.
Glanton *et al.* (2003) (104)	151027	2	Paradoxical association between BMI and mortality was stronger in African American MHD patients. USRDS data.
Johansen *et al.* (2004) (27)	418055	2	High BMI, adiposity, and fat mass were associated with increased survival in all but Asian American MHD patients. USRDS data.
Kalantar-Zadeh *et al.* (2010) (22)	121762	2.5	Larger body size with more muscle mass appears associated with a higher survival rate. A discordant muscle gain with weight loss over time may confer more survival benefit than weight gain while losing muscle. Data from DaVita, Inc.
Molnar *et al.* (2011) (79)	14632	3	Transplant-waitlisted hemodialysis patients with lower BMI or muscle mass and/or unintentional weight or muscle loss were associated with higher mortality. Data from DaVita, Inc. and SRTR.

Table 2. Summary of studies with large sample sizes (>1000 subjects) examined the association between pre-transplant obesity and post-transplant outcome

Reference	Sample size	Follow-up Period (yr)	Findings and source of data
Meier-Kreische *et al.* (2002) (94)	51927	Up to 10	U-shaped risk patterns such that both high and low BMI were related to increased risk of death and graft failure. USRDS data.
Gore *et al.* (2006) (95)	27377	Up to 7	Compared with normal weight patients, morbid obesity was independently associated with an increased risk of delayed graft function, prolonged hospitalization, acute rejection and decreased overall graft survival. Donor BMI did not affect overall graft survival. UNOS data.
Chang *et al.* (2007) (105)	5684	Up to 14	Obesity per se was not associated with poorer kidney transplant outcomes. Underweight was associated with late graft failure, mainly due to chronic allograft nephropathy. Australian and New Zealand Dialysis and Transplant (ANZDATA) Registry
Marcen *et al.* (2007) (106)	1000	10	Pre-transplant high body mass and 1-year post-transplant weight gain were not risk factors for graft or patient survival. Single center.
Streja, Molnar *et al.* (2011) (93)	10090	2.5	Pre-transplant obesity does not appear associated with poor post-transplant outcomes. Larger pre-transplant muscle mass, reflected by higher pre-transplant serum creatinine level, is associated with greater post-transplant graft and patient survival. DaVita, Inc. and SRTR.

over, in one study of over 1300 hemodialysis patients, every one unit increase in the BMI was associated with a reduction of 30 percent in the relative risk of dying (23). This result may be confounded in part by race and gender, since African-American females have the highest BMI (53). This results has arrived the question it is the obesity-mortality association was modified by race?

3. Role of race in the association betwee body composition and survival

CKD is common and associated with major racial and ethnic disparities in the United States (US) (54-56). Approximately one-third of the 400,000 US dialysis patients are African Americans, even though they comprise only 14% of the US general population (57, 58). Hispanics compose close to 1/5 of the dialysis population (57, 58). Such factors as disparities in income, education, diet, and lifestyle, co-morbid conditions and in healthcare have been implicated in the increased mortality of Blacks compared with Whites (59). The racial and ethnic discrepancies in CKD prevalence have persisted over the past decades. The incidence rates for dialysis patients for 2006 in the African American and Hispanic population continued to be 3.6 and 1.5 times, respectively, greater than among non-Hispanic whites (57, 58).

Notwithstanding the racial and ethnic differences in CKD rates, there are some encouraging facts pertaining to interaction of health outcomes and race/ethnicity. About two-thirds of all US dialysis patients die within 5 years of initiating maintenance dialysis treatment, higher than most cancers (59). Nonetheless, African American and Hispanic patients with end-stage renal disease (ESRD) have consistently greater survival over the past several decades than non-Hispanic Whites, with an death rate of 187 and 180 per 1000 patient-years at risk, respectively, compared to 207 per 1000 patient-years at risk for non-Hispanic Whites (57, 58). The causes of these disparities remain largely unknown.

Discovering the factors responsible for survival advantages of African American and Hispanic dialysis patients may have major clinical and public health implications, not only for CKD patients but also for other populations with chronic disease states and poor survival. Understanding these factors might lead to methods for improving clinical outcomes in other groups of dialysis patients as well as in populations with other chronic disease states associated with poor survival (60). These issues are particularly time-sensitive for ESRD patients, since the imminent Bundling Payment for provision of medical care to dialysis patients in the US currently does not include an adjustor for race (61-63).

Some nutritional surrogates such as BMI are associated with both race and survival in maintenance hemodialysis patients, in whom higher BMI is associated with greater survival (21, 24, 47, 64). Glanton *et al.* reported 22% higher adjusted risk of obesity in African-Americans than in White-Americans (65). The same study also reported slightly higher hazard ratio for mortality in non-Caucasian than in Caucasian MHD patients with BMI < 22 kg/m^2 (65). Examining a large cohort of 124,029 adult hemodialysis patients, who were observed for up to 5 years during the first decade of the 21st century, African American and Hispanic patients had greater survival than Whites even after case-mix adjustment (66). After additional multivariate adjustment for surrogates of nutrition and inflammation, Hispanics had essentially the same mortality as White, whereas African Americans had a greater death risk compared to Hispanics or Whites. Our findings suggest that a healthier nutritional and inflammatory status is the main cause of the survival advantages of minorities who undergo hemodialysis treatment (66). Additionally, we found that obesity, as measured by BMI, was associated with greater survival in MHD patients of all races and ethnicity, but different patterns were observed across the three mutually exclusive racial and ethnic groups (67). The survival advantage of obesity was most prominent among Blacks. Our analyses suggest a protective but differential role for higher BMI across racial and ethnic groups of hemodialysis patients (67).

4. Body composition and survival in wait-listed dialysis patients

Kidney transplantation is the treatment of choice in patients with ESRD, since patients with functioning renal grafts have both survival benefits (68) and better quality of life (69) compared to transplant waitlisted patients on maintenance dialysis. Approximately 80,000 (20%) of the 400,000 US dialysis patients are currently on transplant waiting lists, although each year only ~16,500 of these patients receive a renal transplant (70, 71). At least half of these patients receive a deceased kidney, which currently requires a wait period of 3 to 6 years in most regions of the United State (70). During this period, up to 40% of the transplant-waitlisted dialysis patients die (72).

Overweight and obesity are highly prevalent in patients at the time of kidney transplantation (73). Indeed, most transplant centers in US may suspend wait-listing of obese patients with a BMI above 30 or 35 kg/m^2 and refer them for weight reduction procedures such as bariatric surgery as a contingency for the transplant surgery (74). In a recent report BMI≥35 kg/m^2 was the third most common reason to deny patient active transplant-wait-listing, affecting approximately 10% of potential renal transplant candidates (75). However, consequences of obesity or changes in weight during the period of wait-listing, which usually last 4 to 7 years in the United States, remain unclear (76, 77). Weight changes prior to transplantation may be transient, especially since most renal transplant recipients experience weight gain following a successful kidney transplant (78). Hence, weight loss before transplantation might not alleviate the risk of obesity after transplantation. In recent study, by linking the 6-year (7/2001-6/2007) national databases of a large dialysis organization and the Scientific Registry of Transplant Recipients, we identified 14,632 waitlisted hemodialysis patients without kidney transplantation (79). Low BMI or serum creatinine, as a surrogate marker of muscle mass and their decrease over time are associated with increased death risk in transplant waitlisted hemodialysis patients. A 20% higher death risk is observed in patients losing more than 5 kg of dry weight compared to patients with stable weight over time. Compared to the lowest serum creatinine quintile, the 4th and 5th quintiles had death hazard ratio of 0.75 (0.66-0.86) and 0.57 (0.49-0.66), respectively. Controlled trials are needed to examine the effects of intentional pre-transplant weight loss on pre- and post-transplant outcomes.

5. Body composition and survival in kidney transplanted patients

Role of pre-transplant obesity

An obesity paradox has been consistently observed in dialysis patients, but conflicting data have been published about the association of pre-transplant body size and weight with post-transplant graft and patient survival in renal transplant recipients *(Table 2)*. Early studies had reported poorer kidney transplant outcomes in obese dialysis patients (80-83) mainly due to cardiovascular (76) and infectious complications such as surgical wound infections (84). More recent studies, however, have reported that weight change prior to transplantation did not correlate with graft loss and death after kidney transplantation (78), even though obese recipients develop diabetes mellitus or surgical complications more frequently (84-88). Many transplant centers exclude or suspend obese patients with a BMI > 30 or > 35 kg/m^2 from the transplant waitlist and refer them for weight reduction strategies such as bariatric surgery (74). However, clinical trials of bariatric surgery in populations without kidney disease indicate comparable weight loss but higher post-surgery mortality (89). In a recent report BMI≥35 kg/m^2 was the third most common reason to deny transplant wait-listing and affecting 10% of potential renal transplant candidates (75). Since the long term consequences of obesity after transplantation remain unclear (76, 77), it is important to address the potential association between pre-transplant body composition and post-transplant outcomes.

Previous studies of obesity in kidney transplant recipients used solely BMI to define obesity (80-83), but BMI is unable to differentiate between adiposity and muscle mass (90). Reduced muscle mass (sarcopenia) is a predictor of mortality in dialysis patients (51). To better characterize patients' nutritional status, additional parameters such as waist circumference or serum creatinine have been suggested (22, 31, 40, 51, 91, 92). Indeed, in maintenance dialysis patients with minimal residual function under steady-state serum creatinine may better reflect muscle mass compared to BMI (22, 31, 40, 51, 92). Recently we examined a large and contemporary national data of over 10,000 renal transplant recipients, pre-transplant low BMI showed a trend towards higher post-transplant mortality, and lower pre-transplant serum creatinine level, a potential surrogate of sarcopenia, was associated with the unfavorable post-transplant outcomes (93). We categorized renal transplant recipients into four groups, based on their pre-transplant BMI and serum creatinine levels being above or below the median value of these measure (26 kg/m^2 and 10.5 mg/dL, respectively), leading to 2 concordant (high/high and low/low) and 2 discordant (high/low and low/high) groups *(Figure 1)*. The post-transplant death and graft failure hazard ratios are shown in *Figure 1*. Compared to the low creatinine and

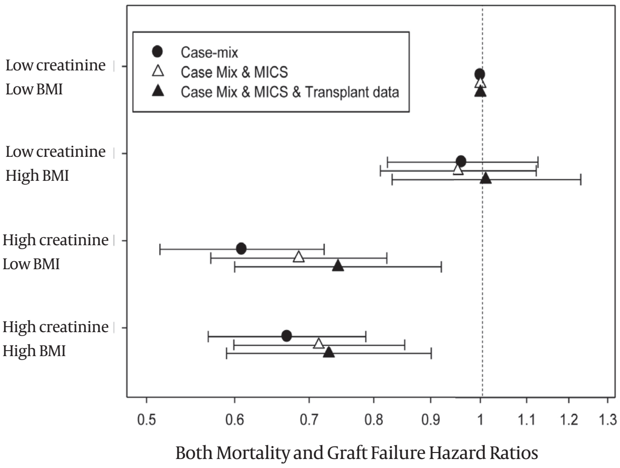

Figure 1. Hazard ratios (and 95% confidence intervals) of death and graft failure across BMI and creatinine categories (subgroup are based on cutoff levels according to the median values of pre-transplant BMI and creatinine levels), using Cox regression analyses in 10,090 MHD patients who underwent renal transplantation and who were observed over a 6-year observation period (7/2001-6/2007)

low BMI groups (reference), the groups with high creatinine and high BMI had 34% lower adjusted death risk (HR: 0.73, [0.57-0.90]) *(Figure 1)*. Adjustment levels in the *Figure 1* present Case-mix adjusted models that included BMI/creatinine, entry calendar quarter, age, sex, race and ethnicity, diabetes mellitus, dialysis vintage, primary insurance, marital status, the standardized mortality ratio of the dialysis clinic during entry quarter, dialysis dose as indicated by Kt/V (single pool), presence or absence of a dialysis catheter, and residual renal function during the entry quarter, i.e. urinary urea clearance, Case-mix, malnutrition-inflammation-complex syndrome (MICS) adjusted models which included all of the covariates in the case-mix model as well as 10 surrogates of nutritional status and inflammation, including 11 laboratory variables with known association with clinical outcomes in MHD patients, i.e. normalized protein catabolic rate (nPCR) as an indicator of daily protein intake, also known as the normalized protein nitrogen appearance (nPNA) and serum or blood concentrations of albumin, TIBC, ferritin, phosphorus, calcium, bicarbonate, peripheral white blood cell count (WBC), lymphocyte percentage, and hemoglobin, and Case-mix, malnutrition-inflammation-complex syndrome (MICS) and transplant data adjusted models which included all of the covariates in the case-mix model and MICS model as well as 5 transplant-related data, i.e., donor type (deceased or living), donor age, panel reactive antibody (PRA) titer (last value prior to transplant), number of HLA mismatches, and cold ischemic time.

Somewhat contrary to our findings, Meier-Kreische *et al.* reported U-shaped risk patterns such that both high and low BMI were related to increased risk of death and graft failure (94), and Gore *et al.* found graded bivariate increases in the risk of delayed graft function, prolonged hospitalization, early graft loss and graft failure with higher BMI level (95). However, the former study examined the USRDS database between 1988 and 1997, whereas the latter study used the UNOS database between 1997 and 1999. During the aforementioned period the immunosuppressive protocols were different (for instance no tacrolimus was available). Moreover, the latter cohort was younger and had less diabetic and African-American patients. Additional studies are needed to better understand the association between obesity, muscle mass and other body compositions and transplant outcomes.

Obesity after transplantation

Obesity contributes to an adverse cardiovascular risk profile and may also be involved in the pathogenesis of allograft dysfunction (96). The deleterious effects of obesity on the kidney are in part mediated by associated cardiovascular risk factors such as diabetes mellitus, hypertension, dyslipidemia, and insulin resistance (97, 98). Recently, Hoogeveen *et al.* reported that one year post-transplant BMI and BMI increment are more strongly related to death and graft failure than pre-transplant BMI among kidney transplant recipients (99). Patients with post-transplant BMI more than 30 kg/m^2 compared with a normal BMI have approximately 20% to 40% higher risk for death and graft failure (99). Previous studies of obesity in kidney transplant recipients used solely BMI to define obesity (80-83), but BMI is unable to differentiate between adiposity and muscle mass (90). We also proved that higher BMI and waist circumference display opposite associations with mortality in kidney transplant recipients (91). Waist circumference appears to be a better prognostic marker for obesity than BMI. Unadjusted death hazard ratios (95%CI) associated with one standard deviation higher BMI and waist circumference were 0.94 (0.78, 1.13), $p = 0.5$ and 1.20 (1.00, 1.45), $p = 0.05$, respectively. Higher BMI was associated with lower mortality after adjustment for waist circumference (0.48 [0.34, 0.69], $p < 0.001$), and higher waist circumference was more strongly associated with higher mortality after adjustment for BMI (2.18 [1.55-3.08], $p < 0.001$) (91).

In summary, we conclude that overweight and obesity have become mass, that are often associated with increased cardiovascular risk and poor survival in the general population appear to confer survival advantage in ESRD patients. This so-called 'obesity paradox' has been consistently reported in other chronic disease states. Whereas the 'reverse epidemiology' of obesity is relatively consistent in maintenance hemodialysis patients, studies in peritoneal dialysis patients have yielded mixed results. The effect of pre- and post-transplant obesity in kidney transplanted patients on long-term graft and patient survival appears to be more complicated. The BMI is unable to differentiate accurately between adiposity and muscle mass, in patients with ESRD. Assessing lean body mass, in particular skeletal muscle, and fat mass separately are needed in ESRD patients using gold standard techniques such as imaging techniques .Alternatively, inexpensive and routinely measured surrogate markers such as serum creatinine, waist and hip circumference or mid-arm muscle circumference can be used.

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Conflict of interest

Dr. Kalantar-Zadeh is the medical director of DaVita Harbor-UCLA/MFI in Long Beach, CA. MZ Molnar has not declared any conflict of interest.

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References

1. U.S. Renal Data System. USRDS 2006 Annual Data Report: Atlas of End-Stage Renal Disease in the United States. Bethesda, MD: NIH/NIDDK; 2008.
2. Kovesdy CP, Kalantar-Zadeh K. Review article: Biomarkers of clinical outcomes in advanced chronic kidney disease. *Nephrology (Carlton)*. 2009;**14**(4):408-15.
3. Chertow GM, Hsu CY, Johansen KL. The enlarging body of evidence: obesity and chronic kidney disease. *J Am Soc Nephrol*. 2006;**17**(6):1501-2.
4. Lavie CJ, Milani RV, Ventura HO. Obesity and cardiovascular disease: risk factor, paradox, and impact of weight loss. *J Am Coll Cardiol*. 2009;**53**(21):1925-32.
5. Lavie CJ, Milani RV, Artham SM, Patel DA, Ventura HO. The obesity paradox, weight loss, and coronary disease. *Am J Med*. 2009;**122**(12):1106-14.
6. Kovesdy CP, Anderson JE, Kalantar-Zadeh K. Paradoxical association between body mass index and mortality in men with CKD not yet on dialysis. *Am J Kidney Dis*. 2007;**49**(5):581-91.
7. Molnar MZ, Lukowsky LR, Streja E, Dukkipati R, Jing J, Nissenson AR, et al. Blood pressure and survival in long-term hemodialysis patients with and without polycystic kidney disease. *J Hypertens*. 2010;**28**(12):2475-84.
8. Kovesdy CP, Anderson JE, Kalantar-Zadeh K. Inverse Association between Lipid Levels and Mortality in Men with Chronic Kidney Disease Who Are Not Yet on Dialysis: Effects of Case Mix and the Malnutrition-Inflammation-Cachexia Syndrome. *J Am Soc Nephrol*. 2007;**18**(1):304-11.
9. Kalantar-Zadeh K, Block G, Humphreys MH, McAllister CJ, Kopple JD. A low, rather than a high, total plasma homocysteine is an indicator of poor outcome in hemodialysis patients. *J Am Soc Nephrol*. 2004;**15**(2):442-53.
10. Oreopoulos A, Padwal R, Kalantar-Zadeh K, Fonarow GC, Norris CM, McAlister FA. Body mass index and mortality in heart failure: a meta-analysis. *Am Heart J*. 2008;**156**(1):13-22.
11. Oreopoulos A, Padwal R, Norris CM, Mullen JC, Pretorius V, Kalantar-Zadeh K. Effect of obesity on short- and long-term mortality postcoronary revascularization: a meta-analysis. *Obesity (Silver Spring)*. 2008;**16**(2):442-50.
12. Oreopoulos A, Kalantar-Zadeh K, Sharma AM, Fonarow GC. The obesity paradox in the elderly: potential mechanisms and clinical implications. *Clin Geriatr Med*. 2009;**25**(4):643-59, viii.
13. Bross R, Chandramohan G, Kovesdy CP, Oreopoulos A, Noori N, Golden S, et al. Comparing body composition assessment tests in long-term hemodialysis patients. *Am J Kidney Dis*. 2010;**55**(5):885-96.
14. Beddhu S, Samore MH, Roberts MS, Stoddard GJ, Pappas LM, Cheung AK. Creatinine production, nutrition, and glomerular filtration rate estimation. *J Am Soc Nephrol*. 2003;**14**(4):1000-5.
15. Keshaviah PR, Nolph KD, Moore HL, Prowant B, Emerson PF, Meyer M, et al. Lean body mass estimation by creatinine kinetics. *J Am Soc Nephrol*. 1994;**4**(7):1475-85.
16. Schutte JE, Longhurst JC, Gaffney FA, Bastian BC, Blomqvist CG. Total plasma creatinine: an accurate measure of total striated muscle mass. *J Appl Physiol*. 1981;**51**(3):762-6.
17. Ramkumar N, Pappas LM, Beddhu S. Effect of body size and body composition on survival in peritoneal dialysis patients. *Perit Dial Int*. 2005;**25**(5):461-9.
18. Kakiya R, Shoji T, Tsujimoto Y, Tatsumi N, Hatsuda S, Shinohara K, et al. Body fat mass and lean mass as predictors of survival in hemodialysis patients. *Kidney Int*. 2006;**70**(3):549-56.
19. Kalantar-Zadeh K, Abbott KC, Salahudeen AK, Kilpatrick RD, Horwich TB. Survival advantages of obesity in dialysis patients. *Am J Clin Nutr*. 2005;**81**(3):543-54.
20. Kalantar-Zadeh K, Kopple JD. Obesity paradox in patients on maintenance dialysis. *Contrib Nephrol*. 2006;**151**:57-69.
21. Kalantar-Zadeh K, Kopple JD, Kilpatrick RD, McAllister CJ, Shinaberger CS, Gjertson DW, et al. Association of morbid obesity and weight change over time with cardiovascular survival in hemodialysis population. *Am J Kidney Dis*. 2005;**46**(3):489-500.
22. Kalantar-Zadeh K, Streja E, Kovesdy CP, Oreopoulos A, Noori N, Jing J, et al. The obesity paradox and mortality associated with surrogates of body size and muscle mass in patients receiving hemodialysis. *Mayo Clin Proc*. 2010;**85**(11):991-1001.
23. Fleischmann E, Teal N, Dudley J, May W, Bower JD, Salahudeen AK. Influence of excess weight on mortality and hospital stay in 1346 hemodialysis patients. *Kidney Int*. 1999;**55**(4):1560-7.
24. Leavey SF, McCullough K, Hecking E, Goodkin D, Port FK, Young EW. Body mass index and mortality in 'healthier' as compared with 'sicker' haemodialysis patients: results from the Dialysis Outcomes and Practice Patterns Study (DOPPS). *Nephrol Dial Transplant*. 2001;**16**(12):2386-94.
25. Salahudeen AK. Obesity and survival on dialysis. *Am J Kidney Dis*. 2003;**41**(5):925-32.
26. Stack AG, Murthy BV, Molony DA. Survival differences between peritoneal dialysis and hemodialysis among "large" ESRD patients in the United States. *Kidney Int*. 2004;**65**(6):2398-408.
27. Johansen KL, Young B, Kaysen GA, Chertow GM. Association of body size with outcomes among patients beginning dialysis. *Am J Clin Nutr*. 2004;**80**(2):324-32.
28. Beddhu S, Pappas LM, Ramkumar N, Samore M. Effects of body size and body composition on survival in hemodialysis patients. *J Am Soc Nephrol*. 2003;**14**(9):2366-72.
29. de Mutsert R, Snijder MB, van der Sman-de Beer F, Seidell JC, Boeschoten EW, Krediet RT, et al. Association between body mass index and mortality is similar in the hemodialysis population and the general population at high age and equal duration of follow-up. *J Am Soc Nephrol*. 2007;**18**(3):967-74.
30. Kalantar-Zadeh K, Abbott KC, Salahudeen AK, Kilpatrick RD, Horwich TB. Survival advantages of obesity in dialysis patients.

Am J Clin Nutr. 2005;**81**(3):543-54.
31. Molnar MZ, Streja E, Kovesdy CP, Bunnapradist S, Sampaio MS, Jing J, et al. Associations of Body Mass Index and Weight Loss with Mortality in Transplant-Waitlisted Maintenance Hemodialysis Patients. *Am J Transplant*. 2011;**11**(4):725-36.
32. Horwich TB, Fonarow GC, Hamilton MA, MacLellan WR, Woo MA, Tillisch JH. The relationship between obesity and mortality in patients with heart failure. *J Am Coll Cardiol*. 2001;**38**(3):789-95.
33. Mohamed-Ali V, Goodrick S, Bulmer K, Holly JM, Yudkin JS, Coppack SW. Production of soluble tumor necrosis factor receptors by human subcutaneous adipose tissue in vivo. *Am J Physiol*. 1999;**277**(6 Pt 1):E971-5.
34. Weber MA, Neutel JM, Smith DH. Contrasting clinical properties and exercise responses in obese and lean hypertensive patients. *J Am Coll Cardiol*. 2001;**37**(1):169-74.
35. Rauchhaus M, Coats AJ, Anker SD. The endotoxin-lipoprotein hypothesis. *Lancet*. 2000;**356**(9233):930-3.
36. Kalantar-Zadeh K, Miller JE, Kovesdy CP, Mehrotra R, Lukowsky LR, Streja E, et al. Impact of race on hyperparathyroidism, mineral disarrays, administered vitamin D mimetic, and survival in hemodialysis patients. *J Bone Miner Res*. 2010;**25**(12):2448-58.
37. Kalantar-Zadeh K, Kovesdy CP. Clinical outcomes with active versus nutritional vitamin D compounds in chronic kidney disease. *Clin J Am Soc Nephrol*. 2009;**4**(9):1529-39.
38. Macleod J, Davey Smith G. Psychosocial factors and public health: a suitable case for treatment? *J Epidemiol Community Health*. 2003;**57**(8):565-70.
39. Kalantar-Zadeh K, Block G, Humphreys MH, Kopple JD. Reverse epidemiology of cardiovascular risk factors in maintenance dialysis patients. *Kidney Int*. 2003;**63**(3):793-808.
40. Noori N, Kovesdy CP, Dukkipati R, Kim Y, Duong U, Bross R, et al. Survival predictability of lean and fat mass in men and women undergoing maintenance hemodialysis. *Am J Clin Nutr*. 2010;**92**(5):1060-70.
41. Kovesdy CP, George SM, Anderson JE, Kalantar-Zadeh K. Outcome predictability of biomarkers of protein-energy wasting and inflammation in moderate and advanced chronic kidney disease. *Am J Clin Nutr*. 2009;**90**(2):407-14.
42. Foley RN, Parfrey PS, Sarnak MJ. Clinical epidemiology of cardiovascular disease in chronic renal disease. *Am J Kidney Dis*. 1998;**32**(5 Suppl 3):S112-9.
43. Fouque D, Kalantar-Zadeh K, Kopple J, Cano N, Chauveau P, Cuppari L, et al. A proposed nomenclature and diagnostic criteria for protein-energy wasting in acute and chronic kidney disease. *Kidney Int*. 2008;**73**(4):391-8.
44. Kalantar-Zadeh K, Kopple JD. Relative contributions of nutrition and inflammation to clinical outcome in dialysis patients. *Am J Kidney Dis*. 2001;**38**(6):1343-50.
45. Kalantar-Zadeh K, Kopple JD, Block G, Humphreys MH. A malnutrition-inflammation score is correlated with morbidity and mortality in maintenance hemodialysis patients. *Am J Kidney Dis*. 2001;**38**(6):1251-63.
46. Molnar MZ, Czira ME, Rudas A, Ujszaszi A, Lindner A, Fornadi K, et al. Association of the Malnutrition-Inflammation Score With Clinical Outcomes in Kidney Transplant Recipients. *Am J Kidney Dis*. 2011;[Epub ahead of print].
47. Kopple JD, Zhu X, Lew NL, Lowrie EG. Body weight-for-height relationships predict mortality in maintenance hemodialysis patients. *Kidney Int*. 1999;**56**(3):1136-48.
48. Kopple JD. Nutritional status as a predictor of morbidity and mortality in maintenance dialysis patients. *Asaio J*. 1997;**43**(3):246-50.
49. Kalantar-Zadeh K, Kilpatrick RD, Kopple JD, Stringer WW. A matched comparison of serum lipids between hemodialysis patients and nondialysis morbid controls. *Hemodial Int*. 2005;**9**(3):314-24.
50. Degoulet P, Legrain M, Reach I, Aime F, Devries C, Rojas P, et al. Mortality risk factors in patients treated by chronic hemodialysis. Report of the Diaphane collaborative study. *Nephron*. 1982;**31**(2):103-10.
51. Noori N, Kopple JD, Kovesdy CP, Feroze U, Sim JJ, Murali SB, et al. Mid-arm muscle circumference and quality of life and survival in maintenance hemodialysis patients. *Clin J Am Soc Nephrol*. 2010;**5**(12):2258-68.
52. McDonald SP, Collins JF, Johnson DW. Obesity is associated with worse peritoneal dialysis outcomes in the Australia and New Zealand patient populations. *J Am Soc Nephrol*. 2003;**14**(11):2894-901.
53. Hakim RM, Lowrie E. Obesity and mortality in ESRD: is it good to be fat? *Kidney Int*. 1999;**55**(4):1580-1.
54. Norris KC, Agodoa LY. Unraveling the racial disparities associated with kidney disease. *Kidney Int*. 2005;**68**(3):914-24.
55. Agodoa L. Racial disparities in kidney health: the puzzle to solve. *Am J Kidney Dis*. 2002;**40**(6):1337-9.
56. Agodoa L, Eggers P. Racial and ethnic disparities in end-stage kidney failure-survival paradoxes in African-Americans. *Seminars in dialysis*. 2007;**20**(6):577-85.
57. United States Renal Data System. United States Renal Data System 2006 Annual Data Report Atlas of Chronic Kidney Disease & End-Stage Renal Disease in the United States. *Am J Kidney Dis*. 2007;**49**(Suppl 1):1-296.
58. United States Renal Data System. Excerpts from the USRDS 2005 Annual Data Report: Atlas of End-Stage Renal Disease in the United States,National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, . *Am J Kid Dis*. 2006;**47**(Suppl 1):1-286.
59. Kalantar-Zadeh K, Kovesdy CP, Derose SF, Horwich TB, Fonarow GC. Racial and survival paradoxes in chronic kidney disease. *Nat Clin Pract Nephrol*. 2007;**3**(9):493-506.
60. Kalantar-Zadeh K, Abbott KC, Kronenberg F, Anker SD, Horwich TB, Fonarow GC. Epidemiology of dialysis patients and heart failure patients. *Semin Nephrol*. 2006;**26**(2):118-33.
61. Zigmond J. New dialysis payment plan. Providers worry about effects of bundling payments. *Mod Healthc*. 2009;**39**(38):10-1.
62. Sullivan J. Bundling and its potential impact on dialysis service providers. *Nephrology news & issues*. 2008;**22**(11):12, 4, 6-7.
63. Coutts LR. Is bundling the solution for managing the cost of care? *Nephrology news & issues*. 2008;**22**(4):11.
64. Kalantar-Zadeh K, Kuwae N, Wu DY, Shantouf RS, Fouque D, Anker SD, et al. Associations of body fat and its changes over time with quality of life and prospective mortality in hemodialysis patients. *Am J Clin Nutr*. 2006;**83**(2):202-10.
65. Glanton CW, Hypolite IO, Hshieh PB, Agodoa LY, Yuan CM, Abbott KC. Factors associated with improved short term survival in obese end stage renal disease patients. *Ann Epidemiol*. 2003;**13**(2):136-43.
66. Streja E, Kovesdy CP, Molnar MZ, Norris KC, Greenland S, Nissenson AR, et al. Role of Nutritional Status and Inflammation in Higher Survival of African American and Hispanic Hemodialysis Patients. *Am J Kidney Dis*. 2011.
67. Ricks J, Molnar MZ, Kovesdy CP, Kopple JD, Norris KC, Mehrotra R, et al. Racial and Ethnic Differences in the Association of Body Mass Index and Survival in Maintenance Hemodialysis Patients. *Am J Kidney Dis*. 2011;[Epub ahead of print].
68. Wolfe RA, Ashby VB, Milford EL, Ojo AO, Ettenger RE, Agodoa LY, et al. Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a first cadaveric transplant. *N Engl J Med*. 1999;**341**(23):1725-30.
69. Kovacs AZ, Molnar MZ, Szeifert L, Ambrus C, Molnar-Varga M, Szentkiralyi A, et al. Sleep disorders, depressive symptoms and health related quality of life – a cross-sectional comparison between kidney transplant recipients and waitlisted patients on maintenance dialysis. *Nephrol Dial Transplant*. 2011;**26**(3):1058-65.
70. Leichtman AB, Cohen D, Keith D, O'Connor K, Goldstein M, McBride V, et al. Kidney and pancreas transplantation in the United States, 1997-2006: the HRSA Breakthrough Collaboratives and the 58 DSA Challenge. *Am J Transplant*. 2008;**8**(4 Pt 2):946-57.
71. Axelrod DA, McCullough KP, Brewer ED, Becker BN, Segev DL, Rao PS. Kidney and pancreas transplantation in the United States, 1999-2008: the changing face of living donation. *Am J Transplant*. 2010;**10**(4 Pt 2):987-1002.
72. Gill JS, Rose C, Pereira BJ, Tonelli M. The importance of transitions between dialysis and transplantation in the care of end-stage renal disease patients. *Kidney Int*. 2007;**71**(5):442-7.
73. Friedman AN, Miskulin DC, Rosenberg IH, Levey AS. Demographics and trends in overweight and obesity in patients at time of kidney transplantation. *Am J Kidney Dis*. 2003;**41**(2):480-7.

74. Scandling JD. Kidney transplant candidate evaluation. *Seminars in dialysis*. 2005;**18**(6):487-94.
75. Holley JL, Monaghan J, Byer B, Bronsther O. An examination of the renal transplant evaluation process focusing on cost and the reasons for patient exclusion. *Am J Kidney Dis*. 1998;**32**(4):567-74.
76. Lentine KL, Rocca-Rey LA, Bacchi G, Wasi N, Schmitz L, Salvalaggio PR, et al. Obesity and cardiac risk after kidney transplantation: experience at one center and comprehensive literature review. *Transplantation*. 2008;**86**(2):303-12.
77. Olarte IG, Hawasli A. Kidney transplant complications and obesity. *American journal of surgery*. 2009;**197**(3):424-6.
78. Schold JD, Srinivas TR, Guerra G, Reed AI, Johnson RJ, Weiner ID, et al. A "weight-listing" paradox for candidates of renal transplantation? *Am J Transplant*. 2007;**7**(3):550-9.
79. Molnar MZ, Streja E, Kovesdy CP, Bunnapradist S, Sampaio MS, Jing J, et al. Associations of Body Mass Index and Weight Loss with Mortality in Transplant-Waitlisted Maintenance Hemodialysis Patients. *Am J Transplant*. 2011;**11**(4):725-36.
80. Holley JL, Shapiro R, Lopatin WB, Tzakis AG, Hakala TR, Starzl TE. Obesity as a risk factor following cadaveric renal transplantation. *Transplantation*. 1990;**49**(2):387-9.
81. Pirsch JD, Armbrust MJ, Knechtle SJ, D'Alessandro AM, Sollinger HW, Heisey DM, et al. Obesity as a risk factor following renal transplantation. *Transplantation*. 1995;**59**(4):631-3.
82. Pischon T, Sharma AM. Obesity as a risk factor in renal transplant patients. *Nephrol Dial Transplant*. 2001;**16**(1):14-7.
83. Ghahramani N, Reeves WB, Hollenbeak C. Association between increased body mass index, calcineurin inhibitor use, and renal graft survival. *Exp Clin Transplant*. 2008;**6**(3):199-202.
84. Lynch RJ, Ranney DN, Shijie C, Lee DS, Samala N, Englesbe MJ. Obesity, surgical site infection, and outcome following renal transplantation. *Annals of surgery*. 2009;**250**(6):1014-20.
85. Howard RJ, Thai VB, Patton PR, Hemming AW, Reed AI, Van der Werf WJ, et al. Obesity does not portend a bad outcome for kidney transplant recipients. *Transplantation*. 2002;**73**(1):53-5.
86. Johnson DW, Isbel NM, Brown AM, Kay TD, Franzen K, Hawley CM, et al. The effect of obesity on renal transplant outcomes. *Transplantation*. 2002;**74**(5):675-81.
87. Bennett WM, McEvoy KM, Henell KR, Valente JF, Douzdjian V. Morbid obesity does not preclude successful renal transplantation. *Clinical transplantation*. 2004;**18**(1):89-93.
88. Massarweh NN, Clayton JL, Mangum CA, Florman SS, Slakey DP. High body mass index and short- and long-term renal allograft survival in adults. *Transplantation*. 2005;**80**(10):1430-4.
89. Modanlou KA, Muthyala U, Xiao H, Schnitzler MA, Salvalaggio PR, Brennan DC, et al. Bariatric surgery among kidney transplant candidates and recipients: analysis of the United States renal data system and literature review. *Transplantation*. 2009;**87**(8):1167-73.
90. Postorino M, Marino C, Tripepi G, Zoccali C. Abdominal obesity and all-cause and cardiovascular mortality in end-stage renal disease. *J Am Coll Cardiol*. 2009;**53**(15):1265-72.
91. Kovesdy CP, Czira ME, Rudas A, Ujszaszi A, Rosivall L, Novak M, et al. Body mass index, waist circumference and mortality in kidney transplant recipients. *Am J Transplant*. 2010;**10**(12):2644-51.
92. Noori N, Kovesdy CP, Bross R, Lee M, Oreopoulos A, Benner D, et al. Novel Equations to Estimate Lean Body Mass in Maintenance Hemodialysis Patients. *Am J Kidney Dis*. 2011;**51**(1):130-9.
93. Streja E, Molnar MZ, Kovesdy CP, Bunnapradist S, Jing J, Nissenson AR, et al. Associations of Pretransplant Weight and Muscle Mass with Mortality in Renal Transplant Recipients. *Clin J Am Soc Nephrol*. 2011.
94. Meier-Kriesche HU, Arndorfer JA, Kaplan B. The impact of body mass index on renal transplant outcomes: a significant independent risk factor for graft failure and patient death. *Transplantation*. 2002;**73**(1):70-4.
95. Gore JL, Pham PT, Danovitch GM, Wilkinson AH, Rosenthal JT, Lipshutz GS, et al. Obesity and outcome following renal transplantation. *Am J Transplant*. 2006;**6**(2):357-63.
96. Armstrong KA, Campbell SB, Hawley CM, Nicol DL, Johnson DW, Isbel NM. Obesity is associated with worsening cardiovascular risk factor profiles and proteinuria progression in renal transplant recipients. *Am J Transplant*. 2005;**5**(11):2710-8.
97. Hsu CY, McCulloch CE, Iribarren C, Darbinian J, Go AS. Body mass index and risk for end-stage renal disease. *Ann Intern Med*. 2006;**144**(1):21-8.
98. Chagnac A, Herman M, Zingerman B, Erman A, Rozen-Zvi B, Hirsh J, et al. Obesity-induced glomerular hyperfiltration: its involvement in the pathogenesis of tubular sodium reabsorption. *Nephrol Dial Transplant*. 2008;**23**(12):3946-52.
99. Hoogeveen EK, Aalten J, Rothman KJ, Roodnat JI, Mallat MJ, Borm G, et al. Effect of Obesity on the Outcome of Kidney Transplantation: A 20-Year Follow-Up. *Transplantation*. 2011;**91**(8):869-74.
100. Leavey SF, Strawderman RL, Jones CA, Port FK, Held PJ. Simple nutritional indicators as independent predictors of mortality in hemodialysis patients. *Am J Kidney Dis*. 1998;**31**(6):997-1006.
101. Wolfe RA, Ashby VB, Daugirdas JT, Agodoa LY, Jones CA, Port FK. Body size, dose of hemodialysis, and mortality. *Am J Kidney Dis*. 2000;**35**(1):80-8.
102. Port FK, Ashby VB, Dhingra RK, Roys EC, Wolfe RA. Dialysis dose and body mass index are strongly associated with survival in hemodialysis patients. *J Am Soc Nephrol*. 2002;**13**(4):1061-6.
103. Lowrie EG, Li Z, Ofsthun N, Lazarus JM. Body size, dialysis dose and death risk relationships among hemodialysis patients. *Kidney Int*. 2002;**62**(5):1891-7.
104. Glanton CW, Hypolite IO, Hshieh PB, Agodoa LY, Yuan CM, Abbott KC. Factors associated with improved short term survival in obese end stage renal disease patients. *Annals of epidemiology*. 2003;**13**(2):136-43.
105. Chang SH, Coates PT, McDonald SP. Effects of body mass index at transplant on outcomes of kidney transplantation. *Transplantation*. 2007;**84**(8):981-7.
106. Marcen R, Fernandez A, Pascual J, Teruel JL, Villafruela JJ, Rodriguez N, et al. High body mass index and posttransplant weight gain are not risk factors for kidney graft and patient outcome. *Transplant Proc*. 2007;**39**(7):2205-7.