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Accepting kidneys from overweight or obese living donors remains a thorny issue

Aceptar riñones de donantes obesos o sobrepeso, sigue siendo un tema controversial

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ABSTRACT

Introduction: due to the immense need for transplants, it is more common in daily practice to accept expanded-criteria living donors (ECLDs), especially within the growing global epidemic of overweight and obesity. The impact on post-nephrectomy residual renal function should be carefully analyzed in this population. Preoperative evaluation should predict a minimum compensation rate of at least 60%. **Objective:** correlate overweight and obesity with renal compensation rate at one year of follow-up. **Material and methods:** a retrospective analytical observational study in southeastern Mexico, between 2015-2021. Renal compensation rate was calculated before and one year after donation. **Results:** 48 kidney donors were included with a median age of 38.98 ± 10.37 years, 56% were men. The average BMI was 27.68 ± 2.84 kg/m^2; 85.4% of the donors had a BMI > 25 kg/m^2. Kidney compensation rate over 60% was 70.9 ± 15.41%. The eGFR < 60 mL/min per 1.73 m^2 12 months after nephrectomy in overweight or obese donors was 18.75%. The calculated cross product ratios (OR) were as follows: eGFR > 90 mL/min per 1.73 m^2 with normal BMI OR = 0.820 (95% CI 0.71-0.95; p < 0.05); eGFR > 90 mL/min per 1.73 m^2 with age < 50 years OR = 0.81 (95% CI 0.70-0.94; p < 0.05); compensation < 60% for high BMI OR = 1.940 (95% CI 0.21-18.07; p > 0.05). **Conclusions:** overweight and obesity

RESUMEN

Introducción: *asociado a la inmensa demanda de trasplantes, cada día es más frecuente aceptar donantes vivos con criterios extendidos (ECLDm, por sus siglas en inglés), en el contexto de la creciente epidemia mundial de sobrepeso y obesidad. El impacto en la función renal residual postnefrectomía debe analizarse cuidadosamente en esta población. La evaluación preoperatoria debe predecir una tasa de compensación mínima de al menos 60%.* ***Objetivo:*** *correlacionar el sobrepeso y la obesidad con la tasa de compensación renal al año de seguimiento.* ***Material y métodos:*** *estudio observacional retrospectivo en el sureste de México, entre 2015-2021. Se calculó la tasa de compensación renal antes y un año después de donar.* ***Resultados:*** *cuarenta y ocho donantes renales de 38.98 ± 10.37 años, 56% hombres, índice de masa corporal (IMC) 27.68 ± 2.84 kg/m^2; 85.4% tenían un IMC > 25 kg/m^2. La tasa de compensación renal superior a 60% en 70.9 ± 15.41%. Filtrado glomerular estimado (eGFR) < 60 mL/min por 1.73 m^2 a los 12 meses de la nefrectomía en donantes con sobrepeso/obesidad en 18.75%. OR calculados: eGFR > 90 mL/min por 1.73 m^2 con IMC normal OR = 0.820 (IC del 95% 0.71-0.95; p < 0.05); eGFR > 90 mL/min por 1.73 m^2 con edad < 50 años OR = 0.81 (IC 95% 0.70-0.94; p < 0.05); compensación < 60% por IMC elevado OR = 1.940 (IC 95% 0.21-18.07; p > 0.05).* ***Conclusiones:*** *el sobrepeso y la obesidad por sí mis-*

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itself may limit acceptability for organ donation, particularly important for younger donor candidates.

Keywords: Yucatan kidney transplantation, expanded-criteria living donors, overweight and obesity.

mos pueden limitar la donación, particularmente importante en donantes jóvenes.

Palabras clave: *trasplante renal Yucatán, donantes vivos con criterios expandidos, sobrepeso y obesidad.*

INTRODUCTION

Kidney transplant donors lose 50% of their kidney mass after nephrectomy, and the remaining kidney must compensate for this loss. Risk factors associated with poor renal compensation after donation are not well understood in southeastern Mexican population.

Given the organ shortage from cadaveric donors, living kidney donation has become an acceptable and safe option for both the donor and the recipient.[1] Our transplant program has performed 469 kidney transplants in the last 20 years, of which 70% have been from living donors.

Due to the immense need for transplants, it is more common in daily practice to accept expanded-criteria living donors (ECLDs), especially within the growing global epidemic of overweight and obesity.[2] The use of suboptimal quality kidneys from marginal living donors have demonstrated comparable short-term and long-term outcomes for recipients but there are few reports on the long-term outcome of these donors.[3] Evaluation in ECLDs should consider elderly donors, borderline estimated glomerular filtration rate (eGFR), high body mass index (BMI), glucose intolerance and controlled hypertension, among other risk factors.

The impact on post-nephrectomy residual renal function should be carefully analyzed, especially since it can differ between donors based on their individual risk factors, which is important for patient selection, counseling and follow-up care.

Preoperative evaluation should predict a minimum compensation rate of at least 60% and long-term risk for end-stage renal disease (ESRD), to identify donors whose risk exceeds the acceptable threshold, and to ensure follow-up after surgery.[4-6]

Some absolute contraindications in our program for living donor nephrectomy include eGFR < 60 mL/min per 1.73 m^2, diabetes mellitus, uncontrolled hypertension, proteinuria > 300 mg/24 hours, microhaematuria as well as BMI > 35 kg/m^2.[5]

The association between obesity and chronic and ESRD is well known, the relative risk (RR) in obese patients increases directly with BMI, from 1.9 in overweight patients, to 3.6 in those with class I obesity, 6.1 in those with class II obesity, and 7.1 for those with extreme obesity (BMI $\geq$ 40 kg/m^2).[7]

The objective of this study was to identify the risk factors that negatively affect the renal compensation rate after donation, especially the association in overweight or obese donors, since 80.4% of adults aged 20 years and over, who attend our institution in the state of Yucatan, are overweight and obese.[8]

MATERIAL AND METHODS

A retrospective analytical observational study was carried out, reviewing the records of living donors for kidney transplants performed at a tertiary care center, in southeastern Mexico, between 2015-2021.

Variables analyzed were age, sex, relationship, BMI, blood group, surgical technique, nephrectomy laterality, serum creatinine and eGFR using the CKD-EPI equation before and one year after donation. Finally, one-year renal compensation rate was calculated.

Table 1: Donor demographic and anthropometric data.

Variables	%
Relationship	
Related	63.0
Wife/husband	23.0
Non-related	14.0
BMI classification	
Normal (< 25 kg/m^2)	14.6
Overweight (25.1-30 kg/m^2)	64.6
Obesity (> 30.1 kg/m^2)	20.8
Age groups (years)	
20-24	4.2
25-29	20.8
30-34	16.7
35-39	12.5
40-44	10.4
45-49	18.8
50-54	8.3
55-60	8.3
Blood type	
A	8.3
0	91.7

BMI = body mass index.

Table 2: Renal function before and after nephrectomy.

Variables	Media ± DE	Minimum	Maximum	p‡
Serum creatinine before nephrectomy	0.82 ± 0.17	0.50	0.90	< 0.05
Serum creatinine one year follow-up	1.15 ± 0.26	0.70	1.90	
Estimated glomerular filtration rate*	105.27 ± 14.9	71.00	133.00	< 0.05
Estimated glomerular filtration rate* one year follow-up	74.14 ± 16.52	40.00	117.00	

* Estimation made through the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) group formula.
‡ p value represents the statistical significance found between the different strata of the BMI classification, according to the WHO, as well as between the age groups.

Table 3: Variation of glomerular filtration by age groups and by BMI.

Variables	Media	CI 95%		Coefficient of variation %
		Lower limit	Upper limit	
Age groups (years)				
20-24	0.84	0.02	1.65	10.8
25-29	0.71	0.58	0.83	25.3
30-34	0.70	0.55	0.84	25.0
35-39	0.68	0.49	0.87	26.7
40-44	0.72	0.55	0.88	18.5
45-49	0.73	0.65	0.82	15.6
50-54	0.76	0.43	1.10	27.6
55-60	0.60	0.44	0.76	16.6
BMI classification (kg/m^2)				
Normal	0.73	0.63	0.83	14.9
Overweight	0.73	0.67	0.80	23.1
Obesity	0.62	0.55	0.69	15.0

BMI = body mass index. CI = confidence intervals.

Table 4: Variation of serum creatinine concentration by age groups and by BMI.

Variables	Media	CI 95%		Coefficient of variation %
		Low limit	Up limit	
Age groups (years)				
20-24	1.157	0.322	1.991	8.0
25-29	1.451	1.248	1.653	19.4
30-34	1.443	1.224	1.661	17.9
35-39	1.437	1.157	1.717	18.3
40-44	1.369	1.126	1.612	15.0
45-49	1.358	1.236	1.479	12.0
50-54	1.369	0.785	1.952	27.3
55-60	1.578	1.186	1.970	17.5
BMI classification (kg/m^2)				
Normal	1.402	1.248	1.556	11.8
Overweight	1.364	1.273	1.455	18.0
Obesity	1.573	1.409	1.737	14.6

BMI = body mass index. CI = confidence intervals.

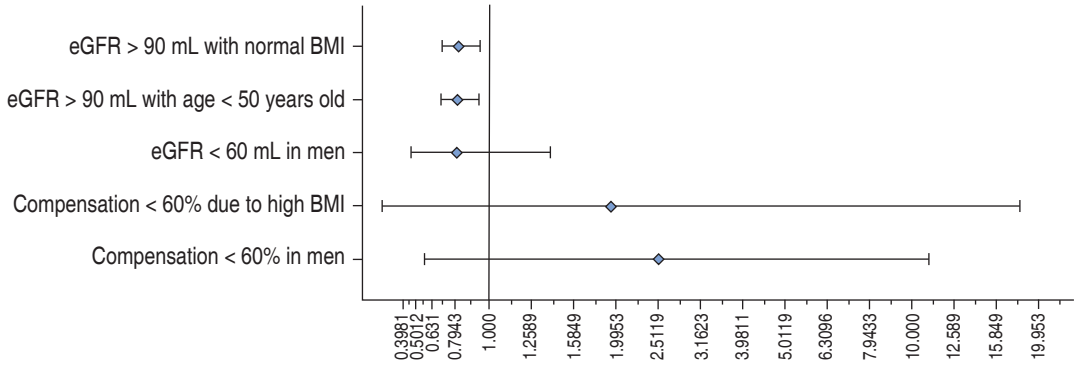

Figure 1:

Association between BMI, age and sex with eGFR and compensation rate for the remaining kidney.
BMI = body mass index. eGFR = estimated glomerular filtration rate.

Descriptive statistics were performed with measures of central tendency and measures of variability (spread). Paired sample t-test was performed to compare baseline and 12 months creatinine and eGFR. Cross-product ratios between BMI classes, age and renal compensation rate (≥ 70%, ≥ 60%, or < 60%) were estimated. These variability percentages in creatinine and eGFR at baseline and at 12 months were estimated using ratio statistics. The cumulative incidence for presenting an eGFR < 60 mL/min and for presenting an eGFR < 60 mL/min due to high BMI (overweight or obesity) was calculated.

Recipient operating characteristic (OC) curves were obtained to determine the performance of diagnostic tests for renal function.

The results are presented in tables, graphs and figures, depending on the type of information.

RESULTS

48 kidney donors were included with a median age of 38.98 ± 10.37 years, 56% of which were men. The average BMI was 27.68 ± 2.84 kg/m^2; 85.4% of the donors had a BMI > 25 kg/m^2; the details on demographic data are shown in *Table 1*. Regarding the surgical technique, 93.8% underwent open nephrectomy and only 6.3% underwent laparoscopic surgery; 81.3% left nephrectomy.

Renal function data

Renal compensation rate over 60% was 70.9 ± 15.41%. Mean creatinine and eGFR before and one year after nephrectomy are shown in *Table 2*.

The eGFR < 60 mL/min per 1.73 m^2 at 12 months after donation was 16.6%; the cumulative incidence for presenting a eGFR < 60 mL/min per 1.73 m^2 12 months after nephrectomy in overweight or obese donors was 18.75%. Variation of glomerular filtration by age groups and by BMI are shown in *Tables 3 and 4*.

The calculated cross product ratios (OR) by associating gender, BMI, and age with eGFR and compensation rate are shown in *Figure 1*; and were as follows: eGFR > 90 mL/min per 1.73 m^2 with normal BMI OR = 0.820 (95% CI 0.71-0.95; p < 0.05); eGFR > 90 mL/min per 1.73 m^2 with age < 50 years OR = 0.81 (95% CI 0.70-0.94; p < 0.05); eGFR < 60 mL/min per 1.73 m^2 in men OR = 0.808 (95% CI 0.468 1.394; p > 0.05); compensation < 60% for high BMI OR = 1.940 (95% CI 0.21-18.07; p > 0.05); compensation < 60% in men OR = 2.526 (95% CI 0.582-11.023; p > 0.05).

The percentile distribution of creatinine and eGFR before and 12 months after nephrectomy, as well as the renal compensation rate, according to age and BMI, are shown in *Figure 2*.

Receiver operating characteristic (ROC) curve showed diagnostic accuracy in predicting favorable compensation (area under the curve = 0.958; 95% CI 0.925-0.991, p < 0.001). Similarly, having a baseline eGFR > 90 mL/min before donation predicted adequate renal compensation one year after nephrectomy. Creatinine quantification before and after surgery allowed us to observe compensation trends at 12 months of follow-up *(Figure 3)*. Percentile graphs were made with creatinine levels, the eGFRs and the percentage of compensation, baseline and at 12 months, in order to observe the trends according to their BMI.

DISCUSSION

Living donor kidney transplantation has been performed at our institution since 1987, and published experience shows that short- and long-term donor

morbidity and mortality is reasonably low.[9] However, this article shows evidence that older donors with overweight, obesity and borderline basal creatinine clearance, have greater difficulty compensating for the remaining kidney.

Functional compensation, morbidity and mortality in kidney donors has been discussed for years, apparently ruling out a higher risk of ESRD or death as compared with the general population.[10]

The above in non-ECLDs groups, but advances in surgical techniques and the increased demand for organ donation and transplantation, has made it necessary to relax the criteria for kidney donation, increasing the use of extended criteria donors, without clearly knowing the long-term functional impact in this group of patients.[11]

Under usual conditions the remaining kidney compensates for the renal mass loss after nephrectomy and it is estimated to be 70% from baseline.[12] The compensation mechanism in healthy individuals is through adaptive hyperfiltration secondary to increased renal blood flow and glomerular hypertrophy.[13] Factors associated with poor post-donation renal compensation may vary depending on different donor risk factors. If a donor candidate postdonation risk is above the transplant program acceptable risk threshold, the risk is not acceptable.[14]

Overweight people are at increased risk for end-stage renal disease (ESRD).[15] The ratio found pre and post-nephrectomy eGFR in patients with high BMI was negatively correlated (-0.53; $p < 0.001$), as described in other series like Altheaby, et. al. who reported that overweight and obese people had a lower glomerular filtration rate one year after nephrectomy.[16] These could be explained because of preexisting obesity-related hyperfiltration that may have a diminished capacity to undergo further adaptive hyperfiltration after nephrectomy compared to a normal weight donor.[17] Hassan N. Ibrahim, et. al. associated in a series of 1338 obese donors with BMI 30-34.9 kg/m^2 a higher risk of eGFR < 60 mL/min per 1.73 m^2, as well as development of diabetes, hypertension, and proteinuria, all well-known risk factors for developing ESRD.[18] The Spanish Society of Nephrology and Spanish National Transplant Organization guidelines define waistline greater than 82 cm in women or

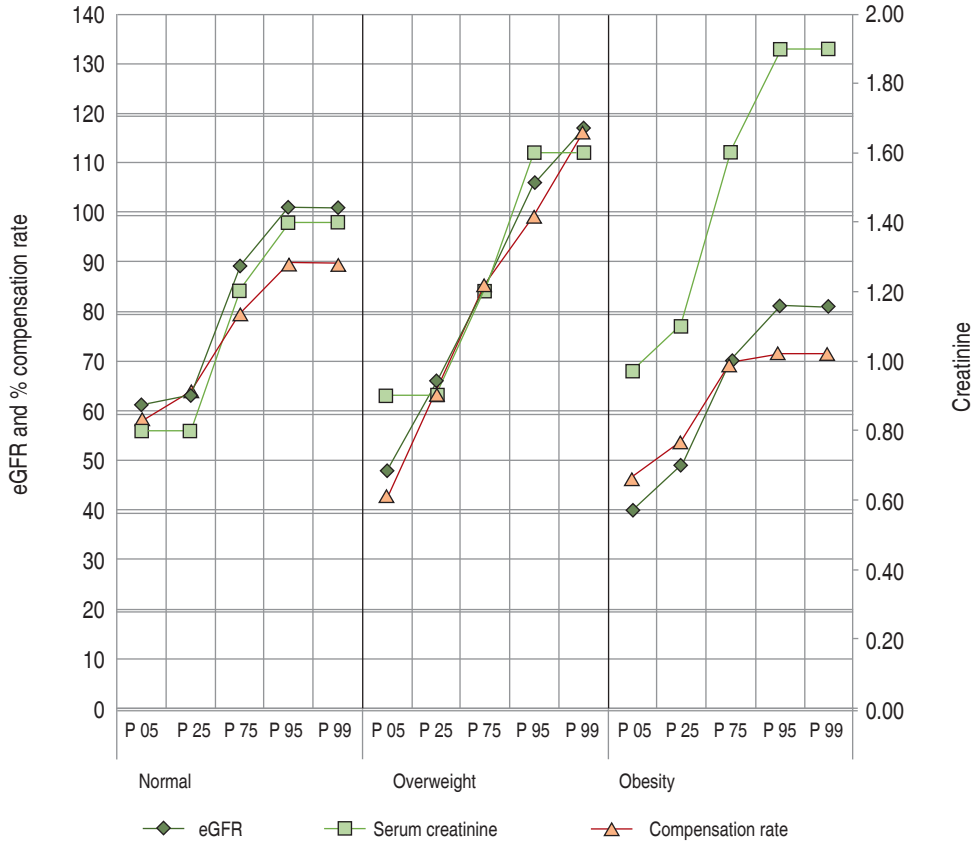

Figure 2:

Renal function variables distributed by age, BMI and ordered by percentiles. One year follow-up.
eGFR = estimated glomerular filtration rate.

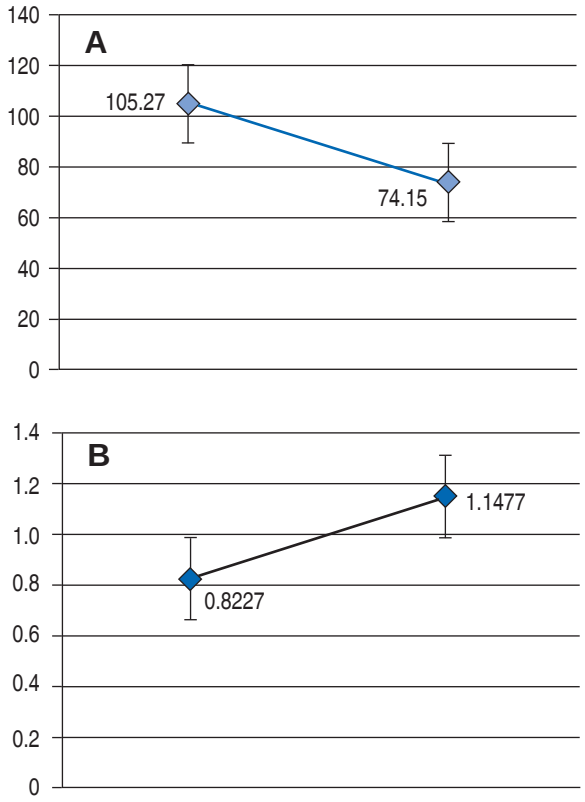

Figure 3: A) Average estimated glomerular filtration rate. **B)** Average serum creatinine level.

greater than 102 cm in men as additional relative contraindications to donation.[19]

These same findings have also been reported in non-donor population; a study of 73 patients who underwent unilateral nephrectomy for reasons other than donation found that patients with BMI > 30 kg/m^2 had a higher rate of proteinuria and renal insufficiency compared to nonobese patients (92% vs 12%) over 10 to 20 years after nephrectomy.[20] Consistent with these data, this study found that the patients who presented greater variability in eGFR were those who were obese and overweight.

These concerns about obese donor higher likelihood of developing hypertension, proteinuria and diabetes (the latter being the most common cause of kidney failure) along with detrimental variations in eGFR trajectory profile should make us reassess the acceptance of overweight or obese donors.

Patients with normal BMI, high glomerular filtration rate and low serum creatinine levels before donation have a better prognosis after nephrectomy, characterized by greater compensation of the remaining kidney.

Donors who are overweight or obese and aged ≥ 50 years have a high risk of low compensation percentage of < 60% one year after surgery.

No association could be established between the degrees of compensation of the remaining kidney with respect to sex.

CONCLUSIONS

Patients with an eGFR > 90 mL/min per 1.73 m^2 before donation and a normal BMI have a better prognosis after nephrectomy.

Overweight and obese donors and those older than 50 years have a low renal compensation rate of less than 60% one year after surgery. Having reduced eGFR by virtue of nephrectomy may put overweight and obese donors at a higher risk for kidney failure, if faced with the development of diabetes or hypertension.

These findings suggest that obesity itself may limit acceptability for organ donation, particularly important for younger donor candidates; and should also be taken into account to modify public policies within the first level of primary care.

It is possible that there is an association between the rate of renal compensation related to male gender, but further studies with a larger sample are needed.

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