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Original article

# Evolution of GFR outcomes during the first year of transplant according to the kidney donor risk Index transplantation in Mexico. The experience of a single center

Jorge L Aguilar-Frasco,* José Manuel Arreola-Guerra,* L Paláu-Dávila,* V Visag,* Mario Vilatobá-Chapa,* Alan Contreras-Saldivar,* A Sanchez,* Josefina Alberú-Gómez*

* Department of Transplantation. Instituto Nacional de Ciencias Médicas y Nutrición «Salvador Zubirán». Mexico, City.

## ABSTRACT

Several scoring systems have been proposed to evaluate the quality of kidneys from deceased donors (DD). Recently, kidney donor risk index (KDRI) was introduced in the USA as a refined version of the dichotomous extended criteria donor (ECD) score versus non-ECD. **Objective:** To evaluate the usefulness of the KDRI as a tool risk predictor of graft loss, delayed graft function and clinical outcomes at one year post-transplant in patients with deceased donor kidney transplantation (DDKT) in our center. **Material and methods:** 96 patients transplanted from Jan/2008 to Nov/2013 with deceased kidney donors were included. DD were on average 41.2 (± 12.6) years old and 49 (51%) were female. The donors had an average KDRI of 0.86 (ratio 0.58~ 1.55). The information for this retrospective cohort study came from the data base of DD kidney transplants at our center. All patients included had at least one year of clinical follow-up. Univariate and multivariate analysis were performed using linear regression adjusted to diverse variables such as, immunological risk, acute rejection and delayed graft function. **Results:** The mean KDRI was 0.86 (range, 0.58~1.55). More than 75% of donors had KDRI < 1.0. The KDRI were divided into three groups: 0.5-0.74, 0.75-0.99 and ≥ 1.0. The incidence of DGF was significantly more frequent in the group with KDRI ≥1.0 (30%) than KDRI < 0.74 (1%), p ≤ 0.01, and higher KDRI was associated with increased episodes of acute rejection and graft loss. Graft function was significantly lower in those with KDRI ≥ 1.0 (p < 0.01). One-year graft survival in the KDRI groups was 100%, 92.3% and 80%, respectively. **Conclusions:** The KDRI discriminated accordingly and in a significant manner patients with DGF

## *RESUMEN*

*Se han propuesto varios sistemas de puntuación para evaluar la calidad de los riñones de donantes fallecidos (DD). Recientemente, el índice de riesgo de donantes de riñón (KDRI, por sus siglas en inglés) se introdujo en los EE.UU. como una versión refinada de la puntuación dicotómica de donantes con criterios extendidos (ECD, por sus siglas en inglés) versus non-ECD.* ***Objetivo:*** *Evaluar la utilidad del KDRI como herramienta para predecir el riesgo de pérdida del injerto, retraso de la función del injerto y resultados clínicos un año después del trasplante en pacientes con trasplante de riñón de donante fallecido (DDKT) en nuestro centro.* ***Material y métodos:*** *Se incluyeron 96 pacientes trasplantados entre enero de 2008 y noviembre de 2013 con donantes de riñón fallecidos. El DD fue en promedio de 41.2 (± 12.6) años de edad y 49 (51%) fueron mujeres. Los donantes tuvieron un KDRI promedio de 0.86 (proporción 0.58- 1.55). La información para este estudio de cohorte retrospectivo provino de la base de datos de trasplantes de riñón DD en nuestro centro. Todos los pacientes incluidos tuvieron al menos un año de seguimiento clínico. Se realizaron análisis univariados y multivariados mediante regresión lineal ajustada a diversas variables como riesgo inmunológico, rechazo agudo y función retardada del injerto.* ***Resultados:*** *El KDRI medio fue de 0.86 (rango, 0.58~1.55). Más del 75% de los donantes tenía KDRI < 1.0. Los KDRI se dividieron en tres grupos: 0.5-0.74, 0.75-0.99 y ≥ 1.0. La incidencia de DGF fue significativamente más frecuente en el grupo con IRC ≥ 1.0 (30%) que con IRC < 0.74 (1%), p ≤ 0.01, y la IRC más alta se asoció con mayores episodios de rechazo agudo y pérdida del injerto. La función del injerto fue significativamente menor en aquéllos*

and correlated with renal function from one month to one year follow up. The correlation between the KDRI and the GFR was persistent and significant during the follow-up. KDRI is a useful prognostic tool for evaluation of graft function during the first year post-transplant.

**Key words:** Deceased donor, donor pool, donor risk, glomerular filtration rate, Kidney Donor Risk Index, scoring system.

*con KDRI ≥ 1.0 ($p < 0.01$). La supervivencia del injerto a un año en los grupos KDRI fue del 100%, 92.3% y 80%, respectivamente.* ***Conclusiones:*** *El KDRI discriminó en consecuencia y de manera significativa a los pacientes con DGF y se correlacionó con la función renal de un mes a un año de seguimiento. La correlación entre el KDRI y la GFR fue persistente y significativa durante el seguimiento. KDRI es una herramienta de pronóstico útil para la evaluación de la función del injerto durante el primer año después del trasplante.*

***Palabras clave:*** *Donante fallecido, grupo de donantes, riesgo del donante, tasa de filtración glomerular, índice de riesgo del donante de riñón, sistema de puntuación.*

**Abbreviations:**

AR = Acute rejection.
DCD = Donation after cardiac death.
DDKT = Deceased donor kidney transplantation.
DGF = Delayed graft function.
ECD = Expanded criteria donor.
eGFR = Estimated glomerular filtration rate.
KDRI = Kidney donor risk index.
MDRD = Modification of diet in renal disease formula.
OPTN = Organ procurement and transplantation network.
SCD = Standard criteria donor.

## INTRODUCTION

The growth of the kidney transplant waiting list in Mexico is an inevitable consequence of the increasing deficit between new enrolling patients and the availability of donor organs each year. The quest to combat this issue has led to diverse innovative solutions such as the use of expanded criteria donor (ECD) versus standard criteria donor kidneys (SCD).[1] Deceased donor kidneys are classified as ECD if they meet either of the following conditions: (1) donor age more than or equal to 60 years or (2) donor age 50 to 59 years, with at least two of the following criteria: serum creatinine more than 1.5 mg/dL, death due to cerebrovascular accident, or history of hypertension. Recent studies show that kidney transplants from ECD donors have at least a 70% greater risk of graft failure than those from the lowest risk, SCD donors.[1] In 2005, ECD kidneys constituted 17% of all transplanted deceased donor kidneys.[2]

The existing ECD or SCD dichotomy has been useful for making decisions about accepting organ offers, counseling patients about risks, and documenting changing practices in the use of higher risk organs.[3] Classifying donor kidneys as ECD versus SCD has simplified the effects of donor characteristics on transplant outcomes and has highlighted the importance for physicians and patients to consider these differences in the transplant process.[4] Furthermore, a continuous kidney donor risk index (KDRI) was also developed to measure the spectrum of risk associated with various factors known to influence graft failure.[3,4] The KDRI combines a variety of donor factors to summarize the risk of graft loss after kidney transplant into a single number. The KDRI scale is a useful tool to assist physicians and transplant candidates when deceased donor kidneys become available. This more specific index results in an improvement over the less accurate ECD classification system.[3] Although the developed classification systems may greatly assists physicians and candidates in assessing their options when a deceased donor kidney becomes available, designation of donor risk may often be assumed to be uniform for recipients. The ECD versus SCD classification and the KDRI can provide estimated relative risks and post transplant survival associated with the quality of the donor organ. However, significant interactions exist with the effect of donor kidney quality and recipient characteristics, which also influence transplant outcomes.[3] The aim of this study was to evaluate the usefulness of the KDRI in the clinical practice to evaluate the risk of delayed graft function, graft function during the first year post-transplantation and evolution of GFR.

## MATERIAL AND METHODS

We analyzed retrospectively the medical records of the donors and recipients for the 96 deceased donor kidney transplantation (DDKT) procedures performed in our center between Jan/2008 to Nov/2013. The KDRI of donor kidneys was calculated and the distribution of kidney donors by standard criteria donor/expanded criteria donor and KDRI was compared. Patients were grouped according to the KDRI score into three groups: 0.5-0.74, 0.75-0.99 and ≥ 1.0. Delayed graft function, graft function and graft survival among KDRI groups were analyzed.

### Data collection

Estimated glomerular filtration rate (eGFR) was calculated from serum creatinine values using the modification of diet in renal disease formula (MDRD). Delayed Graft Function (DGF) was defined as a dialysis requirement during the first week post-transplantation. Acute rejection (AR) confirmed by biopsy (Bx) was stratified according to the Banff 2007 classification criteria. Acute rejection represents the sum of clinical and subclinical events documented by 12 mo protocol Bx and Bx performed for graft dysfunction; borderline lesions are included as AR *(Table 1)*.

Two metrics, the ECD definition and the KDRI, were used to assess donor risk. The KDRI calculated for this study comprised the 10 factors associated with donors including: age, height, weight, race, history of hypertension and diabetes, serum creatinine, cause of death, donation after cardiac death (DCD) and hepatitis C to be consistent with the Organ Procurement and Transplantation Network (OPTN) KDRI calculator[5,6] The KDRI score is a measure of the estimated risk of graft failure relative to a reference donor with KDRI = 1.00 with characteristics as specified by Rao et al.[3,4] As for renal function at one-year follow-up, univariate and multivariate analysis were performed using linear regression adjusted to diverse variables as, immunological risk, acute rejection and delayed graft function. With the aim of assessing the relation between KDRI and diverse cutoff points, in the multivariate analysis, variables with p value < 0.1 were taken into account and considered significant.

## RESULTS

The overall study population included 96 kidney transplant recipients with complete donor risk information that had a median age of 41.2 years at the time of transplant, 51% of which were female. Just 15.63% of recipients had a history of diabetes and all of them were of Hispanic origin *(Table 2)*. All the recipients received thymoglobulin induction therapy and triple drug immunosuppressive therapy based on tacrolimus, mycophenolate mofetil and prednisone.

The median age of the donor was 34.71, 37.2% were female and all of them were of Hispanic origin. Almost ten percent (8.47%) of the donors had a history of hypertension and 8.4% had a history of diabetes. The median terminal creatinine value was 0.97 mg/dL and 54.2% of the donors died secondary to head trauma. None of the donors' population was hepatitis C positive *(Table 3)*.

The mean KDRI was 0.86 (range, 0.58~1.55). More than 75% of donors had KDRI < 1.0. The KDRI were divided into three groups: 0.5-0.74, 0.75-0.99 and ≥ 1.0. The distribution of kidneys by KDRI groups was 38.5%, 40.6%, and 20.8%, respectively. None of the kidneys with KDRI < 0.74 were ECD, whereas 69.2% of the kidneys with KDRI ≥ 1.0 were ECD. The incidence of DGF was significantly more frequent in the group with KDRI ≥ 1.0 (30%) than KDRI < 0.74 (1%), p ≤ 0.01, and higher KDRI was associated with increased episodes of acute rejection and graft loss *(Figure 1)*.

The estimated GFR at six months and one-year post-transplant in the KDRI groups was 67.8, 57.2,

**Table 1. Rejection characteristics.**

| Variable | KDRI (0.5-0.74) (n = 37) | KDRI (0.75-0.99) (n = 39) | KDRI ≥ 1.0 (n = 20) | p value |
|---|---|---|---|---|
| Borderline | 9 (24.32%) | 8 (20.51%) | 7 (35.0%) | NS |
| Celular rejection | 3 (8.11%) | 6 (15.38%) | 3 (15.0%) | NS |
| Humoral rejection | 5 (13.51%) | 4 (10.26%) | 2 (10.0%) | NS |
| Time to 1st AR M (SD, min-max) | 10.41 (3.41, 3-12) | 9.38 (4.35, 1-12) | 6.58 (4.81, 1-12) | 0.062 |

**Table 2. Kidney transplant recipients general demographics.**

| Variables | |
|---|---|
| Recipient gender (female/male) | 49/47 |
| Recipient age (SD) | 41.1 (±12.69) |
| Body mass index (SD) | 24.57 (± 3.83) |
| Recipients with DSA, n (%) | 26 (27.1) |
| ESRD cause: | |
| • Idiopathic, n (%) | 26 (27.1) |
| • Diabetes mellitus, n (%) | 15 (15.63) |
| • Glomerulonephritis, n (%) | 18 (18.75) |
| • ADPKD, n (%) | 13 (13.54) |
| • Second transplant, n (%) | 9 (9.38) |
| • Other causes, n (%) | 15 (15.63) |

SD = Standard deviation; DSA = Donor specific antibody; ESRD = End stage renal disease; AD = Autosomal dominant polycystic kidney disease.

**Table 3. Donor characteristics.**

| Variables | |
|---|---|
| Donor gender (female/male) | 22/37 |
| Donor age (SD) | 34.71 (± 13.7) |
| Weight (SD) | 69.35 (± 9.9) |
| Height (SD) | 1.65 (± 0.07) |
| Hispanic origin n (%) | 59 (100) |
| HCV positive n (%) | 0 (0) |
| Hypertension n (%) | 5 (8.47) |
| Diabetes n (%) | 5 (8.47) |
| Cause of death: | |
| • Head trauma n (%) | 32 (54.23) |
| • Stroke n (%) | 10 (16.94) |
| • Other cause n (%) | 17 (28.8) |
| Cold ischemia time (SD) | 20.2 (± 4.91) |

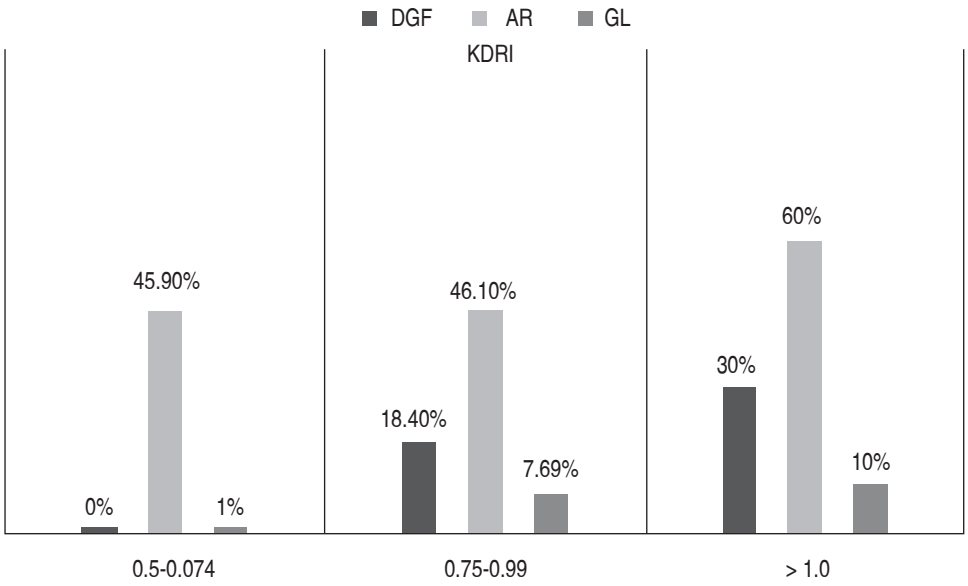


**Figure 1.**

Differences in delayed graft function (DGF), acute rejection (AR) and graft loss (GL) according to the kidney donor risk index (KDRI).

45.1, and 63.1, 57.7, 47.9 mL/min, respectively. Graft function was significantly lower in those with KDRI ≥ 1.0 ($p < 0.01$). One-year graft survival in the KDRI groups was 100%, 92.3% and 80%, respectively *(Table 4)*.

Renal function (eGFR), and related variables were evaluated. In the univariate analysis, only a history of AR episode, DGF and KDRI score were significantly associated with worse renal function and a KDRI cutoff point of 0.8 presented greater correlation. In the adjusted multivariate analysis, AR and DGF showed significance with the dichotomic and continous form of KDRI score *(Table 5)*.

## DISCUSSION

In this study, KDRI discriminated according and significantly with DGF and correlated with renal function from one month to one year follow-up. The correlation between the KDRI and the eGFR was persistent and significant during the follow-up even when adjusting for acute rejection and DGF.

The KDRI is a useful prognostic tool for evaluation of graft function during the first year post-transplant. The impact of KDRI on graft outcome makes it a useful decision-making tool at the time of the deceased donor kidney offer allocation.

**Table 4. Outcomes of deceased donors kidney transplant recipients based on the kidney donor risk index score groups.**

| Variable | KDRI 0.5-0.74 (n = 37) | KDRI 0.75-0.99 (n = 39) | KDRI ≥ 1.0 (20) | p |
|---|---|---|---|---|
| Class I %PRA | 5.7 (0-67) | 8.6 (0-91) | 5 (0-22) | 0.71 |
| Class II %PRA | 5.69 (0-86) | 7.56 (0-83) | 6.25 (0-86) | 0.96 |
| DSA | 12 (32.4%) | 9 (23%) | 5 (25%) | 0.66 |
| AR | 17 (45.9%) | 18 (46.1%) | 12 (60.0%) | 0.54 |
| DGF | 0 (0%) | 7 (18.4%) | 6 (30%) | < 0.01 |
| GFR MO 1 | 69.9 (21.2) | 60.6 (18.1) | 50.7 (26.9) | < 0.01 |
| GFR MO 3 | 68.5 (19.1) | 58.9 (21.2) | 47.5 (19.5) | < 0.01 |
| GFR MO 6 | 67.8 (20.4) | 57.2 (17.1) | 45.1 (18.6) | < 0.01 |
| GFR MO 12 | 63.1 (17.3) | 57.7 (17.7) | 47.9 (18.8) | 0.012 |
| Graft loss | 0 (0%) | 3 (7.69%) | 2 (10%) | 0.177 |

PRA = Panel reactive antibodies, DSA = Donor specific antibodies, DGF = Delayed graft function, GFR (MDRD based), AR = Acute rejection (borderline lesions included), KDRI = Kidney donor risk index, DD = Deceased donors.

**Table 5. Multivariate analysis for eGFR at one year of follow-up.**

| | Univariate | | Model 1 | | Model 2 | |
|---|---|---|---|---|---|---|
| Variable | B coef (CI 95%) | p value | B Coef (CI 95%) | p value | B Coef | p value |
| Recipient age | -0.23 (-0.52-0.06) | 0.128 | | | | |
| Recipient gender | 1.87 (-5.74-9.49) | 0.626 | | | | |
| Class I %PRA | -0.027 (-0.26-0.2) | 0.817 | | | | |
| Class II %PRA | 0.11 (-0.102-0.32) | 0.302 | | | | |
| DSA | 1.18 (-7.34-9.7) | 0.784 | | | | |
| AR | -12.6 (-19.7 to -5.4) | 0.001 | -9.9 (-16.8 to -2.9) | 0.006 | -9.4 (16.3 to -2.5) | 0.008 |
| DGF | -22.27 (-32.8 to -11.7) | < 0.001 | -14.7 (-25 to -3.82) | 0.009 | -13.3 (-24.5 to -2.08) | 0.021 |
| KDRI cont* | -29.4 (-45.1 to -13.75) | <0.001 | | | -18.4 (-34.5 to -2.3) | 0.026 |
| KDRI > 0.8 | -11.07 (-18.3 to -3.8) | 0.003 | -7.59 (-14.6 to -0.51) | 0.036 | | |

Model adjusted for recipient age and gender, class I and class II %PRA, DSA, DGF and KDRI.
*KDRI score as continuous variable.

## CONCLUSIONS

The KDRI discriminated accordingly and in a significant manner patients with DGF and correlated with renal function from one month to one year follow up. The correlation between the KDRI and the GFR was persistent and significant during the follow-up. KDRI is a useful prognostic tool for evaluation of graft function during the first year post-transplant.

## REFERENCES


1. Port FK, Bragg-Gresham JL, Metzger RA, Dykstra DM, Gillespie BW, Young EW et al. Donor characteristics associated with reduced graft survival: An approach to expanding the pool of kidney donors. Transplantation. 2002; 74 (9): 1281-1286.
2. Port FK, Dykstra DM, Merion RM, Wolfe RA. Trends and results for organ donation and transplantation in the United States, 2004. Am J Transplant. 2005; 5 (4 Pt 2): 843-849.
3. Rao PS, Schaubel DE, Guidinger MK, Andreoni KA, Wolfe RA, Merion RM et al. A comprehensive risk quantification score for deceased donor kidneys: the kidney donor risk index. Transplantation. 2009; 88 (2): 231-236.
4. Heaphy EL, Goldfarb DA, Poggio ED, Buccini LD, Flechner SM, Schold JD. The impact of deceased donor kidney risk significantly varies by recipient characteristics. American Journal of Transplantation. 2013; 13 (4): 1001-1011.
5. OPTN KDPI/KDRI Calculator. [Accessed June 20 of 2012] Available in: http://optn.transplant.hrsa.gov/resources/allocationcalculators.asp?index=81.
6. Lee AP, Abramowicz D. Is the Kidney donor risk index a step forward in the assessment of deceased donor kidney quality? Nephrol Dial Transplant. 2014; 30 (8): 1285-1290.




*Mailing address:*
Department of Nephrology
and Mineral Metabolism.
Instituto Nacional de Ciencias Médicas
y Nutrición Salvador Zubirán (INCMNSZ).
Av. Vasco de Quiroga 15, Belisario Domínguez,
Sección XVI, Tlalpan, C.P. 14080, Mexico City.
Phone: +52(55) 5513 5827 y Fax: +52(55) 5655 0382
E-mail: afrascoo@gmail.com