

ORIGINAL ARTICLE

Kidney Donor Profile Index in the Case of Repeated Transplantation

Klinta Gritane*, Janis Jusinkis**, Aleksandrs Malcevs**, Vadims Suhorukovs**, Diana Amerika**, Ieva Ziedina**

* Riga Stradins University, Transplant Research laboratory, Riga, Latvia

**Pauls Stradins Clinical University Hospital, Riga, Latvia

Summary

Introduction. In 2014, new scoring system - Kidney Donor Profile Index (KDPI) was introduced. KDPI is a numerical measure that combines ten donor factors, including clinical parameters and demographics, to summarize into a single number the quality of deceased donor kidneys. There are some publications regarding usefulness of KDPI in the first kidney transplant recipients, however there are no data focusing on repeated transplantation patients.

Aim of the Study. To determine the usefulness of kidney donor profile index as a risk marker of graft failure in repeated transplantation situations.

Material and methods. A single-centre retrospective study was conducted. Patients who underwent a repeated transplantation from deceased donors between 2005. and 2013. were included in the study. Data about donor's risk factors – age, height, weight, race, history of hypertension, history of diabetes, cause of death, serum creatinine, anti-HCV and if donor is after cardiac death – were collected and KDPI was calculated for all participants. Patients were divided into groups according to determined KDPI: Group 1 – KDPI <35%; Group 2 – KDPI 36 – 69%; Group 3 – KDPI >70%. For statistical analysis, IBM Statistical Package for the Social Sciences, version 21.0 was used.

Results. A total of 72 patients were enrolled in the study. There were 17 patients (23.6%) in the 1. group, 38 patients (52.8%) in the 2. group and 17 patients (23.6%) in the 3. group. The most common cause of an end stage renal disease was chronic glomerulonephritis- 59.7% (n=43). Patients with higher KDPI developed acute rejection more often. In the group with KDPI <35% it was observed in 35.3%, while in the groups with KDPI 36 – 69% and KDPI >70% in 60.5% and 64.7% of patients, $p = 0.02$. Graft function differed significantly both, after one ($p = 0.01$) and three years ($p = 0.04$) with the highest eGFR results in the group with the lowest KDPI. The difference in graft survival rates was statistically significant, $p = 0.027$. After three- years it was 88.2% in the first group, 86.8% in the second group and 70.6% in the third group. Patient survival rates showed trend toward significance ($p = 0.076$) with only two patients lost during three- year follow up.

Conclusions. KDPI presents relevance with repeated transplantation outcomes. Lower KDPI indicates better transplantation outcomes – superior graft function and better graft survival. However, there is only trend towards significance in patient survival rates.

Key words: kidney, KDPI, outcomes, transplantation

INTRODUCTION

Kidney transplantation has become the method of choice for treatment of end stage renal disease for eligible patients (6, 8, 12, 16). However, the number of patients waiting for kidney transplantation exceed the number of organs available for this procedure. Since 2002, the number of candidates on the kidney transplant waitlist has nearly doubled from just over 50,000 to more than 96,000 by 2013. (10, 15). This gap has renewed interest in the use of expanded criteria donor (ECD) kidneys in an effort to increase the donor pool (4). In 2014, new scoring system - Kidney Donor Profile Index (KDPI) was introduced. (2) KDPI is a numerical measure that combines ten donor factors, including clinical parameters and demographics, to summarize into a single number the quality of deceased donor kidneys. The KDPI is derived by first calculating the Kidney Donor Risk Index (KDRI) for a deceased donor (1). KDPI allows more gradual evaluation of deceased donor kidneys that ECD definition. Philipse et al. (14) reported that implementing KDRI in their decision-

making practise allowed to increase transplantation rate for 26%.

There are some publications regarding usefulness of KDPI in the first kidney transplant recipients, however there are no data focusing on repeated transplantation patients.

AIM OF THE STUDY

To determine the usefulness of kidney donor profile index as a risk marker of graft failure in repeated transplantation situations.

MATERIAL AND METHODS

Study design and population

A single-centre retrospective study was conducted. We reviewed the medical records of all consecutive repeated kidney transplantations performed between 2005. and 2013. Patients who underwent a repeated transplantation from deceased donors were included in the study. Data about donor's risk factors – age, height, weight, race, history of hypertension, history

of diabetes, cause of death, serum creatinine, anti-HCV and if donor is after cardiac death – were collected and KDPI was calculated for all participants. Patients were divided into groups according to determined KDPI: Group 1 – KDPI <35%; Group 2 – KDPI 36 – 69%; Group 3 – KDPI >70%.

A total of 72 patients were enrolled in the study. There were 17 patients (23.6%) in the 1. group, 38 patients (52.8%) in the 2. group and 17 patients (23.6%) in the 3. group. 55.6% (n=40) of them were female. Mean age of the participants was 42.18 ± 12.55 years. Most of the patients underwent second kidney transplantation 88.9% (n=64), 8.3% (n=6) third and only 2.8% (n=2) underwent third kidney transplantation. The most common cause of an end stage renal disease was chronic glomerulonephritis- 59.7% (n=43).

Data about graft function and patient and graft survival rates after one and three- year follow- up were compared between the study groups.

Immunosuppression regimen

Induction immunosuppression was performed with anti-human T-lymphocyte immunoglobulin (ATG) for the first three to five post-transplant days or basiliximab on the transplantation day and on day four or daclizumab on transplantation day and four times every two weeks (daclizumab was used only until 2008).

All patients received triple maintenance immunosuppressive therapy with a calcineurin inhibitor, mycophenolate mofetil (MMF) and corticosteroids. The initial maintenance immunosuppression consisted of methylprednisolone given intravenously for three days starting from the day of the operation. Beginning from the first post-transplant day, patients received oral prednisone. Calcineurin inhibitors and MMF were commenced on the first post-transplant day. Two calcineurin inhibitors were used: cyclosporine or tacrolimus.

Clinical definitions

Acute rejection was defined as a sudden deterioration in graft function with certain immunopathological changes. All clinically suspected rejection episodes were validated by allograft biopsy. Delayed graft function was defined as a need for at least one dialysis within the first week after transplantation. Graft function was evaluated by estimated glomerular filtration rate (eGFR) through the Modification of Diet in Renal Disease (MDRD) Study Equation. Patient survival time was defined as the time from the last kidney transplantation until death or the end of follow-up. Graft survival time was defined as the time from the last kidney transplantation until permanent return to dialysis, another kidney transplantation, end of follow up or death- censored.

Statistical analysis

For statistical analysis, IBM Statistical Package for the Social Sciences, version 21.0 was used. Descriptive statistics was used for demographical data. Characteristics of patients were described as

mean and standard deviation (SD) or by frequency and percentage. We employed analysis of variance (ANOVA) testing for continuous variables and the Chi-squared test for comparison of categorical variables. Kaplan-Meier analysis was applied for assessing patient and graft survival. A p-value of <0.05 was used to determine significance, p value between 0.05 and 0.1 was considered as trend towards statistical significance.

RESULTS

Acute rejection and delayed graft function:

Patients with higher KDPI developed acute rejection more often. In the group with KDPI <35% (1. group), it developed in 35.3% while in the second (KDPI 36-69%) and third group (KDPI >70%) in 60.5% and in 64.7% of patients. Acute rejection was a significant factor for graft loss, $p = 0.02$.

Rates of delayed graft function did not differ significantly between the study groups, $p = 0.19$.

Graft function:

Mean eGFR after one- and three-year follow-up is presented in Figure 1.

After one year eGFR was 54.35 ± 15.78 ml/min/1.73m² in the group with KDPI <35%, 39.47 ± 11.84 ml/min/1.73m² in the group with KDPI 36-69% and 37.21 ± 17.66 ml/min/1.73m² in the group with KDPI >70%. After three years the results were 47.80 ± 19.56 ml/min/1.73m², 38.0 ± 13.70 ml/min/1.73m² and 32.92 ± 15.16 ml/min/1.73m² respectively. Graft function differed significantly both, after one ($p = 0.01$) and three years ($p = 0.04$). It was inversely proportional to the calculated KDPI – the higher is KDPI the worse becomes graft function after one and three years.

Graft and patient survival:

Graft survival rates are represented in Figure 2. Graft survival rates after one year were 100%, 89.5% and 82.4% respectively in the first, second and third group. After three years graft survival rate had decreased till 88.2% in the first group, 86.8% in the second group and 70.6% in the third group. This difference between groups was statistically significant, $p = 0.027$. Difference can be also observed when comparing mean graft survival time for all the three groups. For the first group, it was 116.94 ± 8.68 months (95% CI 99.93 – 133.95), for the second group 104.10 ± 7.84 months (95% CI 88.74 – 119.46) and significantly less – 73.17 ± 11.36 months (95% CI 50.80 – 95.34) – for the third group with the highest calculated KDPI.

Patient survival rates showed trend toward significance ($p = 0.076$) and are presented in Figure 3. A total of two patients were lost during our three- year follow up. One loss occurred in the group with KDPI 36 – 69% and another in the third group with KDPI more than 70%. Interesting, that both losses occurred during the first four months after repeated transplantation operation. A cause for patient loss was an acute heart failure and Pneumocystis jirovecii pneumonia with sepsis.

DISCUSSION

Influence of KDPI in the case of repeated transplantation has not been studied properly. We believe that repeated kidney transplant recipients should be evaluated separated from the first kidney transplant patients. They are considered as higher risk patients with higher morbidity and mortality rates (17, 9) and it is important to evaluate if KDPI can be used as a "risk marker" for graft loss also in the case of repeated transplantation.

Our findings suggest that KDPI influences the outcomes of repeated kidney transplantation – higher KDPI is associated with worse graft function and lower graft survival rates. However, there is only trend towards significance in patient survival rates. Our data are supported by other authors who suggest that lower KDPI is associated with better transplantation outcomes, still only in the case of the first transplant (5, 7). In their study Gupta et al. (5.) found that KDPI score is a strong predictor of future graft function, but moderate and high KDPI grafts yield similar graft function and survival. Similarly, as repeated transplant recipients, older patients also have longer waiting times on dialysis and have higher mortality rates. Therefore, Jay et al. (7) explored whether older patients gain relative benefits associated with accepting a kidney with a high KDPI opposite to staying on dialysis. Results were as follows: after two- year follow- up patients older than 60 years, accepted a kidney with KDPI more than 85% had significant reduction in mortality compared with those staying on dialysis.

However, not all the studies confirm KDPI as a useful risk predictive tool. Nazarian et al. (11) and Parker et al. (13) proposed that KDPI does not appropriately stratify risk of donor kidney in paediatric population. They wrote that KDPI simplifies too much allocation of the organs for more complex patient populations, for example – children.

Doshi et al. (3) revealed another problem associated with higher KDPI kidneys available worldwide. Despite the fact that kidneys with KDPI of 80% or greater comprise the most resource consuming fraction of donor pool, they still have the highest rates of discard. Their data suggest that some discarded kidneys with KDPI of 80 or greater are viable; however, current tools and biomarkers to identify these viable kidneys are not satisfactory. Therefore, it is necessary to improve methods to assess viability of kidneys with high KDPI. Our study represents only single- centre data and this could lead to some bias while interpreting our results. While knowing that higher KDPI is associated with worse transplant outcomes we should compare survival rates between patients on dialysis and those accepting kidneys with higher KDPI. It would be necessary to find out if the acceptance of the higher KDPI kidneys still provide significant survival benefit over staying on dialysis.

We believe that there should be further work conducted along to this study's lines with the aim to improve the knowledge about this new scoring system which could be very helpful in the future for allocating donor kidneys also in our centre.

CONCLUSIONS

In conclusion, KDPI presents relevance with repeated transplantation outcomes. Lower KDPI indicates better transplantation outcomes – superior graft function and better graft survival. However, there is only trend towards significance in patient survival rates. KDPI could be used as a parameter to predict the risk of kidney graft failure in repeated transplantation recipients.

Conflict of interest: None

REFERENCES

1. A Guide to Calculating and Interpreting the Kidney Donor Profile Index (KDPI). Available: https://optn.transplant.hrsa.gov/media/1512/guide_to_calculating_interpreting_kdpi.pdf
2. Darren E, Stewart DK, Klassen. Early Experience with the New Kidney Allocation System: A Perspective from UNOS // Clin. J. Am. Soc. Nephrol, 2017; 12: 2063-2065
3. Doshi MD, Reese PP, Hall IE et al. Utility of Applying Quality Assessment Tools for Kidneys With KDPI ≥ 80 // Transplant, 2017; 101(6): 1125-1133
4. Filiopoulos V, Boletis JN. Renal transplantation with expanded criteria donors: Which is the optimal immunosuppression? // World J Transplant, 2016; 6(1):103-114
5. Gupta A, Francos G, Frank AM et al. KDPI score is a strong predictor of future graft function: moderate KDPI (35-85) and high KDPI (>85) grafts yield similar graft function and survival // Clin Nephrol, 2016; 86(10):175-182
6. Hricik D. E., Halbert R. J., Barr M. L., et al. Life satisfaction in renal transplant recipients: preliminary results from the transplant learning center // Am J Kidney Dis, 2001; 38(3):580-587
7. Jay CL, Washburn K, Dean PG Survival Benefit in Older Patients Associated With Earlier Transplant With High KDPI Kidneys // Transplantation, 2017; 101(4):867-872
8. Kaplan B., Meier-Kriesche H.-U. Death after graft loss: an important late study endpoint in kidney transplantation // Am J Transplant, 2002; 2(10):970-974
9. Marinaki S., Skalioti C., Boletis J. Patients after kidney allograft failure: immunologic and nonimmunologic considerations // Transplant Proc, 2015; 47(9):2677-82
10. Matas AJ, Smith JM, Skeans MA, et al. OPTN/SRTR 2013 annual data report: kidney // Am J Transplant. 2015; 15:1-34
11. Nazarian SM, Peng AW, Duggirala B, et al. The kidney allocation system does not appropriately stratify risk of pediatric donor kidneys: Implications for pediatric recipients // Am J Transplant, 2018; 18(3): 574-579
12. Oniscu G. C., Brown H., Forsythe J. L. R. Impact of cadaveric renal transplantation on survival in patients listed for transplantation // Journal of the Am Soc Nephrol, 2005; 16(6):1859-1865

13. Parker WF, Thistlethwaite JR, Ross LF. Kidney Donor Profile Index (KDPI) Does Not Accurately Predict the Graft Survival of Pediatric Deceased Donor Kidneys //Transplant, 2016; 100 (11): 2471-2478
14. Philipse E, Alison PK, Bracke LB, et al. Does Kidney Donor Risk Index implementation lead to the transplantation of more and higher-quality donor kidneys? //Nephrol Dial Transplant, 2017; 32 (11): 1934-1938
15. Rege A, Irish B, Castleberry A, et al. Trends in Usage and Outcomes for Expanded Criteria Donor Kidney Transplantation in the United States Characterized by Kidney Donor Profile Index // Cureus, 2016;8(11):e887
16. Sayin B, Colak T, Tural E, Sezer S, Comparison of preemptive kidney transplant recipients with nonpreemptive kidney recipients in single center: 5 years of follow- up //Int J Nephrol Renovasc Dis, 2013; 6:95-99
17. Szabo R. P, Klenk N, Balla J, et al. Prognosis of dialysed patients after kidney transplant failure // Kidney & Blood pressure Research, 2013; 37: 151-157

Address:

Ieva Ziedina
Pauls Stradins Clinical University Hospital,
13 Pilsonu street, Riga, LV-1002, Latvia
E-mail: ieva.ziedina@stradini.lv

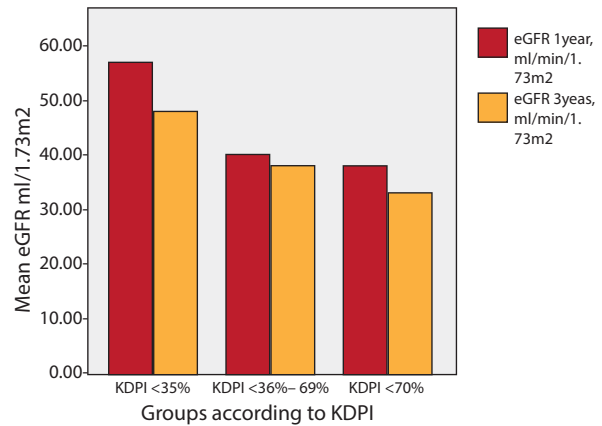


Fig. 1. Graft function

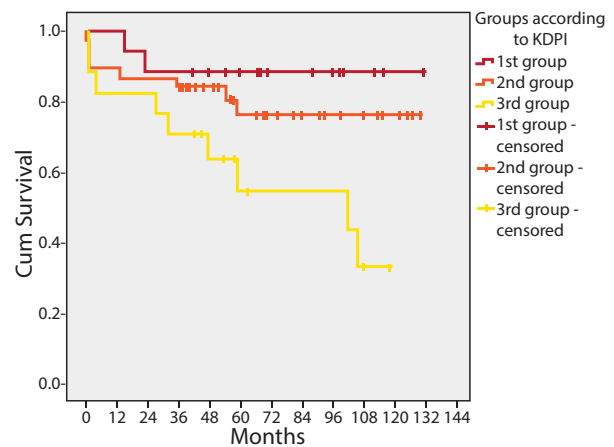


Fig. 2. Graft survival

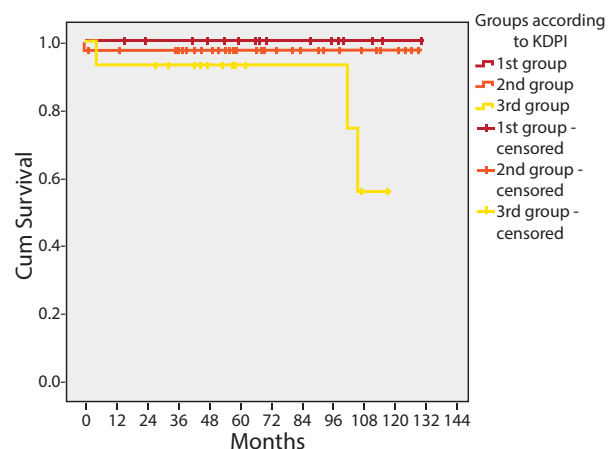


Fig. 2. Patient survival