The impact of kidney weight to recipient weight ratio (Kw/Rw) on kidney graft function after transplantation

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CONFLICT OF INTERESTS
no conflicts of interest

ABBREVIATIONS
Kw/Rw-kidney weight to recipient weight, eGFR-estimated glomerular filtration rate, DGF- delayed graft function, AR-acute rejection, BMI-body mass index, ICU-intensive care unit, ECD-expanded criteria donors, HLA-human leukocyte antigen, CIT-cold ischemia time, KTx-kidney transplantation, CsA-cyclosporin A, BSA-body surface area.

ABSTRACT
Background: Kidney transplantation is the best method of renal replacement therapy. Recent studies assess the suitability of kidney selection for a recipient based on kidney weight to the recipient weight ratio (Kw/Rw). Low ratio can indicate insufficient nephron mass for the recipient. The aim of this study was to calculate Kw/Rw ratio useful to evaluate kidney function until one year post surgery. Materials and Methods: In the years 2010 – 2011 at the Department of General and Transplantation Surgery in Warsaw 262 kidney transplantations were performed. We retrospectively analyzed a group of 103 patients who underwent the transplant procedure from a deceased donor. Collected data considered delayed graft function, acute rejection episodes, creatinine, recipient survival and one year graft survival. Kw/Rw ratio was calculated for all of them. Recipients were divided into two groups: group low-ratio (n=36; Kw/Rw ratio<4,29 g/kg), group high-ratio (n=67; Kw/Rw ratio...
 Progressive kidney failure leads to end-stage renal disease (ESRD). The number of patients suffering from ESRD is increasing worldwide reaching almost 600 million. In Poland, 4 million people suffer from various stages of renal failure [1]. The best renal replacement therapy (RRT), resulting in lower morbidity and mortality rates and improved quality of life for patients with ESRD is kidney transplantation (KT). Moreover, renal transplantation therapy (RTT) is a more cost-effective therapy in comparison to hemodialysis or peritoneal dialysis for patients with chronic kidney disease [2,3]. In 2011, according to Poltransplant’s statistics, there were 2623 people on the National Waiting List for Kidney Transplantation; transplantation was performed in 1074 patients, 998 of whom received a kidney from a deceased donor[4]. Worldwide, there are still not enough donors as compared to the number of recipients. Kidney retrieval from Expanded Criteria Donors [5] or living donors [6] is a possible route to overcome this organ shortage. On the other hand, better graft matching to the recipient is an important aim of contemporary transplantation. The aim is to prolong organ survival time and satisfactory kidney function. Graft function and its survival depends on many immune and non-immune factors. Recent studies, based on kidney weight and recipient weight ratio (Kw/Rw), have assessed the suitability of kidney-recipient matching. This ratio in an adult healthy person has a value of 7g/kg. Low Kw/Rw ratio can indicate insufficient nephron mass for recipient weight, which may lead to hyperfiltration, hypertension and proteinuria [7, 8, 9]. As a result, glomerulosclerosis can develop and the risk of graft rejection is increased [7,8,9]. The aim of the study was to assess, how the ratio kidney/recipient and transplanted nephron mass affect one year graft survival.

MATERIAL AND METHODS

Between January 2010 and December 2011, 262 kidney transplantations were performed in our center. Kidneys were procured from living related donors – LRD (22/262; 8.4%) and deceased donors – DD (240/262; 91.6%). Two hundred twenty DD kidneys were kept in LifePort (Organ Recovery, Itasca, IL, USA) or MOX-100 (Waters Instruments, Rochester, MN, USA) machine perfusion prior to transplantation. The remaining 20 DD kidneys were kept in cold storage.

Demographic, clinical, and laboratory parameters of donors (age, sex, BMI, number of days on ICU, cardiac arrest, hypertension, number of ECD, creatinine level, cause of death) kidney grafts (CIT, weight, preservation methods) and recipients (weight, age, sex, dialysis before transplantation-time and method, HLA matching, immunosuppression) were recorded. Patients were assessed in terms of delayed graft function and acute rejection episodes, creatinine level on 7th, 28th, 180th, 360th day after KTx, eGFR, proteinuria, also hospitalization time and recipient and kidney survival, until one year after transplantation. Data were collected retrospectively. Kidney weight prior to transplantation and recipient’s weight were obtained for 103 kidneys and recipients.

Kw/Rw Ratio
For every recipient Kw/Rw ratio was calculated ([kidney weight (g)/recipient weight (kg)]). Recipients were retrospectively divided into two groups: group low-ratio (n=36; ratio<4.29 g/kg) and group high-ratio (n=67; ratio >4.29 g/kg).

Expanded Criteria Donor was defined according to the Organ Procurement and Transplantation Network (OPTN) / United Network for Organ Sharing (UNOS) definition. Donors aged 60 years old or older, or 50 years old or older with at least two out of three following conditions: history of arterial hypertension, serum creatinine levels >1.5 mg/dL, cause of death from a cerebrovascular incident were considered ECD. All others donors were SCD. Delayed graft function (DGF) was recognized as a need for dialysis in the short term (7 days) following kidney transplantation regardless of reason (hyperkalemia, high serum urea concentration, hyperhydration). Primary Non-Function (PNF) was defined as permanent loss of graft function immediately after transplantation. Acute rejection (AR) was biopsy proven and diagnosed according to Banff 2009 criteria. Cold Ischemia Time (CIT) was recorded as the period between in situ perfusion and vascular anastomosis.

Immunosupression treatment

Triple drug immunosuppression is standard therapy in our center. Cyclosporine or tacrolimus, mycophenolate mofetil, and steroids were the primary immunosuppressive agents. All recipients were administrated 500 mg of intravenous steroids just before restoration of blood flow to the allograft, and intake of steroid was maintained at a dose of 20 mg per day gradually decreasing to 5 mg at 3 weeks following KTx. Cyclosporine or tacrolimus therapy was also started immediately just before surgery.
with dosage subsequently adjusted to maintain a trough concentration of 200–300 nanograms (ng) per mL or 10–12 ng per mL, respectively. Induction immunosuppression (basiliximab or thymoglobulin) was administered in cases of second transplantation, panel reactive antibodies (PRA) above 20%, 4 or more mismatches.

**Kidney storage and preparation**

All kidneys in the study groups (n=103) were kept in LifePort (Organ Recovery, Itasca, IL, USA) or MOX-100 (Waters Instruments, Rochester, MN, USA) machine perfusion prior to transplantation. Following pre-operative bench surgery, all kidneys were weighed on an electronic scale.

**Statistical Analysis**

Short and long-term outcomes of transplantation were compared using Student t-test (statistically significant p<0.05). Creatinine values were represented by linear regression. Continuous variables were expressed by the mean value and standard deviation. The correlation between the kidney and donor weight was verified by the Pearson’s correlation coefficient.

**RESULTS**

**Kw/Rw Ratio**

Mean Kw/Rw Ratio in low-ratio group was 3.5 g/kg vs. 6.06 g/kg in high-ratio group (p<0.00001). Recipients’ characteristics of both groups are presented in table 1. The recipient with low-ratio group had mean weight about 77 kg, compared to mean 67 kg of body weight in high-ratio group (p=0.0062). In the low-ratio group there were more male patients (78%) as compared to the high-ratio group in which the male patients were 58%(p=0.04). Kidney mass in the low-ratio group was about 266.4 g compared to 398.7 g in the high-ratio group: 398.7 g (p<0.001). There were no differences in HLA matching, immunosuppression treatment, duration and type of RRT prior to transplantation (tab.1).

**Donors’ characteristics**

The most common cause of donor’s death was cerebrovascular accident (53% donors). Characteristics of donors in both groups are presented in table 2. Except BMI, there were no differences in donors’ data between the groups.

**Post-transplant results**

Mean surgery time did not differ between the groups and was 170±48 min vs. 178±48 min in high-ratio and low-ratio groups, respectively (p=0.4). Mean Cold Ischemia Time was 29,2±6,5 h vs.27,5±6,9 h in high-ratio and low-ratio groups (p=0.24). Delayed Graft Function occured more often in low-ratio group (Fig.1). Mean serum creatinine concentration was significantly lower for high-ratio group during almost the whole first year following transplantation (Fig.2), although one year graft survival was similar in both groups: 98% vs 97% in high-ratio and low-ratio respectively (p=0.68). One-year patients’ survival was identical in both groups and was 100% vs 100% in high-ratio and low-ratio group respectively. Interestingly, acute rejection rate within the first year was higher in the low-ratio group – 30% (11/36) vs. 15% (10/67) in the high-ratio group (p=0.075), although it did not reach a significant value.

**DISCUSSION**

Numerous authors have found an impact of Kw/Rw ratio on early and late graft outcomes (creatinine, DGF, AR and proteinuria). [10 – 20]. In our analysis we have found a significant impact of Kw/Rw ratio on creatinine level up to one year and DGF. AR episodes were more frequent in the group of patients with low-ratio although this did not reach statistical value. Nevertheless it did not have an influence on one-year graft and patients’ survival. In our study, donor’s and recipient’s BMI significantly differed between the groups. In view of this data it can be noticed that in the group with low-ratio a small kidney, from small donor was received by heavier and taller recipient, whereas in the high-ratio group, larger kidney from heavier donor, went to a smaller recipient. Patients who received smaller kidneys and had an inadequate number of nephrons, also had a higher incidence of DGF and higher level of creatinine up to one year. The risk of hyperfiltration development is high in such patients. It may bring hypertension (although not observed in our patients). Nevertheless it may potentially influence patient and graft survival [21]. Luycx and Brenner found a strong correlation between congenital deficit in nephron number and hypertension and kidney diseases in adults [22]. Hyperfiltration may result in glomerulosclerosis and in further insufficiency of transplanted organ. Generally, most of the publications have found association between low Kw/Rw ratio and long-term kidney function - kidney parenchyma deficiency results in slow graft damage (hyperfiltration->inflammation->glomerulosclerosis) [13,19,23].

As mentioned above, Kw/Rw ratio in a healthy adult person is 7g/kg approximately. Values of the ratio appearing in the literature ranged from about 2,3 g/kg to 4,5 g/kg[13, 18]. In our study, the limit value was 4,29 g/kg. Mean ratio in a group of patients with better functioning grafts was 6,06 g/kg and mean ratio in a group with worse functioning grafts was 3,5 g/kg.

With reference to the conclusion based on better functioning of larger kidney in the recipient, there are also studies denying this relationship. After receiving large kidneys, small patients needed time to adapt the blood flow to the size of the kidney, that may
result in worse graft functioning and, eventually, rejection [24]. Similar results were obtained in the study on kidney transplantation from adults to children. The large kidney transplanted into the small recipient was associated with graft ischemic injury [25]. Such results could be associated with a large disparity between the kidney size and the recipient weight. It should also be mentioned that there are studies with no evidence proving that the size of the graft influences the outcome of kidney transplantation. In another study on kidney transplantation from adult to children, it was shown that much larger kidneys can be successfully transplanted into children. The results of these transplantations were comparable to those where the donor had been selected by size to the recipient [26].

In our study, Kw/Rw ratio impacts graft function, with no effect on graft and patient survival up to one year post transplantation. It is an independent predictor of renal function, therefore may be considered an additional differentiating factor in donor-recipient matching. The most reliable surrogate for nephron mass is kidney weight [19, 27]. However, weighing kidneys is not very useful in practice due to the fact that it is performed during the transplantation. That is the reason why using the kidney size as a one of matching parameters is inconvenient. Therefore, the other surrogates for the number of nephrons, such as Body Surface Area, BMI, renal volume [17, 28, 29], assessment of renal size by ultrasound [14, 30] should be taken under consideration. These methods are much more useful in practice because of the possibility of using the obtained data for donor-recipient matching.

Discrepancies in study results, showing the influence of Kw/Rw ratio on graft function, should stimulate studies of larger populations. Such differences occur probably due to the insufficient number of examined patients and the variety of groups, also due to the usage of various nephron mass surrogates. Taking kidney’s size in kidney-recipient matching into consideration can be the next step to improve results in kidney transplantation.

CONCLUSIONS

Patients who have received insufficient nephron mass at transplantation are more likely to experience delayed graft function, acute rejection and worse kidney function. Kidney mass is an important non-immunological determinant of renal transplant function.

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TABLE 1. RECIPIENT FACTORS RELATED TO KW/RW RATIO

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<thead>
<tr>
<th>Recipient factors</th>
<th>Low-ratio (n=36)</th>
<th>High-ratio (n=67)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>51 ± 13.74</td>
<td>48 ± 14.07</td>
<td>0.23</td>
</tr>
<tr>
<td>% male</td>
<td>77.8%</td>
<td>58.2%</td>
<td>0.038</td>
</tr>
<tr>
<td>BMI (kg/m2)</td>
<td>25.56 ± 3.39</td>
<td>23.78 ± 3.67</td>
<td>0.01</td>
</tr>
<tr>
<td>Time on dialysis prior to KT (months)</td>
<td>40 ± 28</td>
<td>47.4 ± 42</td>
<td>0.29</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>80%</td>
<td>90%</td>
<td>0.3</td>
</tr>
<tr>
<td>HLA mismatch</td>
<td>3.66 ± 1.12</td>
<td>3.41 ± 1.01</td>
<td>0.27</td>
</tr>
<tr>
<td>Ischemic heart disease (%)</td>
<td>11.1%</td>
<td>10.4%</td>
<td>0.91</td>
</tr>
<tr>
<td>Induction therapy (%)</td>
<td>25%</td>
<td>26.8</td>
<td>0.83</td>
</tr>
<tr>
<td>Triple-drug immunosuppression</td>
<td>100%</td>
<td>100%</td>
<td>1.0</td>
</tr>
</tbody>
</table>

TABLE 2. DECEASED DONORS’ ANALYSIS

<table>
<thead>
<tr>
<th>Deceased donor factors</th>
<th>Low-ratio (n=36)</th>
<th>High-ratio (n=67)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>44.4 ± 17.9</td>
<td>45.9 ± 14.1</td>
<td>0.67</td>
</tr>
<tr>
<td>% ECDs</td>
<td>30.5%</td>
<td>28.3%</td>
<td>0.81</td>
</tr>
<tr>
<td>ICU stay (days)</td>
<td>5.08 ± 3.2</td>
<td>4.7 ± 2.57</td>
<td>0.17</td>
</tr>
<tr>
<td>Creatinine level (mg/dl)</td>
<td>1.56 ± 1.16</td>
<td>1.98 ± 1.63</td>
<td>0.13</td>
</tr>
<tr>
<td>% Hypertension</td>
<td>17%</td>
<td>28%</td>
<td>0.19</td>
</tr>
<tr>
<td>Mean BMI (kg/m2)</td>
<td>23.8 ± 2.91</td>
<td>25.6 ± 4.1</td>
<td>0.01</td>
</tr>
</tbody>
</table>

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Fig. 1. Incidence of DGF between the groups
Fig. 2. Mean creatinine concentration

FIGURE 1. INCIDENCE OF DGF BETWEEN THE GROUPS
FIGURE 2. MEAN CREATININE CONCENTRATION

BIBLIOGRAPHY


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