Pretransplant Biopsy in Expanded Criteria Donors: Do We Really Need It?

E. Tavares da Silva¹⁺, R. Oliveira⁵, D. Castelo⁴, V. Marques⁴, V. Sousa⁴, P. Moreira⁵, P. Simões⁴, C.A. Bastos⁶, A. Figueiredo⁶, and A. Mota⁵

¹Urology and Renal Transplantation Department, and ⁵Pathology Department, Coimbra’s Hospital and University Center, Coimbra, Portugal

ABSTRACT

Introduction. Renal transplantation is the best treatment for end-stage renal disease, including when using expanded criteria donors (ECD) kidneys. However, these suboptimal kidneys should be evaluated rigorously to meet their usefulness. Opinions differ about the best way to evaluate them.

Materials and Methods. We retrospectively reviewed kidneys from ECD harvested by a single academic institution between January 2008 and September 2013. Needle biopsies were performed at the time of the harvest when considered relevant by the transplant team. Two pathologists where responsible for their analysis; the Remuzzi classification has been used in all cases.

Results. We evaluated 560 ECD kidneys. Biopsies were made in 197 (35.2%) organs, 20 of which were considered not usable and 36 good only for double transplantation. Sixty-three kidneys (11.3%) were discarded by the transplant team based on the biopsy result and clinical criteria. Donors who underwent a biopsy were older (P < .001) and had a worse glomerular filtration rate (GFR; P = .001). Comparing donors approved and rejected by the biopsy, the rejected donors were heavier (P = .003) and had a lower GFR (P = .002). Cold ischemia time was longer for the biopsy group (P < .001). Regarding graft function, the biopsy overall score correlated with the transplant outcome in the short and long term. Separately, glomeruli and interstitium scores were correlated with recipient’s GFR in the earlier periods (3 months; P = .025 and .037), and the arteries and tubules correlated with GFR in the longer term (at 3 years P = .004 and .010).

Conclusion. The decision on the usability of ECD grafts is complex. At our center, we chose a mixed approach based on donor risk. Low-risk ECD do not require biopsy. In more complex situations, especially older donors or those with a lower GFR, prompted a pretransplant biopsy. The biopsy results proved to be useful as they relate to subsequent transplant outcomes, thereby allowing us to exclude grafts whose function would most probably be less than optimal.
double transplants to maximize nephron mass [3]. Some
groups decide allocation based on peer age [4]; others use
perfusion machines parameters [5], others prefer donor
scores based on clinical data, and still others use histologic
criteria. Even among histologic evaluation supporters there
are some differences, namely, classification used [6–9],
relative importance of a histologic parameter over another
[7,8,10,11], sampling technique [12–15], or sample pro-
cessing [16,17].

This work aims to help in the decision-making process,
based on the analysis of the experience of a single academic
institution, which is the largest Portuguese transplant center.

MATERIALS AND METHODS
We conducted a review of all kidneys harvested at our institution
between January 2008 and September 2013, and selected those
obtained from ECD. We have an on-call transplant team composed
of a senior urologist and a nephrologist. The team, based on clinical
and macroscopic criteria, makes the decision on the kidneys ade-
quacy or the need for a biopsy. When a biopsy is requested, it is
executed using a “Tru-cut” 18-G needle at the time of the harvest,
before clamping. Data from donors including weight, height, serum
creatinine, blood nitrogen urea, proteinuria, age, cause of death,
ventilation time, perfusion liquid, and kidney macroscopic main
features being similar (Table 1). Comparing donors approved and rejected by the biopsy, the latter were heavier
(P = .003) and had a lower GFR (P = .002; Table 2).

There were 467 single transplants and 15 double trans-
plants (Fig 1). When comparing single kidney transplants
recipients from donors who underwent a biopsy with donors
who did not undergo a biopsy, the former group of recip-
ients were older (P < .001)—like the biopsied donors—
and had been under dialysis treatment for a shorter period
(P = .004). The cold ischemia time was longer for the biopsy
group (P < .001). There were no differences regarding
incidence of early, delayed, or absent graft function (P = .839), acute rejection episodes (P = .469), or survival rates
(P = .168) between the biopsied and not biopsied groups
(Table 1; Fig 2).

A subanalysis of all biopsied grafts evaluated the value of
biopsy results and donor’s GFR/age in predicting transplant
functional outcome (Table 3). None of the factors analyzed
was related to graft survival. Concerning graft function,
through 3 years of follow-up, there is no correlation be-

tween donor’s GFR/age and recipient GFR in the different
time frames, but the biopsy overall score was correlated with
both short-term (3 and 6 months; P = .005 and .004) and
long-term (2 and 3 years; P = .015 and .010) transplant
outcomes. Separately, glomeruli and interstitium scores
were correlated with recipient GFR in the earlier periods
(at 3 months P = .025 and .037), whereas the arteries and
tubules scores correlated with GFR in the long term (P = .004
and .010 at 3 years).

DISCUSSION
Kidney transplantation is the best treatment option for end-
stage renal disease patients. Compared with hemodialysis, it
increases overall survival, even in older patients receiving

kidneys from marginal donors [1]. However, there is a lack of
consensus regarding the best way to evaluate the usability of
these suboptimal kidneys. Some European groups rarely
perform biopsies, allocating organs based on age pairing [18].
They assume that grafts from older donors are associated with
worse function and graft and patient survival, even in younger
recipients. Their allocation method maximizes the pairing of
young donors and recipients, which in their experience, gain-
ing 2 years with a functioning graft [18]. Performance of bi-
opsies potentially increases the cold ischemia time [17,19]. At
our center, we also apply age matching, but not so restricted as
others, and age itself is just one among many criteria taken
into account during the allocation process.

An increasing number of groups use perfusion machine
parameters [5,20]. Patel et al [5] compared the results of

Biopsies were taken from 197 organs (35.2%); 20 were
not usable and 36 were usable for double transplantation
(Fig 1). Sixty-three kidneys (11.5%) were discarded by the
transplant team based on the biopsy result and/or clinical
criteria. Comparing donors who underwent a biopsy or not,
we find that the those who required a biopsy for evaluation
were older (P < .001) and had worse GFR (P = .001), other
features being similar (Table 1). Comparing donors
approved and rejected by the biopsy, the latter were heavier
(P = .003) and had a lower GFR (P = .002; Table 2).

There were 467 single transplants and 15 double trans-
plants (Fig 1). When comparing single kidney transplants
recipients from donors who underwent a biopsy with donors
who did not undergo a biopsy, the former group of recip-
ients were older (P < .001)—like the biopsied donors—
and had been under dialysis treatment for a shorter period
(P = .004). The cold ischemia time was longer for the biopsy
group (P < .001). There were no differences regarding
incidence of early, delayed, or absent graft function (P = .839), acute rejection episodes (P = .469), or survival rates
(P = .168) between the biopsied and not biopsied groups
(Table 1; Fig 2).

A subanalysis of all biopsied grafts evaluated the value of
biopsy results and donor’s GFR/age in predicting transplant
functional outcome (Table 3). None of the factors analyzed
was related to graft survival. Concerning graft function,
through 3 years of follow-up, there is no correlation be-

tween donor’s GFR/age and recipient GFR in the different
time frames, but the biopsy overall score was correlated with
both short-term (3 and 6 months; P = .005 and .004) and
long-term (2 and 3 years; P = .015 and .010) transplant
outcomes. Separately, glomeruli and interstitium scores
were correlated with recipient GFR in the earlier periods
(at 3 months P = .025 and .037), whereas the arteries and
tubules scores correlated with GFR in the long term (P = .004
and .010 at 3 years).

DISCUSSION
Kidney transplantation is the best treatment option for end-
stage renal disease patients. Compared with hemodialysis, it
increases overall survival, even in older patients receiving

kidneys from marginal donors [1]. However, there is a lack of
consensus regarding the best way to evaluate the usability of
these suboptimal kidneys. Some European groups rarely
perform biopsies, allocating organs based on age pairing [18].
They assume that grafts from older donors are associated with
worse function and graft and patient survival, even in younger
recipients. Their allocation method maximizes the pairing of
young donors and recipients, which in their experience, gain-
ing 2 years with a functioning graft [18]. Performance of bi-
opsies potentially increases the cold ischemia time [17,19]. At
our center, we also apply age matching, but not so restricted as
others, and age itself is just one among many criteria taken
into account during the allocation process.

An increasing number of groups use perfusion machine
parameters [5,20]. Patel et al [5] compared the results of
biopsies with the flow parameters of the machines and found that kidneys with abnormal biopsies commonly had lower flows and higher resistances. However, kidneys with altered biopsies and normal flows had good results if implanted. Based on their findings, they strongly advised to review the slides or to sample again in case of normal biopsies and altered flows [5]. At our center, we hope to restart at short-term organ preservation using this type of equipment.

The vast majority of groups decide allocation by either donor risk assessment or preimplantation biopsies. Nyberg et al [21] developed a decision process based on donor variables, namely, age, history of hypertension, creatinine clearance, HLA mismatch, and cause of death, which are obtained at harvest, and showed good correlation with creatinine clearance at 12 months and graft survival at 6 years [21]. The validity of this score was confirmed years later by Messina et al, but the allocation system used at his institution includes other variables, like ours [19]. Other groups base their decision solely on the donor GFR. Snanoudj et al [10] allocated kidneys donors >65 years with a GFR of >60 mL/min to a single graft transplant, those with a GFR between 30 and 60 mL/min to a double kidney transplant, and those with a GFR of <30 mL/min were discarded. In their work, histologic evaluation did not exhibit a better performance and results were comparatively better than in the European Senior Transplant Program [10]. In our institution, the decision on ECD grafts usability is based on a mixed system. In most cases, the decision is based on donor age, GFR, cause of death, comorbidities, and kidney macroscopic appearance. In older donors and those with a low GFR, biopsy is a complementary tool.

The relation between GFR with biopsy seems not to be as clear cut as expected [22–24]. Ibernion et al [22] found that histologic and functional parameters are associated with the donor graft function after 3 months. However, Cicora et al [23] compared a donor score with histology and found that only clinical data were related with graft function. Inversely, Snoeij et al [24] conducted a similar comparison and found

![Fig 1. Organs biopsied, biopsy results, and transplantations undertaken. ECD, expanded criteria donor.](image-url)

### Table 1. Biopsied and Not Biopsied Donors, Recipients, and Transplant Characteristics From Expanded Criteria Donors

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Biopsied</th>
<th>Not Biopsied</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Donor</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (y)</td>
<td>69.1</td>
<td>59.5</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>74.9</td>
<td>74.7</td>
<td>.820</td>
</tr>
<tr>
<td>Last hour diuresis (mL)</td>
<td>147.5</td>
<td>152.1</td>
<td>.601</td>
</tr>
<tr>
<td>Ventilation time (h)</td>
<td>46.9</td>
<td>52.8</td>
<td>.241</td>
</tr>
<tr>
<td>GFR (mL/min)</td>
<td>77.0</td>
<td>85.9</td>
<td>.001</td>
</tr>
<tr>
<td><strong>Recipient</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>59.8</td>
<td>53.1</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Weight</td>
<td>71.1</td>
<td>69.3</td>
<td>.205</td>
</tr>
<tr>
<td>Time on dialysis (mo)</td>
<td>50.7</td>
<td>60.0</td>
<td>.004</td>
</tr>
<tr>
<td>GFR at first month (mL/min)</td>
<td>25.2</td>
<td>50.4</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><strong>Transplant</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cold ischemia time (time)</td>
<td>19:25</td>
<td>17:21</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Graft function</td>
<td></td>
<td></td>
<td>.839</td>
</tr>
<tr>
<td>Early</td>
<td>22.2</td>
<td>24.2</td>
<td></td>
</tr>
<tr>
<td>Delayed</td>
<td>73.1</td>
<td>72.1</td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>4.6</td>
<td>3.7</td>
<td></td>
</tr>
<tr>
<td>Acute rejection episode</td>
<td>5.1%</td>
<td>6.8%</td>
<td>.469</td>
</tr>
<tr>
<td>Survival (mo)</td>
<td>38.7</td>
<td>46.2</td>
<td>.168</td>
</tr>
</tbody>
</table>

Abbreviation: GFR, glomerular filtration rate.
that histologic data were the only ones able to predict renal graft function. Our results are similar to those of Snoeij et al. When considering all transplants performed from the biopsied kidneys subpopulation, clinical data (donor age and GFR) were not shown to correlate with transplant outcome, whereas biopsy results—overall and partial scores—correlated with renal function in the short and medium term.

The pretransplant biopsy is the most extensively studied decision maker. The best known classifications are from Remuzzi et al. [25] and the Banff criteria [26], but there are others like Maryland Aggregate Pathology Index (MAPI) [7] and Chronic Allograft Damage Index (CADI) [27,28]. Still others are mixed clinical and histologic classifications such as the one proposed by Anglicheau et al [29]. However, there remain uncertainties about the best way to sample, process, and evaluate these biopsies. Studies comparing wedge with needle biopsies found that wedge biopsies produce better results compared with needle biopsies [12]. There are few studies assessing the ability of biopsies to reproduce the actual kidney condition. The comparison of the biopsy score with histologic evaluation of discarded kidneys seem to show that needle biopsies produce better results compared with wedge samples [15]. Agreement between pathologists is high and improves with increasing sample, achieving reasonable accuracy from 7 glomeruli up [14]. Processing can be done by formaldehyde fixation and paraffin embedding or frozen sectioning [17]. Frozen sections are faster, but histologic evaluation quality is significantly worse. In our center, we perform needle biopsies and the samples are processed by inclusion in paraffin and evaluated by Remuzzi classification.

There remains controversy about which structural parameter relates better with kidney function [17]. Some groups found no relation between the percentage of glomerulosclerosis and renal function [31], although the majority consider it a very important parameter and discard kidneys with glomerulosclerosis of >20% [11,28] or even at lower values [7,8]. The same happens with the other histologic compartments. Although some authors do not find any relationship of tubules, interstitium, and arteries with graft function [7,10,29], others do [8,11,28,31]. In our series, the overall biopsy score correlated with transplant outcome at all time points. Separately, glomeruli and interstitium scores correlated with recipient GFR in the short term, and arteries and tubules correlated with GFR in the long term. This is consistent with the latest results showing that the vascular component is most strongly associated with future renal function [32].

In conclusion, the decision on the usability of ECD grafts is complex. At our center, we chose a mixed approach based on donor risk. Low-risk ECD do not require biopsy. More complex situations, especially older donors or those with a lower GFR, led us to perform a pretransplant biopsy, which is useful because it relates to posttransplant results, allowing us to exclude grafts whose function would clearly be compromised.

**REFERENCES**

[1] Ojo AO, Hanson JA, Meier-Kriesche H, et al. Survival in recipients of marginal cadaveric donor kidneys compared with other...