Kidney Donor Profile in Spain: Risks Factors and Characteristics of the Organs Rejected for Transplantation

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Abstract:
During recent years organ donation in Spain has increased by 100%, with important changes seen in the donor profile. Mean age has increased by more than 10 years, being nowadays more than 33% of our donors over 60 years. Ten years ago road traffic trauma was the main cause of death, while now most of our donors die due to stroke and only 21% die in a traffic accident. This changes lead to an increase in the number of kidneys discarded for transplantation every year. Among the 2517 kidneys retrieved during 2001, 567 were discarded, mainly due to different glomerular, interstitial or vascular pathologic damage. The older is the donor the higher is the percentage of kidneys discarded. It has to be underlined that an increased number of livers from donors, whose kidneys could not be used, are being grafted (141 in 2001 over 281 donors from whom no kidney could be grafted and over a total number of 1335 donors). Only 5% of kidneys were discarded due to technical problems.

An important number of kidneys were discarded due to malignancy suspicion or diagnosis (12.3%). Organ donation has improved but kidney transplantation did not in parallel, due to the increasing number of kidneys discarded for transplantation in close relation with the evolution of donor’s characteristics. Organ donation rate is around 33 donors per million population while efficient organ donation rate is around 30 donors per million. Only from 67% of donors both kidneys can be grafted and from 20% of donors no kidney can be used. These data will not change our policy, at least by the moment, we will continue to evaluate every potential brain death donor with the aim of studying if organs can be used. It is true that in 50% of cases over 70 years no organ can be used after retrieval and microscopic exam, but in the other 50% we can proceed.

Key words: ?????????????????????????????????????????????????????????????????????????????????????

Introduction
Kidney Transplant is nowadays considered as one of the replacement therapy for patients with renal failure. In our country nearly 30,000 than 27000 patients have been transplanted from the beginning of this technique in 1965 (fig. 1). Actually it’s calculated that there are more than 33000 patients with an end stage renal failure, 40% of them having a functioning kidney transplant. Each year, between 4600 and 4800 new cases are diagnosed; this implies an annual rate of incidence about 120 new patients per million in., very similar to the rate reported by other countries [1]. Half of these patients are under of 65 years old and approximately between 40 and 45% of the new patients would have indication of transplant as therapeutic type. That means that a rate of 50 kidney transplants per million people would stabilised the

Figure 1. Kidney Transplant.
balance between the annual needs and the transplant procedures.

In our country the rate of cadaver kidney transplant raised during the last years up to an average of 50 pmp. So, the patients in waiting list decreased during the early nineties till keeping stabilised, and recently showing a swift trend to increase (fig. 2).

It can be said that the Spanish donation and transplantation rate has been enough to cover the demand during some years but not exactly now. Moreover, the historic accumulate of patients in kidney waiting list makes that this global figure of waiting list doesn’t decrease below 4000 patients.

These data, although don’t satisfy us complete, however place Spain in a privilege situation in relation to others countries. In USA, for example, the kidney waiting list had recorded less than 18,000 patients during 1990; while ten years later are more than 50,000, the patients included. The kidney transplants have increased in USA, especially for the living transplant activity, but less than the waiting list. [2]

Also in the European Space the living donation has increased and contributed to the overall increase in transplant figures. However, more than 46,000 patients are waiting for a kidney transplant at this moment [3]

Evolution of the Donation in Spain
Since 1990 and after the establishment of a complete donation and organ procurement infrastructure [5], the number of donors has increased progressively up to 1991, being the stabilised (Fig 3). The donor profile has been changing along this time, as has been described elsewhere [6]

Mean age has increased by ten years average and now, more than 33% of our donors are over 60 years, and 11% over 70 years. During 1992 these percentages were absolutely different as more than half of the donors were less than 45 years old (fig 4). Currently, the main cause of death among our donors is stroke, road traffic accidents account for not more than 21% of all donor’s deaths (fig 5). The percentage of multiorgan donors, whose extra renal organs are retrieved, has increased during the last years, being
now more than 80%. However, the older are the donors, the more organs are discarded. Five years ago we grafted 2.8 organs per donor and nowadays only 2.5 organs per donor are effectively grafted. (Fig 6).

**Donors Whose Organs are Rejected for Transplantation.**

Within the general pool of donors there is always a percentage that are transferred to the surgical theatre and from whom are retrieved solid organs that afterwards cannot be used. Table 1 specifies absolute figures and rates representing all these data. Effective donation means that at least one solid organ has been grafted being a kidney or any other solid organ. In many cases final result was foreseeable, but it must be stated that there are also many doubtful cases and cases without any point for suspicion. There are also many donors with a high degree of suspicion for not being valid and whose organs were grafted. All this justifying the evaluation of all people with brain death and no major contraindications as potential donors, not rejecting anyone prior to the final evaluation before the open body. The rejecting causes range from the technical problems during the retrieval to the existence of a tumour or the unfitness to find the suitable recipient, as it has been published previously. [6]. Kidney rejection causes corresponding to 2001 are specified in table 2. We’ve recorded the cause of rejection in all the 567 kidneys that were not suitable for transplantation during last year. In all cases the corresponding report from the Pathology Department was available.

As has been stated, in the cases of effective donation, not only are the kidneys the grafted organs. Table 3 shows how in several cases kidneys cannot be used but other organs are grafted. Table 4 shows the characteristics of these donors.

Table 5 specifies the characteristics of the donors depending on the number of kidneys used or discarded. Finally table 6 specifies the number and rates of discarded kidneys depending on the donor age.

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**Figure 5.** Organ donors Spain 2001 causes of brain death.

**Figure 6.** Transplanted organs per each donor Spain 1990-2001.
<table>
<thead>
<tr>
<th>Table 1. Organ donors, efficient organ donors and kidneys retrieved/grafted in Spain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Million Population</td>
</tr>
<tr>
<td>------------------------------------------------</td>
</tr>
<tr>
<td>Organ Donors (OD)</td>
</tr>
<tr>
<td>Effcient OD</td>
</tr>
<tr>
<td>Organ Donors pmp</td>
</tr>
<tr>
<td>Effcient OD pmp</td>
</tr>
<tr>
<td>Kidneys Retrieved</td>
</tr>
<tr>
<td>Kidneys Grafted</td>
</tr>
<tr>
<td>Kidneys Discarded</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 2. Causes for Kidney Rejection (2001)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No (%)</td>
</tr>
<tr>
<td>------------------------------------------------</td>
</tr>
<tr>
<td>Previous Kidney disfunction</td>
</tr>
<tr>
<td>Sepsis – Fungal infeccion – HIV</td>
</tr>
<tr>
<td>Hiperteson or Diabetes</td>
</tr>
<tr>
<td>Aortic Aneurism or Kidney artery Areurism</td>
</tr>
<tr>
<td>Donor related causes</td>
</tr>
<tr>
<td>Uncomfirmed malignancy. (Suspicion)</td>
</tr>
<tr>
<td>Confirmed malignancy after retrieved</td>
</tr>
<tr>
<td>Virus B, C combined with aging or absence of edegnete recipient</td>
</tr>
<tr>
<td>Aterometus –Arterosclerosis</td>
</tr>
<tr>
<td>Organ or retrieval process related causes</td>
</tr>
<tr>
<td>Horsetise Kidney</td>
</tr>
<tr>
<td>Litrasis/Hydronephisis</td>
</tr>
<tr>
<td>Decepsulation</td>
</tr>
<tr>
<td>Hypoplasia/Agenesis</td>
</tr>
<tr>
<td>Trauma</td>
</tr>
<tr>
<td>Vascular problems</td>
</tr>
<tr>
<td>Pyelonephritis</td>
</tr>
<tr>
<td>Technical problems/(Vascular/Uretric)</td>
</tr>
<tr>
<td>Multiple Cystis/Polycysstic disease</td>
</tr>
<tr>
<td>Bed perufusion/Thrombosis</td>
</tr>
<tr>
<td>Glomerulosclerosis/Inerstitial fibrosis</td>
</tr>
<tr>
<td>Recipient related causes</td>
</tr>
<tr>
<td>Cross match + and/Overpassed I Time</td>
</tr>
<tr>
<td>Recipient vascular problems</td>
</tr>
</tbody>
</table>
Sometimes the positive serologic test can affect the possibility of grafting a given organ. With increasing frequency it becomes more difficult to find a positive recipient fitting the donor profile. From 1993 to 1995, 75% of the generated kidneys with positive serologic test to virus C were grafted, nowadays this percentage is around 50%. From the 25 virus C donors of 1999 were grafted 26 kidneys and from the 27 virus C donors of 2000 were grafted 34 kidneys. Relating to the HB virus, from the six donors of 1999 were performed four kidney transplants and from the 13 of 2000, only 15 transplants were performed.

Figure 6 shows the evolution of the virus C or B or CMV prevalence among our donors.

**Discussion**

It becomes very clear that donor profile has shown an important change during last years. Advances in the knowledge of better preservation techniques, different grafting techniques, better and more effective immunosuppression therapeutics did allow this evolution, although some changes in patient or graft survival have been observed. On the other hand and simultaneously, recipient admission criteria has also shown an enormous change [7,8] It is hence difficult to state if the results with the so called “suboptimal” donors are so far from the results obtained with “optimal” donors. First of all threshold between both optimal and suboptimal is not so well established. Moreover, there are some factors related with both the process itself and the recipient's characteristics that also have some impact on the graft outcome such as age, clinical circumstances, primary disease, immunosuppressive therapy, centre experience etc. Several authors have described less survival, increased morbidity and higher costs when several risk factors are combined in the same transplant process [4] It becomes mandatory to find the exact middle point between the number of transplants and its quality, moreover when speaking about kidney transplantation and hence having other alternatives. Kidney transplant gives to the kidney patients higher levels of perceived quality of life [9] Nevertheless, the use of organs from elderly donors or from donors with some pathological antecedents can raise ethical questions. [10] Are the patients ready o accept those “marginal” organs?
Recently this question was offered to patients admitted in a kidney centre where the average waiting time was one year. Up to 70% of them would accept an organ of “inferior” quality if this implies less waiting time [10]. It remains very difficult to say what will be the limit.

We have studied the evolution of the characteristics of our donors as well as the characteristics of the rejected

<table>
<thead>
<tr>
<th>Kidneys Used</th>
<th>NONE</th>
<th>ONE</th>
<th>TWO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>197</td>
<td>275</td>
<td>281</td>
</tr>
<tr>
<td>Non Heart Beating</td>
<td>8</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td>Age</td>
<td>60.8 ± 15</td>
<td>58 ± 19</td>
<td>61 ± 17</td>
</tr>
<tr>
<td></td>
<td>61.8 ± 19</td>
<td>51 ± 19</td>
<td>61 ± 19</td>
</tr>
<tr>
<td></td>
<td>61.8 ± 19</td>
<td>53 ± 19</td>
<td>61 ± 19</td>
</tr>
<tr>
<td>Cause of death (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trauma</td>
<td>15</td>
<td>17</td>
<td>14</td>
</tr>
<tr>
<td>Stroke</td>
<td>74</td>
<td>69</td>
<td>76</td>
</tr>
<tr>
<td>Other</td>
<td>11</td>
<td>14</td>
<td>10</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>58</td>
<td>51</td>
<td>58</td>
</tr>
<tr>
<td>No</td>
<td>42</td>
<td>49</td>
<td>42</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>18</td>
<td>26</td>
<td>28</td>
</tr>
<tr>
<td>No</td>
<td>72</td>
<td>74</td>
<td>72</td>
</tr>
</tbody>
</table>

Table 5. Donor characteristics depending on the number of kidneys used or discarder

<table>
<thead>
<tr>
<th>Age (Years)</th>
<th>&lt; 15</th>
<th>15-29</th>
<th>30-44</th>
<th>45-59</th>
<th>60-69</th>
<th>&gt;70</th>
</tr>
</thead>
<tbody>
<tr>
<td>1999</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grafted</td>
<td>85</td>
<td>492</td>
<td>445</td>
<td>545</td>
<td>349</td>
<td>111</td>
</tr>
<tr>
<td>Discarded</td>
<td>5</td>
<td>22</td>
<td>50</td>
<td>142</td>
<td>155</td>
<td>146</td>
</tr>
<tr>
<td>(%) Disc</td>
<td>5.5%</td>
<td>4.3%</td>
<td>10.1%</td>
<td>20.8%</td>
<td>30.7%</td>
<td>56.8%</td>
</tr>
<tr>
<td>2000</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grafted</td>
<td>67</td>
<td>476</td>
<td>371</td>
<td>574</td>
<td>348</td>
<td>108</td>
</tr>
<tr>
<td>Discarded</td>
<td>9</td>
<td>45</td>
<td>68</td>
<td>156</td>
<td>134</td>
<td>155</td>
</tr>
<tr>
<td>(%) Disc</td>
<td>11.8%</td>
<td>8.6%</td>
<td>15.5%</td>
<td>21.4%</td>
<td>28%</td>
<td>59%</td>
</tr>
<tr>
<td>2001</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grafted</td>
<td>58</td>
<td>441</td>
<td>395</td>
<td>608</td>
<td>311</td>
<td>134</td>
</tr>
<tr>
<td>Discarded</td>
<td>16</td>
<td>25</td>
<td>51</td>
<td>91</td>
<td>206</td>
<td>176</td>
</tr>
<tr>
<td>(%) Disc</td>
<td>21.6%</td>
<td>5.4%</td>
<td>11.4%</td>
<td>13%</td>
<td>39.8%</td>
<td>56.8%</td>
</tr>
</tbody>
</table>

Table 6. Kidneys grafted and discarded depending on the age group
It is true that organ donation has improved during last years, but it is also true that the number of rejected kidneys has increased as well. Therefore the number of kidney grafts did not rise in parallel with the number of organ donors. Data from the Catalan kidney patient’s registry shows that while overall survival is not so different, graft function is much worse with kidneys from donors older than 60, and even worst when those kidneys are grafted in old recipients [11]. Hence, donor age is not the only risk factor, in fact the Eurotransplant program elderly donors for elderly patients, reducing other risk factors such as ischemia time is on the way of recording good results [12].

On the basis of the analysis of the causes for kidney rejection we recorded that only 5% of loses are due to technical problems, and hence with the potentiality to be solved. Most kidneys are discarded due to either, glomerular or vascular sclerosis.

It is also true that many organs that some years ago were grafted, are being discarded nowadays. The current practice of performing kidney biopsies when some risk factor is suspected gives the possibility of either rejecting the organ or performing simultaneous graft of both kidneys into the same recipient. This will for sure improve the survival results in forthcoming registry’s reports [13].

Anyway, at this moment, survival rates and graft function data obtained with older kidneys is far from what would be desirable [13-16], although there are many other donor factors that can be considered as risk factors for graft evolution: the extreme ages, below 5 years old and over 60 years old, Hypertension or diabetes history, a serologic profile showing viral infection, the cause of death, etc. The challenge is to establish which organs are going to bear higher risks and in which conditions we could utilise them. [13, 15]

We’ve seen how the age of our donors is increasing progressively, and how more and more kidneys are being rejected every year. We also have seen how the older is the donor the higher is the probability for the kidneys to be rejected. Nearly 60% of all kidneys retrieved from donors over 70 years are rejected. However age is not the only cause for organs to be discarded since 20% of all kidneys from donors between 45 and 59 years are also discarded. This has represented nearly 150 kidneys per year. It has also to be outlined that while organ donor’s average age is increasing every year, mean age of donors from whom both kidneys are grafted is not so high (42-43 years) and is not increasing. We’ve included in this group those donors whose kidneys are grafted in the same recipient following a consensus protocol [17] with encouraging results[18].

Percentage of stroke as cause of death is also in correlation with the percentage of organs discarded: 70 % of donors whose kidneys were discarded died due to stroke. This percentage is reduced to 50% when both kidneys are grafted. Other factors that can affect the organ viability includes pat history of diabetes or...
hypertension. Donors whose kidneys were discarded got antecedents of hypertension or diabetes in 50% and 20% respectively. Nevertheless, it can be said that 20% of donors whose kidneys were used had hypertensive history and 6% got diabetes. This data did not differ from what was previously reported [20]. This means that no donor can be discarded solely because of the past medical history, without a complete and careful examination. Moreover other organs seems not to be so far affected as the kidneys are. Those are recognised risk factors for the long term kidney graft evolution. However this does not mean that those organs should be rejected without a complete and careful evaluation [13, 20].

Moreover, it has been recorded that livers from donors with past history of diabetes or hypertension can be grafted, provided the microscopic inspection, the perfusion and, if necessary, the macroscopic assessment is normal, without an increase in the incidence of primary non function, while more detailed data on the basis of a multivariant analysis is still not available [21].

After the analysis of the donor’s and kidney’s characteristics we know that we can improve the organ availability by 5% if all the technical problems are overcome. But in the other cases, the evidence of kidney damage determined the organ to be discarded.

It becomes clear that the coincidence of more than one donor risk factor deserves less survival probability to the graft, but it also becomes clear that our donor population got the characteristics that we have exposed along the previous pages. Moreover the recipient’s characteristics are also in evolution as a reflect of what is the evolution of the general population profile.

It will be necessary to draw up strategies that could be useful to minimise the effect of the so called risk factors. Probably the secret will be to carefully evaluate the presence of these risk factors and the exact consequences of its use, together with the development of strategies of allocation and recipient’s management that could contribute to the improvement of the survival. It will be necessary to discard only what needs to be discarded after the deep evaluation not only of the functional characteristics of the organ but also its morphologic features and hence the possible damage, both on glomeruli and interstitium. We need to find the most appropriate recipient on the basis of all these data. We know that elderly patients present with less immunological response, and less metabolic requirements; we know that the use of some immunosuppressive drugs will represent an additional nephrotoxic risk; we know that with those kidneys the less ischemia time the better is the prognosis; we know that we can use both kidneys into the same recipient etc. Moreover a careful follow up of the recipient becomes mandatory, having in mind all the features of both, organ and recipient.

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