DISPARITIES IN ACCESS TO LIVER TRANSPLANTATION IN SPAIN

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Background. The maintenance of an equitable system for access to transplantation is a matter of concern to all professionals involved in this field. Any national system must ensure equity.

Methods. The rates of indication for liver transplantation have been reviewed for all Spanish regions. The time to transplantation was evaluated with respect to different recipient characteristics and donor rates. The indication rates for liver transplantation are similar in the different countries with liver transplant programs but are far from similar among different regions in Spain. This suggests that there is not equity in the access to liver transplantation.

Results. A review of the factors affecting the waiting times to transplantation after being registered for the waiting list shows that some groups of patients are currently waiting less time than others. Shorter waiting times occur in patients of the AB group, children, patients with hepatocarcinoma, and patients living in the zone of Valencia, despite similar organ donation rates in all transplant zones.

Conclusion. Neither the rate nor the probability of liver transplantation is affected exclusively by the organ donation rate in Spain but also depends on the number of patients admitted to the waiting list. Despite the existence of an organ allocation system that is center-oriented, liver patients are receiving grafts mainly based on the severity of the illness, because clearance rates from the waiting list of both dead patients and graft patients are the same.

INTRODUCTION

The success of organ transplantation has led to a significant increase in the number of patients admitted to the waiting list. However, organ donor rates have remained unchanged or have increased slightly. Despite all the advantages conferred by organ transplantation, many people cannot benefit from such an opportunity.

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Table 1 shows the evolution of both patients recorded on the liver transplants waiting lists at the end of the year and the number of liver grafts performed by year in some selected Western countries (1). At the same time, annual mortality rates as a result of chronic liver diseases for the same countries are presented (2). As shown, the gap between the supply and the demand is increasing. In such circumstances it becomes an obligation and a matter of concern for all professionals involved in organ transplantation to draw up a system for organ retrieval, allocation, and transplantation that ensures, as far as possible, that equity in the access to such a therapeutic procedure is respected.

In this context, we present how the system works in Spain and the results, in terms of access of the different groups of patients, to liver transplantation.

The System for Organ Procurement and Allocation

Spain is a European Union Country with 41.8 million inhabitants with 17 autonomous regions. Twenty-two liver transplant programs are actively working in the different geographic areas. More than 1,000 liver transplantations are being performed per year.

A network of professionals responsible for the organ procurement and donation process has been set up at all levels (national, regional, and hospital) together with a complete system of coordination and support for organ retrieval, allocation waiting list management, and transplantation (3, 4). The approach to monitoring the organ procurement process has been expanded to most hospitals, and organ donation rates have improved in the last years (5).

The Spanish transplant law for organ procurement was in principle one of presumed consent, but the subsequent legal developments obliged us to approach the deceased patient's next of kin to discuss the wishes of the deceased and, in the absence of this knowledge, the opinion of the relatives. Overall, refusal of consent to donation is maintained at around 20% of all interviews for donation (6).

Organ allocation is based on geographic and medical criteria decided with the consensus of all transplant teams and all of the 17 Regional Transplant Coordinators. Every year criteria are reviewed and modified if large differences among

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groups of patients are found. Allocation rules are public and can be found on the Organizacion Nacional de Transplantes (ONT) website (7).

Waiting list management and allocation procedure is organized by the coordinating offices. The Madrid office is responsible for all Spanish regions except Catalonia; the Barcelona office is responsible for the Catalan territory and for maintaining connections between Spain and other European transplant organizations.

For the purpose of organ allocation, besides the official division into 17 Autonomous Regions, Spain is divided into six zones. This division together with the population distribution and liver transplant center location is shown in Fig. 1.

Patients are registered in the center’s waiting list, which is recorded at the ONT office. Currently urgent patients have national priority on the waiting list. Liver urgency is defined as a primary graft failure within the first 7 days after the graft or fulminant liver failure of any origin but with a healthy liver before the event. In the absence of liver urgencies, livers are offered first locally, then regionally, then to the zone and, if no available recipient can be found, to the rest of the country. Allocation is thus center oriented, but before the organ is offered it must be stated that there is an available recipient meeting the agreed-upon medical criteria to match donors with recipients (ie, age, size, and blood group).

Objective and Methods of the Review

The aim of the review was to analyze the disparities in access to liver transplantation. We have reviewed both the indications for transplantation and transplantation procedures in different groups of patients within the different Spanish regions and zones.

Patients admitted to the waiting list. Every year the number of patients registered on the liver waiting list is recorded. Data are shown by means of the rate per million population (pmp) for each of the 17 officially recognized regions in Spain. Data are analyzed separately and compared depending on the existence or not of a liver transplant unit within the region.

These data have been compared with overall mortality rates due to chronic liver disease, hepatitis, or liver tumor, as published by the National Institute for Statistics for each region. These mortality rates are expressed as number per 100,000 inhabitants and correspond to 1999 (last published data) (8). Liver mortality rates for other countries that are shown in Table 1 have been recorded from the World Health Organization (WHO) website and correspond to 1996 (last published data for the selected countries).

Outcome of patients admitted to the liver transplant waiting list. We have analyzed the outcome of all patients admitted to the waiting list during the last 4 years. The rate of clearance of patients from the waiting list was evaluated by means of time spent on the waiting list using survival actuarial analysis and Wilcoxon test.

The outcome is evaluated in a general way: transplanted, died, still on the waiting list, and excluded. The time to transplantation has been analyzed depending on the following patient characteristics: age, primary disease, region of home address (usual residence), transplant center, blood group.

Analysis of the indication for liver transplantation rates and the probability of undergoing transplantation have been assessed in comparison with the organ donation rate, number of transplant centers, and overall mortality due to chronic liver diseases. This analysis has been performed for each organ allocation zone to see whether geographic differences are present. The Pearson correlation statistic has been used (only data corresponding to 2002 have been included).

RESULTS

Patients Admitted to the Waiting List

Figure 2 shows the rate of liver transplant indications and the corresponding rate for each of the 17 autonomous regions every year from 1991 to 2002. Clear differences have been found in comparing rates from regions with and without a liver transplant team. The average national liver transplant indication rate has been increasing each year, but there seems to be a plateau during the last 2 years.

Rates of indication for liver transplantation are much higher in the United States than in the selected European centers (Table 1). There is no correlation between the rate of indication of liver transplantations and mortality rates due to chronic liver disease.

Outcome of the Patients Admitted to the Waiting List

During the last 4 years, a total of 4,628 patients have been registered on the liver transplant waiting list. Among them, 3,624 received a graft, 558 died while waiting, and 546 were still on the waiting list at the end of the year 2002. Urgent patients and patients excluded from the waiting list have not been considered for this waiting time analysis. There were no differences between the time to a transplantation and the time on the waiting list for patients who died (Fig. 3). Young patients do wait less than adults, as do AB group patients as compared with other blood groups. Patients living in zone 5 waited less than other Spanish citizens (Figure 4). Patients with hepatocarcinoma and those with retransplantation for chronic allograft failure waited less than others.
Table 2 shows the figures for liver transplant candidates, numbers of liver transplants, and transplant probability as well as donor rate, liver transplant centers pmp, and chronic liver disease mortality corresponding to each of the six zones for the year 2002. When the number of patients admitted to the waiting list is higher, the transplant rate is also higher, but the transplant probability is lower (P<0.05, R=-0.85 and +0.8).

No correlation has been found between transplant rates or transplant probabilities and donor rates. There was no correlation between chronic liver disease mortality rates and rates of liver transplantation. No statistical correlation could be found between the number of transplant centers and the number of liver transplants, but there seems to be a tendency toward more liver transplant activity and the number of candidates for liver transplantation (R=0.57).

**DISCUSSION**

Organ transplantation is severely restricted by the number of available organs. There is small possibility of improving this situation merely with more investment and more resources, either in terms of humans or finances. Organ transplantation depends on organ donation either from the living or dead. In such circumstances it becomes an obligation for all professionals involved in organ donation and transplantation to draw up a system for organ retrieval, allocation, and transplantation that ensures, as far as possible, that equity in the access to such therapeutic procedure is achieved. It has been repeatedly claimed that there are geographic differences in the access to organ transplantation (9), and it is true that dramatic differences in the transplant figures from different countries can be found (10). But there are many other factors that deserve our attention.

We reviewed the evolution of the number of patients awaiting liver transplantation in different countries. Although in some of these countries numbers are increasing, in others they remain stable. There are important differences in the rate of indications pmp that cannot be explained by differences in the corresponding mortality rates due to chronic liver diseases. Probably many transplant centers are being extremely selective in the admittance of patients to the waiting list because including patients with no real hope of getting an organ can be pointless (10). In addition, policies for admitting nonresident patients or multiple listings are certainly different among different countries.
In Spain, despite similar rates of chronic liver disease mortality in the different regions, indication rates for liver transplantation are far from similar. Clear differences can be found among regions with or without transplant units. Obviously not all patients who could benefit are being transferred to the transplant centers, and this is the first point that makes it impossible to achieve equity in the access to organ transplantation.

Two main paths are followed in planning the organ allocation system. It can be patient oriented, which is the case for the United States and some European countries, or center oriented, which is the case in other European countries, including Spain. Both have advantages and disadvantages (9, 11, 12). Furthermore, different strategies to manage the enlarging waiting lists, mainly for kidneys, are being proposed (13, 14). However, one must keep in mind that the first and last step in the chain, respectively, are the acceptance of the patient as a candidate for transplantation and a final decision about using or not using a given organ for a given patient; both these decisions remain the responsibility of the physician.

Organ allocation is usually a matter of consensus between transplant teams, organizational bodies, health authorities, and patient’s associations. Independently of the chosen
model, all systems are based on two main categories of factors. In one category, one can list medical criteria such as severity of liver failure, ABO group, HLA matching, and primary disease. In the other category, one can list nonmedical criteria such as geographic distances or available resources. Some factors, such as waiting time or ischemic time, can be listed in both categories. The Committee of Ministers of the Council of Europe, in considering that organ transplantation is severely restricted by the availability of organs for transplantation, underlined the need for a public system with an officially recognized network of transplant centers and officially recognized registries for patients on the waiting list. The Committee also recommended such a system to periodically provide complete information for both health care professionals and the general public. This information should include criteria for registration and allocation, figures and flows of registered patients, and average waiting time for the different groups of patients. The system must ensure, as far as possible, that no group of patients waits longer than another group (15).

We reviewed the outcome of all patients registered in the liver transplant waiting list in Spain between 1999 and 2002. For the purpose of the analysis of transplant probabilities and waiting times, we have excluded those patients admitted for urgent liver transplants, because national priority is given to those cases. A total of 558 patients among the remaining 4,628 patients died while waiting. That is an overall mortality of 12%. A total of 3,524 (76%) received grafts and 546 are still waiting. Figure 3 clearly shows no differences in the rate for clearance from the waiting list between the grafted and dead patients, suggesting that patients are undergoing transplantation on the basis of medical status criteria. Although the Spanish allocation system is center oriented, the final decision for transplantation is based on the severity of the patient’s status, as can be deduced from the overlapping waiting times in both groups, dead and grafted patients (16). It has always been recommended not to transplant O blood group donors into recipients with different blood groups. Despite this, every year some cases escape this allocation rule (6), giving some benefit to patients in the AB group (only 3–4% of the Spanish population) in terms of a higher transplant probability and less waiting time (median time to transplant of 43 days vs. 109 and 107 days for B and O groups, respectively).

No differences between zones are present in terms of clearance rates from the waiting list and waiting times, except for the region of Valencia, which is an exceptional case with a low indication rate and highly concentrated activity. All these factors lead to a higher transplant probability and shorter waiting times (median time, 58 vs. 96 days for overall).

As expected, waiting time for patients with hepatocarcinoma is shorter, this being driven by the life expectancy for those patients (17). On the contrary, the difference observed for liver retransplantation for chronic allograft failure was not expected, basically because of the known discrepancies between liver transplant experts about the indications for chronic retransplantation (18).

The Spanish organ procurement system had similar donation rates among all regions, leading to the conclusion that the rate of liver transplantation does not correlate with organ donation rates but with the number of candidates. The larger the candidate pool, the larger is the absolute number of liver transplants performed. There is always a medically suitable potential recipient for a given donor within the region. But in this scenario, with similar organ donation rates, the transplant probability decreases when the pool for candidates is larger. Differences in the access to transplantation, once the organ donation rate is more than or close to 30 donors pmp in each region, are clearly the result of differences in the indication rate. These indication rates are influenced by the existence of local transplant teams and by the number of transplant teams. The lower the number of transplant centers or the more concentrated the activity, the lower is the indication rate. We must be careful in drawing conclusions from those results or analyzing waiting times and transplant probabilities. It has been already demonstrated that large waiting lists are sometimes the result of the patient’s registration at an earlier stage of the liver disease, hence patients can wait for 2 years or more (16). We strongly believe that candidates’ evaluation before waiting list registration is the answer. Probably not all patients who could benefit are being referred, whereas in some other areas an over-registration can be detected, with those figures also being highly dependent on the number of transplant centers, the registration of nonresidents, and double listing, among other factors.

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GEORGIC VARIANCE IN ACCESS TO RENAL TRANSPLANTATION IN AUSTRALIA

INTRODUCTION

The treatment of end-stage renal failure by both renal dialysis and transplantation in Australia is recorded in a twice yearly census of all treatment centers and includes all patients undertaking chronic treatment for longer than 4 weeks. The data are entered into a single database—the ANZDATA Registry—and the analyses are published in the form of annual reports (1). Single-center survival data are provided only to the submitting center, but state-by-state analyses are available and form the basis of this report. A total of 19 renal transplant units operate in five states: Queensland (QLD) (1 center, population 3.6 million), New South Wales (NSW) also serving the Australian Capital Territory (ACT) (8 centers, population 6.8 million), Victoria (VIC) also serving Tasmania (TAS) (6 centers, population 5.3 million), South Australia (SA) also serving the Northern Territory (NT) (1 center, population 1.7 million), and Western Australia (WA) (3 centers, population 1.9 million). The total population of Australia at the end of 2001 was estimated to be 19,386,663—or approximately one third of the population of France.

Although all dialysis and transplant therapy is available through services that are free-at-point-of-delivery and based in the state-funded public hospitals, the individual policies of each state impact on the availability and types of treatment that are provided. Access to transplantation in Australia is largely dependent upon access to dialysis treatment because the preemptive transplantation rate is currently less than 2% for cadaver grafts and 15% for living donor grafts. The cadaveric renal transplantation allocation system in Australia is managed through the national Renal Transplant Advisory Committee, which has clinical representatives from each state and from each of the national organizations (Transplantation Society of Australia and New Zealand (TSANZ), Australia, New Zealand Society of Nephrology, and the Australian Kidney Foundation) as well as from the tissue typing laboratories and from consumers. Unlike the French environment described by Roudot-Thoraval et al. (2), the cadaveric organ allocation system is thus managed by the