

Liver and pancreas transplantation in Europe – and in Hungary*

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Received: February 2, 2001

Accepted: June 10, 2001

Liver transplantation (LT) is the sole treatment modality of most of diffuse liver diseases. Simultaneous-pancreas-kidney (SPK) transplantation is also a life saving operation for IDDM patients. Both procedures are established treatment options in the European Community (EC) and in the US. These procedures are performed in a significantly smaller number in Hungary. Having a larger demand for LT than the supply of cadaver donors alternative solutions are sought to increase the number of transplantable livers.

In Hungary partly the shortage of donors and the shortage of recipients are the factors rendering the number of LTs and SPKs low. These factors can be changed by better organisation and good survival data that make the two procedures accepted by the community of physicians.

Keywords: Simultaneous-pancreas-kidney (SPK) transplantation, liver transplantation, cadaver donors

In the sixties of the twentieth century renal transplantation became an established treatment of end stage renal disease. At that time Hungarian surgeons and physicians kept up with the front line of the world. The first Hungarian renal transplant was performed by András Németh in 1963. It needed further thirty years for the liver and the pancreas transplant to become an established treatment modality.

Liver transplantation became a routine procedure only during the past decade with a result of 90% one-year survival rate at the best performing transplant centres.

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* The paper was presented at the Scientific Meeting of the Pécs and Veszprém Regional Committees of the Hungarian Academy of Sciences, November 4, 2000, Pécs, Hungary

No other treatment of diffuse liver diseases in the given stage can provide better outcome. The same improvement goes to pancreas transplantation with 90% one-year patient survival and 80% one-year graft survival (12).

The encouraging results of LT increase the demand for it while the resources of transplantable livers remain limited. As most of LTs is performed from cadaver donors, the cadaver donor rate (i.e. the number of donors per million population per year) is one of the main indicators of transplantation activity (Fig. 1).

Due to different reasons not all the otherwise transplantable organs are transplanted from a given donor. Those donors from whom more than one organ, usually kidneys, is procured are quoted as multi-organ donors. The proportion of multi-organ donors vary in different European countries (Fig. 2).

The development of new immunosuppressive drugs, the improvement of technology in surgery and anaesthesia (2) and also the improving global exchange of

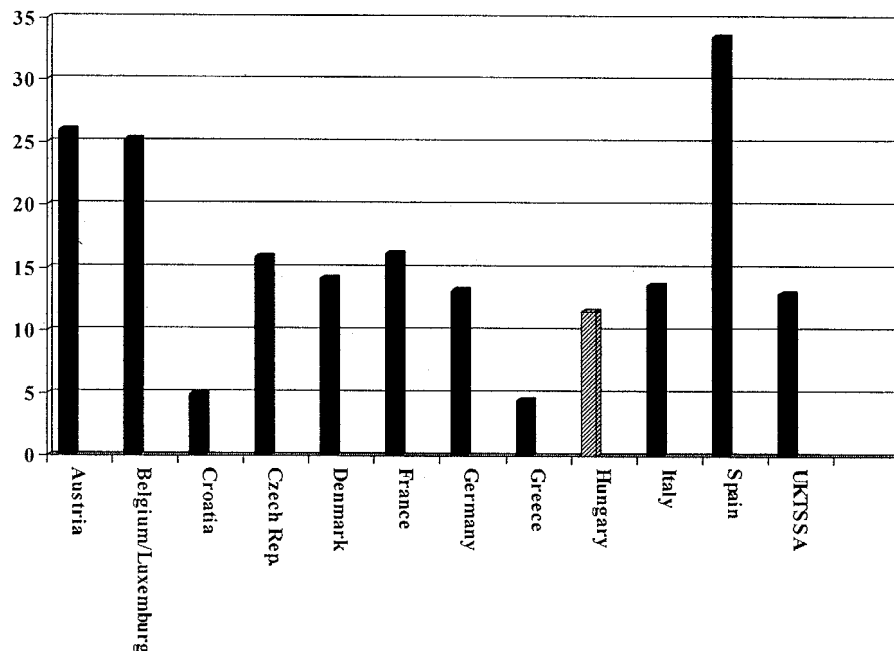


Fig. 1. Cadaveric donors 1999 (per million population)

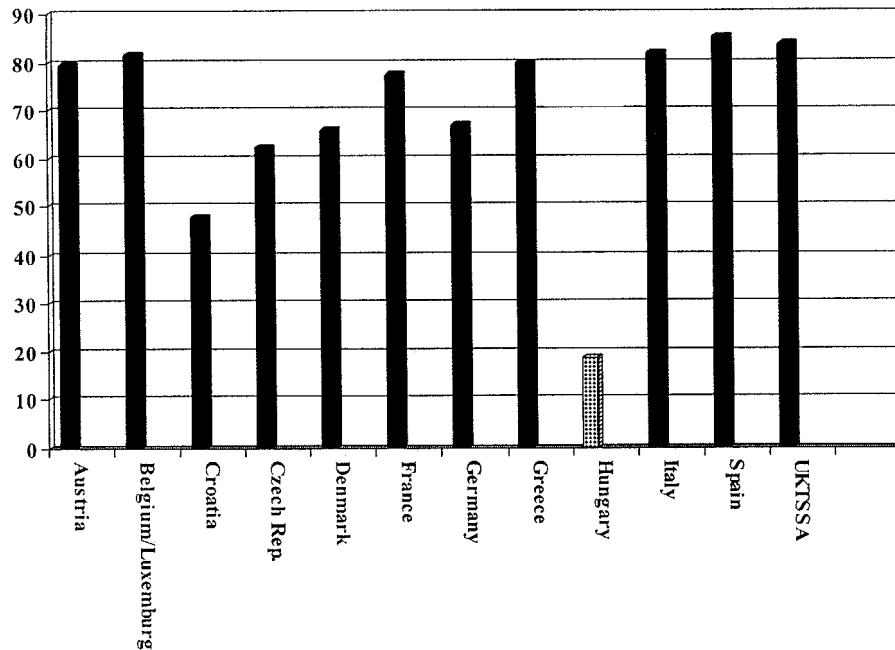


Fig. 2. Multi-organ donors 1999 (%)

information in the field of transplantation had turned liver and pancreas transplantation from an experimental stage into routine. More and more physicians suggest this kind of treatment to their patients. It was in 1994 when the demand for livers outnumbered the supply in the United States. The means of meeting the rapidly growing demand for transplantable organs are the following

- Increase the number of brain dead cadaver donors by better organisation.
- Transplantation of parts of non-paired organs from living donors.
- Splitting the liver of a cadaver donor allowing two liver transplants from one donor.
- Transplantation of organs from so-called non-heart-beating donors.

The number of cadaver donors in a given country is determined by many factors, such as cultural, legal and historical. The cadaver donor activity also reflects the preferences of the health government. The authorities in Spain and Austria put huge effort into the support of organ procurement programs. The result of it is clearly seen in

the statistical data. The main principles of the “Spanish model” are being adopted in many countries. One basic idea of the model is close cooperation between donor hospitals and the organ retrieving centres within a nationwide organization. A local transplant coordinator is employed in every hospital either part-time or full-time in favour of salvage most of the transplantable organs. These coordinators seek and follow every potential donor in the hospital and in case of brain death of a patient they coordinate the process of organ procurement. The specially trained coordinator is the person who contacts the relatives of the deceased potential donor and obtains the consent for organ donation (11). It can be also a promotional factor that the coordinator overtakes the task of donor conditioning from the ICU staff who had fought for the life of the patient before the brain death happened. Donor conditioning is a special medical skill of preservation of viability and function of the organs to be transplanted what is different of the intensive care of the patient. Proper donor conditioning is pivotal for the high rate of multi-organ donation. It can be also a psychological relief to the ICU staff not to be directly involved in organ donation.

Though the criteria of declaration of brain or brainstem death are accepted worldwide the legal rules of organ donation from a cadaver donor is different in many countries. The most significant difference is whether the principle of informed consent or the principle of presumed consent is applied by the legal system. The appliance of the first mentioned one, in other words the opting in principle means the deceased person should have permitted in his life the organ retrieval for transplant purposes or the next of kin to the deceased has to consent it. The principle of opting out or presumed consent means that every person can object any organ removal for the case of his or her death, but the lack of written or orally given objection allows the presumption of consent for organ donation.

The result of a good organ procurement organisation and the application of opting out principle can be seen in the high donation rate in Austria (Fig. 1).

The increasing demand for transplantable livers led to the development of the technique of LT from living donor. As the liver regains almost entirely its volume following a resection, one-third or half of it can be removed safely for transplantation. Most commonly segments II-III or segments II-III-IV are removed for transplantation. On rare occasions the right half of the liver (segments V-VI-VII-VIII) is removed and transplanted (9). Due to cultural and traditional reasons the public opinion in Japan does not recognise brain death and refuse organ transplantation from cadaver donor. Therefore overwhelming majority of LTs in Japan is performed from living donors.

The experience with LT-s from living donors promoted split liver transplantation from cadaver donors. The process of splitting can take place either following the removal from the donor in cold temperature or during the harvest procedure with sustained blood circulation (3). This latter method seems to be more promising with

regard to the primary function of the transplanted halves of the liver (13). Split liver transplantation can theoretically double the number of liver transplants at the same number of cadaver donors.

Another theoretical possibility of expansion of the donor pool is liver transplantation from non-heart-beating donors. In brain-dead cadavers the circulation and the blood supply of the transplantable organs is not compromised while in non-heart-beating cadavers the circulation had also collapsed and a compromised blood supply is provided only by external cardiac massage until preservation with cold solution takes place. A few specialised transplant centres publish encouraging long-term results of non-heart-beating renal transplants in spite of extremely high delayed-graft-function rate (5, 10). The research into the problems of liver transplantation from non-heart-beating donors is promising although there are only sporadic publications in the literature on liver transplants from non-heart-beating donors. For the time being the probability unacceptably high primary non-function rate seems to be prohibitive to liver transplant from non-heart-beating donors.

In some liver transplant centres other means of optimal utilization of the limited number of cadaver donor livers are accepted. As the patient survival rate following liver transplant for primary hepatocellular or cholangiocellular cancer is the same as it is following hepatic resection (8) liver transplant is only very cautiously indicated in primary malignancies not associated with cirrhosis.

In cases of liver failure caused either by primary non-function or any other reason the only chance of survival for the patient can be provided by retransplant within a few days. However the survival rate following such a liver transplant from a second donor is only 50% versus 90% in first transplant cases. As patients can die on the waiting list without liver transplant, there are opinions that in favour of the optimal use of the transplantable livers first liver transplants should be preferred over retransplants.

The development of pancreas transplantation was not as straightforward as that of the liver transplantation. Before the widespread use of the new generation immunosuppressive agents as Tacrolimus and mycophenyl mofetil more complications were observed with an inferior survival rate (6). Only few centres kept on performing pancreas transplants in that era. Most of them were American ones. Long-term experience of these established pancreas transplant programs show that the best graft survival rate is achieved by the simultaneous-pancreas-kidney (SPK) transplant. Therefore 95% of all pancreas transplants is SPK. According to the data of the UNOS (the United Network of Organ Sharing) the US transplant organization the death rate on the SPK waiting list in 1996 was 7.47% per year whereas one-year patient survival rate of patients receiving SPK transplant in 1996 and 1997 is 94.1% expected five-year survival is 81.9%(1). In other words SPK transplant provides better survival for IDDM patients than kidney transplant alone (2).

It also seems to be out of mind that SPK transplant significantly improves the quality of life by making the patient insulin independent, euglycemic and free of dialysis treatment.

It must be admitted however that even with the good results in survival and improved quality of life pancreas transplantation remains the procedure with the highest complication rate among all solid organ transplants. It was in 1994 when the number of patients on both liver and SPK waiting list grown higher than the number of donors.

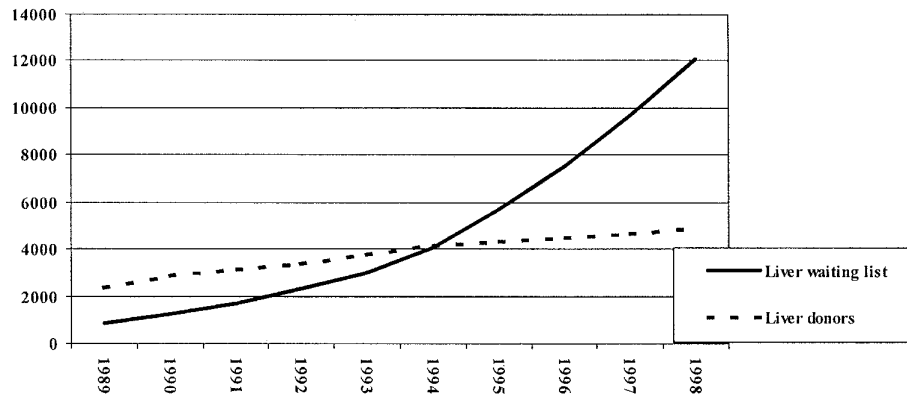


Fig. 3. Liver donors and patients on the waiting list on the last day of the year (UNOS)

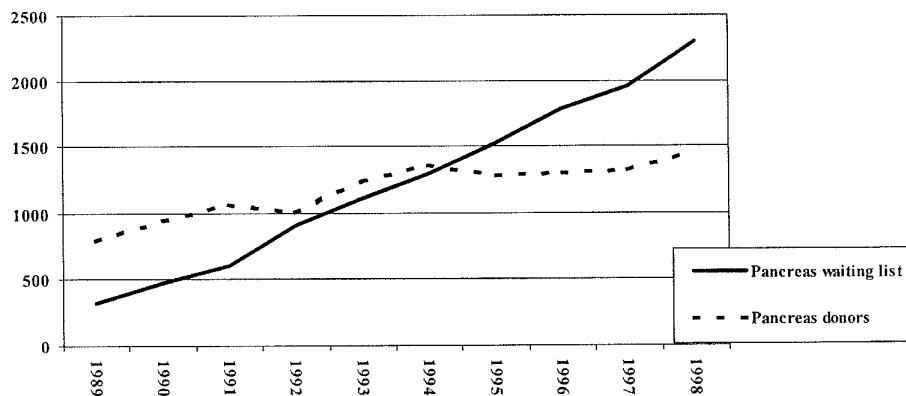


Fig. 4. Pancreas donors and patients on the waiting list on the last day of the year (UNOS)

(Figs 3 and 4). In the author's opinion 1994 was the year when the public opinion of physicians accepted liver and pancreas transplantation as a reliable, standard procedure.

The state of transplantation in Hungary is comparable in some fields with the established western transplant programs. Results and activity of the four Hungarian renal transplant programs are close to the European average. The Hungarian legal rules of organ donation are in harmony with the legislation of more than half of the European Community countries adopting the "soft" opting out principle. As the Hungarian legal rules provide a good balance between the interests of the transplant recipient candidates and the relatives of brain dead donors, the legislation cannot be named as cause of donor shortage. Some other reasons should be sought and found to explain why the data of the Hungarian liver and pancreas transplant programs are inferior to the European and American ones.

The first Hungarian liver transplant was performed in 1985 by Andor Szécsényi 23 years after the world's first. Since 1995 the sole liver transplant program run by the Budapest team performed more than 100 LTs. The 1999 liver transplantation activity of a few voluntarily chosen countries can be seen in Figure 5.

The first Hungarian pancreas transplant was performed at the author's institution in 1998 32 years after the first pancreas transplant in the world. The Pécs pancreas

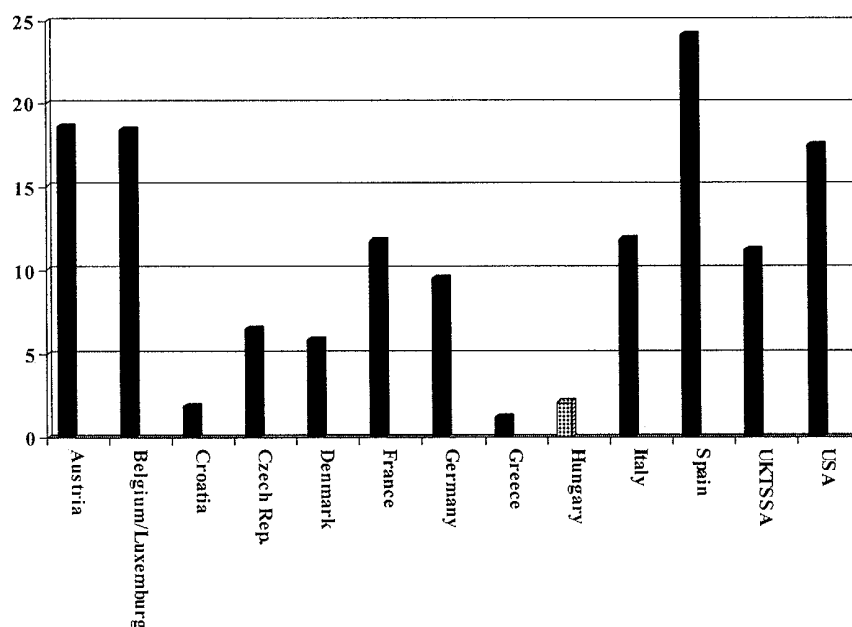


Fig. 5. Liver transplants 1999 (per million population)

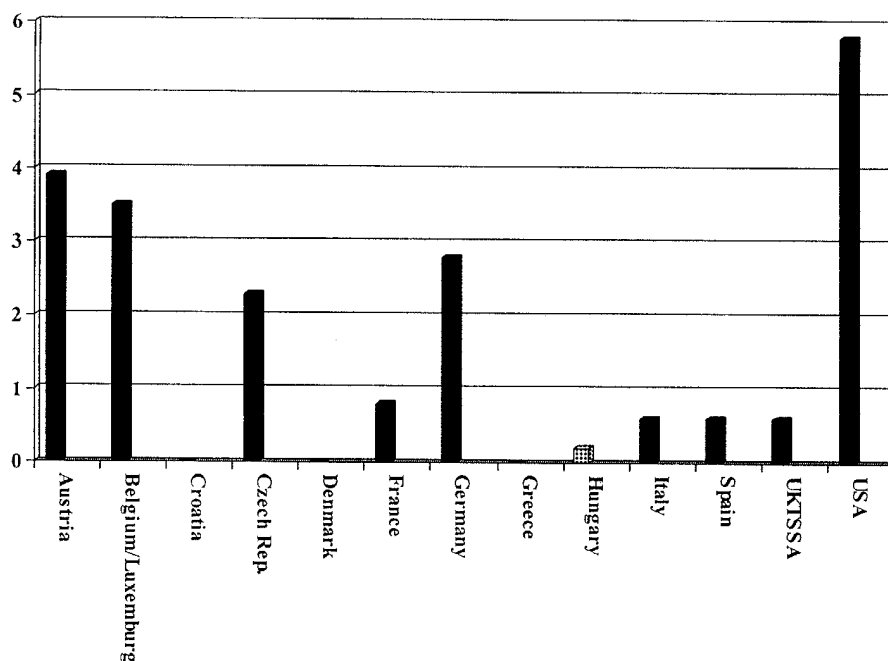


Fig. 6. Pancreas transplants 1999 (per million population)

transplant program is the only one in Hungary for the time being. The program's activity is also behind the activity of the established western programs (Fig. 6). Eleven SPK transplants were performed during the past two years. Ten of them are insulin independent with good renal function. One patient was lost on the 14th postoperative day due to sepsis.

Some more efforts are requested to obtain the same activity in liver and in pancreas transplantation as EC centres produce. Identification of those factors, which should be changed in favour of better performance, is of significant importance.

The donor shortage in itself cannot be blamed for the poorer activity as most of the countries face the same donor shortage. Although every measure should be taken for the increase of the donor pool hence such an increase might allow the choice of optimal organs for transplant. Hungary has some resources to be more exploited, as there are hospital ICUs that never report cadaver donors. The adaptation of the aforementioned "Spanish model" might increase the number of donors and by standardisation of donor conditioning and organ procurement could improve the quality of transplantable organs.

The shortage of recipients might be influential in the low activity. In some cases excellent organs from cadaver donors are refused due to lack of recipient and the waiting

list, rendering the rate of multi-organ donation low. About four thousands of patients die due to diffuse liver diseases every year (4), but the number of patients on the liver transplant waiting list is rarely more than twenty. About 250 IDDM patients are in chronic haemodialysis program in Hungary and only 10 of them are on the pancreas transplant waiting list. The two transplant programs ought to produce and publish convincing results that encourage physicians to put their patients on the lists.

Another possible cause of low Hungarian multi-organ donation rate can be that ICU staff in some hospitals are not familiar with donor conditioning. Long hypotensive periods for instance can turn otherwise transplantable organs unusable. A well-organized organ procurement organization (OPO) might increase the multi-organ donation rate by providing help with donor conditioning.

Financial burdens of liver and pancreas transplantation need not to be considered, as the budget provided for liver and pancreas transplants is regularly under spent.

Certain changes in the policy of the health government might also promote liver and pancreas transplantation. Both programs are in monopolistic position with all of its positive and negative consequences. Only a few European countries with relatively small population afford such monopoly in transplantation. For instance in Austria with 8 million populations has three liver transplant programs. Setting up a second liver and a second pancreas transplant program would generate a fruitful competition resulting in the increase in number and improvement in quality.

It can be concluded that no insurmountable obstacle renders the Hungarian liver and pancreas transplant activity relatively low. Every condition is given to reach in liver and pancreas transplantation the EC average. The planned Hungarian OPO – Hungarotransplant can provide better public control over transplantation and can increase the public sympathy and altruism toward transplantation.

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