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Role of Pancreas Transplantation in People with Diabetes



The first case of pancreas transplantation was performed in the United States, in Minnesota, in 1966. Since then, more than 50,000 pancreas transplants have been conducted worldwide. In Spain, the first pancreas transplant was performed in 1983 at Hospital Clínic of Barcelona (Barcelona, Spain) by Dr. Gil-Vernet and Dr. Fernández-Cruz. Three years earlier, in the same city of Minnesota, Dr. Sutherland had managed to improve both patient survival and graft function—meaning the transplanted pancreas—by modifying the initial surgical techniques.

Many hospitals attempted to implement these changes in the procedure and introduce pancreas transplantation into clinical practice. Spain should be considered one of the pioneers of pancreatic transplantation in Europe. It still is, being one of the 6 countries in the world where the most pancreas transplants are performed each year. Among all European countries, only Germany performs a similar number of procedures. Therefore, we have more than 40 years of experience in pancreatic transplantation, enough to be able to assess the importance of this treatment in the care of people with diabetes mellitus.

One of the questions we must ask is: when would be the right time to transplant a pancreas to a person suffering from diabetes? What restrictions would there be? We start from the premise that the primary reason for the transplant is only one: to achieve normoglycemia. While this is true, it is also true that there are currently other, less complex alternatives to achieve it, such as the glucose sensor-insulin infuser system, which yields very good results. That being the case, why do we propose pancreas transplantation as a therapeutic alternative?

The answer is simple. Pancreas transplantation would be indicated if there is, or there exists, a high risk of diabetes-related complications such as nephropathy, retinopathy, or neuropathy, and if these cannot be managed with other procedures or, if achieved, it comes at the cost of severe hypoglycemia. The most common scenario is that transplantation is indicated for people with diabetes who are already being considered for kidney transplantation. In such cases, a combined kidney-pancreas transplant is opted for.

To transplant a kidney—a procedure that has a vital indication—treatment with immunosuppressive drugs is necessary to prevent rejection. Under these circumstances, a pancreas transplant will not change or will only slightly modify the immunosuppressive regimen. Thus, with the same or minimal changes in the anti-rejection treatment, we can proceed with the pancreas transplant. By doing so, we aim to achieve strict normoglycemia, which will be of utmost importance to prevent the progression of other diabetes-specific complications, as well as possible complications in the transplanted kidney per se. The second indication would be to perform it when normoglycemia cannot be achieved by other means, as previously mentioned, or if it is achieved only at the cost of multiple and severe hypoglycemia episodes. In this case, we would be considering an isolated pancreas transplant, which would be a much more limited >>

» indication. Lastly, we might indicate a pancreas transplant for a person with diabetes who has previously received a kidney transplant, in most cases from a living donor. Any of these 3 options yield good results. The highest survival rates, both for the functioning graft (achieving normoglycemia without the need for insulin) and for the recipient, are achieved with the combined kidney-pancreas transplant, with survival rates > 90% at 1 year and 75% at 5 years post-transplant.

These achievements were reached after several changes to the initial surgical protocols. As the reader may know, the number of beta cells in a pancreas, which produce insulin, is very low, only 2% of all the cells in that organ. In diabetes, only the endocrine cells (primarily the beta cells) are affected, while the exocrine cells remain intact. However, in a pancreas, 98% of the cells are exocrine, meaning they secrete their products into the intestine, aiding digestion, especially of proteins (proteolytic enzymes) and fats (lipolytic enzymes). The patient with diabetes has an intact exocrine function. What benefit is there in receiving it from a donor pancreas? If there is no benefit, how can it be abolished? This was the question posed by the first surgeons performing this transplant, and they tried to answer it by seeking various methods to avoid it.

One option was to eliminate it. Another was to divert this secretion to the recipient's intestine or urinary tract, or wherever it would not cause harm. The idea of abolishing it was discarded after a few initial procedures, as the graft's survival was very short. In Spain and many other countries, the option chosen was to divert this secretion to the urinary tract. Results were good, and it also seemed that determining enzyme levels in the urine could be used as an indicator of rejection. If amylases or lipases stopped appearing in the urine, it indicated that the pancreas was potentially undergoing rejection. If detected in time, it allowed intervention by changing the immunosuppressive regimen. However, currently—in most centers—the digestive route is used. It is more physiological, and better graft survival rates are achieved.

At one point, there was debate over whether it made sense to graft the pancreas when the deficit seen in a person with diabetes was only in a small portion of the cells, about one and a half grams of tissue. Many centers advocated for the transplantation of pancreatic islets instead of the whole organ. However, the graft survival results, although improved, are still worse than those achieved with total pancreas transplantation. Changes will possibly occur in the future, especially when beta cells produced in the laboratory and protective systems that avoid immunosuppression are achieved, but these advancements are

still far away in time. For now, the indication for total pancreas transplantation is the recommendation, particularly when performed simultaneously with the kidney.

More than 50,000 transplants have been reported worldwide. There is no doubt that this is a clinically relevant indication in the management of people with diabetes. The major complication of pancreas transplantation is cardiac complications and infections. Regarding cardiovascular issues, a coronary study (angiography) is recommended before the transplant, and if any vessels are affected, the defect should be corrected, as 30% of people with diabetic nephropathy already have coronary artery disease. Similarly, as with any patient undergoing immunosuppression, follow-up is required for any signs or symptoms that may suggest infection.

Is pancreas transplantation recommended in the described situations? My answer is yes. It is justified by the high survival rates of transplant recipients, both in terms of the recipient and the function of the transplanted pancreas. Let us not forget that those not transplanted, in most cases on a waiting list, have a mortality rate of more than 50% at the 4-year follow-up. This data confirms the need to keep pancreatic transplant programs active in Spain. **D**

IN CONCLUSION:

- Pancreas transplantation is effective in type 1 diabetes mellitus when there is a precise indication, and the most common is the simultaneous pancreas and kidney transplantation in people with diabetes and diabetic nephropathy-related renal failure.
- It is a major procedure that requires lifelong immunosuppressive treatment.
- In Spain, this procedure is performed with results comparable to those of the best international centers of excellence.

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