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Special article

Pancreas transplantation: 50 years of experience☆

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ABSTRACT

In December 1966, the first pancreas transplant ever was performed at the University of Minnesota. R. Lillehei and W. Kelly, transplanted a kidney and a pancreas in a diabetic patient on dialysis, getting function of both organs. Since then, the technical and immunological advances in this transplant have resulted in graft and patient survival results as the rest of the abdominal solid organ transplants. The balance of these 50 years is that more than 50,000 diabetic patients have been transplanted in more than 200 centers around the world. In our country the first transplant was performed 34 years ago in Barcelona and now 12 centers perform about 100 transplants per year. Although advances in diabetes control have been very important, pancreas transplantation continues to be the only method that allows normalization of the carbohydrates metabolism to improve the quality of life and, above all, to increase the survival of these patients.

Trasplante de páncreas: 50 años de experiencia

Palabras clave:
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RESUMEN

En diciembre de 1966 se realizó en la Universidad de Minnesota el primer trasplante de páncreas de la historia. R. Lillehei y W. Kelly, trasplantaron un riñón y un páncreas a una paciente diabética en diálisis, consiguiendo función de ambos órganos. Desde entonces los avances técnicos e inmunológicos en este trasplante, han propiciado resultados en cuanto a supervivencia del injerto y del paciente superponibles al resto de los trasplantes de órganos sólidos abdominales. El balance de estos 50 años es que mas de 50.000 pacientes diabéticos han sido trasplantados en mas de 200 centros en todo el mundo. En nuestro país el primer trasplante se realizó hace 34 años en Barcelona y ahora 12 centros realizan alrededor de 100 trasplantes por año. Aunque los avances en el control de la diabetes han sido muy importantes, el trasplante de páncreas continúa siendo el único método que permite normalizar el metabolismo hidrocarbonado, mejorar la calidad de vida y sobre todo aumentar la supervivencia de estos pacientes.

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Last December 17th was the 50th anniversary of the first pancreas transplantation in the history of medicine (12/1/1966).[1]

We should be reminded that, in the 1960s, the clinical application of organ transplantation was initiated in patients whose diseases had been irreversible until that time. The advent of organ transplantations was a wake-up call that definitively propelled the development of important technical and immunological advances. The era was one of social controversy as well as incredible technological development, culminating in the Space Race and man landing on the Moon in 1969.

Kidney transplantation had been developed before this wave of innovations, thanks to the vision and persistence of Hume, Kuss and, especially, Murray and Merrill who, at the Peter Bent Brigham Hospital in Boston, had successfully performed the first kidney transplantation between 2 twin brothers in 1954. These advances, made fundamentally in the US, were due to the willingness of a series of hospitals, whose objective was the clinical application of organ transplantation after many years of research programs. Liver (1963), lung (1963), heart (1967), pancreas (1967) and colon (1967) transplants and a group of pioneers including Starzl, Calne, Sunway, Barnard, Hardy, Lillehei, Kelly, Murray and Najarian blazed a trail that many surgeons throughout the world have later followed.[2]

For a long time, pancreas transplantation was considered the Cinderella of solid organ transplants. As the objective was to cure diabetes though the normalization of carbohydrate metabolism, it took a while to comprehend that, in order to substitute only 2% of insulin-producing pancreas cells, it was necessary to transplant the entire pancreas, which involved technical and immunological problems. Furthermore, the availability of insulin for the control of diabetes meant that many doctors did not adequately contemplate the deterioration caused by the disease, even with apparently good metabolic control.

The University of Minnesota in Minneapolis is a prestigious hospital with a long tradition of clinical research thanks to a group of physicians who, under the leadership of Professor Wangensteen, were able to develop the first experiences in cardiac surgery thanks to Varco and the Lillehei brothers. Richard Lillehei, who had consolidated an important research program in shock, postulated that a pancreas transplant could be the solution for those patients with diabetes and kidney failure who, until that time, were practically given up on by medicine. Lillehei and Kelly, 2 surgeons with independent laboratories and research fellows, joined forces and, together with the diabetologist Goetz, made the unheard of decision to simultaneously perform kidney and pancreas transplantations in a 28-year-old patient who had been diabetic since the age of 9 and who presented end-stage renal disease. This transplantation, led by Kelly and assisted by Lillehei and Merkel, was done at the Mayo Memorial Hospital in Minneapolis, by the prestigious Surgery Department headed by Wangensteen.[1]

The pancreas transplant consisted of a segmental graft with the pancreas duct ligated. This patient remained insulin free for 6 days; however, after this period, insulin was required, probably related with the high doses of steroids necessary to try to avoid rejection. Likewise, the patient developed pancreatitis of the graft, possibly due to the duct ligation, and on February 14, 1967 Kelly and Lillehei removed the pancreas graft; the kidney was rejected shortly thereafter. The recipient died due to pulmonary embolism 13 days after the transplantectomy (Fig. 1).

This first case is an example of the morbidity that was associated with pancreas transplantation for many years: surgical complications, infections and rejection. In spite of this complicated first case, the Minnesota team demonstrated the technical possibilities of this transplantation. Prior to clinical application, Merkel had developed in the laboratory of Dr. Kelly a canine model of segmental pancreas transplantation, trying to reduce exocrine secretion by graft radiation.[3,4] Meanwhile, in the laboratory of Dr. Lillehei, another 2 surgical fellows, Largiader from Zurich and Idezuki from Tokyo, worked on a canine pancreatic-duodenal transplant model, with drainage of the exocrine secretion by means of Roux-en-Y duodenojejunostomy.[5,6] With this new surgical model, Lillehei led the second pancreas transplantation on the morning of New Year's day (1/1/1967). This transplant functioned for 4.5 months, with excellent follow-up of both organs. Acute rejection was controlled with high doses of prednisone, although in the end the rejection episodes affected the duodenum. After the first case, another 12 were carried out by the same team until 1973, using a complete

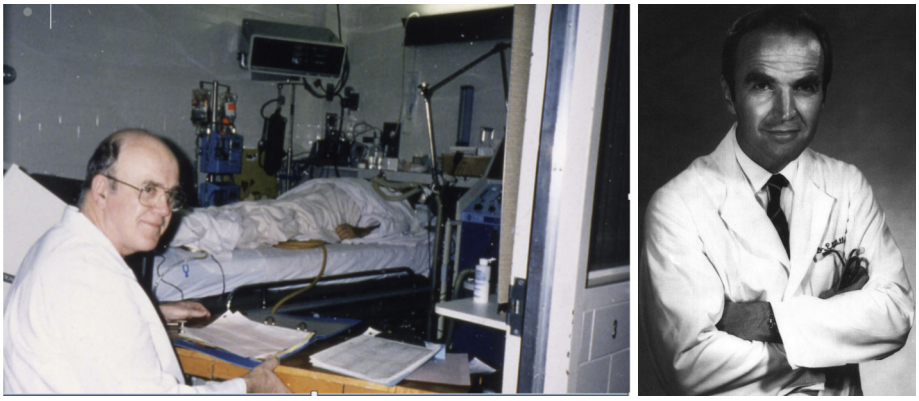

Fig. 1 – William Kelly with the first transplant recipient; Richard Lillehei.