Point of view

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Duct-drained versus duct-occluded pancreatic grafts: a personal view

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The management of pancreatic graft exocrine secretion has been a major concern ever since the start of clinical pancreas transplantation. A variety of techniques have been utilized in an effort to reduce surgical complications related to the acinar pancreatic tissue and to enhance graft survival. After more than a decade's trials of performing pancreatic transplantation by various duct drainage (DD) systems [14, 15, 20, 22], Dubernard, in the late 1970s, introduced the duct occlusion (DO) technique [8]. In contrast to duct drainage, which aims at the preservation of functioning exocrine pancreatic tissue, duct occlusion results in exocrine tissue atrophy.

The technically simple and safe DO technique was adopted by several European and North American transplant centres during the 1980s and led to a rapid increase in pancreas transplantation activity (Fig. 1). Subsequently, some disadvantages of the DO technique were revealed. In the few weeks to a couple of months time from duct occlusion to total acinar atrophy [3], exocrine pancreatic fluid escaping from the graft frequently caused local fluid accumulation and fistulation [5, 18]. Moreover, vascular thrombosis was reported to be responsible for early loss of 15%–20% of the DO grafts. Multiple graft artery stenoses, observed in recipients over time [29], is supposed to be a result of fibrotic parenchymal derangement following duct occlusion. These changes may play a role in additional graft loss through late arterial thrombosis [9, 29] and, thus, contribute to the low, long-term survival rates of DO grafts (Fig. 2).

Because of these problems, an increasing number of transplant centres have during the last 6–7 years, again turned to transplant procedures that include duct drainage (DD). This has been especially true for North American centres, where pancreas transplants registered since 1987 have almost exclusively been performed by pancreatic duct drainage to the urinary bladder (BD) [38]. The evolution of the urinary drainage technique was based on the initial experience with pancreatic duct-to-ureter anastomosis reported by Gliedman et al. [14] in the early 1970s. A decade later, a duct-to-bladder technique was described for segmental pancreas [7, 12], followed by whole organ with duodenal patch [35], and finally by the pancreaticoduodenal transplant with a duodenal segment drained to the bladder [27]. The Stockholm group has refined the technique of enteric drainage (ED), employing pancreaticoduodenal transplants with a direct intestinal anastomosis [39]. This technique may be more physiological than the BD technique, but a high rate of surgical complications have been reported and the technique has so far not been widely adopted.

The refinements of the DD techniques, together with modifications of immunosuppressive protocols, have led to improved results and to continuous growth in the number of pancreas graft recipients each year, at least in the United States. In Europe, on the other hand, pancreas transplant activity seems to have stagnated (Fig. 1), and a consensus on which technique should be given preference has obviously not yet been reached.

After having transplanted 53 duct-occluded segmental grafts during a 5-year period (June 1983–March 1988), the pancreas transplant technique used at the Rikshospitalet, Oslo, was changed in April 1988 to BD pancreaticoduodenal grafting [2]. One reason for changing the technique was that a marker for graft rejection was required in order for us to be able to proceed with our program for transplanting isolated pancreatic grafts. The monitoring of graft function by measuring urinary output of amylase seemed to be feasible, judging from reports from several centres [30, 37].

Thirty-three BD whole pancreas transplantations have been performed at our institution thus far (i.e., up until March 1992). The distribution over the various patient categories is shown in Table 1. Mean recipient age was identical in the DO and BD groups. Triple drug immunosuppression was standard in both groups, although eight patients in the BD group received quadruple induction prophylaxis. The opinion I have formed regarding the two methods of pancreas transplantation, as expressed here, is based on my personal experience performing the surgery and following up on the recipients. In what follows, some pros and cons of the two methods are given, based on my personal experience and on reports from other centres.

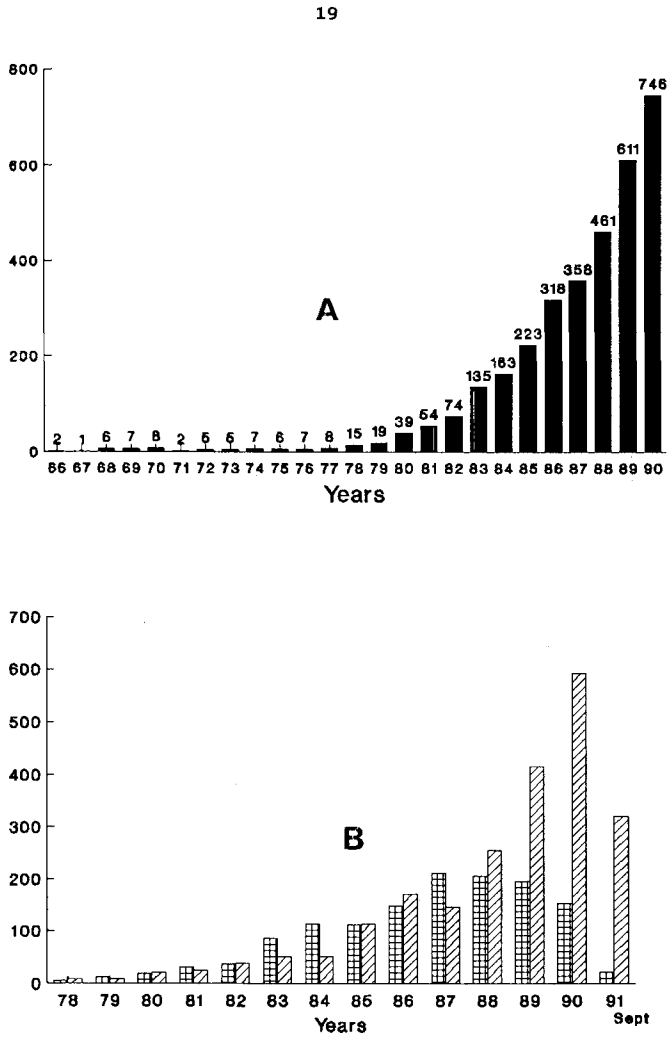

Fig 1. A, B. Annual number of pancreatic transplantations: **A** worldwide; **B** in European (▦) and U.S. (▨) centres (International Pancreas Transplant Registry)

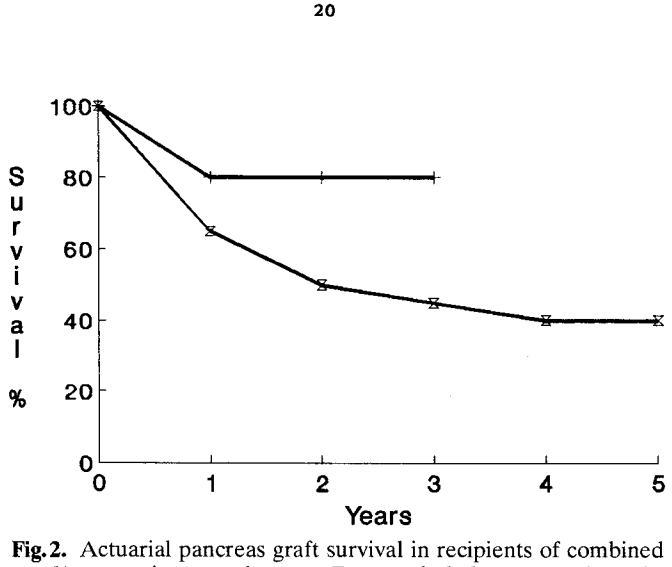

Fig. 2. Actuarial pancreas graft survival in recipients of combined renal/pancreatic transplants. ⧖ Duct-occluded segmental grafts ($n = 46$, June 1983–March 1988), + bladder-drained pancreaticoduodenal grafts ($n = 26$, April 1988–March 1992)

Table 1. Number of pancreas transplantations performed by duct occlusion (1983–1988) and by bladder drainage (1988–March 1992) simultaneously with kidney, after kidney, or alone

	Simultaneous pancreas and kidney	Pancreas after kidney	Pancreas alone
Duct occlusion	46	0	7
Bladder drainage	26	5	2

Surgical techniques

Organ retrieval

The retrieval of a pancreas segment is certainly easier and faster than that of a whole pancreas with a duodenal segment. Moreover, in simultaneous liver harvesting, the preference of most centres to leave the portal vein and coeliac axis with the liver has no impact on the segmental pancreas. For the pancreaticoduodenal technique, the absence of these vascular structures means time-consuming reconstructions when preparing the pancreas for transplantation. Approximately 80% of our whole pancreas donors were also liver donors. In agreement with reports from several other centres [6, 10] however, this did not seem to have any adverse effect on pancreas graft functional survival.

Complications related to the transplantation technique

Wound secretion was experienced in about 40%–50% of the patients with extraperitoneally placed DO segmental grafts. This problem was encountered less frequently when the grafts were placed intraperitoneally. All pancreaticoduodenal grafts were placed intraperitoneally through a midline incision. When changing from DO to DD grafting, an initial increase in postoperative complications and a change in the type of complications were observed. The most frequent types of postoperative complications in our two series (Table 2) are similar to those reported from other centres [5, 16, 18, 19, 36]. Several of the complications observed were chronologically associated with severe rejection episodes and intensified antirejection therapy. Rejection episodes tended to be more severe in BD than in DO grafts, and all recipients of BD grafts experienced at least one steroid-resistant rejection episode, which was treated with ATG, OKT3, or both. In the DO group, about 30% of the recipients had steroid-resistant rejections.

Extended immunosuppression was apparently partly responsible for an increased frequency and severity of cytomegalovirus (CMV) infections in these patients and for the occurrence of lethal, fungal sepsis in two patients. Fascial dehiscence, observed in three recipients of BD grafts 3–4 weeks postoperatively, did not occur after changing from absorbable to non-absorbable fascial sutures. Of eight reoperations in the BD group, five were among the first 15 recipients. Three were for resuturing after fascial dehiscence, two for a leak from the duodenal segment, one for diffuse peritonitis, one for hemorrhage, and in one

patient no abnormality was found. The most frequent reasons for reoperation in the DO group were local fluid accumulation and wound dehiscence. As there is no early marker for rejection of the DO pancreas, graft losses during the first 3 months post-transplantation were registered as having been caused by vascular thrombosis when there were no signs of rejection in the simultaneously transplanted kidney.

One obvious disadvantage of bladder drainage is the constant loss of exocrine pancreatic fluid, leading to metabolic acidosis, electrolyte imbalance, and dehydration [11, 28, 32]. In extreme cases, conversion to enteric drainage [4] or secondary duct occlusion [25] may be indicated. In a recently published study [33], it was demonstrated that active proteolytic enzymes were present in the urine of the majority of recipients of pancreatic transplants drained to the bladder. This may explain the prolonged dysuria in some of the recipients and a significantly increased incidence of infectious and hemorrhagic, lower urinary tract complications in BD pancreatic grafts [34]. Leakage from the duodenocystostomy or from one of the ends of the duodenal segment has been reported to occur in 5%–40% of the cases [16, 19, 25, 36], probably as a result of impaired blood supply and healing conditions subsequent to rejection episodes.

Late graft pancreatitis, probably caused by urinary reflux in BD cases [1, 13, 31] but also seen in ED grafts [23], usually responds well to conservative treatment, but conversion may be necessary in extreme cases.

Results

Patient survival

The 1-year patient survival in our DO series was 97%. There were no deaths related to the surgical procedure or to immunosuppression in this group, but two patients died of acute myocardial infarction during the 1st year after transplantation. However, mortality rates of up to 18% following transplantation of the DO pancreas have been reported [18].

Of the 33 recipients of BD grafts, 3 died of CMV and systemic fungal infection after intensified antirejection therapy with polyclonal and monoclonal antibodies.

Graft survival

The 1-year survival rate of the DO grafts transplanted simultaneously with a kidney remained practically unchanged, at about 60%–67% throughout the 5 years, and this did not improve significantly with increasing experience. When the BD technique was introduced, however, graft survival improved immediately (Fig. 2). In 26 recipients of combined renal/pancreatic grafts, five grafts were lost. The cause of graft loss was patient death in three cases. Only one graft was lost as a result of rejection.

When comparing the influence of the DD and DO techniques on graft survival, the Lyon group failed to demonstrate any difference [24]. However, after analyzing factors influencing pancreas transplant outcome at a single institution having experience with 357 cases, Morel et al. [26] found that the use of BD increased the probability of success twofold over other duct management techniques.

Table 2. Post-transplant complications in duct-occluded and bladder-drained pancreatic grafts

	Duct-occluded ($n = 53$)	Bladder-drained ($n = 33$)
Transplantation-related deaths	0	3 (9%)
Early graft thrombosis	8 (15%)	0
Fascial dehiscence	3/20[a] (15%)	3 (9%)
Bladder leakage	0	3 (9%)
Graft pancreatitis	0	1 (3%)
Fistulation	22 (42%)	3 (9%)
Reoperations	9 (17%)	8 (24%)

[a] Midline incisions

The Oslo experience with the pancreas transplanted alone is limited to a few cases only, as shown in Table 1. Difficulties with the diagnosis of early rejection in the DO grafts motivated the change to BD grafts. Monitoring of urinary amylase in recipients of BD grafts is certainly useful, but not thoroughly dependable. Furthermore, the rejection episodes occurring in recipients of isolated pancreatic grafts proved to be irreversible with the antirejection therapy available. Further transplantations of the pancreas alone were, therefore, deferred.

Metabolic control

Long-term normal carbohydrate metabolism can be achieved with both types of transplants [17, 21]. However, our own data have shown that at 1 year, approximately 40% of the recipients of DO grafts have abnormal glucose tolerance tests (GTT) and borderline HbA_1-values, while 88%–100% of the recipients of BD grafts have normal GTT and HbA_1. Comparing the two graft types, La Rocca et al. [21] found that BD grafts gave better GTT results and lower HbA_1-values at 3, 6, and 12 months than did DO grafts.

Conclusion

My personal experience with DO and BD pancreas transplantation confirms that the DO technique is a safe procedure associated with more frequent, but less serious, complications. However, because of the likelihood of vascular thrombosis, graft survival probability does not reach the same level as that achieved by the BD technique.

With triple drug induction therapy, recipients of BD pancreatic grafts often experience severe rejection episodes requiring intense antirejection therapy. Subsequently, the compromised immune system increases the susceptibility of the recipients to life-threatening infections. However, improved prophylactic and thera-

peutic measures, such as quadruple immunosuppressive induction therapy, CMV prophylaxis, and effective antifungal drugs, are now available. Therefore, these complications may now be prevented or effectively treated in most cases.

The BD technique provides methods for diagnosing early graft rejection, which is obviously of major importance in isolated pancreas transplantation. Nevertheless, the further development of markers for early graft rejection, as well as of immunosuppressive approaches, seems necessary in order to improve the results of isolated pancreas transplantation. When the pancreas is transplanted simultaneously with a kidney using the BD technique, the probability of survival for both grafts is excellent. The problems directly associated with BD may be solved by draining the pancreatic duct to the intestine, which may ultimately prove to be the method that should be given preference.

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