

## Surgical trials for chronic pancreatitis

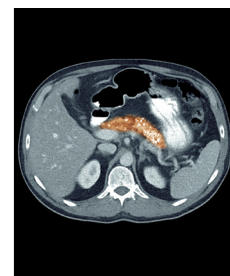
Chronic pancreatitis is associated with a heavy burden for patients and substantial economic costs.<sup>1,2</sup> Patients with chronic pancreatitis might have debilitating pain, opioid dependence, and reduced quality of life; be recurrently admitted to hospital; and be unable to work.<sup>3,4</sup> Yet, for patients and physicians, chronic pancreatitis remains a difficult disease to manage, with few medical options and little consensus on the optimum timing or type of surgical intervention. Reports<sup>5,6</sup> suggest potential superiority of surgical intervention over endoscopic drainage for long-term pain relief. Surgical options for chronic pancreatitis include partial pancreateoduodenectomy (Whipple procedure); lateral pancreaticojejunostomy (Peustow procedure); duodenum-preserving pancreatic head resection (DPPHR); distal pancreatectomy; or total pancreatectomy, with or without islet autotransplantation. Which surgery will most benefit the patient with chronic pancreatitis is often unclear, and few head-to-head randomised trials have been done.<sup>7-9</sup>

In *The Lancet*, Markus Diener and colleagues<sup>10</sup> address this research gap in their multicentre, randomised, controlled ChroPac trial. At 18 centres across Europe—16 in Germany, one in Slovenia, and one in the UK—the investigators randomly assigned 250 patients undergoing elective surgery for treatment of chronic pancreatitis to either DPPHR or partial pancreateoduodenectomy. 226 participants were included in the modified intention-to-treat analysis ( $n=115$  for DPPHR and  $n=111$  for partial pancreateoduodenectomy). The authors found improvements in health-related quality of life at 24 months after surgery in both surgical groups and the primary endpoint of physical functioning according to the European Organisation for Research and Treatment of Cancer QLQ-30 questionnaire was no better with DPPHR than with partial pancreateoduodenectomy. Similarly, significant improvements were seen in the global health and pain scales in both groups for 24 months. Thus, both surgical interventions led to similar benefits in terms of reduction of pain and improved quality of life.

Although operative time was shorter for DPPHR than for partial pancreateoduodenectomy (4.7 h vs 5.3 h;  $p=0.008$ ), both interventions had similar mortality (3% for partial pancreateoduodenectomy and 7% for DPPHR at 24 months;  $p=0.190$ ), morbidity, and length

of initial hospital stay after surgery (16.0 days for partial pancreateoduodenectomy and 18.1 days for DPPHR;  $p=0.710$ ). Development of new diabetes and exocrine insufficiency was also similar between the groups. However, hospital readmissions for chronic pancreatitis occurred more frequently after DPPHR than after partial pancreateoduodenectomy: 31 (27%) of 115 patients in the DPPHR group were readmitted for chronic pancreatitis compared with 12 (11%) of 111 patients in the partial pancreateoduodenectomy group ( $p=0.002$ ). Additionally, in a post-hoc meta-analysis of the ChroPac trial and five previous trials<sup>7-9,11,12</sup> comparing surgical techniques for chronic pancreatitis, the authors found that second operations for management of chronic pancreatitis occurred more frequently after DPPHR than after partial pancreateoduodenectomy, leading them to suggest that partial pancreateoduodenectomy might be the more definitive treatment for chronic pancreatitis. However, the ChroPac trial was not powered for these secondary endpoints, and reoperations within the ChroPac trial were quite rare overall—only two patients in the partial pancreateoduodenectomy group and six patients in the DPPHR group during the 24 months of follow-up ( $p=0.165$ ).

Although the results were optimistic that more than one surgical approach might benefit patients with chronic pancreatitis, the ChroPac trial did highlight some important pragmatic challenges in doing randomised trials of pancreatic surgery. First, surgeons did not adhere to a strict protocol, and surgical variations were allowed on the basis of the expertise and skills of the treating surgeon and centre. Partial pancreateoduodenectomy was done with pylorus-sparing or classic approaches; DPPHR approaches included the original Beger method and Frey and Berne modifications. Because the safety and success of pancreatic surgery are dependent on surgical expertise and volume,<sup>13</sup> allowing surgeons to do the techniques with which they had previous experience was a practical necessity, but one that introduced potential variability in surgical outcomes. Second, all patients with chronic pancreatitis and head disease undergoing surgery were eligible for inclusion, without other specific, patient-related inclusion criteria, allowing for a heterogeneous patient population. Third, outcome data were analysed in an intention-to-treat manner, but, because of



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intraoperative contraindications, the surgical procedure to which the patient was assigned was not done for about one in every seven surgeries—18% of patients assigned to DPPHR underwent a partial pancreatoduodenectomy and 13% of patients assigned to partial pancreatoduodenectomy underwent DPPHR.

Despite these limitations, these findings suggest that more than one surgical procedure could provide clinical benefit for patients with chronic pancreatitis. Still unknown is whether the varied approaches to partial pancreatoduodenectomy or DPPHR affect clinical response; how the risks and benefits of both interventions compare with other surgical procedures to treat chronic pancreatitis; the optimal timing for surgical intervention; whether the morphology of the pancreas affects surgical responses; and whether these findings from (on average) middle-aged adults with a history of smoking or drinking will translate to other populations of patients with chronic pancreatitis, including those with genetic mutations and severe disease in childhood. Head-to-head randomised trials of pancreatic surgery must continue to be done, although the diversity of the patient and disease population must be considered.

Thus, clinical trials are a crucial component of determining the right surgical approaches. However, as we enter the age of precision medicine, the question might not only be whether one surgical procedure is superior for all patients with chronic pancreatitis, but also whether we can select the surgery that is most likely to benefit a particular patient.

\*Melena D Bellin, Gregory J Beilman

Department of Pediatrics (MDB) and Department of Surgery (MDB, GJB), University of Minnesota Medical Center, Minneapolis, MN 55454, USA  
bell0130@umn.edu

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## Penile transplantation is here

Despite high initial mortality, the development of immunosuppressants has allowed solid organ transplantation to become a mainstay of modern medicine, providing a near cure for otherwise fatal conditions. Life-enhancing vascularised composite allotransplantation (VCA), such as face or hand transplantation, has increasingly been used to successfully treat devastating tissue loss. Results from a

recent survey suggest that public attitudes in the USA are favourable overall towards the use of VCA, although concerns remain about seeing familiar body parts on the donor recipient, psychological discomfort, identity loss, and the need for lifelong immunosuppression to treat a non-life-threatening disease.<sup>1</sup>

Given the personal and publicly unnoticeable circumstances of genitalia, penile disfigurement can be

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