

Extreme pancreatic surgery

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Introduction

Pancreatic surgery can be considered extreme surgery by definition for several reasons. In most general hospital pancreatic surgery is rarely performed, it is difficult and requires long learning curve and clinical experience. Moreover, the morbidity and mortality rate remain high and a multidisciplinary team is required to improve the surgical outcome. Pancreaticoduodenectomy (PD), that represent the most frequent procedure, is a complex surgical procedure with substantial risks. Since the '80s, surgeon experience and hospital volume were demonstrated to be major outcome prognostic factors, and such complex surgical procedure were suggested to be performed in centers with sufficient experience and resources for support. This scenario is unchanged to date. A recent observational study of the statewide inpatient database of California showed that in this region, 143 hospital performed their first PD between 1996 and 2010 and that only 5 among them performed more than 50 PD during the study period. In this study, 77 % of the hospitals performed 10 or less PD and the overall mortality rate has remained as high as 9.7%. This report confirms that at the end of the learning process the curve reaches the "plateau" at which point there are no further significant changes in success parameter for surgeon, and results may remain disappointing. In the modern era, other factors contribute to the surgical outcome after PD such as the coalescence of a surgical Unit, an established postoperative recovery pathway, hospital experience, and ancillary support system. The reduction of the mortality rate is mainly due to the management of postoperative complications by a multidisciplinary support system, that represent the "safety net" of the pancreatic surgeon. High volume hospitals have developed such multidisciplinary care and, despite the morbidity rate has remained relatively consistent over the time at 40%, the associated mortality rate has shown a dramatic reduction to less than 4%. We evaluated the surgical outcome of 300 consecutive PD of a single surgical Unit over the past 25 years. In undertaking this study, we hypothesized that once the surgeon learning curve has reached the "plateau", the improvements of surgical outcome rely on the "safety net" that surrounds the surgical Unit.

25 years single institution experience with pancreaticoduodenectomy

We retrospectively reviewed the charts of 308 patients who accepted PD for suspected malignant diseases of the pancreatic head region and were operated on by the same surgical team, in three different hospitals sequentially from 1990 to 2015 in Rome, Italy, (1990-2000: Department of Oncologic Surgery of the Regina Elena Cancer Institute-old location, 2001-3/2007: Department of Digestive Surgery and Liver Transplantation of the Regina Elena Cancer Institute-new location, 4/2007-2015: Department of Surgery and Liver Transplantation of the San Camillo General Hospital). To evaluate the effect of experience, the three periods were compared. All total of 300 patients underwent the conventional pancreaticoduodenectomy (PD) and 8 patients underwent total

pancreatectomy (TP). All procedures were performed by the two senior surgeons (S.E. or E.G.M), or under their supervision. PJ by end-to-side or duct-to-mucosa reconstruction and hepatico-jejunostomy between common hepatic duct stump and jejunum side wall without T tube were became the procedure of choice between 1995 and 2004. Pancreatico-gastrostomy (PG) was performed afterwards. Since 1990, 308 patients underwent PD or total pancreatectomy. Median age was 65 years (range 22-84), and 59 % were male. The clinic-pathological data in the three periods are comparable. Pancreatic duct adenocarcinoma was the most common indication for resection in the three periods (86%). During the three periods, the volume of pancreatic head resections increased from 8.6 procedure per year, to 13 in the intermediate period to 15.5 per year in the last period. Particularly, the number of resections per year increased from 5 to 25. Total pancreatectomy was performed in the first period in 8 patients because of cancer invasion at the frozen section examination of the pancreatic resection margin, and then this procedure was abandoned. Total or partial portal/mesenteric vein resection rate was 9%, and increased in the three periods reaching 15.5% in the last period. Intraoperative blood product transfusion rate was high in the first period and then showed a significant reduction (85% vs. 42% v. 7%, $p < 0.05$). In the last period the median estimated blood loss (EBL) was 300 cc. Median operation time was 305 min (range 160-500 min), and increased with time (290 vs. 300 vs. 320 min). Overall morbidity and reoperation rates were 39% and 10.5%, respectively and remained relatively consistent in the three periods (32% vs. 42% vs. 35% and 9.3% vs. 8.3 % vs 13%, respectively). Overall mortality rate was 4.9%, and there was a significant decrease in the three periods (10.4% vs. 6% vs. 1.6%), with no death in a consecutive series of 144 PD spanning over the last two periods. The incidence of pancreatic fistula in the second and third period was 21% and 23%, respectively. The incidence of delayed massive bleeding associated with POPF was 3% and did not change significantly. Surgical complications represented the main causes of death in the first and second periods, particularly massive bleeding associate with POPF. The cause of death in the two patients that who died since 2005 were not due to pancreatic stump associated complications but were due to respiratory failure following abdominal sepsis, and to massive mesentericoportal vein thrombosis immediately after vascular resection and reconstruction with vein allograft, in one case each. Median hospital stay was 21 days (range 11-117) and was comparable in the three periods (21 vs. 23 vs. 21 days) as well as the 30-days readmission rate that was 4.6% (7% vs. 3.5% vs. 3.9%). The median LOS of patients with uneventful postoperative course was 18 days after PJ and 16 days after PG.

Discussion

Our study confirm that despite the incidence of complications remained unchanged to 40% during the three periods, the refinements of the surgical technique and the advances in critical care provided significant decrease of the mortality rate from 10.4% to 1.6%, as shown in other single institution experiences. The significant reduction of intraoperative blood product transfusion during the study period, despite the expansion of indications to more difficult cases, is an indirect parameter of the refinements of the technique and represents the result of the learning curve of the senior surgeons and his

surgical team. An increase of the operation time was also reported in our study, despite the increasing surgeons experience. This is probably due to the more expanded patient selection criteria, on one side, and on the other side to the adoption of the bloodless surgical technique that is time consuming. As a matter of fact, in our experience a dramatic fall of intraoperative blood product transfusion was seen once our surgical team implemented the number of liver resections (LR) and started the liver transplant (LT) program in 2002, with more than 1700 LR and 350 LT performed to date.

The decrease in the mortality rate in our series, cannot be associated only with surgeon experience and capabilities, but is also associated with the improvements of surgical critical care. Identifying high risk surgical patients in the preoperative workup and the management of POPF in the postoperative course were paramount. Surgeons and intensivists gained clinical experience through the last decades, and preoperative and intraoperative parameters allowed to identify high risk patients. Patients with preoperative and intraoperative risks for complications should be treated differently and followed more closely during the postoperative stay and adopt strategies on individual basis. A very important issue that has not been taken into account in the PREPARE and Braga scores is the preoperative microbial exposition of the patient that represents a predisposing factor for complications. In fact, many of these patients are malnourished and are likely to be colonized with resistant Enterobacteriaceae because of multiple hospitalizations in the course of the preoperative evaluation, including preoperative biliary drainage (PBD). The sharp analysis of postoperative complications after pancreatic surgery at the John Hopkins Hospital provided a new classification in grading complications, and the most common complications were of infections nature. However, no mention was done on the role of the infectious disease specialist in pancreatic surgery. In our recent experience, more than 40% of the patients had positive culture during the postoperative course, and this was significantly associated with higher incidence of preoperative biliary drainage (PBD) and postoperative complications. The rate of grade III or IV Clavien-Dindo complications has remained high at 20% and the ancillary support system has become crucial for treating complicated patients. Particularly, radiologists and interventional radiologists, gastroenterologists and specialists in internal medicine and infectious disease, are involved fruitfully in the management of severe postoperative complications in collaboration with the intensivists. The prevention of pulmonary complications and early detection and treatment of POPF represent the main targets of these pathways, and provided significant results. The different outcome of patients with grade III or IV complications during the study period represents a demonstration of the increased clinical experience and improvements in critical care by all the health care professionals of the hospital during the years.

From the technical point of view, we routinely performed PJ for a more than a decade. In 2004 we decided to perform PG because POPF with massive delayed hemorrhage still represented the most life threatening surgical complication with high mortality rate despite the increasing experience with PJ. In our experience, reoperation for delayed massive arterial bleeding associated with POPF was required after both PJ and PG, and the incidence of this life threatening complication remained unchanged. However, reoperation after PG was easier and the postoperative management provided favorable outcome. So far, despite the reoperation rate increased in the last period, the mortality rate

associated with grade C POPF had a dramatic fall to 0% with a series of 144 consecutive PD without an operative mortality. Relaparotomy has become the treatment of choice in case of massive bleeding associated with POPF. Relaparotomy allows to clean and drain extensively the peritoneal cavity and operating field, and perform microbial cultivation to guide the choice of antimicrobial agents.

The enhanced recovery pathway after surgery (ERAS) represents a new frontier in pancreatic surgery. In our experience, the postoperative median length of stay (LOS) did not show a significant reduction during the study period being 21 days, and we look with interest at the ERAS protocol. However, the readmission rate in our series was as low as 5%. Readmission to a secondary hospital without an adequate safety net is not recommended and our policy has always been to discharge the patients when the predictors and causes of early readmissions are excluded regardless of the length of stay. However, the ERAS protocol is recommended and feasible in selected patients, with the aim to improve the patients' quality of life exclusively, and not the costs containment.

In conclusions, pancreatic surgery can be considered extreme surgery because it is still associated with high morbidity rate. Pancreatic surgeon should continue to use the technique with which they are most familiar, however, all the health professionals of the hospital must be involved in the management of these patients. The multidisciplinary team represents an essential "safety net" to improve results beyond the surgeons skill and experience.

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