Complications of Pancreaticoduodenectomy with Concurrent Colectomies

Subjects: Surgery

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A pancreaticoduodenectomy (PD) is one of the most challenging abdominal surgical procedures and is associated with increased rates of postoperative complications, including severe ones, potentially leading to postoperative deaths. Even at very high-volume centers for pancreatic resections, the morbidity rates after PD are relatively high, while the perioperative mortality cannot be neglected. Multi-visceral resections for colon and pancreatic cancer (PDAC) are feasible, safe, and justified for early and late outcomes. However, the use of pancreaticoduodenectomy (PD) with concurrent colectomies is highly debatable in terms of morbidity and oncological benefits.

Keywords: pancreaticoduodenectomy ; colectomy ; colon cancer ; morbidity ; mortality ; complication

1. Introduction

A pancreaticoduodenectomy (PD) is one of the most challenging abdominal surgical procedures and is associated with increased rates of postoperative complications, including severe ones, potentially leading to postoperative deaths. Even at very high-volume centers for pancreatic resections, the morbidity rates after PD are relatively high, while the perioperative mortality cannot be neglected. Specifically, in the experience in Verona of almost 3000 PDs over 20 years, the overall and severe morbidity rates were 59.9% and 20%, respectively, with postoperative pancreatic fistulas (POPFs) as a leading cause of morbidity (22.4%) and an in-hospital mortality rate of 2.3% [1]. Nationwide studies reporting outcomes of PD showed severe morbidity rates between 20.3% and 33% and in-hospital mortality rates between 1.3% and 9.8%. The centralization of pancreatic surgery has been associated with improvements in terms of failure to rescue, mortality, and re-admission rates [2][3][4][5][6]. Patient-level factors, such as advanced co-morbidities, male sex, and increased age, significantly contribute to increased mortality risks after PD [3].

A malignant periampullary pathology (with pancreatic ductal adenocarcinoma—PDAC as a leading indication), along with a benign pancreatic pathology, is most significant for patients with PD (87–96.4%). Other pathologies, including locally advanced colon cancer, represent an uncommon indication for PD [1][4][5][7].

Extended PD is required for specific pathologies (mainly borderline or locally advanced PDAC) to obtain negative resection margins. Considering that PD is a multi-visceral resection, in 2014, the International Study Group for Pancreatic Surgery defined standard and extended PDs to avoid confusion, particularly for multi-visceral resection and extended lymph node dissection [8][9]. Extended PD usually implies a venous resection (portal/superior mesenteric vein) [10]. In contrast, concurrent resections of the colon, small bowel, stomach, kidney, etc., are uncommon (less than 3% of PDs) [8][11][12][13][14]. Thus, a colon resection during PD is considered extended PD [8].

The en bloc resection of adjacent organs is sometimes required to resect patients with periampullary (particularly PDAC) or colon malignancies with curative intent. Based on the anatomical relationship, periampullary malignancies (with the PDAC as a leading cause) may extend to the mesocolon or colonic lumen. At the same time, a right or right-side transverse colon cancer may extend to the pancreatic head or duodenum. Multi-visceral (extended) resections for colon cancer and PDAC are feasible, safe, and justified for early and late outcomes [11][15][16][17][18][19][20]. However, the use of PD with concurrent colectomies is highly debatable because it may increase morbidity and mortality rates, while the oncological benefits are controversial.

PD and colectomies are surgical procedures with a high risk of morbidity and mortality. The two surgical procedures have specific postoperative complications, and it is widely considered that the severe morbidity and mortality rates for colectomies are far lower than those encountered in PDs. Interestingly, a recent study, based on analyses from the American College of Surgeons National Surgical Quality Improvement Program, showed increased morbidity rates for PDs compared with colectomies (38.5% vs. 26%) but similar 30-day mortality rates (2.7% vs. 2.8%) [21]. Although

uncommonly performed, associations between two complex surgical procedures, such as PDs and colectomies, can potentially increase an operation's complexity, morbidity, and mortality rates. Postoperative complications impact patients' early outcomes and quality of life after PD/colectomies (slow postoperative recovery) and may harm oncological outcomes. Thus, severe postoperative complications correlate with delayed, incomplete, or even lower adjuvant chemotherapy rates in patients with PD for malignancies (mainly but not exclusively PDAC), which is a situation associated with increased recurrence rates and decreased survivals [22][23]. Furthermore, the development of significant morbidities after curative surgery for colon cancer is associated with increased recurrence rates and worse long-term survivals [24]. Thus, carefully selecting patients suitable for PD with concurrent colectomies is paramount to mitigate the potentially severe complications of the two combined surgical procedures and maximize the oncological benefits.

2. Complications of PD with Concurrent Colectomies

POPF and anastomotic leaks are the primary clinically significant complications after PD and colectomies, respectively. The clinically relevant POPF rates after PD vary between 10.9% and 22.4% [1][4][5][7][25]; POPF represents the most common source of surgical mortality after PD. Nationwide population studies showed anastomotic leak rates after colectomies of 6.2% to 7% [26][27]. Recent multi-institutional studies demonstrated overall complications and anastomotic leakage rates after right colectomies of 15.9–38% and 5.6–7.4%, respectively, while the perioperative mortality is 2.1–6.1% [28][29]. Anastomotic leak rates of 1.9% after right colectomies in a study from Australia and New Zealand [30] are worth mentioning. Nevertheless, an anastomotic leak significantly increases the mortality risk after right colectomies [26][28][30].

A few systematic reviews showed an overall morbidity rate of 52.4–53.8% after colectomies with associated PD for locally advanced right colon cancer, which is the most frequent complication represented by POPF (23.8–27.5%) [31][32]. Another systematic review, including patients with PD and concurrent colectomies for PDAC, showed an overall morbidity rate of 25–91.3%, with perioperative mortality rates between 0% and 12% [33].

Several other studies reported overall morbidity and POPF rates of 12.5–100% [34][35][36][37][38][39][40][41][42][43][44][45][46] and between 7% and 100%, respectively [34][35][36][37][38][39][40][41][44][45], after PD with associated colectomies. Operative mortality rates of 2% to 17% were reported for patients with PD and associated colectomies [31][34][37][39][43][47][48][49]. The ileo-colic leak rate after PD with associated right colectomies is reported to be between 6% and 17% [33][34][37][43]. It is worth mentioning studies reporting nil ileo-colic leak and/or mortality rates after PD with associated right colectomies [35][36][39][40][41][42][44][45][50][51][52]. It appears that there are no differences in severe morbidity and mortality rates between patients with PD and concurrent colectomies for PDAC and locally advanced colon cancer, as a study showed [34].

Concurrent colectomies with PD in emergency settings are scarce but associated with exceptionally high mortality rates. A study from a very high-volume center and a recent systematic review showed that standard PD in emergency settings is associated with up to 40% mortality rates [53][54]. However, a few studies reported nil 90-day mortality rates even after colectomies with associated PD in emergency settings [42].

Extended PDs are widely considered to have increased severe morbidity and mortality rates, compared with standard PDs: 42.7–56.5% vs. 30.8–34.2% and 8.8–10.8% vs. 2.9–5.3%, respectively [12][14][55]. However, a few studies did not find any differences in the morbidity and mortality rates between standard PD and extended PD [13][56], albeit extended PD for PDAC was associated with worse survivals compared with standard PD [13][14]. Nevertheless, in a few studies, a colectomy was an independent predictor of mortality and/or severe morbidity in patients with PD [12][47][48][55][57]. Furthermore, a colectomy during PD was independently associated with an increased risk of overall morbidity and infectious complications [48].

Only a few studies assessed the outcomes of patients who underwent PD with or without associated colectomies. A study from Canada did not identify any statistically significant differences between the group of patients with PD and with or without associated colectomies for severe morbidity, POPF, delayed gastric emptying, or operative mortality rates (25% vs. 17%, 7% vs. 13%, 11% vs. 8%, and, respectively, 7% vs. 1%, p values ≥ 0.068) [37]. However, in the group of patients with PD and associated colectomies, the rate of severe hemorrhagic complications was statistically significantly higher than in the group of patients without associated colectomies (14% vs. 1%, $p = 0.002$) [37]. No differences in postoperative morbidity and mortality between the two groups of patients were observed in a Japanese comparative study, including mainly PDAC patients [35], and a study from Australia [58]. Another study from the American College of Surgeons National Surgical Improvement Program database comparing 159 patients with PD and associated colectomies with 10,965 patients with standard PD, including patients who underwent surgery between 2005 and 2012, found statistically significant differences between the two groups of patients for major morbidity (50.5% vs. 26.9%, $p < 0.001$), organ space

infection (22.6% vs. 10.4%, $p < 0.001$), superficial surgical site infection (17.6% vs. 10.3%, $p = 0.003$), sepsis (22% vs. 10.2%, $p < 0.001$), septic shock (10.7% vs. 4.5%, $p < 0.001$), and 30-day mortality rates (8.8% vs. 2.8%, $p < 0.001$), and included a propensity-score matched analysis [47].

An updated analysis of the American College of Surgeons National Surgical Improvement Program database comparing 430 patients with PD and associated colectomies with 23,991 patients with standard PD, including patients who underwent surgery between 2014 and 2019, found statistically significant differences between the two groups of patients for overall morbidity (73% vs. 49%, $p < 0.001$), severe morbidity (68% vs. 42%, $p < 0.001$), clinically relevant POPF (22% vs. 16%, $p = 0.004$), any infectious complication (46% vs. 30%, $p < 0.001$), sepsis (21% vs. 12%, $p < 0.001$), septic shock (7% vs. 3%, $p < 0.001$), severe postoperative hemorrhage (44 vs. 18%, $p < 0.001$), unplanned reintubation and respirator dependence > 48 h (6% vs. 4%, $p = 0.03$, and 7% vs. 3%, $p < 0.001$, respectively), deep vein thrombosis (7% vs. 3%, $p < 0.001$), and re-laparotomy for complications rates (13% vs. 5%, $p < 0.001$). Interestingly, no statistically significant differences were observed between the two groups of patients in this late analysis for 30-day mortality rates (2% vs. 2.8%, $p = 0.767$) [48].

One explanation for the increased rate of infectious complications, sepsis, and septic shock in patients with PD and associated colectomies compared with standard PD might be related to the potential infectious complications of a colic/ileo-colic leak [47]. It is widely accepted that the colon has a higher bacterial load than the upper gastrointestinal tract [48]. Intraoperative bacterial contamination of the abdominal cavity during PD is associated with increased organ space, surgical site infection, and clinically relevant POPF rates [59]. The independent risk factors for abdominal contamination during PD are concurrent colectomies, internal biliary drainage, and longer operative time [59].

The improved mortality rates of both standard PD and PD with concurrent colectomies from the two extensive series analyses of the American College of Surgeons National Surgical Improvement Program database over time might be explained by the improvement of peri- and postoperative care of these patients, with increasing rescue-to-failure rates [48]. Thus, recent studies associated high-volume centers in pancreatectomies with significantly improved mortality, severe morbidity, and rescue-to-failure rates after PD [5][60].

Interestingly, the study by Harris and coworkers published in 2023 found statistically significantly increased rates of small Wirsung duct size and soft pancreatic texture in patients with PD and concurrent colectomies compared with the group of patients with standard PD [48]. This might explain, at least in part, the higher rates of clinically relevant POPF in the group of patients with PD and associated colectomies because small Wirsung duct size and soft pancreas are essential predictors of POPF formation after PD, widely used in recently proposed risk scores for POPF formation after PD [61][62]. Unfortunately, the study mentioned above [48] has no data about treating distal pancreatic stumps after PD. Recent studies have suggested the potential benefits of distal pancreatic stump anastomoses with the stomach over jejunum in patients with small Wirsung duct size and soft pancreatic texture [63][64].

A multicentric national database study compared the outcomes between patients with PD and concurrent colectomies and patients with only colectomies for colon cancer, showing statistically significantly higher rates of surgical site infections, wound dehiscence, and pneumonia in the associated PD group. Interestingly, no differences between the groups were observed for operative mortality (6.3% vs. 1.5%, $p = 0.250$) [49].

It is widely accepted that extended PD is associated with longer hospital stays than standard PD [12][14]. Statistically, significantly more extended hospital stays were reported for patients with PD and associated colectomies compared with standard PD in a few studies [47][48]. In contrast, no differences were reported in other studies [35][37].

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