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Recent Advances in the Study of Risk Factors and Prevention and Treatment Strategies for Postoperative Bleeding following Laparoscopic Pancreaticoduodenectomy

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Abstract

Laparoscopic pancreaticoduodenectomy (LPD) is an established but complex approach for ampullary and periampullary tumours, causing postoperative complications in 30% - 50% of cases. Postpancreatectomy haemorrhage (PPH) occurs in 1% - 8% of patients with an 11% - 38% mortality, making it one of the most lethal complications; early prevention and recognition are therefore essential. However, its risk factors remain incompletely characterized, and optimal management is not yet established. In order to inform perioperative management, this narrative review synthesized evidence on the presentation, classification, pathogenesis, and risk factors of PPH, together with preventive and therapeutic strategies. The review found risk factors distributed across preoperative (hyperbilirubinemia, advanced age, hypertension, ASA grade ≥ III, and elevated body mass index), intraoperative (soft pancreatic parenchyma, main pancreatic duct ≤ 3 mm, transfusion, increased blood loss, and prolonged operative time > 610 min), and postoperative phases, in which pancreatic fistula and intra-abdominal infection drive delayed haemorrhage via the cascade of fistula → infection → vascular erosion → pseudoaneurysm → haemorrhage. This review indicates that PPH arises from converging perioperative factors and warrants risk-stratified, whole-period prevention, with treatment following a severity-stratified algorithm: conservative management for mild haemorrhage, endovascular intervention first-line for moderate-to-severe haemorrhage, and prompt surgery for haemodynamically unstable patients.

Keywords

Laparoscopic Pancreaticoduodenectomy, Postoperative Hemorrhage, Risk

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Factors, Prevention, Treatment

1. Introduction

Laparoscopic pancreaticoduodenectomy (LPD) is an accepted surgical option for malignant and selected borderline tumours of the ampulla of Vater and pancreas, and ranks among the most technically demanding procedures in general surgery, owing to the complexity of the resection, the number of reconstructive anastomoses required, and the steep learning curve. LPD was first reported by Gagner *et al.* in 1994 [1]. Advances in laparoscopic instrumentation and technique have since driven a steady increase in the number of LPDs performed worldwide. In a single-center series of 550 consecutive cases, Wang *et al.* [2] demonstrated that LPD can be performed safely in high-volume centers. Using the Clavien-Dindo classification, Song *et al.* [3] found that LPD was associated with a lower rate of severe complications, and a systematic review by Li *et al.* [4] confirmed reductions in intraoperative blood loss and length of stay, with long-term outcomes comparable to those of open pancreaticoduodenectomy (OPD). A multicenter randomized controlled trial by Wang *et al.* [5] subsequently provided level I evidence: when performed by experienced surgeons at high-volume centers, LPD did not differ significantly from OPD with respect to 90-day mortality, the incidence of Clavien-Dindo grade III - IV complications, the comprehensive complication index, or postoperative length of stay.

Current evidence indicates that, relative to OPD, LPD is associated with less intraoperative blood loss, lower postoperative pain scores, fewer intra-abdominal infections, a shorter hospital stay, a greater lymph node yield, and a lower incidence of postoperative pancreatic fistula [6]-[10]. Nevertheless, the overall complication rate after LPD remains high, at 30% - 50% [11]. Postpancreatectomy haemorrhage (PPH) is among the most serious of these complications. In this review, PPH is used in its broad ISGPS sense, encompassing haemorrhage after any form of pancreatic resection; haemorrhage following LPD is the principal focus. Meta-analyses of randomized controlled trials have found no statistically significant difference between LPD and OPD in the incidence of PPH or in 90-day mortality [12] [13], and perioperative mortality after LPD is approximately 2% - 5% [13] [14]. Contemporary international guidelines and consensus statements—including the Brescia Internationally Validated European Guidelines on Minimally Invasive Pancreatic Surgery (EGUMIPS) [15] and the International Study Group for Pancreatic Surgery (ISGPS) consensus on complexity and experience grading for patient selection in minimally invasive pancreatoduodenectomy [16]—do not report pooled haemorrhage or mortality rates, but both emphasize that LPD should be performed only by adequately trained surgeons at high-volume pancreatic centers, with strict patient selection, in order to safeguard operative safety.

Recent reviews have addressed PPH after pancreaticoduodenectomy either broadly across treatment strategies [17] or with a narrow focus on the learning curve in minimally invasive pancreaticoduodenectomy [18]; however, none has systematically integrated preoperative risk stratification, laparoscopy-specific technical factors (pneumoperitoneum, energy-device thermal injury), and severity-stratified management for PPH after LPD. The present review therefore synthesizes current evidence on the risk factors, prevention, and management of PPH after LPD, with particular emphasis on these laparoscopy-specific dimensions.

According to the ISGPS, PPH occurs in 1% - 8% of patients, with a reported mortality of 11% - 38% [11]. In a series of 1122 patients, Correa-Gallego *et al.* [19] observed a significant increase in the reported incidence of PPH following adoption of the ISGPS definition. Beyond its direct threat to patient survival, PPH imposes a substantial clinical and psychological burden on the operating team. Therefore, systematic identification of the risk factors for PPH and the development of evidence-based preventive and therapeutic strategies are central to reducing its incidence and improving patient outcomes.

2. Materials and Methods

This narrative review was informed by a structured literature search of PubMed, Web of Science, and Scopus, covering the period from January 1994 to August 2026. Eligible publications comprised peer-reviewed original research (retrospective and prospective cohort studies, randomized controlled trials, and multicenter series), systematic reviews and meta-analyses, and expert consensus statements and clinical guidelines. The search strategy combined the following terms with Boolean operators: (“laparoscopic pancreaticoduodenectomy” OR “LPD”) AND (“post pancreatectomy hemorrhage” OR “PPH” OR “postoperative bleeding”) AND (“risk factors” OR “prevention” OR “management”). Supplementary free-text terms included “pancreatic fistula”, “pseudoaneurysm”, and “transcatheter arterial embolization”; the search was further expanded using MeSH headings in PubMed. Only peer-reviewed studies involving human subjects were considered. When multiple reports addressed the same question, studies were prioritized according to methodological quality, sample size, and relevance to the scope of this review. Although studies reporting ISGPS-defined PPH as the primary endpoint were preferred, many eligible reports evaluated related but broader outcomes—such as overall severe complications, intraoperative blood loss, or postoperative pancreatic fistula—rather than ISGPS-defined PPH per se. Such data were retained and are explicitly labelled in the text as indirect evidence for PPH risk rather than direct estimates. The search identified a total of 249 records; after removal of duplicates, 249 records were screened by title and abstract, and 91 studies met the inclusion criteria and were included in this review. Because several publications drew on the same institutional series or overlapping patient populations, overlapping cohorts were treated as a single source of evidence, with the largest or most representative report prioritized. In view of the heterogeneity in outcome definitions across studies, quantitative pooling was not performed; findings were synthesized narratively, with study-specific definitions noted where relevant. Two reviewers independently screened records; disagreements were resolved by consensus. Extracted data comprised study design, sample size, PPH incidence, risk factor effect sizes, and preventive or therapeutic interventions evaluated.

3. Clinical Manifestations and Classification of Postoperative Bleeding

3.1. Clinical Manifestations of Postoperative Hemorrhage

The clinical manifestations of PPH may be grouped as follows. 1) Blood in surgical drains—sanguineous output from abdominal drains or the nasogastric tube; this is typically the earliest and most readily observed sign. 2) Gastrointestinal bleeding—manifesting as haematemesis or melaena; with high-volume bleeding, both may occur concurrently. 3) Haemodynamic changes reflecting compensation for blood loss—tachycardia (≥100 beats/min), tachypnoea (≥20 breaths/min), hypotension (a systolic pressure < 90 mmHg indicates shock), a narrowed pulse pressure (<20 mmHg), and orthostatic hypotension (a fall of ≥20 mmHg on standing) [11] [20]. 4) Laboratory findings—a progressive fall in haemoglobin (Hb) on serial full blood counts, the magnitude of which broadly reflects the volume of blood lost. 5) Haemorrhagic shock—blood pressure below 90/60 mmHg, accompanied by agitation, altered consciousness, thirst, cold and clammy skin, oliguria (<0.5 mL/kg/h), and pallor of the conjunctivae and nail beds [11]. Early recognition of these features is critical to the timely diagnosis and management of PPH [20]-[24].

3.2. Classification and Clinical Significance of Postoperative Bleeding

PPH is conventionally classified according to three parameters: the timing of onset, the anatomical site, and the severity of bleeding.

1) Classification by timing: Using a 24-hour cut-off, PPH is classified as early (≤24 h) or late (>24 h). Early haemorrhage typically reflects technical failure of intraoperative haemostasis—vascular injury, inadequate ligation, clip displacement, or incomplete vessel occlusion [22]. Late haemorrhage arises predominantly from vascular erosion secondary to pancreatic fistula, biliary leak, or intra-abdominal infection, and from rupture of a pseudoaneurysm [11]. Gao *et al.* [25] have proposed subdividing early PPH into <24 h and 24 - 48 h intervals, on the grounds that these represent distinct aetiological groups. In our view, the principal value of this temporal classification is that it enables rapid triage between technical failure of intraoperative haemostasis and erosive processes that arise later; management options range from conservative measures and endoscopic haemostasis to endovascular embolization and re-operation [22].

2) Classification by site: PPH is classified as intra-abdominal or gastrointestinal in origin. Intra-abdominal haemorrhage typically arises from the resection bed, vascular stumps, or pseudoaneurysms, and presents as sanguineous drain output.

The reported distribution of bleeding sites is: the gastroduodenal artery (GDA) stump (26%), the common hepatic artery and its branches (24%), the splenic artery and its branches (11%), the superior mesenteric artery and its branches (7%), othervessels (21%), and an unidentified source (11%) [26]-[28]. Gastrointestinal haemorrhage originates from the pancreaticojejunal, hepaticojejunal, or gastrojejunal anastomoses, or from stress ulceration, and manifests as blood in the nasogastric tube, T-tube, or feeding jejunostomy, or as haematemesis or melaena [11]. Anatomical classification is clinically useful because it directs the choice of haemostatic modality: minor bleeding may be managed conservatively, intra-abdominal haemorrhage is generally amenable to endovascular embolization or surgical control, and gastrointestinal haemorrhage to endoscopic or endovascular therapy.

3) Classification by severity: According to the ISGPS, severity is graded A (mild), B (moderate), or C (severe) on the basis of the clinical impact of bleeding, together with the diagnostic work-up and the therapeutic intervention required, rather than on laboratory thresholds alone [11] [19] [20] [29]. Grade A (mild) denotes haemorrhage with no or only minimal clinical impact: the patient remains haemodynamically stable, and the bleeding is usually detected incidentally by drain inspection, serial full blood counts, or abdominal ultrasound or CT, without the need for a specific therapeutic intervention; conservative management—cardiac monitoring, proton-pump inhibitors, somatostatin analogues, haemostatic agents, nutritional support, and transfusion as required—is sufficient. Grade B (moderate) denotes haemorrhage that causes clinical deterioration but is not immediately life-threatening; it requires adjustment of the clinical pathway and a specific therapeutic intervention, such as transfusion, intermediate care or ICU admission, therapeutic endoscopy, endovascular embolization, or operative control, depending on whether the bleeding is intraluminal or intra-abdominal; a fall in haemoglobin of <30 g/L (<3 g/dL) and a transfusion requirement of ≤3 units of packed red cells are typical of this grade but do not by themselves define it. Grade C (severe) denotes life-threatening haemorrhage that requires immediate, often emergency, intervention—angiography with embolization, covered stent placement, or re-operation—together with intensive care; such bleeding is frequently accompanied by haemorrhagic shock, a fall in haemoglobin of >30 g/L, and a transfusion requirement exceeding 3 units of packed red cells, but it is the severity of the clinical impact and the need for emergency treatment that determine the grade [11].

4) Brodsky and Turnbull [30] introduced the concept of the sentinel bleed—a small, self-limiting herald haemorrhage that frequently precedes delayed massive bleeding and serves as a critical early warning sign of severe PPH (discussed further in Section 5.3). A further practical distinction may be drawn between overt and occult haemorrhage, according to whether blood loss is externally apparent. Overt haemorrhage is externally evident—as haematemesis, melaena, wound bleeding, or fresh blood in the drains—and its source is usually readily identified.

Occult haemorrhage accumulates within a body cavity or the tissues and is not externally visible; it is signaled by a falling haemoglobin concentration and blood pressure, and confirmation requires cross-sectional imaging or diagnostic aspiration. Retroperitoneal haematoma and contained intra-abdominal bleeding are characteristic examples.

4. Analysis of Risk Factors Associated with Postoperative Bleeding

Throughout this section, the evidence base comprises cohorts with differing surgical approaches. Where findings derive from open, robotic, or mixed pancreatic resection cohorts rather than LPD-specific populations, this is indicated explicitly, and such data are interpreted as supportive (indirect) evidence rather than as direct LPD-specific estimates.

4.1. Preoperative Risk Factors

The patient's baseline physiological status and comorbid burden significantly influence the risk of PPH. The best-characterized preoperative determinants include serum total bilirubin (TBIL), advanced age, hypertension, American Society of Anesthesiologists (ASA) physical status, and body mass index (BMI) [2] [31]-[34].

4.1.1. Preoperative Serum Total Bilirubin

Several studies have identified elevated preoperative TBIL as an independent risk factor for haemorrhage after LPD. Tumor-related biliary obstruction causes cholestasis, which in turn impairs hepatic functional reserve, reduces synthesis of vitamin K-dependent clotting factors, and diminishes intestinal absorption of vitamin K; coagulopathy is thus established before surgery. This pre-existing coagulopathy predisposes to bleeding after a technically demanding resection. In 793 patients undergoing LPD, Song *et al.* [3] found a preoperative TBIL > 170 μmol/L was independently associated with severe postoperative complications, including major haemorrhage (OR 1.523; $P = 0.029$). In a bicenter analysis of 879 LPD patients, Meng *et al.* [33] similarly identified severe obstructive jaundice (TBIL ≥ 171 μmol/L) as an independent predictor of severe postoperative complications, and Lin *et al.* [35], a cohort of 1722 patients undergoing pancreaticoduodenectomy that was not LPD-specific, found a preoperative TBIL > 200 μmol/L to be independently associated with increased perioperative blood loss (95% CI 6.948 - 16.797; $P < 0.001$). Collectively, these data indicate a positive association between preoperative bilirubin concentration and bleeding risk, although the threshold above which risk rises most steeply remains undefined—reported cut-offs range from 170 to 200 μmol/L. Prospective randomized trials or large multicenter cohorts will be required to resolve this uncertainty. Of note, the studies of Song, Meng, and Lin used related but broader endpoints—severe postoperative complications including haemorrhage, or perioperative blood loss—rather than ISGPS-defined PPH as the primary outcome; they therefore provide indirect evidence for the bilirubin-haemorrhage association rather than direct PPH risk estimates.

4.1.2. Advanced Age

Advanced age, conventionally defined as ≥65 years, is an established risk factor for postoperative haemorrhage. Aging is accompanied by a progressive decline in organ function—reduced cardiovascular reserve, diminished arterial compliance, and a greater burden of microvascular disease—which reduces physiological tolerance of major resection. In a nationwide Japanese study of predominantly open pancreaticoduodenectomies, Aoki *et al.* [36] identified advanced age as an independent determinant of severe complications after pancreatoduodenectomy—a broader endpoint that constitutes indirect evidence for PPH risk. In 326 patients undergoing LPD, Wang *et al.* [34] found that the risk of postoperative intra-abdominal haemorrhage rose with each additional year of age (OR 1.065; $P = 0.045$). Older patients are also at higher risk of pancreatic fistula and intra-abdominal infection, both of which are key triggers of delayed erosive haemorrhage [35] [37]-[39]. Perioperative assessment and management should therefore be intensified in this group.

4.1.3. Hypertension

Long-standing hypertension causes systemic arteriolosclerosis, reduced arterial wall compliance, and endothelial dysfunction [37], thereby increasing the risk of intraoperative vessel rupture and postoperative bleeding from vascular stumps or anastomoses. In a series of 183 patients undergoing pancreatoduodenectomy (not an LPD-specific cohort), Uggeri *et al.* [32] identified hypertension as an independent risk factor for postoperative haemorrhage. Three mechanisms may be operative. First, hypertension is associated with an imbalance between coagulation and fibrinolysis, which predisposes to bleeding. Second, hypertension has been linked to an increased incidence of postoperative pancreatic fistula after LPD [38], which in turn predisposes to delayed haemorrhage. Third, hypertensive vascular remodeling complicates intraoperative vascular control.

4.1.4. American Society of Anesthesiologists Classification

The American Society of Anesthesiologists (ASA) physical status classification is a standard instrument for preoperative risk assessment. The system comprises six classes (I - VI), with ascending class denoting greater comorbid burden and operative risk [40] [41]. Patients in ASA class III or above frequently have cardiopulmonary impairment, coagulation abnormalities, or metabolic syndrome, each of which increases the risk of complications after major laparoscopic surgery [23] [41]. In a non-LPD-specific cohort of 1722 patients undergoing pancreatoduodenectomy, Lin *et al.* [35] found ASA class IV to be independently associated with perioperative blood loss (95% CI 45.934 - 105.485; $P < 0.001$). In an international multicentre study of 9631 patients undergoing open, laparoscopic, or robotic pancreatic resections, Duan *et al.* [41] used Lasso and logistic regression to identify ASA class ≥ III as one of five independent preoperative predictors of PPH. In a nationwide Japanese analysis of 17,564 predominantly open pancreaticoduodenectomies, Aoki *et al.* [36] likewise found ASA class ≥ III to be an independent risk factor for severe postoperative complications, including haemorrhage ($P < 0.05$). Moreover, because of their comorbid burden and limited physiological reserve, such patients tolerate blood loss poorly once PPH occurs, and are correspondingly more difficult to manage. The findings of Lin *et al.* (perioperative blood loss) and Aoki *et al.* (severe complications including haemorrhage) relate to broader endpoints and thus constitute indirect evidence for PPH risk, whereas the model of Duan *et al.* was specifically developed to predict PPH. (Level III: international multicenter retrospective study)

4.1.5. Body Mass Index

Body mass index (BMI) is the standard index of adiposity. BMI is calculated as weight (kg) divided by the square of height (m^2). The reference range is 18.5 - 24.9 kg/m^2 according to WHO criteria [42] and 18.5 - 23.9 kg/m^2 according to Chinese criteria [43]. Lin *et al.* [35] identified a BMI > 24 kg/m^2 as an independent risk factor for postoperative haemorrhage in a pancreaticoduodenectomy cohort that was not LPD-specific; this threshold denotes overweight by Chinese criteria, with obesity defined as ≥28 kg/m^2. Several mechanisms may underlie this association. First, abundant visceral adipose tissue impedes exposure and dissection, and hinders complete haemostasis of the resection bed. Second, obesity frequently coexists with metabolic syndrome—insulin resistance and chronic low-grade inflammation—which may impair tissue healing and haemostasis. Third, an elevated BMI is an established risk factor for postoperative pancreatic fistula [38] which itself predisposes to haemorrhage.

In summary, preoperative factors act through distinct mechanisms: impaired hepatic and coagulation reserve (hyperbilirubinemia), diminished physiological reserve (advanced age), accelerated vascular pathology (hypertension), aggregate comorbidity burden (high ASA class), and increased technical difficulty (obesity). Because these factors frequently coexist, multivariable preoperative assessment is likely to predict risk more reliably than any single index. The optimal bilirubin threshold for preoperative biliary drainage remains unsettled, and the reported cut-offs are study-specific rather than universally established: Kanani *et al.* [44] proposed 14.6 mg/dL (≈250 μmol/L), whereas Chu *et al.* [45] advocated a lower target. Zhu *et al.* [46] further reported that drainage in patients with mild jaundice may increase the incidence of intra-abdominal infection. Preoperative biliary drainage is therefore not appropriate for all patients with obstructive jaundice, and the decision should be individualized according to the severity of jaundice, the presence of cholangitis, the anticipated surgical delay, and local expertise.

4.2. Intraoperative Risk Factors

Several intraoperative variables are likewise associated with haemorrhage after LPD. These include pancreatic parenchymal texture, main pancreatic duct diameter, operative duration, blood loss, and the surgeon's position on the learning curve. Each may influence bleeding risk directly or through the intermediate development of pancreatic fistula.

4.2.1. Pancreatic Texture and Pancreatic Duct Diameter

A soft pancreatic parenchyma and a narrow main pancreatic duct are the intraoperative characteristics most strongly associated with postoperative pancreatic fistula (POPF), which is the principal cause of delayed haemorrhage. In a quantitative study, Belyaev *et al.* [47] showed that the suture-holding capacity of soft pancreatic tissue was only 63% of that of firm tissue, and that suture-holding capacity correlated closely with parenchymal firmness ($r = 0.98$; $P < 0.001$)—a finding that accounts for the high fistula rate associated with a soft gland. A main pancreatic duct diameter ≤ 3 mm renders the pancreatic jejunal anastomosis technically demanding and increases the risk of POPF, and has been identified as a risk factor for postoperative haemorrhage [47] [48]. Wu *et al.* [49] have described reconstruction of the pancreatic remnant as the "Achilles heel" of laparoscopic pancreatectomy, and it remains the most technically demanding step of the operation. In an analysis of risk factors for POPF after LPD, Xu *et al.* [38] identified soft pancreatic parenchyma as an independent predictor of clinically relevant fistula (OR 42.015; $P < 0.001$). In high-risk patients with a soft gland and a narrow duct, the anastomotic technique should be selected individually.

4.2.2. Intraoperative Transfusion and Intraoperative Blood Loss

Substantial intraoperative blood loss may reflect anatomical complexity, difficult vascular control, or inadvertent vascular injury. Transfusion is both a marker of operative complexity and a potential contributor to coagulopathy through dilution and transfusion-related immunomodulation. In 793 patients undergoing LPD, Song *et al.* [3] found intraoperative transfusion to be independently associated with overall postoperative complications (OR 1.517; $P = 0.033$) and with severe complications, including haemorrhage (OR 2.123; $P = 0.004$). In a retrospective, predominantly open multicenter study of 5323 patients undergoing pancreaticoduodenectomy, Seykora *et al.* [50] reported that the transfusion rate rose sharply from 8.14% to 40.9% once intraoperative blood loss exceeded 750 mL ($P < 0.001$), an intraoperative blood-loss surrogate rather than a direct PPH estimate. Few studies, however, have examined transfusion and blood loss specifically in LPD cohorts. The independent predictive value of these two variables therefore requires validation in larger prospective studies confined to patients undergoing LPD.

4.2.3. Surgical Duration and Technical Proficiency

LPD is associated with a well-documented learning curve. Prolonged operative time increases tissue retraction, thermal injury, and systemic inflammatory activation, each of which may raise the risk of postoperative complications. In a retrospective analysis of 453 patients undergoing predominantly open pancreaticoduodenectomy, Chipaila *et al.* [51] used receiver operating characteristic analysis to define optimal cut-offs, and identified an operative time > 610 min and >657 min as an independent risk factor for arterial pseudoaneurysm formation and fatal pseudoaneurysm rupture, respectively. Cioltean *et al.* [52] retrospectively analyzed 121 LPD procedures and observed significant improvements in blood loss, operative time, and length of stay after the first 50 cases. Applying risk-adjusted cumulative sum (RA-CUSUM) analysis to 115 LPD procedures, Kim *et al.* [53] found that the rates of overall complications (Clavien-Dindo > IIIa), POPF, and haemorrhage fell significantly after 42 cases, thereby providing an objective benchmark for the LPD learning curve.

Taken together, these data suggest that the contribution of operative time to bleeding risk diminishes as surgical experience accumulates. Comparative studies of LPD and OPD support this interpretation: although LPD requires longer operating times, in experienced hands it confers advantages in operative trauma, blood loss, recovery, and length of stay, with rates of haemorrhage and overall complications comparable to or lower than those of OPD [4] [54] [55]. In a randomized controlled trial, Wang *et al.* [5] found short-term outcomes after LPD for pancreatic ductal adenocarcinoma to be non-inferior to those after OPD, with lower intraoperative blood loss in the LPD group (145 vs 200 mL; $P = 0.02$). Longer operative times therefore do not necessarily translate into greater bleeding risk once technical proficiency is achieved. LPD should accordingly be undertaken in high-volume centers with established expertise in both pancreatic and minimally invasive surgery to shorten the learning curve and improve operative safety.

In summary, intraoperative risk is determined by three interacting domains: the anatomical constraints imposed by parenchymal texture and duct diameter, the interplay between blood loss and transfusion, and the surgeon's position on the LPD learning curve. The precise inflection points of the LPD learning curve remain uncertain: Cioltean *et al.* [52] placed it at 50 cases and Kim *et al.* [53] at 42. This discrepancy may reflect differences in case mix, the surgeon's prior laparoscopic experience, and the outcome measures used to define proficiency. Multicenter data will be needed to clarify learning-curve thresholds for surgeons with differing backgrounds and to inform standardized training in LPD.

4.3. Postoperative Risk Factors

Postoperative pancreatic fistula (POPF), intra-abdominal infection, and delayed gastric emptying (DGE) are the principal postoperative determinants of PPH. Each directly influences postoperative outcome.

4.3.1. Pancreatic Fistula

POPF is the single most important risk factor for PPH. The underlying mechanism is well characterized: leakage of enzyme-rich pancreatic secretions causes progressive erosion of adjacent exposed vessels and arterial stumps, and loss of vessel wall integrity permits pseudoaneurysm formation and, ultimately, rupture with haemorrhage. Numerous studies have identified POPF as an independent risk factor for haemorrhage after LPD [11] [48] [49]. In a review of emerging approaches to the early diagnosis of pancreatic fistula, Coppola *et al.* [56] noted that, beyond drain amylase kinetics and CT features, inflammatory markers—C-reactive protein, procalcitonin, and presepsin (soluble CD14 subtype)—and serial drain volumes carry some predictive value. Findings across studies remain inconsistent, however, and no single marker has achieved general acceptance; integrated validation and the identification of novel biomarkers are required. In a retrospective analysis of 500 mixed pancreatic resections (open and minimally invasive), Ansari *et al.* [57] reported an overall PPH rate of 13.6%. The median time to grade C haemorrhage was 13 days (range 1 - 85 days), and a sentinel bleed preceded the event in 63.2% of these patients; grade B or C pancreatic fistula (OR 5.2; P = 0.003) and biliary fistula were independent risk factors for severe PPH. In an analysis of unplanned re-operation within 30 days of LPD, Zhang *et al.* [48] found haemorrhage to be the leading indication (82.6%), with pancreatic fistula the predominant cause of delayed bleeding—further confirming the clinical importance of the fistula-haemorrhage sequence.

4.3.2. Intra-Abdominal Infection

Intra-abdominal infection is <u>another</u> important risk factor for haemorrhage after LPD. The local inflammatory response produces tissue edema, increased vascular permeability, and coagulopathy, all of which predispose to haemorrhage. In a multivariable analysis of 326 patients undergoing LPD, Wang *et al.* [34] identified intra-abdominal infection as an independent risk factor for postoperative intraperitoneal haemorrhage (OR 6.347; 95% CI 1.454 - 27.716; P = 0.014), and intra-abdominal infection was likewise among the principal factors associated with unplanned re-operation in the series of Zhang *et al.* [48] Intra-abdominal infection and enteric fistulae—pancreatic, biliary, or intestinal—frequently coexist and are casually reciprocal, constituting the sequence of fistula → infection → haemorrhage [38] [58].

4.3.3. Delayed Gastric Emptying

Although DGE is not a direct cause of PPH, it may indirectly increase bleeding risk. DGE commonly coexists with intra-abdominal infection, pancreatic fistula, and inadequate nutritional intake, delaying recovery and adding to the overall complication burden. Gastric stasis may also promote acid accumulation, compromise the mucosal barrier, and predispose to gastric mucosal bleeding. Li *et al.* [59] reported that preserving the hepatic branch of the vagus nerve during LPD significantly reduced the incidence of DGE (23.08% vs 46.61%; P < 0.001) and shortened hospital stay, indicating that nerve preservation may help mitigate DGE and its associated indirect bleeding risk. Specific preventive strategies are discussed in Section 5.

In summary, POPF is the dominant postoperative risk factor. Through enzymatic erosion, synergy with intra-abdominal infection, and the indirect contribution of DGE, it drives the characteristic sequence of pancreatic fistula → intra-abdominal infection → haemorrhage. The self-reinforcing cycle between pancreatic fistula and intra-abdominal infection is the key mechanism underlying delayed PPH. Therefore, the principal objective of postoperative management is to interrupt this cycle at any point (**Table 1**).

Table 1. Summary of risk factors associated with postoperative bleeding following laparoscopic pancreaticoduodenectomy.

Type	Risk Factor	Possible Mechanism	Clinical Prevention and Management Recommendations
Preoperative factors	Elevated preoperative serum total bilirubin	Impaired liver function, coagulation disorders	Assess liver function and coagulation status; perform biliary drainage if necessary
Preoperative factors	Advanced age (≥65 years)	Decreased organ reserve and increased risk of complications	Comprehensively assess general health status and enhance perioperative management
Preoperative factors	Hypertension	Increased vascular fragility; blood pressure fluctuations can easily lead to bleeding	Control blood pressure preoperatively and perioperatively
Preoperative factors	ASA Classification	High burden of comorbidities, reduced cardiopulmonary reserve, and impaired coagulation function	Complete a thorough preoperative ASA assessment and optimize cardiopulmonary function and coagulation status
Preoperative factors	Elevated body mass index (BMI)/obesity	Difficulty with surgical exposure; increased risk of pancreatic fistula and infection	Assess obesity and metabolic status; perform precise intraoperative maneuvers
Intraoperative factors	Soft pancreatic tissue	Difficult anastomosis, increased risk of pancreatic fistula	Select an appropriate pancreaticojejunal anastomosis; enhance anastomotic site protection
Intraoperative factors	Small main pancreatic duct diameter	Poor pancreatic juice drainage, increased risk of anastomotic leakage	Perform meticulous anastomosis; place a pancreatic duct stent if necessary
Intraoperative factors	intraoperative blood loss	Reflects anatomical complexity or vascular injury; may induce dilutional coagulopathy	Optimize hemostasis and ensure thorough hemostasis
Intraoperative factors	Prolonged surgery	Increased tissue damage and inflammatory response	Improve surgical efficiency and reduce unnecessary procedures
Intraoperative factors	Surgeon inexperience/learning curve	Inconsistent hemostasis and anastomotic quality	Enhance training and standardize surgical procedures
Postoperative factors	Postoperative pancreatic fistula	Pancreatic juice corrodes blood vessels, leading to pseudoaneurysms	Monitor amylase levels in drainage fluid and ensure adequate drainage
Postoperative factors	Intra-abdominal infection	Inflammation and digestive fluids erode blood vessels	Antibiotic therapy to control the source of infection
Postoperative factors	Delayed postoperative gastric emptying	Delayed recovery and increased risk of complications	Promote recovery of gastrointestinal function and provide nutritional support

Abbreviations: ASA: American Society of Anesthesiologists; BMI: Body Mass Index; POPF: Postoperative Pancreatic Fistula.

5. Strategies for Preventing Postoperative Bleeding

Preventing PPH requires an integrated approach spanning the entire perioperative period. Within a multidisciplinary framework, this approach comprises targeted correction of preoperative risk factors, refinement of operative technique with reinforced vascular protection, and structured postoperative surveillance. Together, these constitute a continuum from risk assessment to early intervention.

5.1. Preoperative Optimization

Preoperative optimization is the primary step in reducing the risk of postoperative hemorrhage after LPD and forms the foundation for minimizing PPH risk. The goal of preoperative optimization should be to correct as many preoperative risk factors as possible.

The indications for and timing of preoperative biliary drainage require careful consideration. In a single-center retrospective study of 665 patients undergoing pancreaticoduodenectomy (not an LPD-specific cohort), Kanani *et al.* [44] identified a preoperative bilirubin level of ≥14.6 mg/dL (≈250 μmol/L) as an independent predictor of 90-day mortality. Among patients with severe hyperbilirubinemia who did not undergo drainage, 90-day mortality was 13.3%, significantly higher than in the remaining groups (2.9% - 5.7%; P = 0.001). In 148 patients with obstructive jaundice undergoing (open or mixed) pancreaticoduodenectomy, Zhu *et al.* [46] similarly concluded that drainage should be undertaken routinely when bilirubin exceeds 250 μmol/L, with the drainage interval limited to two weeks; conversely, drainage in patients with mild jaundice increased the incidence of intra-abdominal infection. With respect to technique, a Chinese expert consensus [60] recommends selective preoperative drainage in patients with cholangitis, severe jaundice (bilirubin > 300 μmol/L in distal biliary obstruction), malnutrition, or planned neoadjuvant therapy. For distal obstruction, endoscopic nasobiliary drainage (ENBD) or endoscopic biliary stenting (EBS) is preferred over a 4 - 6 week drainage interval. However, that document does not specify a target preoperative bilirubin concentration for pancreatoduodenectomy. However, preoperative biliary diranage (PBD) remains controversial: some evidence suggests PBD may increase overall complications in certain subgroups. Current evidence therefore supports selective rather than routine PBD, reserving it for patients with severe jaundice, cholangitis, or anticipated surgical delay.

Cao *et al.* [61] proposed a goal-directed drainage strategy in a retrospective analysis of 194 patients with pancreatic cancer and obstructive jaundice, defining a target of TBIL ≤ 93.0 μmol/L or a reduction of ≥68.5%. Achievement of this target, at a median of three weeks, was associated with a lower incidence of PPH. In a non-LPD-specific cohort of 292 patients undergoing pancreatoduodenectomy, Chu *et al.* [45] found that reducing TBIL below 151.8 μmol/L before surgery was associated with significantly fewer severe postoperative complications (P = 0.047). These thresholds and targets derive from individual retrospective studies and shouldbe regarded asstudy-specific rather than universal recommendations. Taken together, they suggest that a preoperative TBIL above approximately 250 μmol/L is commonly used as an indication forbiliary drainage in LPD candidates, with ENBD or EBSpreferredwhere endoscopic expertise isavailable andpercutaneous transhepatic cholangial drainage (PTCD) an acceptable alternative; a drainage interval of approximately 2 - 3 weeks, aiming for a study-derived target such as TBIL ≤ 93 μmol/L (or a reduction of ≥68.5%), may be reasonable. Such astrategy permits recovery of hepatic reserve and correction of coagulopathy while limiting the risk of infection from prolonged or unnecessary drainage.

In older patients and those with comorbidity, operative decisions should be based on physiological reserve rather than chronological age alone. In a meta-analysis of robotic pancreatoduodenectomy, Chrysikos *et al.* [62] found that older patients had significantly higher rates of severe complications (Clavien-Dindo ≥ III: OR 2.20), DGE (OR 2.34), and mortality (OR 3.42) than younger patients; complication risk appeared to rise beyond 70 years and mortality beyond 80 years. Preoperative evaluation should therefore include ASA grading, cardiopulmonary assessment, and frailty screening, with targeted optimization—including correction of anemia and rate control—in patients with limited functional reserve [63] [64]. In high-risk patients of ASA class III or above, preoperative management should focus on correcting coagulation abnormalities and improving cardiopulmonary reserve; where appropriate, a multidisciplinary team should assess the risk-benefit balance of surgery and formulate an individualized perioperative plan [65]. In hypertensive patients, blood pressure should be managed throughout the perioperative period: preoperatively it should be brought below 180/110 mmHg and as close to baseline as feasible; intraoperatively, marked fluctuation should be avoided; and postoperatively, stress-related elevation should be monitored and treated promptly [39]. In overweight and obese patients, preoperative weight reduction and meticulous dissection are advisable to minimize tissue trauma. Zhang *et al.* [66] reported that protein-energy malnutrition significantly worsened in-hospital outcomes after open pancreatoduodenectomy in patients with pancreatic cancer; preoperative nutritional support should therefore form part of routine preparation in high-risk patients.

Evidence for pharmacological prophylaxis remains limited. In a randomized controlled trial, Chen *et al.* [67] found that intraoperative dexmedetomidine attenuated the early postoperative inflammatory response after LPD, with a non-significant trend towards fewer pancreatic fistulae, less DGE, and fewer severe intra-abdominal infections. Whether this translates into a reduction in infection-related PPH remains to be established. A systematic review and meta-analysis by Wang *et al.* [68] found the efficacy of prophylactic octreotide across open and minimally invasivepancreatic resections to be inconclusive, and its use is best reserved for selected high-risk patients.

In summary, preoperative optimization should center on goal-directed biliary drainage and on assessment of organ reserve in older and comorbid patients, supplemented by nutritional support and selective pharmacological prophylaxis. Together these measures improve baseline physiological status and reduce the underlying risk of haemorrhage. Given ongoing debate, PBD is best reserved for selected patients, for example thosewith severe jaundiceor cholangitis, and the decision should be individualized according to jaundice severity, the presence of cholangitis, the anticipated surgical delay, and local expertise, with study-specific bilirubin thresholds used as guidance rather than fixed rules.

5.2. Improvements in Surgical Techniques

Improvements in surgical techniques are a key factor in reducing the risk of PPH, encompassing four aspects: optimization of pancreatico-intestinal anastomosis techniques, intraoperative hemostasis, protection of vascular stumps, and management of the learning curve. The quality of the pancreaticojejunal anastomosis is a principal determinant of POPF, which in turn is the main driver of delayed PPH. Although numerous anastomotic techniques have been described, guidelines recommend that surgeons use the method with which they are most experienced. Several modifications have been evaluated specifically for high-risk glands—those with soft parenchyma and a main duct ≤ 3 mm. In 112 patients undergoing LPD with Chen's pancreaticojejunostomy, Zhu *et al.* [69] reported an overall grade B fistula rate of 7.1%, with no significant difference between subgroups with a soft versus firm gland (11.1% vs 4.5%; P = 0.264) or a narrow versus wide duct (9.8% vs 5.6%; P = 0.461), indicating stable performance under unfavorable anatomical conditions, with a mean anastomotic time of 27 min. The modified Kakita duct-to-mucosa technique described by Zhao *et al.* [70] requires only six sutures and, in a series of 98 patients, had a median anastomotic time of 17 min; the overall grade B fistula rate was 4.1%, and 4.4% in the high-risk subgroup with a soft gland and a duct ≤ 3 mm, suggesting that the technique performs consistently regardless of parenchymal texture or duct caliber. Li *et al.* [71] reported, in a series of 184 patients, a single-layer continuous duct-to-mucosa anastomosis reinforced with two figure-of-eight sutures (the "1 + 2" technique), with a median anastomotic time of 15 min (range 10 - 20) compared with 50 min for conventional two-layer interrupted anastomosis (P < 0.001). Grade B/C fistula occurred in 4.21% versus 12.34% (P = 0.044), with correspondingly lower rates of intra-abdominal infection (2.11% vs 8.99%; P = 0.040) and a shorter hospital stay (11 vs 13 days; P = 0.013). The "double-R" technique described by Tang *et al.* [72] isolates the anastomosis from pancreatic secretions, with a mean anastomotic time of 34 ± 5 min. Among 35 patients undergoing LPD, no bleeding-related deaths occurred, though the small sample size and lack of a control group limit interpretation. Comparative data for representative anastomotic techniques are summarized in **Table 2**.

Modifications to pancreatic duct drainage have also been reported. Tu *et al.* [73] described a split pancreatic duct stent, and Li *et al.* [74] reported that a variable-diameter duct catheter reduced the pancreatic leak rate from 9.89% to 2.70%.

The relative merits of pancreaticogastrostomy (PG) and pancreaticojejunostomy (PJ) remain debated. In a meta-analysis of open and mixed pancreatic

Table 2. Comparison of representative pancreaticojejunal anastomotic techniques evaluated for pph prevention during LPD.

Technique	Author/Ref	N	Anastomotic Time (min)	Grade B/C Fistula (%)	Key Feature	Evidence Level
Chen's pancreaticojejunostomy	Zhu *et al.* [69]	112	27	7.1% Grade B (soft 11.1% vs. firm 4.5%, P = 0.264)	Stable fistula rate across gland types and duct calibers	Level III (retrospective)
Modified Kakita duct-to-mucosa	Zhao *et al.* [70]	98	17	4.1% Grade B (high-risk: 4.4%)	Only 6 sutures; consistent in high-risk glands	Level III (retrospective)
"1 + 2" single-layer continuous duct-to-mucosa	Li *et al.* [71]	184	15 (10 - 20) vs. 50 (conv.) P < 0.001	4.21% vs. 12.34% Grade B/C P = 0.044	Reduced infection (2.11% vs. 8.99%) and hospital stay (11 vs. 13 d)	Level III (comparative retrospective)
Double-R	Tang *et al.* [72]	35	34 ± 5	0%* Grade B/C (0/35)	Isolates anastomosis from pancreatic secretions	Level III (small sample, no control)

Abbreviations: conv., conventional two-layer interrupted anastomosis; Grade B/C, clinically relevant postoperative pancreatic fistula. Evidence levels follow the Oxford Centre for Evidence-Based Medicine (OCEBM) 2011 classification. *Grade B/C (clinically relevant) fistula rate of 0% derived from Tang *et al.*: no clinically relevant pancreatic fistula was recorded among the 35 patients.

resections, Salman *et al.* [75] found a significantly lower incidence of clinically relevant POPF after PG than after PJ (P = 0.043), but a significantly higher overall incidence of PPH after PG (P = 0.018). Rates of clinically significant postoperative bleeding did not differ between the two (P = 0.287). PG may therefore reduce CR-POPF at the cost of a higher overall haemorrhage rate. In practice, PJ remains the preferred reconstruction because it is more physiological, and PG is reserved for selected cases.

Intraoperative blood-flow control and protection of vascular stumps are central to the prevention of PPH. In a predominantly open multicenter cohort of 5323 patients undergoing pancreatoduodenectomy, Seykora *et al.* [50] found that increased intraoperative blood loss was significantly associated with adverse outcomes, including PPH, supporting the use of an intraoperative blood-loss alert threshold. Tan *et al.* [76] described blood-flow control strategies—including early devascularization and dual-system pre-occlusion—that reduced intraoperative blood loss and, in their series, the risk of postoperative haemorrhage. Vascular anatomy and its variants should be assessed preoperatively by contrast-enhanced CT, and the gastroduodenal artery (GDA), common hepatic artery, and superior mesenteric vein should be handled with meticulous dissection. Rupture of the GDA stump is a major cause of PPH. Yu *et al.* [77] and Wang *et al.* [78] reported that wrapping the GDA stump and the hepatic artery at the porta hepatis, respectively, with the ligamentum teres hepatis was associated with a lower incidence of PPH after LPD. In 272 patients undergoing LPD, Liu *et al.* [79] found that wrapping the GDA stump with the ligamentum teres hepatis and the falciform ligament, combined with a modified Blumgart anastomosis, reduced the incidence of clinically relevant postoperative pancreatic fistula and Clavien-Dindo grade ≥ II complications. Finally, as discussed in Section 4.2.3, blood loss, operative time, and complication rates all improve with accumulated experience; LPD should therefore be performed in high-volume centers with an established pancreatic surgery program, and the learning curve managed through structured training under senior supervision. Specifically, Yu *et al.* [77] reported that LTH wrapping reduced GDA stump bleeding from 7.9% to 0% (n = 148). Wang *et al.* [78] confirmed LTH as an independent protective factor (PPH 0% vs. 11.3%, P = 0.019, n = 131) with shorter hospital stay (12 vs. 15 days, P < 0.001). The two-parts wrapping technique has also demonstrated significant efficacy [80]. Hepaticojejunostomy insufficiency represents an additional source of arterial hemorrhage after pancreatic surgery [58].

In summary, technical refinement should proceed across four domains: precision in pancreaticojejunal anastomosis, systematic control of blood flow, deliberate protection of vascular stumps, and structured management of the learning curve. The optimal material for wrapping the GDA stump—ligamentum teres hepatis, falciform ligament, autologous liver tissue, or greater omentum—has not been established in randomized trials and warrants further study. LTH wrapping reduces GDA stump bleeding from 7.9% to 0% [77] and is independently protective against PPH (0% vs. 11.3%, P = 0.019) [78].

5.3. Postoperative Monitoring and Early Intervention

Postoperative surveillance and early intervention represent the final opportunity to interrupt the fistula-infection-haemorrhage sequence and to improve outcomes in PPH. Routine monitoring should encompass vital signs (blood pressure, heart rate, respiratory rate), the character and volume of abdominal drain output, serial haemoglobin concentrations, and coagulation indices. In a review of coagulation disorders in sepsis, Iba *et al.* [81] observed that serial trends in platelet count, prothrombin time/international normalised ratio, fibrinogen, and D-dimer are more informative than isolated threshold values—a principle that applies equally to coagulation monitoring after LPD. Shiozaki *et al.* [82] reported that a second fall in the eosinophil ratio after (open or mixed) pancreatoduodenectomy predicted severe complications, including PPH, with an area under the receiver operating characteristic curve of 0.96 (95% CI 0.93 - 0.99), although this finding requires external validation. Where haemorrhage is suspected, CT angiography (CTA) or digital subtraction angiography (DSA) should be undertaken promptly to localise the source and direct treatment.

Recognizing sentinel bleed provides a critical window to pre-empt delayed major haemorrhage. In 1991, Brodsky and Turnbull [30] described the sentinel bleed: a small volume of blood appearing in the abdominal drain or nasogastric tube before major haemorrhage, in a patient whose vital signs remain stable and whose haemoglobin has fallen only slightly. Such an event frequently heralds subsequent, potentially fatal haemorrhage, most often from rupture of a pseudoaneurysm. Arterial bleeding from a ruptured pseudoaneurysm may rapidly precipitate haemorrhagic shock, and mortality from severe PPH has been reported to reach 29% [23]. In 76 patients with pseudoaneurysm after mixed open and minimally invasive pancreatic surgery, Liu *et al.* [83] found that pseudoaneurysm formation was significantly associated with POPF, intra-abdominal infection, and a serum albumin < 30 g/L. Patients with a sentinel bleed therefore warrant intensive monitoring. Even when haemodynamically stable, they should undergo contrast-enhanced CT, CTA, or DSA without delay to exclude a pseudoaneurysm or arterial stump rupture. If either is confirmed, prompt embolization, covered stent placement, or operative repair is indicated.

Preventing and managing pancreatic fistula and intra-abdominal infection require several concurrent measures: judicious antimicrobial therapy, somatostatin analogs to reduce exocrine secretion, and adequate drainage to limit enzymatic erosion of adjacent vessels. In established pancreatic fistula, conservative measures should be initiated without delay: nil by mouth, gastrointestinal decompression, suppression of pancreatic secretion, and double-lumen tube irrigation. Nutritional support should be optimized, fluid and electrolyte balance maintained, and conditions favorable to anastomotic healing preserved. In patients with active bleeding or haemodynamic instability, resuscitation should be goal-directed, guided by haemoglobin concentration, coagulation status, and indices of tissue perfusion, with packed red cells, fresh frozen plasma, platelets, and fibrinogen concentrate administered as required.

In summary, postoperative surveillance should be based on serial assessment of vital signs and drain output, with recognition of the sentinel bleed as the principal early-warning signal and cross-sectional imaging for localization, thereby establishing an uninterrupted pathway from detection to intervention. Novel biomarkers, such as a second fall in the eosinophil ratio, [82] may further improve the timeliness and accuracy of early warning. Prevention of haemorrhage after LPD thus rests on a continuous perioperative model comprising preoperative risk assessment, intraoperative technical optimization, and early postoperative detection (**Figure 1**). Close multidisciplinary collaboration offers the best prospect of reducing both the incidence and the mortality of PPH. Emerging biomarkers such as the second-drop eosinophil ratio [82] may enhance early detection.

6. Treatment Strategies for Postoperative Bleeding

Management of haemorrhage after LPD should follow a stepwise algorithm determined by haemodynamic status, the timing of bleeding, and ISGPS severity grade. The ISGPS grades PPH as A (mild), B (moderate), or C (severe). Treatment principles may be summarized as follows: conservative management for mild bleeding; endovascular intervention as first-line therapy for moderate-to-severe bleeding; and prompt surgical exploration when the patient is haemodynamically unstable or endovascular treatment has failed. These approaches are considered below in order of increasing intensity.

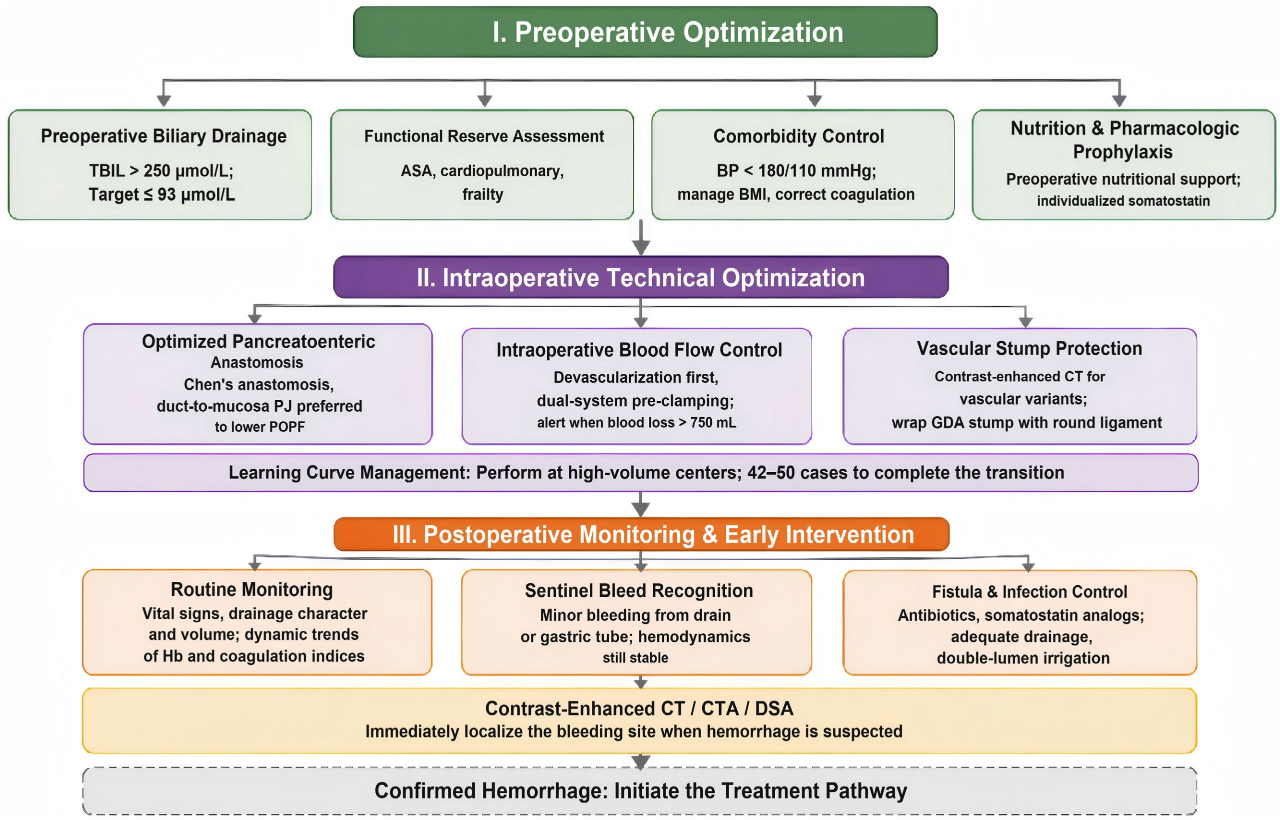

Figure 1. Perioperative prevention flowchart for postoperative bleeding following laparoscopic pancreaticoduodenectomy. Abbreviations: LPD, laparoscopic pancreaticoduodenectomy; TBIL, total bilirubin; ASA, American Society of Anesthesiologists classification; BMI, body mass index; POPF, postoperative pancreatic fistula; PJ, pancreaticojejunostomy; GDA, gastroduodenal artery; Hb, hemoglobin; CTA, computed tomography angiography; DSA, digital subtraction angiography.

Treatment should also be tailored to the site of bleeding. In haemodynamically stable patients with intraluminal (gastrointestinal) bleeding—presenting as haematemesis, melaena, or blood via the nasogastric tube—upper gastrointestinal endoscopy should generally precede CTA or angiography, because it permits direct identification and endoscopic haemostasis of anastomotic bleeding (for example, from the gastrojejunostomy, hepaticojejunostomy, or pancreaticojejunostomy) or stress ulceration. By contrast, CTA or DSA should be the first-line investigation when the bleeding is extraluminal (sanguineous drain output), when the patient is haemodynamically unstable, when a sentinel bleed raises suspicion of a pseudoaneurysm or arterial stump rupture, or when endoscopy has been negative or cannot be completed; these situations point to an arterial source requiring angiographic localization and endovascular or surgical control. Distinguishing intraluminal anastomotic bleeding from suspected arterial or pseudoaneurysmal bleeding in this way avoids unnecessary delay in definitive treatment. Of note, the evidence for interventional and surgical management of PPH derives predominantly from open or mixed pancreatic resection cohorts, because LPD-specific treatment series remain limited; the underlying haemostatic principles are nevertheless directly applicable to bleeding after LPD.

6.1. Conservative Treatment

Conservative management is appropriate for haemodynamically stable patients with minimal blood loss (ISGPS grade A) and no evidence of active arterial bleeding [11]. Key measures comprise continuous cardiac monitoring; nil by mouth; fluid resuscitation and transfusion to correct hypovolaemia; correction of coagulopathy with fresh frozen plasma, platelets, fibrinogen concentrate, or prothrombin complex concentrate; gastric mucosal protection with proton-pump inhibitors; somatostatin or its analogs to suppress pancreatic secretion and thereby limit enzymatic erosion of adjacent vessels; and hemostatic agents and antimicrobial therapy where indicated [84] [85]. Somatostatin-like drugs have a dual effect in these patients: on the one hand, they reduce corrosion of the vascular stumps by inhibiting pancreatic secretion; on the other hand, their pharmacological properties—which constrict visceral blood vessels and reduce visceral blood flow—theoretically also help reduce bleeding volume, although this effect is primarily based on studies of portal hypertension and variceal bleeding [86]. Many patients with grade A PPH resolve with conservative management alone. Close observation is nonetheless essential: a progressive fall in haemoglobin, increasing sanguineous drain output, haemodynamic instability, or rising transfusion requirement should raise suspicion of active arterial bleeding and prompt escalation to endovascular or surgical treatment.

6.2. Interventional Treatment

Endovascular therapy is the principal treatment for moderate-to-severe PPH in patients who are haemodynamically stable or have been stabilized by resuscitation, and is indicated for arterial bleeding, ruptured pseudoaneurysm, and failure of conservative management. DSA permits simultaneous localization and treatment of the bleeding source. Fang *et al.* [26] reported a diagnostic yield of 66.7% for DSA in PPH, with successful haemostasis by transarterial embolization (TAE) in 87.5% (14/16) of cases. In a multicentre cohort of 4062 pancreatic resections, Gao *et al.* [25] found that early haemorrhage after pancreatoduodenectomy arose most often from branches of the common hepatic and superior mesenteric arteries; endovascular embolization permitted rapid localisation and selective occlusion, with significant reductions in ICU admission and postoperative mortality. In a nine-year series of 76 postoperative pseudoaneurysms, Liu *et al.* [83] found that these arose most frequently from the common hepatic artery and its branches (32.9%) and the superior mesenteric artery and its branches (28.9%), followed by the GDA and its branches (15.8%); technical and clinical success were both achieved in 100% of cases, although the small single-center sample limits generalisability. Pottier *et al.* [27] employed endovascular therapy as first-line treatment for delayed PPH in 69 patients. Technical success at the initial procedure was 70%, and re-bleeding occurred in 43%; with repeated intervention, 74% were ultimately managed by endovascular means alone, while 26% required surgery. For patients with negative angiography, Guan *et al.* [28] suggested that empirical embolization of high-risk feeding vessels—the GDA stump, hepatic artery, left gastric artery, splenic artery, and dorsal pancreatic artery—may be preferable to conservative management in reducing re-bleeding. Ono *et al.* [87] reported successful percutaneous transhepatic coil embolization and covered stent placement for extrahepatic portal venous bleeding after pancreatic surgery, extending minimally invasive options to the portal system.

Endovascular therapy has become the first-line treatment for haemodynamically stable patients with moderate-to-severe PPH, with reported technical success rates of 70% - 100%. Compared with surgery, it is less invasive, more selective, and associated with faster recovery. Covered stents achieve haemostasis while preserving flow in critical arteries, whereas superselective embolization of peripheral branches limits the risk of organ ischemia. Selected cases of portal venous haemorrhage may likewise be managed by percutaneous puncture with coils or covered stents [87]. When angiography is negative, however, the choice between empirical embolization and conservative management remains unresolved. Guan *et al.* [28] found that empirical embolization may reduce re-bleeding, at the cost of ischaemic complications—hepatic, biliary, or gastrointestinal ischemia and splenic infarction. Conservative management avoids procedural risk but may delay definitive treatment of occult haemorrhage. The decision must therefore take account of the rate of bleeding, the presence of infection, and the adequacy of collateral circulation. Long-term complications of endovascular therapy—stent infection, in-stent thrombosis, and restenosis—also remain incompletely characterized.

6.3. Surgical Intervention

Surgery is indicated for persistent massive haemorrhage, haemodynamic instability (ISGPS grade C), or failure of conservative and endovascular treatment [84] [85] [88]. The objectives are rapid haemostasis, debridement of infected and necrotic tissue, control of associated pancreatic or biliary fistula, and prevention of re-bleeding. Exploration should be systematic: the operative field is first fully exposed, the bleeding source identified, and the responsible vessel suture-ligated, with vascular clips applied as an additional safeguard where necessary [23] [89] [90].

Where haemorrhage is complicated by pancreatic or biliary fistula and peritoneal infection, marked local inflammation and edema obscure the tissue planes, and the bleeding source may be difficult to identify at exploration. Evacuation of intraperitoneal blood and clot should be performed first. Exploration should then proceed from superficial to deep and from distal to proximal, so progressively exposing the suspected source and avoiding iatrogenic vascular or bowel injury from blind dissection. Once blood has been evacuated, the field should be irrigated copiously with normal saline and necrotic tissue around the anastomoses should be removed. Where adhesions are dense, the field is deep, or anatomical planes are indistinct, adjunctive measures include local compression, ligation, packing, tissue coverage, and intraoperative ultrasound. When slow bleeding cannot be localized despite thorough exploration, haemostasis may be achieved by mass suture of the affected area together with adjacent healthy tissue, and suspected sources should be ligated with non-absorbable suture (for example, polypropylene). Zhang *et al.* [48] reported that re-operation after LPD was performed predominantly for haemorrhage and pancreatic fistula, underlining the need to address fistula and intra-abdominal infection during the same procedure. Exposed vascular stumps should be covered with autologous tissue—the ligamentum teres hepatis, falciform ligament, or greater omentum—to reduce the risk of re-bleeding [77]-[80]. Attention should also be given to revision of the pancreaticojejunal anastomosis and to optimizing drainage, using techniques such as a modified anastomosis, pancreatic duct stenting, and retro-anastomotic drainage, so as to reduce the risk of recurrent fistula and secondary haemorrhage [71]-[75] [91].

In summary, surgery is the definitive recourse within the graded management of PPH, and its principal value lies in addressing haemorrhage, infection, and fistula at a single procedure. The optimal timing of re-operation remains undefined: early surgery may be technically more difficult and carry a higher risk of re-bleeding because of inflammation and oedema, whereas delay risks irreversible haemorrhagic shock and multi-organ failure. Current evidence favours early exploration after adequate resuscitation, although the decision should be taken by a multidisciplinary team, weighing the rate of bleeding, the patient's physiological reserve, and the interval since failure of endovascular treatment.

Management of haemorrhage after LPD should therefore proceed stepwise: assessment of haemodynamic status, characterisation of the bleeding, and selection of conservative, endovascular, or operative treatment accordingly (**Figure 2**).

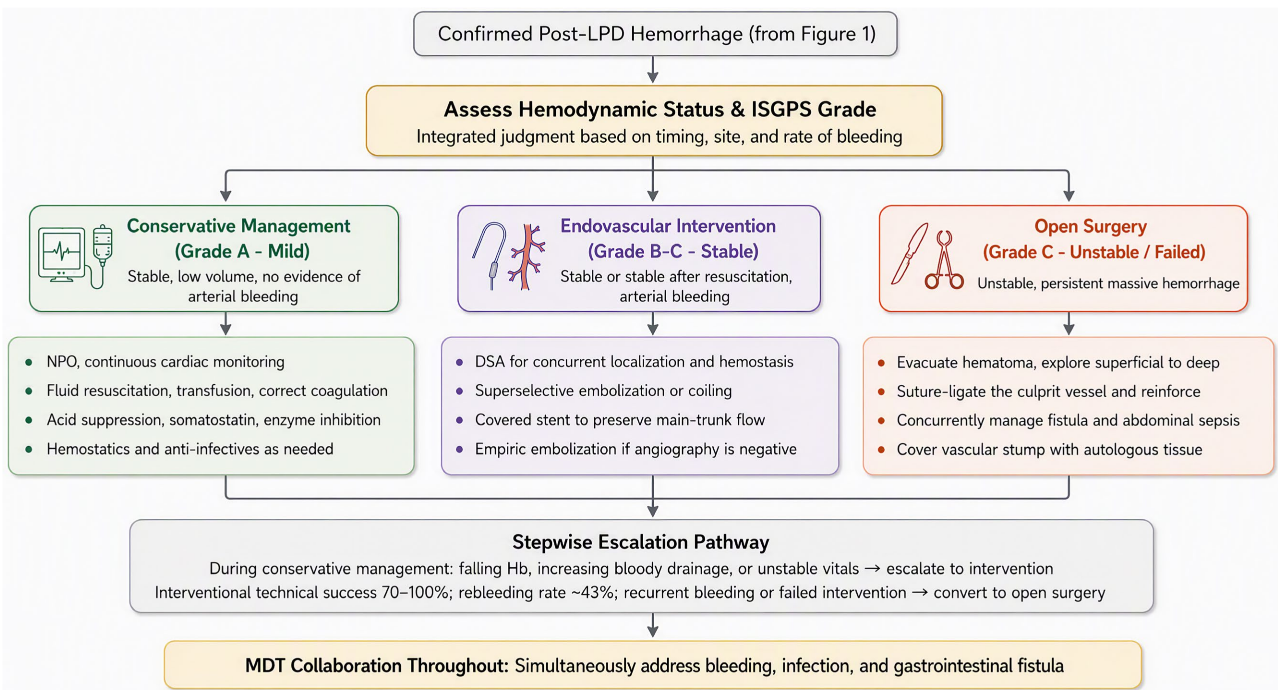

Figure 2. Flowchart for the treatment of postoperative bleeding following laparoscopic pancreaticoduodenectomy. Abbreviations: LPD, laparoscopic pancreaticoduodenectomy; PPH, post-pancreatectomy hemorrhage; ISGPS, International Study Group of Pancreatic Surgery; Hb, hemoglobin; DSA, digital subtraction angiography; MDT, multidisciplinary team.

7. Future Prospects

Management of haemorrhage after LPD is largely reactive at present; the field is likely to shift towards earlier prediction and more targeted intervention. First, risk prediction models that draw on large clinical datasets, radiomics, and machine learning may allow high-risk patients before major haemorrhage occurs. Second, diagnostic and therapeutic pathways following a sentinel bleed require standardization, with explicit indications for CTA, DSA, and pre-emptive embolization. Third, endovascular technique may be refined further, including superselective embolization, covered stent materials, empirical embolization for angiographically negative bleeding, and minimally invasive management of portal venous haemorrhage. Novel topical haemostatic agents, enzyme-resistant vascular wrapping materials, biodegradable covered stents, and robot-assisted re-operation also merit investigation. With continued development of multidisciplinary pathways, the management of PPH should evolve from reactive haemostasis towards an integrated strategy of risk prediction, early detection, targeted intervention, and prevention of recurrence.

8. Conclusion

Haemorrhage after LPD is a serious complication that significantly affects outcome, and its pathogenesis spans the preoperative, intraoperative, and postoperative periods. As noted above, PPH occurs in 1% - 8% of patients, with a mortality of 11% - 38%. Contributing factors include preoperative hyperbilirubinaemia, advanced age, hypertension, high ASA class, and elevated BMI; substantial intraoperative blood loss and transfusion, a soft pancreatic parenchyma (with correspondingly reduced suture-holding capacity), and a main pancreatic duct ≤ 3 mm; and postoperative pancreatic fistula and intra-abdominal infection. Among these, the sequence pancreatic fistula → intra-abdominal infection → vascular erosion → pseudoaneurysm → delayed haemorrhage is of greatest clinical importance. Prevention should span the whole perioperative period: preoperatively, individualized biliary drainage according to jaundice severity, cholangitis, anticipated surgical delay, and local expertise (with study-specific thresholds and targets), blood pressure control, correction of coagulopathy, and nutritional support; intraoperatively, meticulous dissection, thorough haemostasis, an optimised pancreaticojejunal anastomosis (for example, a modified Chen's or duct-to-mucosa technique), and vascular protection by wrapping with the ligamentum teres hepatis or the falciform ligament; and postoperatively, close monitoring of vital signs, drain output, and emerging predictive biomarkers to identify a sentinel bleed. Treatment should be stratified by severity and haemodynamic status, with conservative, endovascular, or operative management selected accordingly; DSA with TAE, which achieves success rates of 70% - 100%, is the first-line option for haemodynamically stable patients. Refined risk prediction (for example, nomograms), improved endovascular technique, and better-defined multidisciplinary pathways should together reduce both the incidence and the mortality of PPH.

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Author Contributions

Kaiming Zhang: Conceptualization, Investigation, Visualization, Writing—original draft; Yanliang Yang: Investigation, Writing—review & editing; Hongping Zuo: Writing—review & editing; Zichen Yang: Validation; Haofeng Lu: Conceptualization, Funding acquisition, Project administration, Supervision, Writing—review & editing. All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Gagner, M. and Pomp, A. (1994) Laparoscopic Pylorus-Preserving Pancreatoduodenectomy. *Surgical Endoscopy*, **8**, 408-410. https://doi.org/10.1007/bf00642443

[2] Wang, X., Cai, Y., Jiang, J. and Peng, B. (2020) Laparoscopic Pancreaticoduodenectomy: Outcomes and Experience of 550 Patients in a Single Institution. *Annals of Surgical Oncology*, **27**, 4562-4573. https://doi.org/10.1245/s10434-020-08533-3

[3] Song, X., Ma, Y., Shi, H. and Liu, Y. (2023) Application of Clavien-Dindo Classification-Grade in Evaluating Overall Efficacy of Laparoscopic Pancreaticoduodenectomy. *Frontiers in Surgery*, **10**, Article ID: 1043329. https://doi.org/10.3389/fsurg.2023.1043329

[4] Li, L., Bo, Z., Liu, Q., Wang, G., Zhang, W. and Liang, Q. (2023) Comparative Analysis of Clinical Efficacy between Laparoscopic and Open Pancreaticoduodenectomy. *Medicine*, **102**, e33588. https://doi.org/10.1097/md.0000000000033588

[5] Wang, M., Pan, S., Qin, T., Xu, X., Huang, X., Liu, J., *et al.* (2023) Short-Term Outcomes Following Laparoscopic vs Open Pancreaticoduodenectomy in Patients with Pancreatic Ductal Adenocarcinoma: A Randomized Clinical Trial. *JAMA Surgery*, **158**, 1245-1253. https://doi.org/10.1001/jamasurg.2023.5210

[6] Palanivelu, C., Senthilnathan, P., Sabnis, S.C., Babu, N.S., Srivatsan Gurumurthy, S., Anand Vijai, N., *et al.* (2017) Randomized Clinical Trial of Laparoscopic *versus* Open Pancreatoduodenectomy for Periampullary Tumours. *British Journal of Surgery*, **104**, 1443-1450. https://doi.org/10.1002/bjs.10662

[7] Qin, R., Kendrick, M.L., Wolfgang, C.L., Edil, B.H., Palanivelu, C., Parks, R.W., *et al.* (2020) International Expert Consensus on Laparoscopic Pancreaticoduodenectomy. *Hepatobiliary Surgery and Nutrition*, **9**, 464-483. https://doi.org/10.21037/hbsn-20-446

[8] Fall, S., Souche, R., Bardol, T., Fabre, J. and Borie, F. (2025) Laparoscopic versus Open Pancreaticoduodenectomy for Pancreatic or Periampullary Tumors: A Multicenter Propensity Score-Matched Comparative Study. *Surgical Endoscopy*, **39**, 3037-3048. https://doi.org/10.1007/s00464-025-11677-6

[9] Zhang, B., Xu, Z., Gu, W., Zhou, J., Tang, N., Zhang, S., *et al.* (2023) Postoperative Complications and Short-Term Prognosis of Laparoscopic Pancreaticoduodenectomy vs. Open Pancreaticoduodenectomy for Treating Pancreatic Ductal Adenocarcinoma: A Retrospective Cohort Study. *World Journal of Surgical Oncology*, **21**, Article No. 26. https://doi.org/10.1186/s12957-023-02909-x

[10] Zhang, L., Sun, D., Zhang, Y., Gao, F. and Guo, Y. (2020) Natural Orifice Specimen Extraction Surgery in Laparoscopic Pancreaticoduodenectomy: A Single-Center Case Series. *International Journal of Surgery*, **82**, 95-99. https://doi.org/10.1016/j.ijsu.2020.07.043

[11] Wente, M.N., Veit, J.A., Bassi, C., Dervenis, C., Fingerhut, A., Gouma, D.J., *et al.* (2007) Postpancreatectomy Hemorrhage (PPH)—An International Study Group of Pancreatic Surgery (ISGPS) Definition. *Surgery*, **142**, 20-25. https://doi.org/10.1016/j.surg.2007.02.001

[12] Zhang, J., Chen, F., Tang, G., Chen, R. and Zhou, R. (2025) Minimally Invasive versus Open Pancreaticoduodenectomy for Periampullary Tumors: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Surgical Endoscopy*, **39**, 7666-7679. https://doi.org/10.1007/s00464-025-12163-9

[13] Ricci, C., D'Ambra, V., Alberici, L., Ingaldi, C., Minghetti, M., Bonini, G., *et al.* (2025) Minimal Invasive Pancreatoduodenectomy: A Comprehensive Systematic Review and Metanalysis of Randomized Controlled Clinical Trials. *Annals of Surgical Oncology*, **32**, 3614-3622. https://doi.org/10.1245/s10434-025-16990-x

[14] Barrera Gutierrez, J.C., Vivian, E., Shah, J. and Mejia, A. (2025) Mortality and Complications in Patients with Obesity after Open, Robotic or Laparoscopic Pancreaticoduodenectomy: A Systematic Review and Meta-Analysis. *International Journal of Obesity*, **49**, 1921-1928. https://doi.org/10.1038/s41366-025-01844-z

[15] Abu Hilal, M., van Ramshorst, T.M.E., Boggi, U., Dokmak, S., Edwin, B., Keck, T., *et al.* (2024) The Brescia Internationally Validated European Guidelines on Minimally Invasive Pancreatic Surgery (EGU-MIPS). *Annals of Surgery*, **279**, 45-57. https://doi.org/10.1097/sla.0000000000006006

[16] Barreto, S.G., Strobel, O., Salvia, R., Marchegiani, G., Wolfgang, C.L., Werner, J., *et al.* (2025) Complexity and Experience Grading to Guide Patient Selection for Minimally Invasive Pancreatoduodenectomy: An International Study Group for Pancreatic Surgery (ISGPS) Consensus. *Annals of Surgery*, **281**, 417-429. https://doi.org/10.1097/sla.0000000000006454

[17] Montorsi, R.M., Zonderhuis, B.M., Daams, F., Busch, O.R., Kazemier, G., Marchegiani, G., *et al.* (2024) Treatment Strategies to Prevent or Mitigate the Outcome of Postpancreatectomy Hemorrhage: A Review of Randomized Trials. *International Journal of Surgery* (*London*, *England*), **110**, 6145-6154. https://doi.org/10.1097/js9.0000000000000876

[18] Chan, K.S., Wang, Z.K., Syn, N. and Goh, B.K.P. (2021) Learning Curve of Laparoscopic and Robotic Pancreas Resections: A Systematic Review. *Surgery*, **170**, 194-206. https://doi.org/10.1016/j.surg.2020.11.046

[19] Correa-Gallego, C., Brennan, M.F., D'Angelica, M.I., DeMatteo, R.P., Fong, Y., Kingham, P.T., *et al.* (2012) Contemporary Experience with Postpancreatectomy Hemorrhage: Results of 1,122 Patients Resected between 2006 and 2011. *Journal of the*

American College of Surgeons, **215**, 616-621.
https://doi.org/10.1016/j.jamcollsurg.2012.07.010

[20] Darnis, B., Lebeau, R., Chopin-Laly, X. and Adham, M. (2013) Postpancreatectomy Hemorrhage (PPH): Predictors and Management from a Prospective Database. *Langenbeck's Archives of Surgery*, **398**, 441-448.
https://doi.org/10.1007/s00423-013-1047-8

[21] Grützmann, R., Rückert, F., Hippe-Davies, N., Distler, M. and Saeger, H. (2012) Evaluation of the International Study Group of Pancreatic Surgery Definition of Post-Pancreatectomy Hemorrhage in a High-Volume Center. *Surgery*, **151**, 612-620.
https://doi.org/10.1016/j.surg.2011.09.039

[22] Lu, J.W., Ding, H.F., Wu, X.N., *et al.* (2018) Intra-Abdominal Hemorrhage Following 739 Consecutive Pancreaticoduodenectomy: Risk Factors and Treatments. *Journal of Gastroenterology and Hepatology*, **34**, 1100-1107. https://doi.org/10.1111/jgh.14560

[23] Khoo, C.Y., Tan, H.L., Tan, T.Q.W., Yeo, D.B.X., Koh, Y.X., Teo, J.Y., *et al.* (2025) Critical Appraisal of Postpancreatectomy Hemorrhage after Pancreatoduodenectomy: An Analysis of Risk Factors, Treatment and Outcomes in 860 Consecutive Cases. *Pancreatology*, **25**, 743-751. https://doi.org/10.1016/j.pan.2025.05.015

[24] Liu, Z.J., Hong, J.Y., Zhang, C., She, J. and Zhai, H.H. (2025) Gastrointestinal Bleeding after Pancreatoduodenectomy: Report of Four Cases. *World Journal of Gastrointestinal Surgery*, **17**, Article ID: 100119. https://doi.org/10.4240/wjgs.v17.i1.100119

[25] Gao, Y., Wang, Y.Z., Dai, Y.R., Zhang, K., Yan, H., Lu, Z.P., *et al.* (2025) Early Postpancreatectomy Hemorrhage: Is an Update of the ISGPS Definition Required? *Langenbeck's Archives of Surgery*, **411**, Article No. 1.
https://doi.org/10.1007/s00423-025-03896-1

[26] Fang, Y., Han, X., Liu, L. and Lou, W. (2018) Diagnosis and Treatment Efficacy of Digital Subtraction Angiography and Transcatheter Arterial Embolization in Post-Pancreatectomy Hemorrhage: A Single Center Retrospective Cohort Study. *International Journal of Surgery*, **51**, 223-228. https://doi.org/10.1016/j.ijsu.2018.01.045

[27] Pottier, E., Ronot, M., Gaujoux, S., Cesaretti, M., Barbier, L., Sauvanet, A., *et al.* (2016) Endovascular Management of Delayed Post-Pancreatectomy Haemorrhage. *European Radiology*, **26**, 3456-3465. https://doi.org/10.1007/s00330-016-4213-x

[28] Guan, Y., Zhang, J.L., Li, X.H. and Wang, M.Q. (2021) Postpancreatectomy Hemorrhage with Negative Angiographic Findings: Outcomes of Empiric Embolization Compared to Conservative Management. *Clinical Imaging*, **73**, 119-123.
https://doi.org/10.1016/j.clinimag.2020.12.009

[29] Harnoss, J.C., Ulrich, A.B., Harnoss, J.M., Diener, M.K., Büchler, M.W. and Welsch, T. (2014) Use and Results of Consensus Definitions in Pancreatic Surgery: A Systematic Review. *Surgery*, **155**, 47-57. https://doi.org/10.1016/j.surg.2013.05.035

[30] Brodsky, J.T. and Turnbull, A.D. (1991) Arterial Hemorrhage after Pancreatoduodenectomy. The "Sentinel Bleed". *Archives of Surgery* (*Chicago*, *Ill.*: 1960), **126**, 1037-1040. https://doi.org/10.1001/archsurg.1991.01410320127019

[31] Rystedt, J., Tingstedt, B., Ansorge, C., Nilsson, J. and Andersson, B. (2019) Major Intraoperative Bleeding during Pancreatoduodenectomy—Preoperative Biliary Drainage Is the Only Modifiable Risk Factor. *HPB*, **21**, 268-274.
https://doi.org/10.1016/j.hpb.2018.07.024

[32] Uggeri, F., Nespoli, L., Sandini, M., Andreano, A., Degrate, L., Romano, F., *et al.* (2019) Analysis of Risk Factors for Hemorrhage and Related Outcome after Pancreatoduodenectomy in an Intermediate-Volume Center. *Updates in Surgery*, **71**, 659-

667. https://doi.org/10.1007/s13304-019-00673-w

[33] Meng, C., Li, X., Wu, D., Wang, R., Zhou, Y., Tian, Y., *et al.* (2026) Impact of Obstructive Jaundice Severity and Preoperative Biliary Drainage on Laparoscopic Pancreaticoduodenectomy: A Bicentric Retrospective Cohort Analysis of 879 Cases. *Surgical Endoscopy*, **40**, 3012-3021. https://doi.org/10.1007/s00464-026-12570-6

[34] Wang, S., Li, D., Du, C., Yang, X. and Haitao, L. (2025) Development and Validation of a Nomogram for Predicting Postoperative Intraluminal Hemorrhage in Patients Undergoing Laparoscopic Pancreaticoduodenectomy. *Frontiers in Surgery*, **12**, Article ID: 1507434. https://doi.org/10.3389/fsurg.2025.1507434

[35] Lin, Y.M., Yu, C. and Xian, G.Z. (2025) Retrospective Analysis of Delta Hemoglobin and Bleeding-Related Risk Factors in Pancreaticoduodenectomy. *World Journal of Gastrointestinal Surgery*, **17**, Article ID: 100999. https://doi.org/10.4240/wjgs.v17.i3.100999

[36] Aoki, S., Miyata, H., Konno, H., Gotoh, M., Motoi, F., Kumamaru, H., *et al.* (2017) Risk Factors of Serious Postoperative Complications after Pancreaticoduodenectomy and Risk Calculators for Predicting Postoperative Complications: A Nationwide Study of 17,564 Patients in Japan. *Journal of Hepato-Biliary-Pancreatic Sciences*, **24**, 243-251. https://doi.org/10.1002/jhbp.438

[37] Alfaro-Lara, V., Muñoz-Hernández, R., Giménez-Miranda, L., Beltrán-Romero, L., Castell-Montsalve, F.J. and Stiefel, P. (2022) Pancreas Fat Content, Insulin Homeostasis and Circulating Endothelial Microparticles in Male Essential Hypertensive Patients. *The Journal of Clinical Hypertension* (*Greenwich*, *Conn.*), **25**, 38-46. https://doi.org/10.1111/jch.14600

[38] Xu, H., Meng, Q., Hua, J. and Wang, W. (2024) Identifying the Risk Factors for Pancreatic Fistula after Laparoscopic Pancreaticoduodenectomy in Patients with Pancreatic Cancer. *World Journal of Gastrointestinal Surgery*, **16**, 1609-1617. https://doi.org/10.4240/wjgs.v16.i6.1609

[39] Gill, R. and Goldstein, S. (2023) Evaluation and Management of Perioperative Hypertension. StatPearls Publishing.

[40] Foley, C., Kendall, M.C., Apruzzese, P. and De Oliveira, G.S. (2021) American Society of Anesthesiologists Physical Status Classification as a Reliable Predictor of Postoperative Medical Complications and Mortality Following Ambulatory Surgery: An Analysis of 2,089,830 ACS-NSQIP Outpatient Cases. *BMC Surgery*, **21**, Article No. 253. https://doi.org/10.1186/s12893-021-01256-6

[41] Duan, Y., Du, Y., Mu, Y., Guan, X., He, J., Zhang, J., *et al.* (2025) Development and Validation of a Novel Predictive Model for Postpancreatectomy Hemorrhage Using Lasso-Logistic Regression: An International Multicenter Observational Study of 9631 Pancreatectomy Patients. *International Journal of Surgery* (*London*, *England*), **111**, 791-806. https://doi.org/10.1097/js9.0000000000001883

[42] (2000) Obesity: Preventing and Managing the Global Epidemic. Report of a WHO Consultation. World Health Organization Technical Report Series, 894, i-253.

[43] National Health Commission of the People's Republic of China (2024) Guidelines for the Diagnosis and Treatment of Obesity (2024 Edition). NHC. (In Chinese)

[44] Kanani, F., Messer, N., Cohen, B., Falk, E., Goykhman, Y. and lubezky, N. (2025) Impact of Preoperative Biliary Drainage on Outcomes of Pancreaticoduodenectomy in Severe Hyperbilirubinemia. *Surgical Endoscopy*, **39**, 6504-6513. https://doi.org/10.1007/s00464-025-12027-2

[45] Chu, X., Tong, K., Liu, K., Wu, H., Li, H., Liu, J., *et al.* (2025) A Retrospective Study

to Determine the Preoperative Bilirubin Level for Conducting Preoperative Biliary Drainage to Reduce Pancreaticoduodenectomy Complications. *International Journal of General Medicine*, **18**, 6769-6781. https://doi.org/10.2147/ijgm.s546424

[46] Zhu, L., Yang, Y., Cheng, H., Cai, Z., Tang, N., Mao, L., *et al.* (2023) The Role of Preoperative Biliary Drainage on Postoperative Outcome after Pancreaticoduodenectomy in Patients with Obstructive Jaundice. *Gland Surgery*, **12**, 593-608. https://doi.org/10.21037/gs-22-648

[47] Belyaev, O., Rosenkranz, S., Munding, J., Herzog, T., Chromik, A.M., Tannapfel, A., *et al.* (2013) Quantitative Assessment and Determinants of Suture-Holding Capacity of Human Pancreas. *Journal of Surgical Research*, **184**, 807-812. https://doi.org/10.1016/j.jss.2013.04.017

[48] Zhang, S., Yadav, D.K., Wang, G., Jiang, Y., Zhang, J., Yadav, R.K., *et al.* (2024) Causes and Predictors of Unplanned Reoperations within 30 Days Post Laparoscopic Pancreaticoduodenectomy: A Comprehensive Analysis. *Frontiers in Oncology*, **14**, Article ID: 1464450. https://doi.org/10.3389/fonc.2024.1464450

[49] Wu, J., Zhang, G., Yao, X., Xiang, Y., Lin, R., Yang, Y., *et al.* (2020) Achilles' Heel of Laparoscopic Pancreatectomy: Reconstruction of the Remnant Pancreas. *Expert Review of Gastroenterology & Hepatology*, **14**, 527-537. https://doi.org/10.1080/17474124.2020.1775582

[50] Seykora, T.F., Ecker, B.L., McMillan, M.T., Maggino, L., Beane, J.D., Fong, Z.V., *et al.* (2019) The Beneficial Effects of Minimizing Blood Loss in Pancreatoduodenectomy. *Annals of Surgery*, **270**, 147-157. https://doi.org/10.1097/sla.0000000000002714

[51] Chipaila, J., Kato, H., Iizawa, Y., Motonori, N., Noguchi, D., Gyoten, K., *et al.* (2020) Prolonged Operating Time Is a Significant Perioperative Risk Factor for Arterial Pseudoaneurysm Formation and Patient Death Following Hemorrhage after Pancreaticoduodenectomy. *Pancreatology*, **20**, 1540-1549. https://doi.org/10.1016/j.pan.2020.08.021

[52] Cioltean, C.L., Bartoş, A., Muntean, L., Brânzilă, S., Iancu, I., Pojoga, C., *et al.* (2024) The Learning Curve for Pancreaticoduodenectomy: The Experience of a Single Surgeon. *Life* (*Basel*, *Switzerland*), **14**, Article No. 549. https://doi.org/10.3390/life14050549

[53] Kim, H., Choi, H.Z., Kang, B.M. and Lee, J.W. (2022) Learning Curve in Laparoscopic Pancreaticoduodenectomy: Using Risk-Adjusted Cumulative Summation Methods. *Journal of Laparoendoscopic & Advanced Surgical Techniques*, **32**, 401-407. https://doi.org/10.1089/lap.2021.0260

[54] Dang, C., Wang, M., Zhu, F., Qin, T. and Qin, R. (2021) Comparison of Laparoscopic and Open Pancreaticoduodenectomy for the Treatment of Nonpancreatic Periampullary Adenocarcinomas: A Propensity Score Matching Analysis. *The American Journal of Surgery*, **222**, 377-382. https://doi.org/10.1016/j.amjsurg.2020.12.023

[55] Qiu, H., Zhang, L., Wang, D., Miao, H. and Zhang, Y. (2023) Comparisons of Short-Term and Long-Term Results between Laparoscopic between Open Pancreaticoduodenectomy for Pancreatic Tumors: A Systematic Review and Meta-Analysis. *Frontiers in Genetics*, **13**, Article ID: 1072229. https://doi.org/10.3389/fgene.2022.1072229

[56] Coppola, A., Cammarata, R., La Vaccara, V., Farolfi, T. and Caputo, D. (2022) New Frontiers of Early Diagnosis of Pancreatic Fistula after Pancreaticoduodenectomy. *Journal of Clinical Medicine*, **11**, Article No. 6423. https://doi.org/10.3390/jcm11216423

[57] Ansari, D., Tingstedt, B., Lindell, G., Keussen, I., Ansari, D. and Andersson, R. (2017) Hemorrhage after Major Pancreatic Resection: Incidence, Risk Factors, Management,

and Outcome. *Scandinavian Journal of Surgery*, **106**, 47-53. https://doi.org/10.1177/1457496916631854

[58] Herzog, T., Skrobisch, M., Abdelsamad, A., Uhl, W., Belyaev, O., Aghalarov, I., *et al.* (2026) Hepaticojejunostomy Insufficiency-Associated Arterial Hemorrhage in Patients after Pancreatic Surgery. *Journal of Clinical Medicine*, **15**, Article No. 2900. https://doi.org/10.3390/jcm15082900

[59] Li, X., Qin, T., Zhu, F., Wang, M., Dang, C., He, L., *et al.* (2021) Clinical Efficacy of the Preservation of the Hepatic Branch of the Vagus Nerve on Delayed Gastric Emptying after Laparoscopic Pancreaticoduodenectomy. *Journal of Gastrointestinal Surgery*, **25**, 2172-2183. https://doi.org/10.1007/s11605-021-05024-y

[60] Study Group of Biliary Tract Surgery in Chinese Society of Surgery of Chinese Medical Association, Hepatobiliary Committee of Bethune Charitable Foundation and Editorial Board of Chinese Journal of Surgery (2021) Expert Consensus on Enhanced Recovery Concept for the Application of Standardized Management on Obstructive Jaundice. *Chinese Journal of Surgery*, **59**, 241-248.

[61] Cao, H., Li, T., Li, Z., Zhao, B., Liu, Z. and Wang, W. (2024) Goal-Oriented Preoperative Biliary Drainage Is More Precise and Conducive to Seize the Opportunity for Pancreaticoduodenectomy. *World Journal of Surgical Oncology*, **22**, Article No. 331. https://doi.org/10.1186/s12957-024-03615-y

[62] Chrysikos, D., Taprantzis, N., Delis, S., Shihada, A., Samolis, A. and Troupis, T. (2026) Robotic Pancreaticoduodenectomy in Elderly vs. Younger Patients: Systematic Review with Meta-Analysis. *Journal of Clinical Medicine*, **15**, Article No. 2744. https://doi.org/10.3390/jcm15072744

[63] Wang, T., Qiu, Y., Luo, Y., Wei, R., Xu, L., Huang, J., *et al.* (2025) Analysis of Outcomes in Pancreaticoduodenectomy for Elderly Patients Aged 80 and Above: A Retrospective Study Using Inverse Probability of Treatment Weighting. *Aging Medicine* (*Milton* (*N.S.W*)), **8**, 447-457. https://doi.org/10.1002/agm2.70048

[64] Xu, J.Y., Tian, X.D., Yang, Y.M., Song, J.H. and Wei, J.M. (2022) Preoperative Anemia Is a Predictor of Worse Postoperative Outcomes Following Open Pancreatoduodenectomy: A Propensity Score-Based Analysis. *Frontiers in Medicine*, **9**, Article ID: 818805. https://doi.org/10.3389/fmed.2022.818805

[65] Kuiper, B.I., Janssen, L.M.J., Versteeg, K.S., ten Tusscher, B.L., van der Spoel, J.I., Lubbers, W.D., *et al.* (2024) Does Preoperative Multidisciplinary Team Assessment of High-Risk Patients Improve the Safety and Outcomes of Patients Undergoing Surgery? *BMC Anesthesiology*, **24**, Article No. 9. https://doi.org/10.1186/s12871-023-02394-5

[66] Zhang, Y.X., Yang, Y.F., Han, P., Ye, P.C. and Kong, H. (2022) Protein-Energy Malnutrition Worsens Hospitalization Outcomes of Patients with Pancreatic Cancer Undergoing Open Pancreaticoduodenectomy. *Updates in Surgery*, **74**, 1627-1636. https://doi.org/10.1007/s13304-022-01293-7

[67] Chen, Y.X., Du, L., Wang, L.N., Shi, Y.Y., Liao, M., Zhong, M., *et al.* (2022) Effects of Dexmedetomidine on Systemic Inflammation and Postoperative Complications in Laparoscopic Pancreaticoduodenectomy: A Double-Blind Randomized Controlled Trial. *World Journal of Surgery*, **47**, 500-509. https://doi.org/10.1007/s00268-022-06802-8

[68] Wang, C., Zhao, X. and You, S. (2017) Efficacy of the Prophylactic Use of Octreotide for the Prevention of Complications after Pancreatic Resection: An Updated Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Medicine*, **96**, e7500. https://doi.org/10.1097/md.0000000000007500

[69] Zhu, Y., Yu, J., Li, X., Wang, H., Sun, H., Chen, Y., *et al.* (2025) Efficacy of Chen's Pancreaticojejunostomy for Patients with Soft Pancreatic Texture and Small Main Pancreatic Duct in Laparoscopic Pancreaticoduodenectomy. *BMC Surgery*, **25**, Article No. 248. https://doi.org/10.1186/s12893-025-02984-9

[70] Zhao, A., Zhu, Q., Qin, X., Wang, K., Tan, K., Liu, Z., *et al.* (2023) A Duct-to-Mucosa Pancreaticojejunostomy for Small Main Pancreatic Duct and Soft Pancreas in Minimally Invasive Pancreaticoduodenectomy. *Surgical Endoscopy*, **37**, 3567-3579. https://doi.org/10.1007/s00464-022-09830-6

[71] Li, D., Du, C., Zhao, W., Li, S., Lv, H. and Wang, W. (2023) Application of Single-Layer Continuous Duct-To-Mucosa Pancreaticojejunostomy with Two Figure-of-Eight Sutures in Total Laparoscopic Pancreaticoduodenectomy. *Langenbeck's Archives of Surgery*, **408**, Article No. 434. https://doi.org/10.1007/s00423-023-03155-1

[72] Tang, W., Qiu, J.G., Li, G.Z., Zhao, Y.F. and Du, C.Y. (2021) Clinical Application of "Double R" Anastomosis Technique in Laparoscopic Pancreaticoduodenectomy Procedure. *Medicine*, **100**, e26204. https://doi.org/10.1097/md.0000000000026204

[73] Tu, J., Huang, C., Xu, W., Gong, S., Cao, Z., Wan, P., *et al.* (2023) Application of Split Pancreatic Duct Stent in Laparoscopic Pancreaticoduodenectomy. *Medicine*, **102**, e34049. https://doi.org/10.1097/md.0000000000034049

[74] Li, Q., Zhou, X., Duan, J., Xing, Z., Wu, Z., Zhao, W., *et al.* (2022) Decreased Pancreatic Leakage Rate in the Application of a Measurable Variable-Diameter Pancreatic Duct Catheter in Laparoscopic Pancreaticoduodenectomy. *Gland Surgery*, **11**, 1546-1554. https://doi.org/10.21037/gs-22-478

[75] Salman, M.A., Elewa, A., Elsherbiny, M., Tourkey, M., Emechap, E.N., Chikukuza, S., *et al.* (2024) Postoperative Pancreatic Fistula after Pancreaticogastrostomy versus Pancreatojejunostomy after Pancreatic Resection, a Comparative Systematic Review and Meta-Analysis. *World Journal of Surgery*, **48**, 1467-1480. https://doi.org/10.1002/wjs.12173

[76] Tan, Z.J., Zhong, X.S., Qiu, C.J., Yu, Z.M., Chen, G.H., Zhang, S., *et al.* (2025) "Blood Flow Control Techniques" in Laparoscopic Pancreaticoduodenectomy: Strategy and Application. *Chinese Journal of Surgery*, **63**, 1005-1008.

[77] Yu, Z., Wu, X., Zhou, X., Hu, X., Lu, J., Fang, S., *et al.* (2023) Ligamentum Teres Hepatis Wrapping of the Gastroduodenal Artery Stump for Protection in Total Laparoscopic Pancreaticoduodenectomy: A Single-Center Experience. *Journal of International Medical Research*, **51**, No. 8. https://doi.org/10.1177/03000605231188288

[78] Wang, Z., Wang, Y., Zhu, C., Pan, H., Chen, S., Hu, X., *et al.* (2024) Prevention of Postpancreatectomy Hemorrhage after Laparoscopic Pancreaticoduodenectomy by Wrapping Ligamentum Teres Hepatis Surrounding Hepatic Portal Artery. *Scientific Reports*, **14**, Article No. 18332. https://doi.org/10.1038/s41598-024-69292-9

[79] Liu, W., Li, Z., Zhou, C., Ji, S., Xu, W., Shi, Y., *et al.* (2024) A Ligamentum Teres Hepatis and Falciform Ligament 'belt and Braces' Approach in Laparoscopic Pancreaticoduodenectomy Using a Modified Blumgart Anastomosis to Minimize Severe Pancreatic Fistula and Post-Operative Complications. *Surgical Oncology*, **57**, Article ID: 102152. https://doi.org/10.1016/j.suronc.2024.102152

[80] Huang, L., Jiang, B., Lai, J., Wu, D., Chen, J., Tian, Y., *et al.* (2024) Efficacy of the Two-Parts Wrapping Technique in Reducing Postoperative Complications in Laparoscopic Pancreaticoduodenectomy. *Surgical Endoscopy*, **38**, 4731-4744. https://doi.org/10.1007/s00464-024-11028-x

[81] Iba, T., Tanigawa, T., Wada, H., Kondo, K., Ferrer, R. and Levy, J.H. (2026) Recognizing Coagulation Disorders in Sepsis in the Emergency Room: A Narrative Review.

Journal of Clinical Medicine, **15**, Article No. 488.
https://doi.org/10.3390/jcm15020488

[82] Shiozaki, H., Fujioka, S., Takano, Y., Shimazaki, T., Suka, M., Sakamoto, T., *et al.* (2026) The Second-Drop Eosinophil Ratio Is Useful for the Early Detection of Severe Complications after Pancreaticoduodenectomy. *Surgery Today*, **56**, 275-282.
https://doi.org/10.1007/s00595-025-03128-5

[83] Liu, J., Fei, X., Liu, X., Shan, Q., Wang, S., Wu, Z., *et al.* (2025) Endovascular Intervention and Risk Factor Assessment for Postoperative Pseudoaneurysms after Pancreatic Surgery: A 9-Year Retrospective Study. *Quantitative Imaging in Medicine and Surgery*, **15**, 10834-10846. https://doi.org/10.21037/qims-2025-1012

[84] Kobayashi, K., Inoue, Y., Omiya, K., Sato, S., Kato, T., Oba, A., *et al.* (2023) Diagnosis and Management of Postpancreatectomy Hemorrhage: A Single-Center Experience of Consecutive 1,096 Pancreatoduodenectomies. *Pancreatology*, **23**, 235-244.
https://doi.org/10.1016/j.pan.2023.01.004

[85] Wu, X., Chen, G., Wu, W., Zhang, T., Liao, Q., Dai, M., *et al.* (2020) Management of Late Hemorrhage after Pancreatic Surgery: Treatment Strategy and Prognosis. *Journal of International Medical Research*, **48**, No. 6.
https://doi.org/10.1177/0300060520929127

[86] Reynaert, H. and Geerts, A. (2003) Pharmacological Rationale for the Use of Somatostatin and Analogues in Portal Hypertension. *Alimentary Pharmacology & Therapeutics*, **18**, 375-386. https://doi.org/10.1046/j.1365-2036.2003.01657.x

[87] Ono, S., Yamazoe, S., Takigawa, Y. and Hasegawa, H. (2022) Percutaneous Transhepatic Coil and Cover Technique with Small System for the Extrahepatic Portal Vein Hemorrhage after Pancreaticoduodenectomy. *Radiology Case Reports*, **17**, 1246-1250. https://doi.org/10.1016/j.radcr.2022.01.036

[88] Habib, J.R., Gao, S., Young, A.J., Ghabi, E., Ejaz, A., Burns, W., *et al.* (2022) Incidence and Contemporary Management of Delayed Bleeding Following Pancreaticoduodenectomy. *World Journal of Surgery*, **46**, 1161-1171.
https://doi.org/10.1007/s00268-022-06451-x

[89] Preston, W.A., Collins, M.L., Gönen, M., Murtha, T., Rivera, V., Lamm, R., *et al.* (2024) Hemorrhage Sites and Mitigation Strategies after Pancreaticoduodenectomy. *JAMA Surgery*, **159**, 891-899. https://doi.org/10.1001/jamasurg.2024.1228

[90] Goev, A.A., Berelavichus, S.V., Karchakov, S.S. and Galkin, G.V. (2021) Postpancreatectomy Hemorrhage. *Khirurgiya. Zhurnal im. N.I. Pirogova*, **1**, 77-82.
https://doi.org/10.17116/hirurgia202101177

[91] Zhou, Y., Lu, F., Lin, X., Yang, Y., Wang, C., Fang, H., *et al.* (2024) Drainage Posterior to Pancreaticojejunostomy Reduces the Severity of Postoperative Pancreatic Fistula after Pancreaticoduodenectomy. *World Journal of Surgical Oncology*, **22**, Article No. 315. https://doi.org/10.1186/s12957-024-03597-x