Background. Postoperative hemorrhage is one of the most severe complications after pancreatic surgery. Due to the lack of an internationally accepted, universal definition of postpancreatectomy hemorrhage (PPH), the incidences reported in the literature vary considerably, even in reports from randomized controlled trials. Because of these variations in the definition of what constitutes a PPH, the incidences of its occurrence are not comparable.

Methods. The International Study Group of Pancreatic Surgery (ISGPS) developed an objective, generally applicable definition of PPH based on a literature review and consensus clinical experience.

Results. Postpancreatectomy hemorrhage is defined by 3 parameters: onset, location, and severity. The onset is either early (<24 hours after the end of the index operation) or late (>24 hours). The location is either intraluminal or extraluminal. The severity of bleeding may be either mild or severe. Three different grades of PPH (grades A, B, and C) are defined according to the time of onset, site of bleeding, severity, and clinical impact.

Conclusions. An objective, universally accepted definition and clinical grading of PPH is important for the appropriate management and use of interventions in PPH. Such a definition also would allow comparisons of results from future clinical trials. Such standardized definitions are necessary to compare, in a nonpartisan manner, the outcomes of studies and the evaluation of novel operative treatment modalities in pancreatic surgery. (Surgery 2007;142:20-5.)
Perioperative mortality of pancreatic surgery, especially in high-volume centers, has declined markedly in the last 2 decades; it is currently less than 5%. These improved results have been due to technical advances in operative techniques, critical care management, percutaneous interventional radiology, and better patient selection and preparation. In contrast, the postoperative morbidity of pancreatic resections continues to remain high at 30% to 50%. The most frequent postoperative complications include delayed gastric emptying (19% to 23%), anastomotic leakage or fistula from the pancreaticenterostomy (9% to 18%), intraabdominal abscess (9% to 10%), and gastrointestinal or intraabdominal hemorrhage.

Gastrointestinal or intraabdominal hemorrhage occurs in somewhere between 1% to 8% of all pancreatic resections and accounts for 11% to 38% of overall mortality. The clinical significance of postoperative hemorrhage after pancreatic surgery, therefore, is of substantive importance. The reported variation in incidence and mortality of these hemorrhages is due, in part, to the lack of a uniform and objective definition of this complication and possibly to differences in the expertise of the responsible surgeons. Our aim is to establish a generally acceptable, objective definition of postoperative hemorrhage after major pancreatic surgery.

METHODS

The consensus definition in this manuscript was developed by the International Study Group of Pancreatic Surgery (ISGPS), which was founded in the spring of 2006. All participating surgeons are specialists from high-volume centers with long-term experience in pancreatic surgery and scientific research. An extensive Medline search was performed to identify the existing literature on definitions of postoperative hemorrhage after pancreatic resection. All available major publications from the past 20 years, primarily from high-volume surgical centers, were considered when creating the basis for this definition. All participants reviewed the literature and contributed to the consensus definition. Draft definitions were circulated between the participants over a period of 8 months, and all comments and suggestions were taken into account to arrive before a final consensus statement was agreed to by all cosignatories of the ISGPS.

RESULTS

Terminology. For the purposes of the definition and this paper, “pancreatic surgery” includes the following procedures: pylorus-preserving or classic pancreaticoduodenectomy, pancreatic left resection, duodenum-preserving pancreatic head resection, pancreatic segment resection, or total pancreatectomy. The terms used most commonly to identify this complication (postoperative hemorrhage after pancreatic resection) were as follows: intraabdominal or gastrointestinal hemorrhage; early or delayed postoperative bleeding; or hemorrhage after pancreatic surgery, biliary surgery, or pancreaticoduodenectomy.

We propose use of the term postpancreatectomy hemorrhage (PPH) as the uniform descriptor for all postoperative episodes of hemorrhage. In the literature reviewed, postoperative bleeding was classified on the basis of 3 criteria: (I) time of onset, (II) location and cause, and (III) severity.

Time of onset (I). We suggest that PPH be differentiated into early and late onset. Whereas early PPH is caused most likely by technical failure of appropriate hemostasis during the index operation or an underlying perioperative coagulopathy, late PPH occurs typically from complications of the operation, with a usual delay of several days or even weeks (eg, after intraabdominal abscesses, erosion of a peripancreatic vessel secondary to pancreatic fistula or intraabdominal drains, ulceration at the site of an anastomosis, or in association with an arterial pseudoaneurysm that has developed).

Delayed hemorrhage after pancreatic surgery, as defined by several high-impact papers, usually begins more than 24 hours and can occur up to several days or weeks after the operation. This type of bleeding has also been defined as delayed massive hemorrhage when it was clinically severe.

Tien et al distinguished between early (<1 week) and late (>1 week) postoperative periods. For Choi et al, the cut-off point chosen for delayed massive hemorrhage was postoperative day 5. In a large retrospective analysis, Meinke et al suggested a further classification of postoperative hemorrhage into early (from postoperative day 2 until postoperative day 30) and late (after postoperative day 30).

Based on our review of the literature and the clinical scenario, we suggest a definition that includes 2 times of onset: early PPH occurring in the first 24 hours postoperatively, meaning 24 hours after end of the index operation, and late PPH occurring more than 24 hours postoperatively.

Location and cause (II): PPH may originate from the following: (a) arterial or venous vessels; (b) suture lines of the anastomoses (gastroenteric, duodenoenteric, jejunojejunostomy or pancreaticoenteric); (c) areas of resection (eg, pancreas stump, retroperitoneum); (d) gastric/duodenal ulcer or...
diffuse gastritis; (e) eroded and ruptured pseudoaneurysms; or (f) hemobilia from previously placed endobiliary stents. In addition, PPH can be grouped into (a) intraluminal and (b) extraluminal according to the definite location.

PPH has been correlated with bile leaks, pancreatic anastomotic leak or fistula, intraabdominal abscess, or generalized sepsis. The role of preoperative jaundice and increased serum bilirubin concentration is a subject of controversy. In a large trial, the type of resection, texture of the pancreatic parenchyma, extent of lymph node resection, and pathologic findings did not show a clear correlation with PPH. Possible pathophysiologic explanations for late PPH include enzymatic digestion of the blood vessel wall by trypsin, elastase, and other pancreatic exocrine enzymes secondary to a pancreatic leak; intraabdominal infection with involvement of peripancreatic vessels; or vascular injury during resection that leads to a pseudoaneurysm. Peripancreatic vascular structures that may be the source of PPH are the stump of the gastroduodenal artery; splenic artery; branches of the superior mesenteric artery (eg, inferior pancreaticoduodenal artery); the splenic vein stump; or, rarely, an intrapancreatic artery (Fig 1 & Fig 2).

**Severity (III):** Many different definitions of PPH based on severity have been published. According to these definitions, the severity of bleeding can be differentiated into 2 categories based on the amount of blood loss or transfusion requirements: (a) mild (no clinical impairment and transfusion requirements), or (b) severe (more than 4 or 6 units of packed cells transfused within 24 hours; a decrease in hemoglobin of more than 4 g/dl; or need for relaparotomy or interventional angiographic therapy due to severe blood loss). In 1983, Meinke et al proposed 3 grades of hemorrhage severity: (a) mild hemorrhage, defined as “bleeding indicated by coffee ground emesis or bright red blood in nasogastric tube output and response to treatment with nasogastric suction, antacids, cimetidine and occasionally gastric lavage;” (b) moderate hemorrhage, defined as “transfusion of up to 2 units of blood and hospital admission were required;” and (c) severe hemorrhage, defined as “transfusion of more than 2 units of blood and other circulatory support or reoperation required.” Many of these definitions overlap in several respects, but no general agreement or consensus has been reached on how to classify PPH.

**Suspicion and diagnosis.** PPH becomes apparent due to one or more of the following signs: blood loss through abdominal drains or nasogastric tube;
hematemesis or melena; clinical deterioration of the patient; unexplained hypotension or tachycardia; or laboratory findings such as a decreasing hemoglobin concentration. A so-called “sentinel bleed”—a small amount of blood loss via abdominal drains or nasogastric tube several hours before massive hemorrhage—may be present (30% to 100%)6,17,25; recognizing this event as a sentinel

Table I. Proposed definition of postpancreatectomy hemorrhage (PPH)

<table>
<thead>
<tr>
<th>Time of onset</th>
<th>Location</th>
<th>Severity of Hemorrhage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early hemorrhage (≤24 h after the end of the index operation)</td>
<td>Intraluminal (intraenteric, eg, anastomotic suture line at stomach or duodenum, or pancreatic surface at anastomosis, stress ulcer, pseudoaneurysm)</td>
<td>Mild</td>
</tr>
<tr>
<td>Late hemorrhage (&gt;24 h after the end of the index operation)</td>
<td>Extraluminal (extraenteric, bleeding into the abdominal cavity, eg, from arterial or venous vessels, diffuse bleeding from resection area, anastomosis suture lines, pseudoaneurysm)</td>
<td>Severe</td>
</tr>
</tbody>
</table>

Table II. Proposed classification of PPH: clinical condition, diagnostic and therapeutic consequences

<table>
<thead>
<tr>
<th>Grade</th>
<th>Time of onset, location, severity and clinical impact of bleeding</th>
<th>Clinical condition</th>
<th>Diagnostic consequence</th>
<th>Therapeutic consequence</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Early, intra- or extraluminal, mild</td>
<td>Well</td>
<td>Observation, blood count, ultrasonography and, if necessary, computed tomography</td>
<td>No</td>
</tr>
<tr>
<td>B</td>
<td>Early, intra- or extraluminal, severe</td>
<td>Often well/intermediate, very rarely life-threatening</td>
<td>Observation, blood count, ultrasonography, computed tomography, angiography, endoscopy†</td>
<td>Transfusion of fluid/blood, intermediate care unit (or ICU), therapeutic endoscopy,† embolization, relaparotomy for early PPH</td>
</tr>
<tr>
<td>C</td>
<td>Late, intra- or extraluminal, severe</td>
<td>Severely impaired, life-threatening</td>
<td>Angiography, computed tomography, endoscopy†</td>
<td>Localization of bleeding, angiography and embolization, (endoscopy†) or relaparotomy, ICU</td>
</tr>
</tbody>
</table>

ICU, Intensive care unit; PPH, postpancreatectomy hemorrhage.

*Late, intra- or extraluminal, mild bleeding may not be immediately life threatening to patient but may be a warning sign for later severe hemorrhage ("sentinel bleed") and is therefore Grade B.

†Endoscopy should be performed when signs of intraluminal bleeding are present (melena, hematemesis, or blood loss via nasogastric tube).
bleed in a timely fashion may prevent severe and fatal outcomes. The diagnosis of PPH may be confirmed by upper gastrointestinal endoscopy, angiography, scintigraphy, computed tomography, and reoperation.

**Suggested definition of PPH.** Our proposed definition of PPH is based on three parameters: time of onset, location, and severity of hemorrhage: (1) Onset is either early (≤24 hours after end of the index operation) or late (>24 hours); (2) Location is either intraluminal (eg, pancreatic surface, anastomoses, gastric/duodenal ulcer/erosion, or hemorrhilia) or extraluminal (eg, arterial or venous vessel, operating field, external suture or staple line, or pseudoaneurysm); (3) Severity of bleeding may be mild or severe. Mild bleeding is characterized as a small or medium volume blood loss (drop of hemoglobin concentration of <3 g/dl) with no or minimal clinical impairment, no need for invasive intervention (reoperation or interventional angiography), and successful conservative treatment (fluid resuscitation and blood transfusion of 2 to 3 units packed red blood cells within 24 hours after the end of pancreatic surgery [ie, early bleed] or <3 units while hospitalized, if more than 24 hours after operation [ie, late bleed]). Severe bleeding is a larger volume blood loss (decrease in hemoglobin concentration of ≥3 g/dl) and potentially life-threatening clinical impairment with tachycardia, hypotension, and/or oliguria; treatment involves the need for blood transfusion (>3 units packed red blood cells) and/or invasive treatment (reoperation or interventional angiography) (Table I).

To summarize the different factors influencing PPH and establishing a clinical grading system, 3 different grades of PPH (grades A, B, and C) are defined according to the time of onset, location, and severity of the hemorrhage, and considering the cumulative overall risk and clinical severity of the hemorrhage (Table II). PPH Grade A results only in a temporary and marginal variation of the standard postoperative course of the patient after pancreatectomy. In general, PPH Grade A has no major clinical impact, and its occurrence should not be associated with a major delay of the patient’s hospital discharge. PPH Grade B requires adjustment of a given clinical pathway, including further diagnostics and intervention; this grade of PPH will lead to therapeutic consequences such as the need for transfusion, the (re-)admission to an intermediate or intensive care unit, and potential invasive therapeutic interventions, such as relaparotomy or embolization. Most likely, the occurrence of PPH Grade B will prolong the patient’s hospital stay.

**PPH Grade C** leads to severe impairment of the patient and should always be considered potentially life threatening. Immediate diagnostic and therapeutic consequences are mandatory and often needed. The hospital stay of this group of patients is always prolonged and sometimes necessitates that the patient stay longer in the intensive care unit.

**DISCUSSION**

Unlike for other complications after pancreatic surgery, such as postoperative pancreatic fistula, an internationally accepted, objective definition is lacking for PPH. Previously reported “definitions” of postoperative hemorrhage vary widely and are heterogeneous regarding time of onset, grade, severity, and clinical impact.

A clear, objective differentiation into early and late hemorrhage will allow further analysis and comparison of causes of PPH, such as a direct failure of intraoperative hemostasis; coagulopathy; complications of the pancreatectomy such as pseudoaneurysms, fistula, or anastomotic leak; or consequences of technique of resection or reconstruction. Early and late PPH should be considered as 2 different entities of morbidity in pancreatic surgery.

A consistent, objective clinical grading of the severity of PPH, as outlined in the present definition also seems essential to further determine the impact of the occurrence of PPH on the clinical course of the individual patient and the impact on mortality and duration of hospital stay in any reported cohort of patients undergoing pancreatic resections.

In the present report, we provide an objective, universally applicable, nonpartisan classification of hemorrhage after pancreatectomy. To date, in most publications on pancreatic surgery, a clear, concise, and quantifiable characterization of postoperative bleeding is lacking. This deficiency leads to discrepancies and potential misunderstandings when trying to compare results of pancreatic surgery from different centers. Only the use of an acknowledged, generally acceptable, simple, and objective definition will allow accurate comparison of different studies. Our study offers such a unifying definition and classification.

**REFERENCES**


