

Assessment of Complications According to the Clavien-Dindo Classification After Distal Pancreatectomy

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ABSTRACT

Context The absence of a definition and a widely accepted ranking system to classify surgical complications has hampered proper interpretation of the surgical outcome. **Patients** Sixty-one patients undergoing distal pancreatectomy. **Main outcome measures** The complications were classified according to the Clavien-Dindo classification; each grade was evaluated regarding the length of the postoperative stay and was compared to the most important complications. **Results** Thirty (49.2%) patients had no complications; out of the thirty-one (50.8%) patients with complications, 9 (14.5%) had grade I, 15 (24.6%) had grade II, 6 (9.8%) had grade III, and 1 (1.6%) had grade IV. There were no postoperative deaths (grade V). A progressive increase in the length of hospitalization from patients with no complications to those having grade IV ($P < 0.001$) was noted. Postoperative pancreatic fistula and postpancreatectomy hemorrhage rates did not significantly increase from Clavien-Dindo grade I to grade IV ($P = 0.118$ and $P = 0.226$, respectively). The severity of a postpancreatectomy hemorrhage, instead, was positively related to the grade of the Clavien-Dindo classification ($P = 0.049$) while postoperative pancreatic fistula resulted near the significant value ($P = 0.058$). **Conclusions** The Clavien-Dindo classification is a simple way of reporting all complications following distal pancreatectomy. It allows us to distinguish a normal postoperative course from any deviation and the severity of complications and it may be useful for comparing postoperative morbidity between different pancreatic centers.

INTRODUCTION

Distal pancreatectomy is a technically complex procedure usually performed on an older population with significant comorbidities, with a perioperative mortality rate inferior to 5% in high volume centers [1], but with a high morbidity rate, ranging from 22.7% to 57% [2, 3]. How is it possible to justify this wide range? Are there really important differences between the different centers or does a common method for evaluating surgical outcome not exist? In fact, while mortality is an easily quantifiable outcome parameter, overall morbidity and its severity are only poorly defined and this has hampered comparison among the different centers and within the same institution over time. It should be pointed out that the definition and severity of the most common complications after pancreatic resection are widely accepted to be postoperative pancreatic fistula [4], post-

pancreatectomy hemorrhage [5] and delayed gastric emptying [6], but there is no internationally accepted grading system of all types of complications which allows a proper interpretation of the surgical outcome. In 1992, a novel approach was presented for ranking complications by severity based on the therapy used to treat the complications but it did not gain widespread acceptance [7]. The same authors revised this grading system in 2004, introducing a new five-scale classification system with the aim of presenting an objective, simple, reliable and reproducible way of reporting all complications after surgery [8]. From January 2004 to March 2009, Clavien *et al.* [9] reported 214 citations of this classification system, 49 of them from the hepato-pancreatico-biliary field. Nevertheless, to our knowledge, there is no study which has tested the Clavien-Dindo classification after distal pancreatectomy. Thus, the aim of our study was to test the usefulness of the Clavien-Dindo classification in patients undergoing distal pancreatectomy in clinical practice by considering the length of the hospital stay as the principal outcome indicator.

METHODS

A prospective study of 61 consecutive patients who underwent distal pancreatectomy in the First Surgical

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Clinic of the University of Bologna, S.Orsola-Malpighi Hospital, from January 2006 to June 2010, was conducted. Demographic data (age and sex), preoperative factors (presence and number of co-morbidities), operative parameters (type of distal pancreatectomy, treatment of the pancreatic stump, extension of resection), and pathological diagnosis (benign or malignant disease) were reported. The clinical course was documented for each patient and the complications were classified according to the criteria of Clavien and Dindo [7, 8] (Table 1).

Briefly, distal pancreatectomy was performed for pancreatic diseases of the body-tail, always with a standard lymphadenectomy, frequently with a splenectomy (44, 72.1%), rarely spleen-preserving (17, 27.9%). A left pancreatectomy consisted in a pancreatic resection to the left of the portal mesenteric vein; in a subtotal pancreatectomy, instead, the pancreatic resection was to the right of the portal mesenteric vein. Manual or stapler closure of the pancreatic stump was performed.

A postoperative pancreatic fistula was defined as a drain output of any measurable volume of fluid on or after the third postoperative day, with amylase content greater than three times the serum amylase activity. The grading system for a postoperative pancreatic fistula which was used in the present study was that proposed by the International Study Group of Pancreatic Fistula (ISGPF: grades A, B, and C) [4]. Postpancreatectomy hemorrhage was defined as intra-abdominal or intestinal bleeding according to the criteria of the International Study Group of Pancreatic Surgery (ISGPS). The definition of postpancreatectomy hemorrhage is based on three parameters: onset (early: less than, or equal to, 24 hours; late: more than 24 hours), location (intraluminal or extraluminal) and severity (mild or severe). Three different grades of postpancreatectomy hemorrhage (grades A, B, and C) were recognized and, in general, postpancreatectomy hemorrhage grade A has no major

clinical impact, postpancreatectomy hemorrhage grade B requires adjustment of a given clinical pathway, including additional diagnostic examinations and intervention and, finally, postpancreatectomy hemorrhage grade C should always be considered potentially life threatening [5]. Postoperative mortality was defined as all deaths within 30 days after surgery; postoperative morbidity included all complications following surgery up to the day of discharge. The length of the postoperative period was defined as the interval from the day of surgery to discharge. Reoperation was defined as any surgical procedure performed in the first 30 postoperative days or before discharge from the hospital.

The characteristics of the 61 patients are summarized in Table 2. There were 24 (39.3%) males and 37 (60.7%) females, having a mean age of 58.9±16.0 years. Co-morbidities were present in 29 patients (47.5%) and, among them, the most frequent were cardiovascular diseases (44.3%). The majority of patients had an American Society of Anesthesiologists (ASA) score of II and III (45.9% and 47.5%, respectively) whereas a score of IV was present in only a few patients (6.6%). The type of distal pancreatectomy included 40 (65.6%) left pancreatectomies and 21 (34.5%) subtotal pancreatectomies. Standard resections were routinely performed (47, 77.0%); extended resections (14, 23.0%) included 5 liver resections and 9 resections of neighboring structures (stomach, kidney, etc.). The majority of the patients had malignant disease (38, 62.3%), while 23 patients (37.7%) had various benign pancreatic diseases.

ETHICS

No approval of institutional review committee was needed because the data of the present study were collected in the course common clinical practice and, accordingly, the signed informed consent was obtained from each patient for any surgical and clinical

Table 1. Classification of surgical complications adopted for pancreatic surgery [7, 8].

Grade	Definition
I	Any deviation from the normal postoperative course without pharmacologic treatment or surgical, endoscopic, and radiological interventions. Allowed therapeutic regimens are: drug as antiemetics, antipyretics, analgesics, diuretics, electrolytes, and physiotherapy. This grade also includes wound infections opened at the bedside.
II	Requiring pharmacologic treatment with drugs other than ones allowed for grade I complications. Blood transfusion and total parenteral nutrition ^a are also included.
III:	Requiring surgical, endoscopic, or radiologic intervention:
- IIIa	- Intervention not under general anesthesia;
- IIIb	- Intervention under general anesthesia.
IV:	Life-threatening complications (including central nervous system complications) ^b requiring intermedie care/ICU management:
- IVa	- Single-organ dysfunction (including dialysis);
- IVb	- Multiorgan dysfunction.
V	Death of a patient.
“d” suffix	If the patient suffers from a complication at the time of the discharge, the suffix “d” (for disability) is added to the respective grade of complication (including resection of the pancreatic remnant). This label indicates the need for a follow-up to fully evaluate the complication.

^a Note regarding delayed gastric emptying: the insertion of a central line for TPN or nasojejunal by endoscopy is a grade IIIa. However, if a central line is still in place or a feeding tube has been inserted at the time of surgery, then a TPN or enteral nutrition is a grade II complication.

^b Brain hemorrhage, ischemic stroke, subarachnoidal bleeding, but excluding transient ischemic attacks.

ICU: intensive care unit

Table 2. Clinical and demographic characteristics of 61 patients who underwent distal pancreatectomy.

Variables	N. of cases
Sex:	
- Female	37 (60.7%)
- Male	24 (39.3%)
Age, (mean±SD)	58.9±16.0years
Comorbidity:	
- None	32 (52.5%)
- One or more	29 (47.5%)
Cardiovascular disease:	
- No	34 (55.7%)
- Yes	27 (44.3%)
Renal disease:	
- No	59 (96.7%)
- Yes	2 (3.3%)
Chronic obstructive pulmonary disease:	
- No	57 (93.4%)
- Yes	4 (6.6%)
Diabetes:	
- No	54 (88.5%)
- Yes	7 (11.5%)
American Society of Anesthesiologists (ASA) score:	
- II	28 (45.9%)
- III	29 (47.5%)
- IV	4 (6.6%)
Type of resection:	
- Left pancreatectomy	40 (65.6%)
- Subtotal pancreatectomy	21 (34.5%)
Splenectomy:	
- No	17 (27.9%)
- Yes	44 (72.1%)
Laparoscopic approach:	
- No	39 (63.9%)
- Yes	22 (36.1%)
Extension of resection:	
- Standard resection	47 (77.0%)
- Extended or liver resection	14 (23.0%)
Treatment of pancreatic stump:	
- Manual closure	25 (41.0%)
- Stapler closure	36 (59.0%)
Pathological diagnosis:	
- Benign disease	23 (37.7%)
- Malignant disease	38 (62.3%)

procedure. The study protocol conforms to the ethical guidelines of the "World Medical Association Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects" adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964, as revised in Tokyo 2004.

STATISTICS

Means, standard deviations, ranges, and frequencies were used to describe the data. Box and whiskers plot showed the interquartile ranges, the medians and the extreme values. The logarithmic transformation of the hospital stay was applied before analysis because these data were not normally distributed at the Kolmogorov-Smirnov test and showed a positive skewness. Data were analyzed by means of the one-way ANOVA; the linear trend and the simple contrast were applied. The linear by linear chi squared test was applied to discrete

variables. All statistical analyses were made by running SPSS for Windows (version 13.0) on a personal computer. Two-tailed P values less than 0.05 were considered statistically significant.

RESULTS

Using the Clavien-Dindo classification, 30 out of 61 (49.2%) patients had no complications and 31 (50.8%) had at least one complication. The postoperative mortality rate (grade V) was 0%. The 31 complicated patients had the following grades: 9 patients (14.5%) had grade I, 15 (24.6%) had grade II, 6 (9.8%) had grade III and 1 (1.6%) had grade IV. The absence of major complications, as well as postoperative pancreatic fistula and postpancreatectomy hemorrhage, was reported in 4 out of 9 (44.4%) patients with grade I and in 7 out of 15 (46.7%) with grade II. Major complications were always present in grades III and IV. All patients with grade III required radiologic intervention not under general anesthesia (grade IIIa) and the patient with grade IV, who required the intensive care unit (ICU), underwent surgery under general anesthesia.

The mean length of the postoperative stay was 12.7 days (range 7-118 days.) The length of the postoperative stay, according to the grades of the Clavien-Dindo classification, is reported in Table 3 and Figure 1. The length of hospital stay progressively increased ($P < 0.001$) from non-complicated patients to grade IV patients. The patient with grade IV was excluded from the analysis. It should be pointed out that the length of the postoperative stay was not significantly different between non-complicated patients and patients with grade I ($P = 0.303$) while it was significantly shorter in non-complicated patients

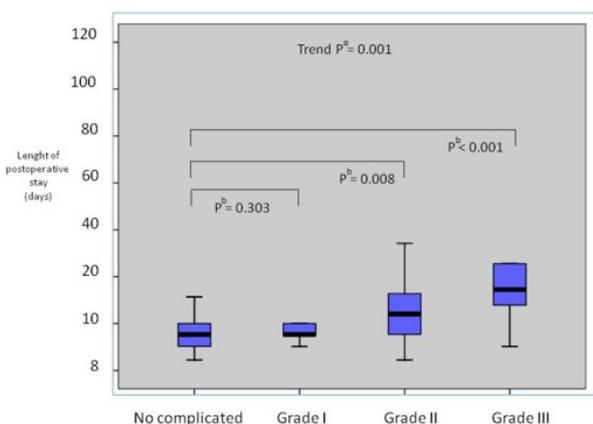


Figure 1. Box and whiskers plot showing the relationship between the length of the postoperative stay and the Clavien-Dindo classification. The boxes represent the interquartile ranges and the lines within the boxes show the median values. The whiskers represent the extreme values. The comparison between non-complicated patients and complicated patients demonstrates a significantly shorter length of hospital stay ($P < 0.001$) in non-complicated patients (grade IV was excluded due to the small sample: No. 1).

^a Progressive increase: linear trend ANOVA

^b Comparison of each grade with non complicated patients: ANOVA with simple contrast

Table 3. Length of postoperative stay related to Clavien-Dindo classification in 61 patients who underwent distal pancreatectomy.

Clavien-Dindo classification	N. of cases	Length of postoperative stay (days; mean±SD)
No complication	30 (49.2%)	9.2±2.2
Grade I	9 (14.7%)	10.4±3.0
Grade II	15 (24.6%)	12.3±4.7
Grade III	6 (9.8%)	16.8±9.4
Grade IV	1 (1.6%)	118
Grade V	0	-

with respect to patients having grades II or III (P=0.008 and P<0.001, respectively).

The most important complications following distal pancreatectomy were postoperative pancreatic fistula (14 patients, 23.0%) and postpancreatectomy hemorrhage (11 patients, 18.0%). One case of postoperative pancreatic fistula A was not considered to be a complicated patient in the Clavien-Dindo classification because it did not change the normal postoperative course as well as did not require any additional treatment. The frequency of the most important complications following pancreatic resection is reported according to the grade of the Clavien-Dindo classification in Table 4. Postoperative pancreatic fistula and postpancreatectomy hemorrhage rates did not significantly increase from Clavien-Dindo grade I to grade IV (P=0.118, and P=0.226, respectively). Regarding the severity of the major complications, postoperative pancreatic fistula and postpancreatectomy hemorrhage were positively related (P=0.046 and P=0.023, respectively) with the grade of the Clavien-Dindo classification (Table 5). Postpancreatectomy hemorrhage showed a significant value (P=0.049) while postoperative pancreatic fistula was near the significant level (P=0.058); in particular, postoperative pancreatic fistulas and postpancreatectomy hemorrhages of grade A were present in Clavien-Dindo grades I and II only.

DISCUSSION

To our knowledge, this is the first prospective study evaluating the usefulness of the Clavien-Dindo classification, a grading system designed to classify postoperative course after distal pancreatectomy according to the treatment used for complications. In this classification, grades I and II include only a minor deviation from the normal postoperative course which can be treated with drugs, blood transfusions,

Table 4. Frequency of postoperative pancreatic fistula and postoperative pancreatic hemorrhage according to the Clavien-Dindo classification grade. The 30 uncomplicated patients have been excluded.

Clavien-Dindo classification	Postoperative pancreatic fistula (No. 13)	Postoperative pancreatic hemorrhage (No. 11)
Grade I	3/9 (33.3%)	2/9 (22.2%)
Grade II	5/15 (33.3%)	6/15 (40.0%)
Grade III	4/6 (66.7%)	2/6 (33.3%)
Grade IV	1/1 (100%)	1/1 (100%)
Total	13/31 (41.9%)	11/31 (35.5%)
P value^a	0.118	0.226

^a Linear by linear chi squared test

physiotherapy and nutrition, while grades III and IV require surgical, endoscopic or radiologic intervention, and intermediate care or ICU management [7, 8, 9].

This grading system was objective and simple because the data recorded in our database were easily converted into this new classification. First, we noted that using this system, the rate of patients with any deviation from the normal postoperative course was very high (50.8%); only 49.2% of the patients had an uneventful postoperative course. In the literature, the lack of a stratified grading system for complications after surgery has not allowed proper evaluation of the surgical outcome. Probably, for this reason, the overall postoperative morbidity rate after a distal pancreatectomy was reported as lower and had a wide range [1, 2, 3]. Some authors have recently reported an overall morbidity rate after distal pancreatectomy using the Clavien-Dindo classification [3, 10]; Yoshioka *et al.* [3] recognized an overall morbidity rate of 65% of which 61% were grades I-II whereas only 4% were grades III-IV; Seeliger *et al.* [10] had an overall morbidity rate of 56.4% of which 32.7% were grades I-II and 18.2% were grades III-IV.

In the present study, the complicated patients were also more frequently in grades I and II, constituting about two-thirds of the complicated patients requiring only pharmacological treatment, whereas one-third of the complicated patients required management in the ICU or interventional treatment.

Patients with a normal postoperative course (i.e. those with no complications) had a significantly shorter hospital stay than patients defined as complicated in the Clavien-Dindo grading system. Thus, in our opinion, this grading system seems to be useful in recognizing a normal postoperative course from a

Table 5. Distribution of the Clavien-Dindo classification according to the severity of postoperative pancreatic fistula and postoperative pancreatic hemorrhage.

Complications	Clavien-Dindo classification				P value ^a
	Grade I	Grade II	Grade III	Grade IV	
Postoperative pancreatic fistula (No. 13)					0.058
- Grade A (No. 4)	2 (50.0%)	2 (50.0%)	0	0	
- Grade B (No. 9)	1 (11.1%)	3 (33.3%)	4 (44.4%)	1 (11.1%)	
Postoperative pancreatic hemorrhage (No. 11)					0.049
- Grade A (No. 3)	2 (66.7%)	1 (33.3%)	0	0	
- Grade B (No. 8)	0	5 (62.5%)	2 (25.0%)	1 (12.5%)	

^a Linear by linear chi squared test

complicated one; nevertheless, patients with no complications and patients with grade I are similar because grade I did not include particular pharmacologic treatment but only wound infections which opened at bedside. The length of the hospital stay significantly increased for grades II-III, demonstrating that the Clavien-Dindo classification is a useful tool for distinguishing among the increased grade of severity of the complications. Moreover, this result suggests that patients undergoing interventional treatment had a greater clinical impact on the length of hospital stay than patients who needed only medical treatment.

Regarding the relationship between the Clavien-Dindo classification and the most important complications after distal pancreatectomy, first of all, it should be pointed out that postoperative pancreatic fistulas A are sometimes not included in the complicated cases of the Clavien-Dindo grading system. This is probably due to the fact that, for the most part, postoperative pancreatic fistulas A do not have a clinical impact and they do not require any treatment. Moreover, patients with grades I or II did not have major complications in approximately 50% of the cases while, in grades III and IV, there were always major complications. Thus, the Clavien-Dindo classification appropriately selected those patients requiring additional surgical, radiologic or endoscopic intervention; in fact, the severity of both postoperative pancreatic fistula and post-pancreatectomy hemorrhage was positively related with the severity of the Clavien-Dindo classification.

In conclusion, the Clavien-Dindo classification represents an objective and simple, way of reporting all complications in patients undergoing distal pancreatectomy. This classification system allows us to distinguish a normal postoperative course from any deviation and it satisfactorily distinguishes the severity of complications. Finally, according to our experience, this classification system seems to be of particular interest in comparing the various complications between different pancreatic surgical centers. However a definite statement on the clinical value is not yet possible due to the small case number, but the

promising results should encourage further evaluation in larger cohort with the goal to possibly establish a standard classification.

Conflicts of interest The authors have no potential conflicts of interest

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