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ORIGINAL ARTICLE

A modified fast-track program for pancreatic surgery: a prospective single-center experience

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Abstract
Objective The objective of this study is to evaluate the impact of a fast-track protocol in a high-volume center for patients with pancreatic disorders.
Background The concept of fast-track surgery allowing accelerated postoperative recovery is accepted in colorectal surgery, but efficacy data are only preliminary for patients undergoing major pancreatic surgery. We aimed to evaluate the impact of a modified fast-track protocol in a high-volume center for patients with pancreatic disorders.
Methods Between February 2005 and January 2010, 145 subjects had resective pancreatic surgery and were enrolled in the program. Essential features of the program were no preanaesthetic medication, upper and lower air-warming device, avoidance of excessive i.v. fluids perioperatively, effective control of pain, early reinstitution of oral feeding, and immediate mobilization and restoration of bowel function following surgery. Outcome measures were postoperative complications such as pancreatic fistula, delayed gastric emptying, biliary leak, intra-abdominal abscess, post-pancreatectomy hemorrhage, acute pancreatitis, wound infection, 30-day mortality, postoperative hospital stay, and readmission rates.
Results On average, patients were discharged on postoperative day 10 (range 6–69), with a 30-day readmission rate of 6.2%. Percentage of patients with at least one complication was 38.6%. Pancreatic anastomotic leakage occurred in seven of 101 pancreatico-jejunostomies, and biliary leak in three of 109 biliary jejunostomies. Postoperative hemorrhage occurred in ten (6.9%) patients and wound infection in nine (6.2%) cases. In-hospital mortality was 2.7%. Fast-track parameters, such as normal food and first stool, correlated significantly with early discharge (<0.05). At multivariate analysis, lack of jaundice, and resumption of normal diet by the 5th postoperative day were independent factors of early discharge.
Conclusion Fast-track programs are feasible, easy, and also applicable for patients undergoing a major surgery such as pancreatic resection.

Keywords Fast-track surgery · Pancreatic cancer · Chronic pancreatitis · Hospital stay · Complications

Abbreviations
NSAID Non-steroidal anti-inflammatory drug
ISGPS International Study Group on Pancreatic Surgery

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Introduction

Traditional concepts for both perioperative and postoperative care for patients undergoing major surgical procedures have not yet received experimental support. When assessed using the principles of evidence-based medicine, these concepts have been questioned with regard to efficacy. In a meta-analysis of 13 randomized controlled trials with a total of 1,173 participants undergoing gastrointestinal surgery, no advantage was appreciated in keeping patients "*nil by mouth*" following surgery, as early feeding reduced the incidence of anastomotic leakage, length of hospital stay, and mortality [1]. Moreover, a further meta-analysis of six randomized trials investigating prophylactic drainage for colorectal surgery found no benefit in routine drainage in elective colonic surgery [2].

Currently, attention is being directed toward multimodal strategies that reduce surgical stress and maintain patient homeostasis. These consist of a number of evidence-based interventions that individually have been associated with improved outcome following major surgery. Physiological stress reduction, support of vital functions, and reduction of postoperative morbidity are the three main targets for enhanced recovery after surgery. Multimodal use of these strategies has been included in the commonly termed fast-track or enhanced recovery programs: by targeting factors that delay postoperative recovery (pain, poor gut function, and immobility), such programs have been shown to accelerate postoperative recovery and reduce length of hospital stay [3–8]. The most relevant dissemination of fast-track peri-operative care is currently in colonic surgery, where consensus reviews have been published on clinical care of patients undergoing colonic resection [9, 10]. However, peri-operative interventions with strong evidence to support their beneficial effect are not yet in use in other major gastrointestinal and non-gastrointestinal procedures. Postoperative hospital stay after pancreatic resection is usually 12 to 17 days at high-volume centers outside the United States [11–15]. With respect to pancreatic surgery, very few reports show that fast-track surgery is feasible and safe and promotes earlier discharge without compromising patient outcome [16, 17]. In this article, we report on a single-center experience with a modified fast-track program for pancreatic surgery.

Patients and methods

In February 2005, we commenced a fast-track peri-operative care program for pancreatic surgery at our hospital. The aim of this study was to evaluate the impact of this program on major patient outcome parameters, particularly complications, as well as to assess the reduction in length of stay at the intensive care unit (ICU), and in total length of stay in the hospital. Between February 2005 and January 2010, 299 consecutive patients underwent pancreatic procedures (resection or derivative by-pass) at the Department of Surgery of IRCCS - Casa Sollievo della Sofferenza Hospital in San Giovanni Rotondo, Italy. The study group consisted of 145 consecutive patients enrolled in the fast-track program following elective pancreatic resection. Pre- and peri-operative data were prospectively collected. The fast-track surgery protocol used at our institution was based on our protocol for colonic surgery and modified for elective pancreatic resection, as follows: all patients received infection prophylaxis with a single shot of ampicillin/sulbactam in a dosage of 3 g and of metronidazole in a dosage of 0.5 g 30 min before surgery; the drugs had to be re-administered if surgery lasted longer than 4 h. Moreover, weight-adapted thrombosis prophylaxis with low-molecular weight heparin until discharge from hospital and pancreatic secretion inhibitor octreotide in a dosage of 0.2 mg three times daily from day 0 to day 7 were also administered [18]. We avoided bowel preparation, and water drinking was allowed until 2 h before surgery, while patients had to stop eating at 10 pm on the day before surgery. Following pancreatic resection, patients were transferred to either the ICU or the normal ward according to their American Society of Anesthesiologists (ASA) status, as assessed by the attending anesthesiologist. Postoperative pain control was achieved by means of an elastomeric pump (ketoprofen 960 mg, tramadol 600 mg, ranitidine 450 mg, metoclopramide 90 mg, morphine 15–30 mg in 300-ml saline solution in 4 ml/h) until the third postoperative day with transition to a non-steroidal anti-inflammatory drug (NSAID) administered orally until discharge. Routine gastrointestinal tubes were usually removed as soon as the anesthetic drugs wore off [19, 20]. Oral intake of clear liquids was resumed on the day of surgery or 4 to 6 h after extubation. On the first postoperative day, or as soon as the patient returned to the normal ward, he was mobilized to a chair and oral intake was increased stepwise from liquid to mashed, light, and normal diet. In addition, patients received antiemetics (metoclopramide 10 mg three times daily) to prevent nausea and promote bowel movement [21]. Details of the fast-track protocol are given in Table 1. Discharge criteria were (1) adequate pain control with oral medication, (2) absence of nausea, (3) passage of first flatus and/or stool, (4) ability to tolerate solid food, (5) mobilization as preoperative, and (6) acceptance of discharge by the patient.

Outcome measures were postoperative complications (both in-hospital regardless of total hospital stay and within 30 days following discharge to home), length of postoperative hospital stay, readmission rates within 30 days from initial discharge, and 30-day mortality. Evaluated complications were pancreatic fistula, delayed gastric emptying, biliary leak, relaparotomy, intra-abdominal abscess, post-

Table 1 Care plan for patients on the fast-track surgery program

Day before surgery
Normal oral nutrition until 10 pm
No preanaesthetic medication
Day of surgery
Analgesia by elastomeric pump (ketoprofen 960 mg, tramadol 600 mg, ranitidine 450 mg, metoclopramide 90 mg, morphine 15–30 mg dissolved in 300-ml saline solution)
No nasogastric drainage; when used, removal immediately after extubation
Warm i.v. fluids, and upper and lower body air-warming device
Avoidance of excessive i.v. fluids (peri-operative CVP<5 mmHg, max 500 ml/h infusion)
Patient eventually transferred to the ICU
First postoperative day
Patient sent back to surgical ward
Patient mobilized at least four times a day
Recommence oral intake of clear liquids
Continue elastomeric pump analgesia
Paracetamol 1,000 mg every 6 h
Metoclopramide i.v.
Second postoperative day
Continue elastomeric pump analgesia
Continue mobilization minimum four times per day
Metoclopramide per os
Light diet (yogurt and toast)
Third postoperative day
Stop elastomeric pump and transition to NSAIDs
Remove urinary catheter
Continue mobilization
Broaden diet (soup)
Fourth postoperative day
Normal diet
Seventh postoperative day
Plan discharge

pancreatectomy hemorrhage, acute pancreatitis, and wound infection. Pancreatic fistula was defined as persisting secretions of drainage fluid on or after postoperative day 3 with an amylase content greater than three times the upper normal serum value [22]. In addition, pancreatic fistula was classified as grade A, B, or C according to the clinical impact on the patient's hospital course in agreement with the classification issued by the International Study Group on Pancreatic Surgery (ISGPS) [22]. The definition of abdominal abscess was collection of fluid of at least 5 cm in diameter, diagnosed by CT scan and/or ultrasound, associated with fever and leukocytosis [22]. Acute pancreatitis was defined as an at least threefold increase in normal plasma amylase or lipase values 48 h following surgery in the context of an appropriate clinical picture [22]. Delayed gastric emptying was defined as continuous drainage via the gastric tube of more than 500 ml/day over more than 5 days after surgery, or recurrent vomiting in combination with swelling of the gastrojejunostomy/duodenojejunostomy and dilatation of the stomach at radiological contrast examination, following the recommendation of the ISGPS [22]. It includes mild, moderate, and severe forms of delayed gastric emptying [23]. Biliary fistula was defined as fluid with a high level of bilirubin (>3 times the bilirubin serum level) secreted for more than 5 days [16]. Post-pancreatic hemorrhage was defined along guidelines setup by the ISGPS [24].

The same team of three surgeons was in charge of all pancreatic resections. The pancreatico-jejunostomy was performed in a standard technique, as described by Büchler et al. [25]; the duodenojejunostomy was performed side-to-end antecolic in two-layer fashion, and the hepaticojejunostomy side-to-end with a single layer.

Statistical analysis

All analyses were performed using the SPSS (version 13, SPSS Inc, Chicago, III, USA). Categorical variables were reported as percentage values and compared using the chi-square test or Fisher's exact test, where appropriate. To detect predictors of early discharge, several patient-related parameters [age <70 years, low ASA class (I and II), lack of jaundice, and the presence of benign disease], surgical factors [short (≤6 h) operation time, no need for blood transfusion, and resection type] and parameters of fast-track surgery [time to resumption of normal diet (≤5 days), day of first liquid intake by mouth (≤1 day), passage of first stool by the 5th postoperative day, and removal of the nasogastric tube on the day of surgery] were included in a multivariate analysis. Significant or nearly significant predictors were included in a multivariate analysis performed by stepwise logistic regression model with backward stepwise selection of terms.

Results

The study population comprised 145 consecutive patients undergoing pancreatic resection. Average age was 65 years (range 25–85), with 89 (61.4%) patients of male gender. Indication for surgery was pancreatic tumor in 80 (55.2%) cases, periampullary tumor in 30 (20.7%), chronic pancreatitis in 15 (10.3%), and other tumors (duodenal, endocrine, stromal, etc.) in the remaining 20 (13.8%) patients. Pylorus-preserving pancreaticoduodenectomy was performed in 90 (62.1%), a classical Whipple procedure in four (2.7%), duodenum-preserving pancreatic head resection in four (2.7%), distal pancreatectomy in 20 (13.8%), central pancreatectomy in three (2.1%), total pancreatectomy in

ten (6.9%), completion pancreatectomy in two (1.4%), and other types of resection in 12 (8.3%) patients. Overall median operating time was 340 min and varied between 120 and 614 min. Intraoperative blood transfusions were required in 30 patients (20.7%). Blood loss was a median of 300 ml (range 50–1200 ml), and an average of 2 U (range 1–6) of packed red blood cells were transfused for each patient (Table 2).

Postoperative course Sixty-four (44.1%) patients were transferred to the ICU, where they stayed for a median of 43 h (range 14–114 h). The remaining 81 (55.9%) patients were transferred directly from the recovery room to the ward.

The nasogastric tube was removed a few hours after surgery in 35 (24.1%), on postoperative day 1 in 61 (42.1%), and at a later time in 49 (33.8%) patients. Median time of nasogastric decompression was 1 day (range 0–8). However, 14 patients (9.7%) who underwent pancreaticoduodenectomy had the nasogastric tube reinserted. In nine (8.3%) of them, this was due to delayed gastric emptying and in the remaining five patients because of relaparotomy. In addition, six additional patients who underwent a procedure other than pancreaticoduodenectomy required reinsertion of the nasogastric tube. The urinary catheter was removed on median day 3 (range 1–9 days), the central venous line on median day 7 (range 5–30 days), the intra-abdominal drains on median day 5 (3–23 days) for the right drain, and on median day 6 (3–29 days) for the left drain; seven patients were discharged with a drain still in place owing to the development of a pancreatic or biliary fistula. Patients received first liquid on median day 1 (range 0–8 days), and normal oral food on day 5 (range 3–11 days). Median time for first flatus passage was 3 days (range 1–7 days), and 5 days (range 2–9 days) for initial stool passage. Metoclopramide was administered to 132 patients (91%).

Table 2 Patient population

n=145	
Age (years)	65 (25–85)
Gender	
Male	89 (61.4%)
Female	56 (38.6%)
Underlying disease	
Pancreatic tumor	80 (55.2%)
Periampullary tumor	30 (20.7%)
Other tumor	20 (13.8%)
Chronic pancreatitis	15 (10.3%)
Type of Surgery	
Pylorus-preserving Whipple resection	90 (62.1%)
Classical Whipple resection	4 (2.7%)
Duodenum-preserving head resection	4 (2.7%)
Central pancreatectomy	3 (2.1%)
Distal pancreatectomy	20 (13.8%)
Total pancreatectomy	10 (6.9%)
Other pancreatic resection	12 (8.3%)
Completion pancreatectomy	2 (1.4%)
Operation	
Operating time (min)	340 (120–614)
Blood loss	300 ml (50–1,200)
Transfusion (units of PRBCs)	2 (1–6)

Values are median (range). *PRBCs* packed red blood cells

Complications Overall morbidity rate, i.e., the percentage of patients with at least one complication, was 38.6%. The majority of complications could be managed by non-surgical means. Pancreatic anastomotic leakage occurred in seven out of 101 patients who received a pancreaticojejunostomy: three patients suffered from grade A pancreatic fistula, two from grade B, and two developed a grade C fistula that necessitated relaparotomy and drainage. Eleven patients required second-look surgery due to complications: two for postoperative bleeding, one for duodenal leak, two for abdominal abscess (one caused by a pancreatic fistula), one for biliary leak, two for postoperative pancreatitis, and one for peritonitis, one for pancreatic fistula, and one for duodenojejunostomy leak. Bleeding occurred in ten (6.9%) patients, and wound infection in nine (6.2%); biliary leak occurred in three of the 109 patients who required a hepaticojejunostomy (2.7%).

Four (2.7%) patients died during hospitalization: one from acute hemorrhage secondary to portal hypertension on postoperative day 9, two from acute heart failure on postoperative days 29 and 51, respectively, and one because of multiorgan failure with sepsis secondary to leakage of the hepatico-jejunostomy on day 43. On average, patients were discharged home on postoperative day 10 (range 6–69 days). The 30-day readmission rate was 6.2% (nine patients): two patients were readmitted for abscess (one for abscess of the abdominal wall and one for an intra-abdominal abscess), three patients for fever, one for delayed gastric emptying, and one for persistent pancreatic fistula, one for wound infection, and one for abdominal pain (Tables 3, 4).

Factors influencing early discharge

The impact of fast-track parameters, such as the intake of normal food, first stool, and complete mobilization, and both patient and surgical factors on early discharge, defined as <10 days, is shown in Table 5. At univariate analysis,

Table 3 Complications

(*Pts*=145)	
Total complications	56 (38.6)
Delayed gastric emptying	9 (8.3)
Bleeding	10 (6.9)
Pancreatic fistula	7 (6.9)
Wound infection	9 (6.2)
Pulmonary complication	7 (4.8)
Biliary leak	3 (2.7)
Abdominal abscess	3 (2.1)
Sepsis	2 (1.4)
Pancreatitis	2 (1.4)
Acute renal insufficiency	2 (1.4)
Duodenal leak	1 (0.7)
Duodenojejunostomy leak	1 (0.7)
Relaparotomy	11 (7.6)
Hemorrhage	2
Abdominal abscess	2
Pancreatitis	2
Biliary leak	1
Duodenal leak	1
Duodenojejunostomy leak	1
Peritonitis	1
Pancreatic fistula	1
Mortality	4 (2.7)
Heart failure	2
Sepsis with MOF	1
Acute hemorrhage	1
Readmission rate	9 (6.2)
Fever	3
Abscess	2
Delayed gastric emptying	1
Persistent pancreatic fistula	1
Wound infection	1
Abdominal pain	1

Values in parentheses are percentages

age (<70 years), absence of jaundice, resumption of normal diet by the 5th postoperative day, and passage of first stool by the 5th postoperative day were all predictors of early discharge. No need for blood transfusion showed a trend towards significance. Other factors, such as disease type, resection type, prompt removal of nasogastric tube, and early resumption of liquid diet, were not predictive. At multivariate analysis of significant or nearly significant predictors, lack of jaundice (odds ratio (OR)=2.6 [95% confidence interval (CI) 1.1–6.1] p=0.029) and early normal food intake (OR=3.1 [95%CI 1.3–7.2]; p=0.008) retained independent power for predicting early discharge.

Table 4 Gastrointestinal function

N=145	
Nasogastric tube	
Median time of nasogastric decompression (days)	1 (0–8)[a]
Removal on day of surgery	35 (24.1%)
Removal on first postoperative day	61 (42.1%)
Later removal	49 (33.8%)
Feeding	
First liquid (days)	1 (0–8)[a]
Complete oralization (days)	5 (3–11)[a]
Gastrointestinal function	
First flatus (days)	3 (1–7)[a]
First stool (days)	5 (2–9)[a]
Pharmacological support	
Metoclopramide	132 (91%)

Values in parentheses are percentages

[a] Median with range

Discussion

In the last decade, several studies have focused on optimal perioperative and postoperative care of surgical candidates and led to a new concept known as "fast-track surgery", multimodal rehabilitation, or enhanced recovery after surgery [3, 6, 9]. Fast-track surgery is an interdisciplinary multimodal concept based on modern intraoperative anesthesia and analgesia, which, in combination with the immediate mobilization of patients and resumption of early oral nutrition after surgery, along with a coordinated effort

Table 5 Factors influencing early (≤10 days) discharge in 145 patients undergoing pancreatic resection with enhanced recovery after surgery at univariate analysis

		p value
Patient factors		
Age (years)	(<70, ≥70)	0.056
Disease	(Benign, malign)	NS
ASA score	(≤II, >II)	NS
Resection type	(Whipple vs. other)	NS
Blood transf. i.o.[a]	(No, yes)	0.066
Operation time (hours)	(≤6 h, >6 h)	NS
Jaundice	(No, yes)	0.023
Fast-track parameters		
Removal of NG tube	(≤1 p.o. day >1)	NS
First liquid	(≤1 p.o. day >1)	NS
Normal diet	(≤5 p.o. day >5)	0.007
First stool passage	(≤5 p.o. day >5)	0.028

p.o. postoperative, *i.o* intraoperative, *NS* not significant, *Blood transf* blood transfusion

for patient education and collaboration between surgeons, anesthesiologists, and nurses, aims to reduce morbidity during the post-surgical period.

Pancreatic resection has always been considered a high-risk procedure with high postoperative morbidity and mortality. Postoperative hospital stay following pancreatic resection is usually 12 to 17 days outside the United States. Advancements in modern surgery have evolved pancreatic surgery, so that mortality rates are currently under 5% at specialized high-volume medical centers; however, the postoperative morbidity rate remains high, with figures ranging from 30% to 60% [11–15]. Postoperative complications, such as pancreatic fistula, delayed gastric emptying, and biliary complications, constitute the main reasons for a prolonged stay. Fast-track perioperative and postoperative programs in pancreatic surgery were developed to cut the well-known stress responses in surgery with the aim of possibly reducing morbidity, postoperative hospital stay, and readmission rate, as already established for patients undergoing other surgical procedures [3, 6, 9, 10].

In this present study, we applied a modified fast-track protocol for pancreatic surgery. In detail, nasogastric tubes were usually removed as soon as the anesthetic drugs wore off, and abdominal drain was left in place until normalization of amylase content. Most of the patients included in the study did not experience problems in complying with the fast-track protocol; however, nausea and vomiting were the main discomforts for some of them. The symptoms were unrelated to the insertion of a nasogastric tube, but appeared to be associated with the occurrence of other complications, such as fistula or abscess. In addition, recent data demonstrated that nasogastric tube placement was unnecessary in elective abdominal surgery and could lead to pulmonary complications [19, 20]. In our study population, the nasogastric tube was removed on postoperative day 1 in the majority of patients. However, 14 patients needed reinsertion because of delayed gastric emptying or relaparotomy.

Median time for removing abdominal drains was day 6. Early removal of drains appears to be of particular relevance, because a prospective randomized trial showed that long dwelling times were associated with more abscesses or fistula formation during the postoperative course [2]. In our experience, the left drain was left in place until normalization of the amylase and lipase content in the drainage fluid, and we feel this approach allowed us to safely manage most postoperative pancreatic fistulas. Univariate analysis showed the lack of early removal of the NG tube and abdominal drains in our cohort of patients to not influence the postoperative course or early discharge.

In the present study, we report a fistula percentage of 6.9% and a delayed gastric emptying of 8.3% in patients on the fast-track protocol. The rate of pancreatic fistulas encountered in our series of patients who underwent pancreatico-jejunostomy as described by Büchler et al. [25] was in keeping with the fistula rate reported by those authors. Similarly, the delayed gastric emptying rate following antecolic duodenojejunostomy in our patients was well comparable with the rate reported in the recent meta-analysis by Diener et al. [26] who compared outcome after retrocolic vs. antecolic duodenojejunostomy [27, 28].

With our modified protocol, we discharge patients to home at median day 10. These data are in line with those reported by Berberat et al. [16] and Balzano et al. [17], which, to our knowledge, are the only two articles dealing with a fast-track program in pancreatic surgery, both of them produced by high-volume centers in Europe.

In conclusion, implementation of a fast-track program for major pancreatic surgery, such as duodenopancreatectomy, is feasible, does not affect patient survival, accelerates recovery, improves patient quality of life, and consequently shortens length of hospital stay.

Conflicts of interest None.

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