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ABBREVIATIONS:

NGT: Nasogastric tube

PD: Pancreaticoduodenectomy

LOS: Length of hospital stay

DGE: Delayed gastric emptying

ERAS: Enhanced recovery after surgery

FT: Fast track

POD: Postoperative day

POPF: Postoperative pancreatic fistula

OFA: opioid-free anesthesia

ABSTRACT

BACKGROUND:

Since the spread of enhanced recovery programs, early withdrawal of the nasogastric tube (NGT) is recommended after pancreaticoduodenectomy (PD), although few data on the safety of this practice are available. The aim of the present study was to evaluate the absence of nasogastric decompression after PD on postoperative outcome.

Study Design: All consecutive patients undergoing PD between January 2014 and December 2015 at a single center were retrospectively analyzed. Since May 2015, all operated patients had the NGT removed immediately after the procedure (NGT− group) and were compared to patients operated on before this practice (NGT+ group), who had the NGT maintained until at least postoperative day 3.

RESULTS: During the study period, 139 patients underwent PD, of whom 40 (29%) were in the NGT− group and 99 (71%) were in the NGT+ group. The length of hospital stay (LOS) and rate of postoperative complications of grade 2 or higher according to the Clavien-Dindo grading system were significantly higher in the NGT+ group [14 (11-25) vs. 10 (8-14.25), *P*=0.005 and 82,8% vs. 40% *P*<0,001, respectively). Incidence and severity of delayed gastric emptying (DGE) grade B-C were also higher in the NGT+ group (45,5% vs. 7,5%, *P*<0.001). There was no difference between the two groups concerning the 90- day postoperative mortality (P= 0.18).

CONCLUSION: Absence of systematic nasogastric decompression after PD might reduce postoperative complications, DGE, and length of hospital stay. These encouraging results deserve to be confirmed in a prospective randomized study (NCT: 02594956).

INTRODUCTION

Pancreaticoduodenectomy (PD) is the most suitable curative treatment for multiple benign and malignant periampullary diseases. With recent advances in surgical techniques, perioperative management, and postoperative care, PD has become increasingly common, and the mortality rate associated with this major procedure has decreased, especially in high-volume centers [1, 2]. The mortality rate after PD is less than 5%, which has been markedly improved by the centralization of pancreatic surgery. Conversely, the morbidity rate following PD remains high, reaching to 30% to 50% [3, 4], owing to pancreatic fistula, hemorrhage [5], and delayed gastric emptying (DGE) [6–8].

Enhanced recovery after surgery (ERAS) programs are one of the most promising approaches to optimize postoperative outcomes after abdominal surgery, whether it is elective or emergency surgery [9]. The feasibility and safety of fast-track (FT) programs have been validated in colorectal [10], hepatic [11], and pancreatic surgery [12, 13]. Fast-track perioperative care employs a number of elements aimed at enhancing recovery and reducing the profound stress response after surgery. ERAS protocols might decrease mortality, morbidity, length of hospital stay (LOS), and cost by 30% to 50%[14].

This program combines various working axes as minimally invasive techniques, optimal pain control, and early postoperative rehabilitation (e.g., early mobilization, non-routine use of postoperative nasogastric decompression, and early oral feeding). The selective use of a nasogastric tube (NGT) represents the keystone of enhanced recovery, because it allows early mobilization and early oral feeding, and reduces the morbidity rate [15]. Many studies have demonstrated that elective colorectal [16, 17], liver [18], and gastric [19] surgery can be safely performed without systematic postoperative nasogastric decompression. Some previous retrospective studies showed the safety of no NGT after pancreatic surgery [20, 21], but without large results in PD specifically.

The aim of the present study was to evaluate the impact of non-systematic nasogastric decompression after PD on postoperative morbidity.

MATERIEL AND METHODS

Patient selection:

All consecutive patients who underwent PD at a single tertiary referral center between January 2014 and December 2015 were included and analyzed. Data were collected from a prospectively maintained database and analyzed retrospectively. Data such as demographics [age, sex, body mass index (BMI)], surgical variables, NGT placement, LOS, morbidity, and mortality were assessed. Indication for surgery was systematically confirmed by a multidisciplinary meeting including surgeons, gastroenterologists, and radiologists. Indications for PD were malignant or benign tumor, chronic pancreatitis, and intraductal papillary mucinous neoplasm (IPMN), with no exclusion regarding the indication. The study protocol was approved by the institutional review board.

From May 2015, NGT was systematically withdrawn postoperatively following fast track protocol [22]. To avoid management bias, the study was restricted to patients who underwent surgery between 2014 and 2015, and patients were managed with the same protocol of postoperative care, except regarding NGT during the study period.

Surgery

All PD were performed according to standardized procedure by a senior pancreatic surgeon. The operative analgesia used was epidural anesthesia or intravenous xylocaine. PDs were performed according to the Whipple procedure without pylorus preservation. The Child technique (i.e., pancreaticojejunal anastomosis, biliary-jejunal anastomosis, and antecolic gastrojejunal anastomosis in sequential order) was used for the reconstruction.

A NGT and a urinary catheter were systematically used during surgery. Intraoperatively, an NGT was used in all patients to maintain the gastric remnant in a decompression state. Through the same nostril that NGT, a nasojejunal tube was inserted and manually placed 15cm downstream from the gastrojejunostomy in the efferent jejunal lib, immediately after reconstructing the posterior layer. Intra-abdominal drainage was routinely performed to look for postoperative pancreatic fistula as defined by the International Study Group on Pancreatic Fistula (ISGPF) [23]. Intraabdominal non-aspirating drain (Ch 10) were used. External trans-anastomotic drainage was performed when pancreatic duct diameter was less than 3 mm with an Escat drain (Ch 6 or 10). One intravenous dose of antimicrobial prophylaxis was systematically administered during the surgery, except for patients with preoperative biliary drainage, who received intravenous antibiotics during the first 72 hours.

Postoperative care

In the two groups, a protocol of fast track was used and standardized. Postoperative care used low-molecular-weight heparin (LMWH) from postoperative day (POD) 0 until 1 month after discharge, and an antiemetic combination of ondansetron and metoclopramide. Pain control was achieved by a patient-controlled pump device with intravenous opiates or oral opiates combined with paracetamol.

Urinary catheter and epidural analgesia were removed on POD 2. All patients received nasojejunal early enteral nutrition (NJEEN) after PD from POD 1 until discharge, which was maintained through the nasojejunal tube, complementary oral feeding. On POD 1, NJEEN was started as 500 mL and 750 Kcal/day, increasing to 1125 Kcal/day on POD 2, and progressively increasing to 1500 Kcal/day. Assisted mobilization started on the night of the surgery with the aim of full mobilization as soon as possible.

Drain amylase level and serum amylase level were analyzed on POD 3 and POD 5 to detect postoperative pancreatic fistula (POPF). Intra-abdominal drains were removed on POD 3 if there was no POPF, or maintained if the sample confirmed POPF, until drain output was less than 50 mL per day.

In the NGT+ group, the NGT was removed on POD 3 if the NGT volume was less than 600 mL or on POD 5 in the absence of DGE. A liquid diet was initiated the same day as removal NGT. If the liquid diet was well tolerated, the solid diet was introduced progressively. In the NGT−group, NGT was systematically removed in the operating room at the end of surgery. After surgery, on POD 0, only water was allowed. Liquid diet (water, soup and yoghurt) was started on POD 1 and advanced as tolerated to solid diet the next day.

In the two groups, reinsertion of the NGT was done in any of the following conditions: persistent hiccups, nausea, or vomiting, and when patients required reintubation or relaparotomy. After reinsertion, the NGT was removed only according to clinical tolerance and if its volume was less than 600 mL per day.

Defining adverse events

Postoperative outcomes were collected during the hospital stay and follow-up period. Complications were defined as: mortality (in-hospital death or death occurring within 90 days of surgery), POPF according to the recent definition of the International Study Group on Pancreatic Fistula (ISGPF) [23], DGE according to the definition of the International Study Group of Pancreatic Surgery Classification (ISGPS) [24].

Postoperative complications were defined by the international Clavien-Dindo grading system [25], and a grade 3b or higher was considered to be a major complication.

Statistical analysis

For descriptive analyses, qualitative variables were reported as number of patients with percentages, and for quantitative variables as medians with the inter-quartile range (IQR). For comparisons between the NGT+ and the NGT− group, qualitative variables were compared using a chi-square test or a Fisher exact test, as appropriate, and quantitative variables were compared using a Mann-Whitney U test, as appropriate. A *P*-value < 0.05 was considered statistically significant. Statistical analyses were performed using R statistical software (http://www.r-project.org/).

RESULTS

Demographics and operative data

During the study period, 139 patients underwent PD (87 men and 52 women). Forty patients (28.8%) had early withdrawal of NGT, whereas 99 patients (71.2%) were classically managed with NGT during the postoperative period (control group: NGT+). Patient and surgical characteristics in each group were similar, particularly for DGE risk factors such as diabetes and age (*Table 1*). The median age was 67 years in the two groups. The median BMI was 24.3 (20.8-26.6) kg/m^2 and 24 (22.4-26.1) kg/m^2 in in the no NGT and control groups, respectively (P = 0.52). There was no statistically significant difference regarding the indication for surgery, preoperative chemotherapy rate, and biliary drainage rate between the two groups.

The surgical data are summarized in Table 2. No difference was found between the two groups regarding duration of surgery, rate of vascular resection, or rate of adjacent organ resection and per and postoperative analgesia.

Postoperative outcomes

Postoperative complications are shown in *Table 3*. Patients in the NGT+ group presented more major complications (≥2 according Clavien-Dindo grading), 82 (82,8%) versus 16 (40%) in the NGT− group (P<0,001). Rates of pancreatic fistula grades B and C according to ISGPF classification were 6 (15%) and 19 (19.2%) in the NGT+ group and the NGT− group, respectively (*P* = 0.73). The rate of DGE (grade B-C according to ISGPS classification) was significantly higher in the NGT+ group compared to the NGT− group (45.5% vs. 7.5%, *P*<0.001). Consequently, the length of postoperative hospital stay was significantly shorter in the NGT− group [10 (8-14.2) vs. 14 (11-25) days, *P* = 0.005].

Concerning postoperative mortality, the 30 day and the 90 day mortality rates were not different between the NGT+ and NGT− groups (3% vs. 0%, *P*=0.56 and 6% vs. 0%, *P*=0.18, respectively).

Nasogastric tube reinsertion

Reinsertion of a NGT was required in nine (22.5%) patients in the NGT− group, after a mean of 3 ± 1 days following surgery. Indications for NGT reinsertion are detailed in Table 5. Among these nine patients, five (55.6%) required NGT reinsertion for secondary DGE due to postoperative complication.

22 patients of NGT+ group required reinsertion of NGT after primary removal. Detailed characteristics of these patients are summarized in the table 4.

DISCUSSION

A large number of studies have widely proved the feasibility, safety, and benefits of no nasogastric decompression after major abdominal surgery. Indeed, the early withdrawal of an NGT allows earlier return of gastrointestinal functions and decreases postoperative pulmonary complications [15, 26]. This approach, which has been clearly proved in many digestive surgeries (e.g., colorectal, liver, and gastric), is now recommended after pancreatic surgery (including PD) by the ERAS Society, without major data on safety. The results of the present study, which included 139 consecutive patients who underwent PD in a modern area of pancreatic surgery, provides an important set of data. In fact, the absence of NGT was associated with a lower rate of major complication, DGE, and a shorter LOS. Moreover, it was not related to increased mortality and POPF rates.

Despite the recommendation of the ERAS Society, the absence of NGT following PD has not been widely adopted by most pancreatic surgeons. This mistrust can be related to different causes, including the lack of data in this precise indication, the type of pancreatic anastomosis performed, and, importantly, the DGE induced by this surgery. In fact, DGE is so frequent following PD that the ISGPS proposed a consensual definition in 2007 that was composed of a three-grade classification [24]. The rate of DGE can be as high as 25% to 40% and significantly affects the quality of life, prolongs hospital stay, and increases hospital cost [27]. The DGE can be primitive and related to the surgical procedure, the pathophysiology of which is still not clearly understood and widely debated. Some authors hypothesize that DGE is the result of gastric denervation due to the loss of parasympathetic nerves, resulting in the reduction of peristaltic contractions and secretion of prokinetic drugs, such as motilin [28]. The classical modifications of postoperative glycemia usually observed after PD might also play a pivotal role in primitive DGE. In contrast, DGE may be secondary to a complication such as a POPF or an intra-abdominal abscess. The present results show that reinsertion of an NGT is necessary in 22.5% of patients, especially when postoperative complications occurred. These results suggest that maintaining an NGT in the postoperative period might represent a major factor inducing primitive DGE. Among the various other factors that might influence the occurrence of primitive DGE, the three most easily modifiable factors are the preoperative and early postoperative control of glycemia [29], the use of opioid-free anesthesia protocols (OFA) [30], and the type of gastro-enteric anastomosis used. A recent meta-analysis published by Hanna *et al.* suggested that antecolic reconstruction without pylorus preserving was associated with a lower incidence of clinically relevant DGE [31, 32]. These results were conflicting with a previous prospective randomized trial published in 2014 by Eshuis and colleagues, where antecolic gastro-enteric anastomosis did not influence postoperative DGE [33]. This small impact has been confirmed in *the Cochrane Database* review published by Hüttner et al. [34].

Indeed, in the present study, all patients underwent systematically a pylorus-resecting pancreaticoduodenectomy (PD). During the study period, pancreatic surgeries were performed by 2 expert pancreatic surgeons and pylorus resecting PD was systematic due to the lack of evidence on the benefits of pylorus preserving PD. In fact, the most recent literature did not clearly demonstrated the potential impact of pylorus preserving PD on the incidence of delayed gastric emptying (DGE). A recent randomized controlled trial [35] comparing PD with pylorus-resecting or pylorus-preserving did not showed significant difference in DGE rate. Finally, a recent meta-analysis [36] showed superiority for pylorus-resecting pancreaticoduodenectomy regarding DGE when all studies are included.

Regarding anesthesia and ERAS protocol, the goal at the present time is to obtain optimal analgesia that allows rapid rehabilitation without pain, through the use of drugs and/or techniques to avoid the need for opioid medications [37]. In particular, OFA using dexmedetomidine, lidocaine, and propofol infusions may be an interesting alternative in digestive surgery [38]. However, to date no work has evaluated the feasibility of this protocol in pancreatic surgery. The feasibility of the early withdrawal of the NGT after PD was previously suggested by Kunstman et al. in a retrospective study [21]. In their study, the rate of the DGE was lower in the selective NGT group, but without significant difference concerning overall postoperative morbidity using the Clavien-Dindo classification. Although the size of the study population is larger than ours (250 patients), the main limitation of their work is a fairly long recruitment period (9 years). This factor may limit the impact on morbidity because the overall management of perioperative care has significantly changed during the last years. It can be assumed that this fact partly explains the difference between their work and the present study regarding the absence of NGT on morbidity. Another hypothesis is that it may be associated with the systematic use of early enteral nutrition via a nasojejunal tube as previously published [39]. However, these results have not been confirmed in a recent controlled randomized study [40].

Of course, some possible weaknesses of the present study should be mentioned.

First, the retrospective and the monocentric character of this study is one of its critical points. Second, the limited number patients, especially in the NGT− group, could induce bias. On the other hand, the short and recent period of recruitment may limit these biases. Obviously, these encouraging results need to be validated by a controlled randomized trial, which was started in our center since January 2016 (NCT: 02594956).

In conclusion, pending the results of a randomized controlled trial, a systematic nasogastric decompression after PD might be avoided in most cases of PD, reducing postoperative DGE and the length of hospital stay.

ETHICAL APPROVAL

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For this type of study formal consent is not required.

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Titles and legend to tables

Table 1: Demographics data

Table 2: Perioperative data

Table 3: Postoperative data

Table 4: Characteristics of patients requiring secondary nasogastric decompression in the 2 groups

Table 5: Detailed characteristics of patients requiring secondary nasogastric decompression in the NGT- group

TABLE 1

	Nasogastric decompression		
Variable	**NGT− (n=40)**	**NGT+ (n=99)**	**P value**
Age [a]	67 [60-74.2]	67 [59.5-73]	0.48
Gender Ratio (F:M)	15:25	37:62	1
BMI [a]	24.3 [20.8-26.6]	24 [22.4-26.1]	0.52
ASA score			0.81
<2	10 (25)	21 (21.2)	
≥2	30 (75)	77 (77.8)	
Diabetes			0.9
No	34 (85)	81 (81.8)	
Yes	6 (15)	18 (18.2)	
Previous sus-mesocolic surgery	35 (87.5)	81 (81.8)	0.57
Jaundice	23 (57.5)	49 (49.9)	0.54
Biliary drainage	15 (37.5)	36 (36.6)	1
Preoperative chemotherapy	4 (10)	13 (13.1)	0.77
Diagnosis			0.43
Pancreatic ductal adenocarcinoma	17 (42.5)	50 (50.5)	
Cholangiocarcinoma	4 (10)	14 (14.1)	
Ampullary cancer	3 (7.5)	4 (4)	
Neuroendocrine tumor	2 (5)	2 (2)	
Other cancer	1 (2.5)	9 (9.1)	
Intraductal papillary mucinous neoplasm	6 (15)	7 (7.1)	
Chronic pancreatitis	2 (5)	3 (3)	
Other benign lesion	5 (12.5)	10 (10.1)	

Values in parentheses are percentages

[a] Median-interquartile range

BMI: Body mass index

ASA: American Society of Anesthesiologists

NGT: Nasogastric tube

TABLE 2

	Nasogastric decompression		
Variable	**NGT− (n=40)**	**NGT+ (n=99)**	**P value**
Epidural analgesia	9 (22.5)	21 (21.21)	1
Length of surgery (min)[a]	300 [248.8-342.5]	270 [210-337]	0.1
Adhesiolysis	12 (30)	22 (22.2)	0.45
Vascular resection	9 (22.5)	22 (22.2)	1
Organ associated resection	1 (2.5)	9 (9.1)	0.28

Values in parentheses are percentages

[a] Median-interquartile range

NGT: Nasogastric tube

TABLE 3

	Nasogastric decompression		
Variable	**NGT− (n=40)**	**NGT+ (n=99)**	**P value**
Length of stay [a] (day)	10 [8-14.2]	14 [11-25]	0.005
Surgical revision	2 (2.0)	19 (19.9)	0.06
Pancreatic fistula[b]			0.21
None	34 (85.0)	80 (80.8)	
B	6 (15.0)	12 (12.1)	
C	0 (0.0)	7 (7.1)	
Pancreatic fistula[b]			
None	36 (85.0)	80 (80.8)	0.73
B-C	6 (15.0)	19 (19.9)	
Dindo-Clavien grade			0.18
<3A	36 (90.0)	78 (78.8)	
≥3A	4 (10.0)	21 (21.2)	
Dindo-Clavien grade			<0.001
<2	24 (60.0)	17(17.17)	
≥2	16(40.0)	82 (82.82)	
Delayed gastric emptying (Grade)[c]			<0.001
None	30 (75.0)	23 (23.2)	
A	7 (17.5.0)	31 (31.3)	
B	2 (5.0)	25 (25.2)	
C	1 (2.5.0)	20 (20.2)	
Delayed gastric emptying (Grade)[c]			<0.001
None-A	37 (92.5)	54 (54.5)	
B-C	3 (7.5)	45 (45.5)	
30-day mortality	0 (0.0)	3 (3.0)	0.56
90-day mortality	0 (0.0)	6 (6.0)	0.18

Values in parentheses are percentages

[a] Median-interquartile range

[b] According to classification ISGPF

[c] According to classification ISGPS

NGT: Nasogastric tube

Table 4

Variable	**NGT+**	**NGT-**
Age, years * (median, [IQR])	67 [64;71]	65 [59;75]
Gender ratio H:F	7:2	17:8
Day of NGT removal, *n* (%)		
POD 3	14 (63.6)	-
POD 5	4 (18.2)	-
POD >5	4 (18.2)	-
Delay for reintroduction of NGT (days)**	3.9	2.5
POPF B-C	6	2
Clavien Dindo Score, n (%)		
<3a	11 (50)	8 (89)
≥3a	11 (50)	1(11)
DGE Grade, n (%)		
A	4 (18.2)	6 (67)
B	7 (31.8)	2 (22)
C	11 (50)	1 (11)
Length of hospital stay, days* (median[IQR])	25 [17;37]	13 [11;19]

Value in parenthese are percentage

NGT : Nasogastric Tube

POD : Postoperative Day

DGE : Delayed gastric empty

POPF : Postoperative pancreatic fistula

*median

**mean

Table 5:

Patients	Histology	Time before NGT reinsertion (days)	Length of ND (days)	Secondary DGE	Type of complications	Clavien-Dindo	LOS (days)
1	PDAC	5	2	No	PF grade A	2	14
2	PDAC	2	5	No	No	2	11
3	PDAC	1	2	No	No	2	10
4	Ampullary neoplasm	3	2	Yes	PF grade A / Gastrointestinal bleeding	2	11
5	Distal cholangiocarcinoma	1	6	No	No	2	10
6	PDAC	2	14	Yes	PF grade B	2	28
7	IPMN	3	5	Yes	PF grade B	2	13
8	IPMN	2	6	Yes	Post-operative ascites	2	22
9	Neuroendocrine tumor	3	3	Yes	Evisceration	3b	19

PDAC: Pancreatic ductal adenocarcinoma

IPMN: Intaductal papillary and mucinous neoplasm

ND: Nasogastric decompression

PF: Pancreatic fistula

LOS: Length of hospital stay

DGE: Delayed gastric emptying