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Early Closure of Ileostomy Is Associated with Less Postoperative Nausea and Vomiting

Mathias Worni[a, d] André Witschi[c] Beat Gloor[a] Daniel Candinas[a]
Urban T. Laffer[c] Claudia E. Kuehni[b]

[a]Department of Visceral Surgery and Medicine and [b]Institute of Social and Preventive Medicine, University of Bern, Bern, and [c]General Surgery, Regional Hospital of Biel, Biel, Switzerland; [d]Department of Surgery, Duke University Medical Center, Durham, N.C., USA

Key Words
Ileostomy closure · Postoperative nausea and vomiting · Morbidity · Loop ileostomy · Early closure

Abstract
Background/Aims: Temporary loop ileostomy is increasingly used in colorectal surgery but necessitates secondary closure. We evaluated postoperative complications, particularly nausea and vomiting, in patients with early, intermediate, or late elective ileostomy closure. ***Methods:*** We included all patients undergoing ileostomy closure from 2001 to 2008. Time from ileostomy construction to closure was classified as early (EC, <12 weeks), intermediate (IC, 12–18 weeks), and late (LC, >18 weeks). Using multivariable logistic regression, we compared the frequency of postoperative complications between the groups. ***Results:*** We included 134 patients (87 males; median age 71 years, range 29–91). Carcinoma of the rectum (n = 67, 50%) was the main reason for ileostomy construction. The median time to ileostomy closure was 103 days (range 8–461). Among patients with EC, IC, and LC, postoperative nausea occurred in 50.0, 73.1, and 78.6%, respectively (p = 0.006), and postoperative vomiting in 22.5, 57.7, and 59.5%, respectively (p = 0.001). Adjusting for important covariates, the odds ratio for postoperative nausea was 2.0 (95% CI 0.76–5.1) for IC and 4.1 (95% CI 1.2–14.3) for LC compared to EC (p = 0.069). For postoperative vomiting, adjusted odds ratios were 3.8 (95% CI 1.4–10.4) for IC and 4.6 (95% CI 1.4–15.5) for LC (p = 0.012). Other complications did not differ between the groups. ***Conclusions:*** These findings suggest that early ileostomy closure might reduce postoperative nausea and vomiting.

Introduction

In the wake of increasingly complex large bowel surgery, particularly of the rectum, protective loop ileostomies become more and more common. They facilitate the management of anastomotic leakage and reduce the morbidity of anastomotic insufficiency [1–4]. Despite these benefits, the presence of a stoma reduces quality of life for patients and can lead to stoma-related problems [5–7]. Therefore, re-establishment of bowel continuity is of major interest in general and visceral surgery.

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Urban T. Laffer, MD, FRCS
Spitalzentrum Biel
Vogelsang 84
CH–2502 Biel (Switzerland)
Tel. +41 32 324 37 84, E-Mail urban.laffer@szb-chb.ch

Little is known, however, about the ideal time point for ileostomy closure. On average, published intervals between primary and ileostomy closure range from 10 to 34 weeks [8–11]. Since the main aim of a loop ileostomy is to increase the safety of colorectal operations, it is important that its closure entails the least possible discomfort, morbidity, and mortality. Of the potential postoperative complications, nausea and vomiting are among the most frequent ones, leading to significant discomfort for patients and increased workload for nursing staff [12, 13]. To the best of our knowledge, no study so far has investigated the impact of the time point of ileostomy closure on postoperative nausea and vomiting.

In this single-center retrospective analysis, we compared postoperative morbidity, particularly postoperative nausea and vomiting, between patients with early (EC, less than 12 weeks postoperatively), intermediate (IC, 12 to less than 18 weeks postoperatively), and late (LC, 18 weeks or more postoperatively) closure of ileostomy.

Methods

This is a retrospective study based on all patients who underwent elective ileostomy closure between January 2001 and December 2008 in the Regional Hospital of Biel, Switzerland, a secondary surgical clinic covering a population of about 200,000 inhabitants. We obtained approval of the ethics committee of the Regional Hospital of Biel. The decision to construct a loop ileostomy in the primary operation was taken by the operating surgeon depending on the intraoperative situation. No hospital guidelines for the timing of ileostomy closure presently exist. Accordingly, the timing of closure was decided on patients and doctors availability.

Data Collection

Two authors (M.W., A.W.) reviewed all patient charts, looking at documents from physicians (operation reports, anesthesia files, medical notes, discharge letters) and records from nurses. Demographic and clinical characteristics of the patients prior to the initial operation and to the ileostomy closure, together with details on surgery and anesthesia of both operations, were extracted to a predefined Excel worksheet. All stoma-related preoperative problems and all postoperative complications and their management were recorded, taking particular care to register all in-hospital events of postoperative nausea and vomiting. Throughout the hospital stay of a patient, nurses in Switzerland are obliged to record all events of nausea, vomiting, stool passage, and medication intake at least thrice daily.

Surgical Procedure

The surgical procedure remained constant throughout the whole study period. Prior to ileostomy closure, a stoma care specialist nurse and a consultant surgeon saw all patients. The anastomotic region was visualized by a water-soluble contrast enema the day before surgery in most patients and by intraoperative rectoscopy in the remaining to guarantee that only patients with an intact anastomotic region were operated on. The technique for ileostomy closure did not vary over the time period. All patients fasted overnight and received one dose of prophylactic antibiotics (second-generation cephalosporin) at induction of anesthesia. The operation was always performed under general anesthesia. Ileostomy closure was approached via a circumstomal incision and mobilization of the stoma. Dissection was performed down to the fascia and peritoneal cavity. Adhesiolysis was performed through this incision until the afferent and efferent loops could be mobilized to perform the end-to-end anastomosis. A short small bowel segment was resected. All anastomoses were hand-sewn with a single-layer serosubmucosal Monocryl 4-0® running suture. The mesenteric gap was then closed by single stitches to prevent an internal hernia. The fascia was closed with Prolene® or PDS®. Subcutaneous suction drainage was installed depending on the surgeon's preference. The skin was closed after wash out of the subcutaneous cavity in all patients with Dermalon 3-0® single stitches.

Postoperative Treatment

Liquid diet was permitted as soon as the patient was fully awake, and gradual return to solid food was established according to clinical signs. Routinely, all patients received metoclopramide 10 mg four times daily for at least 24 h. Patients with repeated vomiting received a gastric tube for a maximum of 24 h. Acetaminophen 1 g four times daily was administered as basic analgesic regimen to all patients. Morphine was added as needed. Patients with adequate oral intake, stool passage, and sufficient analgesia were released from hospital.

Timing of Ileostomy Closure

We stratified patients into three groups according to the time elapsed between the date of the primary surgical procedure resulting in an ileostomy and the date of ileostomy closure. To obtain three groups of comparable size, we divided patients a priori into those with EC, those with IC, and those with LC.

Patient Characteristics/Confounders

We extracted demographic and clinical variables that could be associated both with timing of ileostomy closure and occurrence of nausea, vomiting, and other postoperative complications and thus act as confounders: age, sex, primary disease, primary operation, prior abdominal operations, any previous chemotherapy (neoadjuvant and adjuvant), stomal prolapse, parastomal hernia, the experience of the surgeon performing the ileostomy closure, and duration of the operation.

Postoperative Outcomes

Our primary outcome of interest was postoperative nausea and vomiting, defined as at least one event per day. The day of surgery was defined as day 0. Events were recorded for each day separately but pooled for the main analysis as any nausea and any vomiting, respectively.

Secondary outcomes were the length of hospital stay (in days), postoperative gastric tube insertion, minor postoperative complications (urinary retention, urinary tract infection, dehiscence of the abdominal fascia, wound infection, pneumonia), and major complications (anastomotic leak, gastrointestinal bleeding, septic symptoms, reoperation).

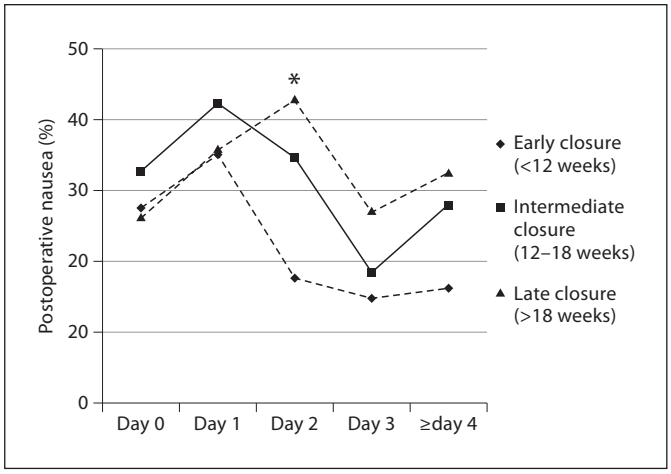

Fig. 1. Postoperative nausea, by day of hospitalization. Day 0 relates to the operation day, days 1, 2, 3, and 4 to the following days. Values are given as percentage of all patients per group. * $p < 0.05$ (χ^2 test). p = 0.012 between groups by repeated measures logistic regression. 231 × 164 mm (150 × 150 DPI).

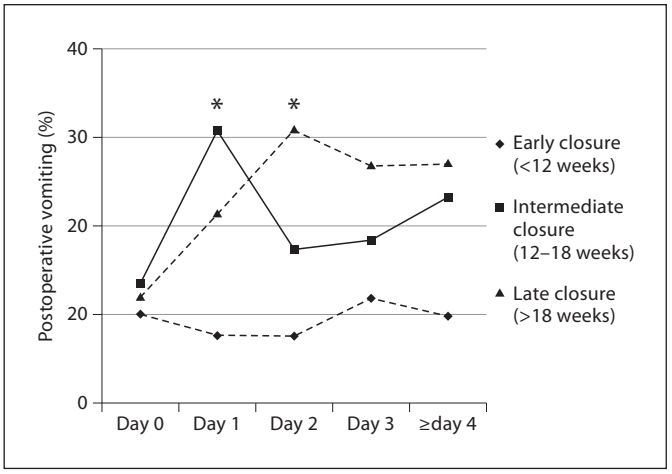

Fig. 2. Postoperative vomiting, by day of hospitalization. Day 0 relates to the operation day, days 1, 2, 3, and 4 to the following days. Values are given as percentage of all patients per group. * $p < 0.05$ (χ^2 test). p = 0.0087 between groups by repeated measures logistic regression. 237 × 168 mm (150 × 150 DPI).

Statistical Analysis

Pearson's χ^2 test, χ^2 test for trend and Kruskal-Wallis test were used to compare postoperative outcomes between the three groups. Then, we compared the occurrence of postoperative nausea and vomiting between the groups using logistic regression. Models were adjusted for the following covariates: age, sex, primary disease, primary operation, prior abdominal operation, any previous chemotherapy, parastomal hernia, the experience of the surgeon performing the ileostomy closure, and duration of the operation. For analysis of repeated outcomes (fig. 1, 2; nausea and vomiting on subsequent days), we used a logistic regression model for repeated measures.

We performed two sets of sensitivity analyses. First, we performed the multivariate logistic regression models including total number of relevant comorbidities as a covariate, and second we performed the adjusted models including subcutaneous suction drainage as a covariate to calculate the odds of postoperative events of nausea, vomiting, and gastric tube insertion among EC, IC, and LC patients. Since all estimates and 95% CI for both sets of sensitivity analysis remained stable, we do not report these results.

Two-sided tests were used in all analyses and p values <0.05 were considered statistically significant. Data were analyzed using Stata 11.0 (Stata Corporation, Austin, Tex., USA).

Results

Characteristics of the Study Population

A consecutive series of 134 patients underwent closure of loop ileostomy from January 2001 to December 2008. One patient was excluded due to missing medical records. The sample included 64.9% males (87/134), the median age was 71 years (range 29–91), and the primary diagnosis had been rectal cancer in 50.0% (67/134), colon cancer in 8.2% (11/134), diverticulitis in 23.9% (32/134), and other disease in 17.9% (24/134) (table 1). The primary operation had been low anterior resection in most of the patients (77%, 103/134). Only 2 patients took immunosuppressive drugs, 1 in the IC and 1 in the LC group.

All ileostomies were successfully closed after a median of 103 days (range 8–461). Ileostomy closure occurred earlier than 12 weeks after construction in 40 patients (30.0%), at 12–18 weeks in 52 patients (38.8%), and at 18 weeks or later in 42 patients (31.3%). Patient characteristics did not differ between the three groups apart from a difference in primary disease, the frequency of adjuvant chemotherapy, and a history of prior abdominal operations. None of the parastomal hernias led to relevant obstructive symptoms, and there was no stomal retraction. Experience of the surgeons and time of surgery did not differ between the groups. Total postoperative opioid use did not differ between the three groups, with a median use of morphine equivalent of 20.0 mg (interquartile range, IQR, 10.0–40.0), 20.0 mg (IQR 10.0–35.0), and 20.0 mg (IQR 10.0–35.0) in the EC, IC, and LC groups, respectively (p = 0.73).

Nausea and Vomiting

Overall, 67.9% (91/134) of the patients suffered from nausea during hospitalization following ileostomy closure, 47.8% (64/134) vomited, and 14.9% (20/134) need-

Table 1. Characteristics of the study population by timing of ileostomy closure

	All patients (n = 134)	EC (n = 40)	IC (n = 52)	LC (n = 42)	p value
Time to ileostomy closure, days	103 (8–461)	49 (8–83)	103 (85–122)	206 (126–461)	NA
Age, years	71 (29–91)	71 (29–89)	72 (42–91)	69.5 (41–84)	0.589
Males	87 (64.9)	25 (62.5)	31 (59.6)	31 (73.8)	0.278
Relevant comorbidities, n (IQR)	2 (1–3)	2 (1–3)	2 (1–3)	2 (1–3)	0.549
Data relating to initial diagnosis					
Primary disease					
Rectal cancer	67 (50)	16 (40.0)	23 (44.2)	28 (66.7)	0.016
Colon cancer	11 (8.2)	6 (15.0)	3 (5.8)	2 (4.8)	
Diverticulitis	32 (23.9)	13 (32.5)	14 (26.9)	5 (11.9)	
Other	24 (17.9)	5 (12.5)	12 (23.1)	7 (16.7)	
Primary operation					
Low anterior resection	103 (76.9)	31 (77.5)	38 (73.1)	34 (81.0)	0.739
Sigmoid resection	13 (9.7)	4 (10.0)	7 (13.5)	2 (4.8)	
Other	18 (13.4)	5 (12.5)	7 (13.5)	6 (14.3)	
History of prior abdominal operations	53 (39.6)	20 (50.0)	22 (42.3)	11 (26.2)	0.028
Neoadjuvant chemotherapy[1]	18 (13.5)	4 (10.3)	4 (7.7)	10 (23.8)	0.070
Adjuvant chemotherapy	36 (26.9)	2 (5.0)	6 (11.5)	28 (66.7)	<0.001
Data relating to ileostomy closure					
Stomal prolapse	2 (1.5)	0	1 (1.9)	1 (2.4)	0.379
Parastomal hernia	17 (12.7)	1 (2.5)	9 (17.3)	7 (16.7)	0.057
Surgeon					
Registrar	41 (30.6)	8 (20.0)	18 (34.6)	15 (35.7)	0.127
Consultant	93 (69.4)	32 (80.0)	34 (65.4)	27 (64.3)	
Subcutaneous suction drainage	94 (70)	29 (73)	38 (73)	27 (64)	0.604
Operation time, min	85 (38–170)	85 (45–161)	85 (38–170)	85 (40–154)	0.932

Values in parentheses are percentages or ranges, if not otherwise indicated. p values are from χ^2 test for trends for categorical variables and Kruskal-Wallis test for continuous data.

[1] One missing value.

ed postoperative insertion of a gastric tube (table 2). All these problems were significantly less common in patients with EC: among patients with EC, IC, and LC, nausea occurred in 50.0% (20/40), 73.1% (38/52), and 78.6% (33/42), respectively (p = 0.006), vomiting in 22.5% (9/40), 57.7% (30/52), and 59.5% (25/42), respectively (p = 0.001), and postoperative gastric tube insertion in 2.5% (1/40), 17.3% (9/52), and 23.8% (10/42), respectively (p = 0.007). The rate of nausea and vomiting over time was significantly lower in EC than in IC and LC patients (p for trend of 0.012 for nausea and 0.009 for vomiting; fig. 1, 2).

After controlling for demographic and clinical covariates in the multivariable logistic regression (table 3), the adjusted odds ratio for postoperative nausea compared to patients with EC was 2.0 (95% CI 0.76–5.1) and 4.1 (95% CI 1.2–14.3) for patients with IC and LC, respectively (p = 0.069); the adjusted odds ratio for vomiting was 3.8 (95% CI 1.4–10.4) and 4.6 (95% CI 1.4–15.5) for patients with IC and LC, respectively (p = 0.012), and the adjusted odds ratio for postoperative gastric tube insertion was 8.2 (95% CI 0.9–73.6) and 10.0 (95% CI 1.0–97.8) for patients with IC and LC, respectively (p = 0.039).

Other Adverse Postoperative Outcomes

The occurrence of minor or major postoperative complications did not differ between patients with EC, IC, and LC (table 2, middle and lower third), and the length of hospital stay was similar. No patient died.

Most postoperative complications were minor: urinary retention (12.7%, 17/134), urinary tract infection (1.5%, 2/134), wound infection (4.5%, 6/134), and pneumonia (3%, 4/134). Major complications were rare over-

Table 2. Postoperative outcomes after ileostomy closure by timing of closure

	All patients (n = 134)	EC (n = 40)	IC (n = 52)	LC (n = 42)	p value
Gastrointestinal problems					
Nausea (postoperative)	91 (67.9)	20 (50.0)	38 (73.1)	33 (78.6)	0.006
Vomiting (postoperative)	64 (47.8)	9 (22.5)	30 (57.7)	25 (59.5)	0.001
Gastric tube insertion	20 (14.9)	1 (2.5)	9 (17.3)	10 (23.8)	0.007
Minor complications					
Urinary retention	17 (12.7)	4 (10)	8 (15.4)	5 (11.9)	0.805
Urinary tract infection	2 (1.5)	0	1 (1.9)	1 (2.4)	0.379
Wound infection	6 (4.5)	3 (7.5)	1 (1.9)	2 (4.8)	0.581
Pneumonia	4 (3.0)	1 (2.5)	1 (1.9)	2 (4.8)	0.543
Any minor complications	26 (19.4)	8 (20)	10 (19.2)	8 (19.1)	0.914
Major complications					
Anastomotic leak	0	0	0	0	NA
GI bleeding	1 (0.8)	0	1 (1.9)	0	0.985
Septic symptoms	3 (2.2)	0	2 (3.9)	1 (2.4)	0.477
Reoperation	1 (0.8)	0	1 (1.9)	0 (0)	0.985
Any major complications	5 (3.7)	0	4 (7.7)	1 (2.4)	0.591
Median hospital stay, days (range)	5.8 (1.9–40.1)	5.8 (1.9–40.1)	5.0 (2.0–28.0)	5.9 (1.9–21.0)	0.362

Values are numbers with percentages in parentheses, if not otherwise indicated. p values are from χ^2 test for trend for categorical variables and Kruskal-Wallis test for continuous data.

Table 3. Unadjusted and adjusted odds ratios for postoperative nausea and vomiting in patients with IC and LC (compared to those with EC)

	Unadjusted odds ratio (95% CI)			p value	Adjusted odds ratio (95% CI)			p value
	EC	IC	LC		EC	IC	LC	
Nausea (postoperative)	1	2.7 (1.1–6.5)	3.7 (1.4–9.6)	0.014	1	2.0 (0.8–5.1)	4.1 (1.2–14.3)	0.069
Vomiting (postoperative)	1	4.7 (1.9–11.8)	5.1 (1.9–13.3)	0.0005	1	3.8 (1.4–10.4)	4.6 (1.4–15.5)	0.012
Gastric tube insertion	1	8.2 (0.98–67.4)	12.2 (1.45–100.3)	0.0084	1	8.2 (0.9–73.6)	10.0 (1.0–97.8)	0.039

Adjustment for age, sex, primary disease, primary operation, prior abdominal operation, any previous chemotherapy, parastomal hernia, surgeon, and duration of operation.

all: 3 patients (2.2%) had postoperative sepsis treated in intensive care, but none was directly related to the surgical site, no anastomotic leak was found, and all 3 patients recovered with antibiotic treatment. One patient (0.8%) was re-operated due to clinical signs of a mechanical ileus and assumed incarcerated scar hernia. This was not confirmed intraoperatively, but massive small bowel adhesions were found.

Discussion

This is the first investigation showing a reduced incidence of postoperative nausea and vomiting in patients undergoing early ileostomy closure compared to patients in whom ileostomy was closed after a longer time interval. Other minor and major postoperative complications as well as length of hospital stay did not differ between the groups.

The overall frequency of nausea and vomiting in our population is comparable to data reported by Apfel et al. [14]. Interestingly, we found no difference in the incidence of postoperative nausea and vomiting between the three groups on the day of operation (day 0). Instead, the gap between the groups opened at postoperative day 1 for vomiting and at postoperative day 2 for nausea. This might be a clue for explaining the underlying reasons for nausea and vomiting per se, and the differences found between patients with EC, IC, and LC. One possibility is a physiological obstruction at the site of anastomosis due to tissue edema or reduced compliance of the distal segment. Reduced intestinal compliance could explain particularly well the higher incidence of nausea and vomiting with a prolonged time interval from construction to closure of ileostomy. Williams et al. [15] demonstrated that motility and compliance of the distal segment may be reduced in proportion to the time of dysfunction. An alternative explanation for prolonged nausea and vomiting might be the presence of intra-abdominal adhesions leading to diminished bowel motility. Some investigators postulated that increased length of time between ileostomy formation and closure might be responsible for intestinal obstruction after stoma closure [8, 16].

Loop ileostomies are done mainly for improving patient handling and safety. Therefore, it is important that the operation necessary for their closure is a safe procedure. In fact, apart from urinary retention, we had a very low incidence of minor or major complications in the whole patient series. Major complications occurred in 6/134 patients (4.5%), and no patient died. Other published patient series reported morbidity rates of 4–33% and mortality rates of 0–2.5% [8, 9, 17–21]. Differences between studies are mainly due to different definitions of postoperative complications; thus, a direct comparison is difficult.

The optimal timing for ileostomy closure is still under debate. Perez et al. [10] reported a higher rate of postoperative complications in patients operated earlier than 8.5 weeks after the primary surgery and concluded that the time interval should not be shorter. Bakx et al. [22], however, showed that loop ileostomy closure is possible as early as 7–21 days after its construction in selected patients. Mansfield et al. [23] reported more postoperative complications in patients with a shorter interval to ileostomy closure, whereas Hallböök et al. [24] did not find any differences. Carlsen and Bergan suggested that intervals greater than 6 months cause a higher incidence of intestinal obstructions [16]. Our study adds significant evidence on this disputed topic, supporting a relatively early ileostomy closure (before 12 weeks) for the following reasons: (1) minor and major complications were not more common, but (2) nausea and vomiting occurred much less in patients with EC. The more frequent events of nausea and vomiting in the IC and LC groups did not translate into longer hospital stays. Still, beside the short-term, in-hospital quality of life improvements, it is likely to decrease the workload for nursing staff and, on average, patients also experience increased quality of live after ileostomy closure, mainly through improved social and physical function [5]. To achieve the goal of early closure, the date for ileostomy closure should be defined at the day of the patient's discharge after the primary operation [11]. Since one of the reasons for delays of ileostomy closure in cancer patients is adjuvant chemotherapy, mutual consent with the treating oncologists has to be achieved to guarantee early ileostomy closure.

We acknowledge several potential limitations of this study. Due to the retrospective design, additional confounding cannot be ruled out. For example, we could not determine if body mass index (i.e. missing data on height) or postoperative complications after the primary operation (e.g. postoperative hemorrhage, abscess formation, abdominal wound problems) influenced the time point of ileostomy closure. Postoperative complications could also lead to more intra-abdominal adhesions and therefore to more postoperative nausea and vomiting after ileostomy closure. We were unable to support or discard this hypothesis, but this should be addressed in future investigations. In addition, it is possible that not all episodes of nausea and vomiting were recorded and that nurses differed with respect to assessing nausea. However, in case of any missing values or varying interpretations of nausea, this would be a non-differential bias and thus unlikely to have influenced our conclusions.

In summary, this study suggests that early ileostomy closure is associated with significantly reduced postoperative nausea and vomiting, without entailing additional morbidity. Further investigations concerning the optimal time point of ileostomy closure should be performed in a prospective way and include even shorter time intervals between ileostomy construction and its closure to maximize the patients' quality of life.

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