

## Intraluminal Postpancreatoduodenectomy Hemorrhage – Last 5 Years' Experience

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### Rezumat

*Hemoragia intralumenală postduodenopancreatectomie – experiența ultimilor 5 ani*

**Introducere:** Hemoragia postoperatorie reprezintă una dintre cele mai semnificative complicații după duodenopancreatectomia cefalică.

**Scop:** Studiul prezentat în acest articol analizează cazurile de hemoragie intralumenală de la nivelul anastomozei gastrojejunale mecanice secundară duodenopancreatectomiei cefalice.

**Material și metodă:** În perioada ianuarie 2012 – ianuarie 2017, 84 de rezecții cefalo-pancreatice consecutive au fost efectuate de aceeași echipă chirurgicală. Procedul preferat de reconstrucție a fost Whipple (76 pacienți). Anastomoza gastrojejunală a fost efectuată mecanic la toți pacienții, folosindu-se staplerul Panther liniar tip GIA. Clasificarea propusă de ISGPS a fost folosită pentru evaluarea severității hemoragiei.

**Rezultate:** Din cei 84 de pacienți, un număr de 7 cazuri de hemoragie intralumenală (8,33 %) a fost observat, în medie în ziua 4 postoperator. Relaparotomia a fost inevitabilă în două cazuri. Trei pacienți din subgrupul cu hemoragie intralumenală postpancreatectomie au decedat. În lotul studiat nu au fost înregistrate cazuri de hemoragie de la nivelul anastomozelor pancreatico-jejunală sau hepatico-jejunală.

**Concluzii:** Anastomoza mecanică poate ridica controverse, sângerarea severă necesitând relaparotomie de urgență și fiind corelată cu rate mari de mortalitate. Hemoragia intralumenală postduodenopancreatectomie rămâne o complicație importantă, al cărei management depinde de multipli factori și care poate avea potențial devastator.

**Cuvinte cheie:** hemoragie, duodenopancreatectomie, management, mortalitate

### Abstract

**Background:** One of the most significant complications following pancreaticoduodenectomy is represented by postoperative hemorrhage.

**Aim:** This study undertook an analysis of the cases that presented intraluminal bleeding of mechanical gastrojejunal anastomosis following pancreatico-

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duodenectomy (PD) in the last five years.

**Methods:** From January 2012 until January 2017, 84 consecutive pancreaticoduodenectomies were performed and managed by the same surgical team. The preferred procedure of reconstruction was Whipple (76 patients). The gastrojejunal anastomosis was performed with Panther linear stapler GIA in all cases. ISGPS classification regarding postpancreatectomy hemorrhage was used to evaluate severity.

**Results:** Out of 84 consecutive PD, a total of 7 cases of intraluminal bleeding (8.33 %) were observed, detected on average on postoperative day 4. Relaparotomy was inevitable in two patients. Three patients from the studied group with intraluminal postpancreatectomy hemorrhage died. In the studied group there were no cases of bleeding from the pancreatico-enteric or bilio-enteric anastomosis.

**Conclusion:** Mechanical anastomosis might be questionable, severe hemorrhage demanding urgent relaparotomy which is correlated with high mortality rates. Intraluminal postpancreatoduodenectomy hemorrhage is a significant complication whose management depends on multiple factors and with a potentially fatal outcome.

**Key words:** postpancreatectomy hemorrhage, pancreaticoduodenectomy, management, mortality

## Introduction

In 2006 The International Study Group of Pancreatic Surgery (ISGPS) developed a broadly valid definition of postpancreatectomy hemorrhage (PPH) based on a literature review and clinical experience consensus. Three parameters were used for defining the PPH, namely severity, onset and location. The location may be either extraluminal or intraluminal. The severity of the hemorrhage may be mild or severe and the onset is referred to as less than 24 hours after the end of the operation or late (after 24 hours). Three grades of severity were proposed (A, B and C), and are denoted according to the site of bleeding, the time of onset, severity and clinical impact (1).

Immediate postoperative mortality and within 30 days after pancreaticoduodenectomy procedure has dropped remarkably, specifically in tertiary care centers, being currently less than 5% (2-4). Factors subscribed to these results have been represented by improved perioperative and critical care management, heightened patient selection and background, radiologic interventional drainage procedures for asymptomatic postoperative fluid collections and technical improvements in operative and reconstruction techniques (5). Perioperative morbidity rates still remains high despite progress, with incidence between 30% and 50% (6-9), with most commonplace complications represented by fistula of the pancreatocenteric anastomosis, delayed gastric emptying, anastomotic leakage, intraabdominal abscess and intra-peritoneal or gastrointestinal hemorrhage (10,11). Hemorrhage following pancreaticoduodenectomy has a reported incidence from 1% to 8%, being responsible for 11% to 38% of procedure related mortality (6,7). Therefore, the clinical outcome

and connotations of postoperative bleeding related to the pancreaticoduodenectomy is of substantive concern (12).

Practice has expanded and the routine use of gastrointestinal staplers in digestive surgery is currently on a large scale. They are currently associated with low rates of postoperative complications (13). Hemorrhage from mechanical gastrotrojejunal anastomosis represents a peculiar postoperative problem, with incidence fluctuating between 0,6% and 16%, being regularly self-limited (50% - 70% of the cases) (22,23). Without perceiving it post-operatively or intraoperatively, due to poor haemostasis of the anastomotic suture lines, it can become life-threatening. Endoscopic examination might have both diagnostic and therapeutic role, with effective haemostasis, low risk of procedure related fistula and avoidance of emergency relaparotomy (13-15).

## Aim

This study undertook an analysis of intraluminal bleeding in 84 consecutive patients that underwent a pancreatoduodenectomy in the last 5 years.

## Methods

Between January 2012 and January 2017, 84 consecutive patients that underwent a pancreaticoduodenectomy were included in a prospectively maintained pancreatic database, approved by the Ethics Commission. Perioperative management was done by the same pluridisciplinary team. Classic resectional procedures were performed in all patients, with Whipple reconstruction in 76 cases and Traverso – Longmire in 5 cases. Three patients

underwent a total pancreatectomy due to multicentric adenocarcinoma. Gastrojejunal mechanical anastomosis in Whipple procedure is a standard in our current practice, being performed in all cases with Pantherlinear stapler GIA. Non-absorbable 3.0 continous interrupted suture is preferred for Traverso – Longmire reconstruction. All three cases of total pancreatectomy due to positive lymph node stations 5 and 6 underwent antrectomy and reconstructive technique as Whipple.

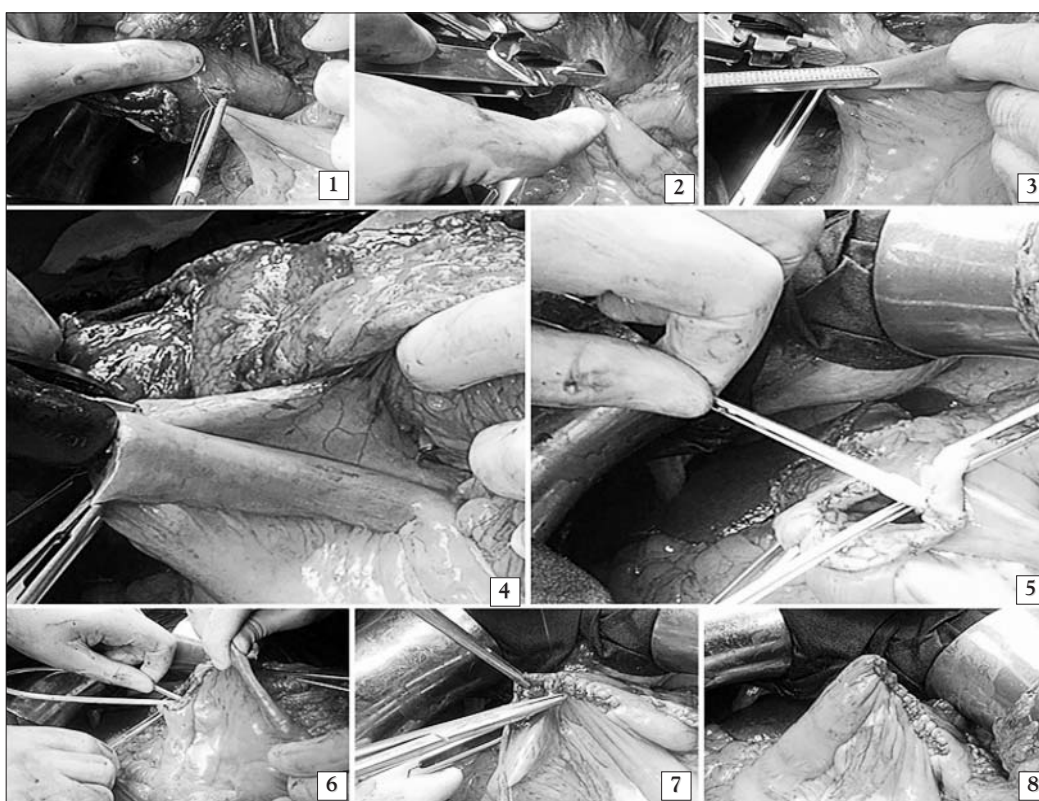
Our standard method of reconstruction after Whipple resection consists of double-layer end-to-side pancreatico-jejunostomy of the pancreatic remnant with “duct-to-mucosa” anastomosis, hepaticojejunal anastomosis at 6 to 10 cm distance from the pancreatico-enteric one, with the jejunal loop passed through and fixed to the transverse mesocolon. After wards, 45 to 50 cm from the biliary anastomosis, an antecolic mechanical gastrojejunal anastomosis using GIA stapler is performed, with running interrupted monofilament non-absorbable 3.0 suture of the anterior line of the anastomosis. Nasojejunal feeding tube and

gastrojejunal tube are inserted intraoperatively and stitched to the nose (*Fig. 1*). Patients receive post-operatively proton pump inhibitor therapy in dosage of 80 mg per day and we have dramatically decreased the usage of non-steroidal anti-inflammatory drugs or derivatives in the immediate postoperative and follow-up period.

In 54 cases we used a linear GIA 60 reloadable stapler. Due to non-existing units at the time of operation, in 25 cases we used GIA 45 and 80 staplers (*Table 1*).

Green cartridge with 4.8 mm staples was preferred in more than 85% of the cases, blue one with 3.8 mm staples being used in cases of unavailability (*Table 2*).

The severity of anastomotic bleeding was classified according to the International Study Group on Pancreatic Surgery regarding postpancreatectomy hemorrhage, with moderate bleeding defined as less than 2 or 3 units of blood transfusion requirements within 24 hours, minimal clinical deterioration or none, with successful conservative management and severe as a decrease in hemoglobin levels of more



**Figure 1.** Gastrojejunal anastomosis technique. (1) approaching anastomotic partners; (2) introducing the linear stapler into the stomach; (3) introducing the stapler into the jejunum; (4) performing the side-to-side mechanical gastrojejunal anastomosis; (5 and 6) introducing the naso-jejunal feeding tube; (7) suturing the anterior breach. (8) final aspect

**Table 1.** Types of linear staplers used

Gastrojejunal anastomosis details		
	Frequency	Percent (%)
GIA 45	9	10.7
GIA 60	54	64.3
GIA 80	16	19.0
Surjet Prolene 3.0	5	6.0
Total	84	100.0

than 3 g/dl, with transfusion necessary of more than 4 to 6 units of blood within 24 hours and clinical impact requiring intensive nonsurgical treatment or emergency relaparotomy. Grades of postpancreatectomy bleeding were defined given the proposed classification by ISGPS based on clinical condition, diagnostic and therapeutic corollary and management. Sentinel bleeding was defined as minor blood loss via the nasogastric tube, melena or haematemesis before severe massive hemorrhage (1,6,16,17).

Nonsurgical management of bleeding was achieved by sustainment of hemodynamic stability by crystalloids and colloids, transfusion with packed red blood cells, cryoprecipitate and fresh frozen plasma. Upper digestive endoscopy was performed in case of good clinical impairment and hemodynamic stability, with usage of vasoconstrictors as diluted 1:1000 adrenaline or endoscopic hemoclips. Evidence of gastrojejunal fistula following endoscopy was questioned by radiological examination with contrast substance administered per os usually on postoperative day 7 for early bleeding, and after a minimum of 5 days after the endoscopy in late hemorrhage, if no other signs of fistula were present. Pharmacotherapy of choice was proton pump inhibitors in dosage of 200 mg per day in continuous endovenous infusion with 8 mg per hour, hemostatic agents and procoagulants in the first 48 hours of bleeding such as calcium, vitamine K, ethamsylate or tranexamic acid. Use of low molecular weight heparin, routinely used post surgery, was carefully assessed in these patients.

Surgical reexploration was based on the following facts: 1) acute hemodynamic depreciation with decrease of hemoglobin more than 3 g/dl and clinical impairment involving tachycardia, hypotension and/or oliguria, evaluated as life-threatening; 2) critical hemodynamic instability despite intensive care nonsurgical management and blood transfusion exceeding 6 units per 12 hours; 3) life-threatening situations based on clinical findings with bedside

**Table 2.** Type of cartridge used

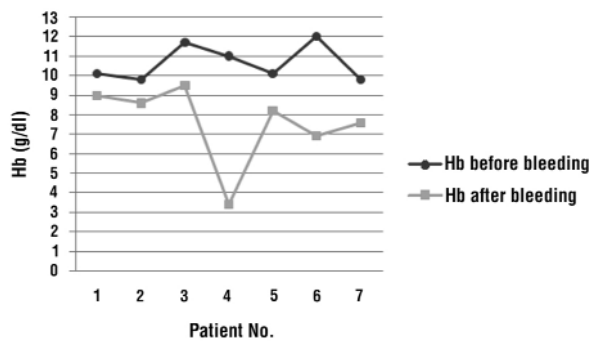
Cartridge details		
	Frequency	Percent (%)
	5	6.0
Blue	7	8.3
Green	72	85.7
Total	84	100.0

decisions; 4) nonsurgical treatment of bleeding failure.

## Results

The global prevalence for postpancreatectomy hemorrhage in the overall studied group was 21.42 % (n=18), with two patients presenting both intra and extraluminal bleeding. Extraluminal bleeding, due to eroded right hepatic artery on POD 16 following hepatico-jejunal fistula in one patient, and due to retroperitoneal diffuse venous bleeding on POD 12 secondary to ligature skid, did not appear concomitant with the gastrointestinal hemorrhage. Intraluminal bleeding was present in 8.33% (n=7), detected on average on postoperative day 4 (range from 0 to 8 POD), with no cases of hemorrhage from the pancreato-enteric or biliary anastomosis, therefore early or late gastrojejunal anastomosis bleeding representing the only cause. We encountered no intraoperative bleeding of the anastomosis, but all seven cases presented arterial bleeding in the immediate or late postoperative period. The underlying diseases in 3 patients was poorly differentiated ductal adenocarcinoma, one case of moderate differentiated ductal adenocarcinoma, one moderate and one poorly differentiated carcinoma of the ampulla of Vater and one case of severe peri-ampullary duodenal dysplasia. Primarily severe bleeding (decrease of Hb more than 3 g/dL) was found in 2 patients, while 71.5% (5 patients) presented moderate bleeding (decrease of Hb less than 3 g/dL), with depletion of less than 1.5 g/dL in two cases (*Fig. 2*). One patient was primarily subjected to observational monitoring due to drop of Hb levels of only 1.1 g/dL and because he was hemodynamically stable. Six patients, in their further clinical course after appearance of bleeding, required consequential intervention, namely upper digestive endoscopy with injection of adrenaline or hemoclips usage and surgery respectively, with emergency relaparotomy in 2 patients hemodynamically





**Figure 2.** Hemoglobin serum levels before and after hemorrhage in every case

unstable with conservative treatment failure (*Table 3*). Interventional radiology was not attempted.

Sentinel bleeding was found in 28.5% (n=2), with severe bleeding appearing within 2 hours in one case, and 8.5 hours in another. Immediate endoscopy was performed in both cases, with lack of success in one case and stop of bleeding after repeating the endoscopy in the other one. Relaparotomy rate correlated with "sentinel" bleeding was 50% (1 of 2). In the subset of the 7 patients with intraluminal post-pancreatectomy hemorrhage, 2 patients developed pancreatic fistula: one on POD 15 due to disruption of pancreatico-jejunal anastomosis subsequent to grade C hemoperitoneum with relaparotomy on POD 12, and another on POD 11 without correlation with the intraluminal postoperative bleeding. No gastrojejunal fistula related to the endoscopy was found.

The 2 patients who experienced relaparotomy due to nonsurgical management failure presented active arterial bleeding of the jejunal mucosa between the staple lines of the anastomosis. In both cases continuous interrupted non-absorbable monofilament 3.0 suture was performed.

Stratifying patients for absence or presence of

intraluminal PPH resulted in adjusted mortality associated with gastrointestinal bleeding of 14.3% (1 of 7), while it could be triumphantly treated in 6 patients (85.7%). In the subset studied group there were 3 deaths, only one correlated with intraluminal bleeding. The patient with lethal outcome PPH-related suffered from poorly differentiated ductal adenocarcinoma and rheumatoid polyarthritis treated with immunosuppressants, and developed severe bronchopneumonia with sepsis following Mendelson syndrome (aspiration on POD 7 of bile and blood). Reasons of the other two postoperative deaths were as follows: 1) complications of hemorrhagic shock following eroded right hepatic artery due to hepatico-jejunal fistula; 2) complications related to grade C pancreatic fistula diagnosed on POD 15.

Mean necessary of blood was 10 red blood cell packs (range from 5 to 22) and 7 of fresh frozen plasma (range from 3 to 19), with mean hospitalization costs and stay of 26876.5 RON and 23 postoperative days compared with 16743.9 RON and 17 postoperative days in the non-PPH group and 13361 RON and 13 postoperative days in the absolute no postoperative morbidity group.

## Discussion

Although it has a reported incidence varying from 1% to 5-12% (6,15,18), postpancreatectomy intraluminal hemorrhage is considered a therapeutic challenge and presents standardized steps of its management. The associated outcome and mortality after early reoperation is at the moment still at high rates, with incidence fluctuating between 13-60% (23,24,25,26). The distinction between late and early hemorrhage may have a decisive impact on the therapeutic management, early hemorrhage being in most studies reported to

**Table 3.** Patient characteristics

Patient No	POD	Severity	Grade (ISGPS)	PPI	Endoscopy	Sentinel bleeding	Relaparotomy
1	8	Mild	B	200 mg	No	No	No
2	1	Mild	B	200 mg	Adrenaline - failure	No	Yes*
3	2	Mild	B	200 mg	Adrenaline	No	No
4**	6	Severe	C	200 mg	Adrenaline, Hemoclips	No	No
5**	4	Mild	B	200 mg	Adrenaline, Hemoclips	No	No
6	0	Severe	B	200 mg	Adrenaline, Hemoclips - failure	Yes	Yes
7**	6	Mild	B	200 mg	Adrenaline, Hemoclips	Yes	No

\* Relaparotomy bedside decided, due to severe hypotension and rebleeding after endoscopy

\*\* Bleeding stopped after repeating the therapeutic endoscopy

POD = postoperative day diagnosis, PPI = proton pump inhibitor dose per 24 hours

ISGPS = International Study Group on Pancreatic Surgery

have a better prognosis than late bleeding (20,21). Based on these facts, some proposed setting the limit for separating early and late bleeding at the fifth (21), respectively seventh (7) postoperative day, contrary to ISGPS recommendations. Some stated that a modified classification of postpancreatectomy hemorrhage is needed, dividing the outbreak of bleeding in early (less than 24 hours), late (more than 5 days) and intermediate (between 24 hours and 5 days), leading to an algorithm of treatment for severe bleeding (26). This might predict the outcome and influence the pluridisciplinary management, with emergency relaparotomy in severe early hemorrhage and therapeutic angiography in late bleeding, surgery being reserved only in cases of failure. In patients with intermediate onset of hemorrhage, endoscopic treatment of intraluminal bleeding must be attempted, and angiography if extraluminal bleeding is present. Surgery is indicated if interventional treatment fails (26). We consider that by sorting patients with postpancreatoduodenectomy bleeding into three distinct groups and following a diagnostic and therapeutic algorithm, we might increase efficiency and reduce the mortality rates.

Due to a total of 18 cases, postpancreatectomy hemorrhage (PPH) represented a substantial problem for us, with an overall incidence in the studied series of 21.42%. We experienced 10 postoperative deaths with an adjusted mortality of 55.5% in the group with postpancreatectomy hemorrhage, 20% of the patients (n=2) presenting both intra and extraluminal bleeding. Extraluminal bleeding was determined in 70% of the cases (9 of 13) by erosion of major blood vessels due to grade B or C pancreatic fistula and was direct responsible for 5 deaths which involved massive bleeding and hemorrhagic shock. It involved the increase of logistic resources, coordination between the surgeon, anaesthesiologist and gastroenterologist, reasoning under emergency conditions only to optimize therapeutic gestures, aggressive management involving multidisciplinary approach for rebalancing the biological constants, bedside decisions involving relaparotomy due to life-threatening conditions, managing massive blood transfusions in some patients and of course, increasing costs and length of stay.

Both early and late intraluminal PPH in the studied series developed subsequent to technical failure in terms of deficient hemostasis along the mechanical anastomotic lines, leading uniformly to gut bleeding even on the same postoperative day (range from 0 to 8 POD). All cases were jaundice

related, with bilirubin levels higher than 10 mg/dl in 71.4 % (n=5), ranging from 6.87 mg to 24.93 mg and a mean value of 12.84 mg, but with the lack of statistical significance (irrelevant results when applying linear regression function with SPSS). Despite this, in our current clinical practice, it represents a predisposing factor for anastomotic hemorrhage, together with the usage of non-steroidal medication in the postoperative period. Therefore, we totally excluded this type of medication in the immediate postoperative period and up to 7 days. From the total of 7 cases, in 85.7% (n=6) a green reloadable cartridge of 4.8 mm was used, with no statistical correlation between the type of cartridge used, the bleeding or the postoperative day ( $p>0.05$ ). Despite a reported safety and time-winning technique, mechanical anastomosis can be questionable and with potentially devastating outcome. Even with risks, interventional therapeutic endoscopy was practiced in 85.2% of the cases (n=6), with success in 4 cases (57.1%) and had no correlation with anastomotic bursting at the follow-up. Emergency relaparotomy was restrained as a heroic procedure to patients in whom endoscopy and nonsurgical intensive care management was not technically feasible or failed.

Postpancreatectomy hemorrhage represents a major problem for the surgeon, both intra and extraluminal bleeding being able to appear simultaneously. Our preference for immediate postoperative enteral nutrition is based on the ability of digestive feeding to exercise a trophic effect on the bowel, thus, leading to functional and structural integrity of the mucosa, and thereby reducing the risk of bacterial translocation across the bowel wall and pancreatic infections of the remnant stump. Therefore, on the grounds that enteral nutrition is stopped in cases of intraluminal hemorrhage at patients with underlying pancreatic disease, in our opinion it leads to a poor nutritional status and deficient intestinal immune system, decreases the overall immuno-competence and bioavailability of the proteins needed in the postoperative period, consecutively increasing the risk of postoperative fistula.

Fortunately, we have not encountered cases of intraluminal bleeding from pancreatico-enteric and bilio-enteric anastomosis, which are a major concern in our daily practice and, we believe, for every pancreatic surgeon. Our growing experience with these cases has in the intervening time induced expanded attention when performing the gastrojejunal mechanical anastomosis, with careful examination of the operative field and adequate

hemostasis represented by continuous interrupted suture with non-absorbable monofilament thread.

We acknowledge some limitations of this study, with complete comparative statistical analysis of the multitude of variables introduced in the prospectively maintained database not practically possible, due to the small number of cases (n=7) in the substudied group.

## Conclusion

Postpancreatectomy hemorrhage, although noteworthy, represents a grave complication following pancreatoduodenectomy correlated with high mortality rates and management depending on various factors. Mechanical anastomosis technique might be debatable, due to severe hemorrhage with conservative treatment failure demanding urgent relaparotomy. Intraluminal postpancreatoduodenectomy hemorrhage is a significant problem, requiring proper management and with potentially fatal outcome. Endoscopy and angiography should be the procedures of choice, surgery being the therapeutic option if patients cannot be revitalized for interventional treatment or if interventional radiology is unavailable.

Complications related to major pancreatic surgery represent a substantial challenge for the surgeon and the pluridisciplinary team involved in the postoperative management, with increased morbidity, length of hospital stay, costs and are potentially life-threatening. Thus, we believe that intense perioperative care and follow-up is needed to optimize the outcome and decrease the procedure related morbidity.

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