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Cholangiopancreatoscopy-guided laser dissection and ablation for pancreas and biliary strictures and neoplasia

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Authors
Samuel Han, Raj J. Shah

Institution
Division of Gastroenterology and Hepatology, University of Colorado Anschutz Medical Campus, Aurora, Colorado, United States

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Corresponding author
Raj J Shah, MD, FASGE, AGAF, FACG, Professor of Medicine, Division of Gastroenterology and Hepatology, University of Colorado Anschutz Medical Center, 1635 Aurora Ct, Mail Stop F735, Rm. AIP 2.031, Aurora, CO 80045
Fax: +1-720-848-2757
Raj.Shah@cuanschutz.edu

ABSTRACT

Background and study aims Cholangiopancreatoscopy-guided laser dissection or ablation (CPL) is a novel therapeutic modality for refractory benign strictures. Our aim was to describe the safety and efficacy of CPL for pancreaticobiliary disorders.

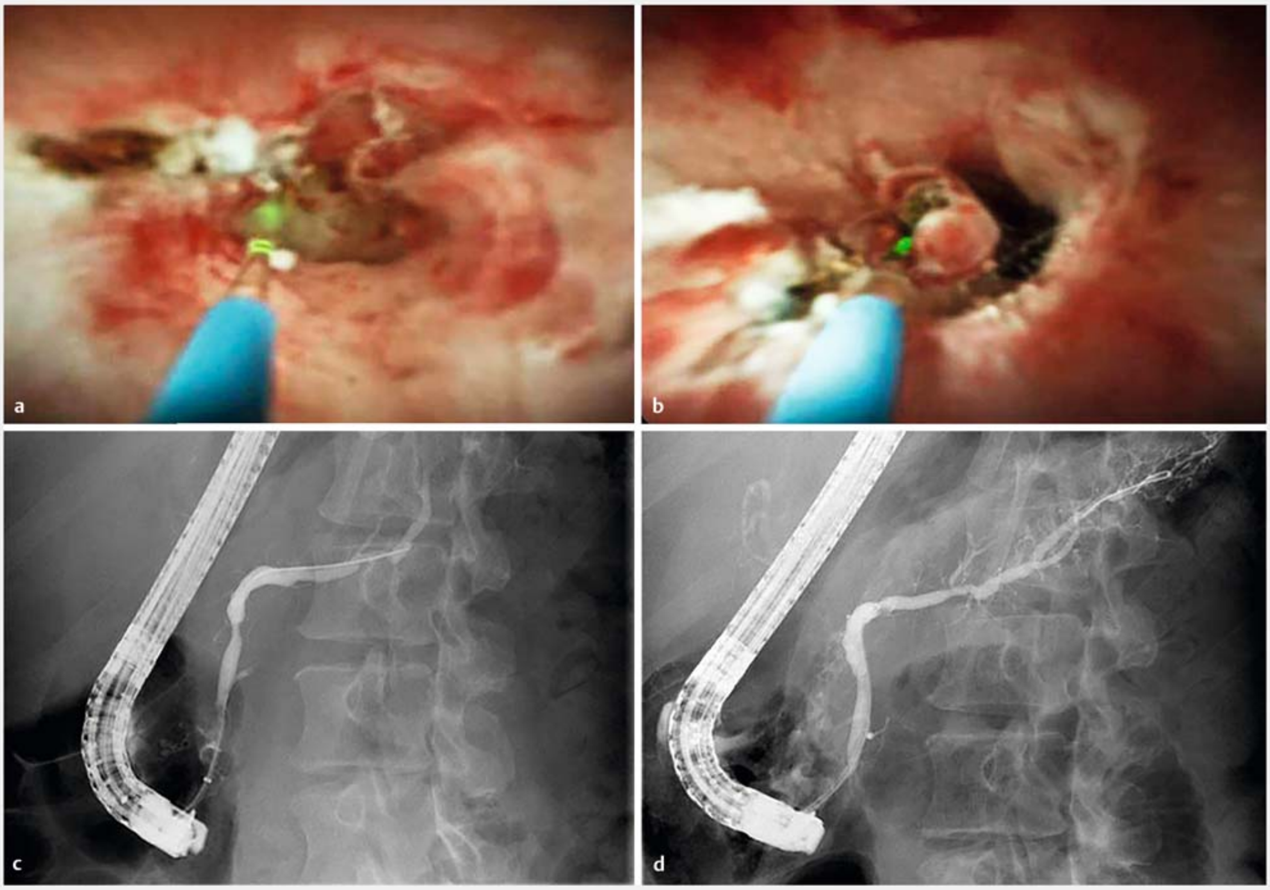
Patients and methods Patients who underwent CPL using holmium or thulium laser between February 2017 and September 2019 were included. For stricture dissection, gentle strokes of the laser fiber from a distal to proximal approach were applied until luminal patency permitted advancement of the cholangiopancreatoscope. Immediate technical success was defined as ability to traverse the stricture with the cholangiopancreatoscope after CPL. Short-term technical success was defined as > 90 % resolution of the stricture on follow-up pancreatogram.

Results Eleven patients underwent a mean of 3.6 ERCPs (mean total diameter of 14.2 Fr of stenting) prior to CPL. Indications included pancreatic duct stricture (n = 8), pancreaticojejunostomy anastomotic stricture (n = 1), bile duct stricture (n = 1) and pancreatic intraductal papillary mucinous neoplasm ablation (n = 1). Immediate technical success was 94.1 % and short-term technical success rates was 88.2 %. At a mean follow-up of 12.1 months, there have been no stricture recurrences.

Conclusions CPL may be an effective therapy for strictures refractory to conventional dilation and multiple stenting.

Introduction

For all the advances in endoscopic retrograde cholangiopancreatography (ERCP), benign pancreaticobiliary strictures refractory to conventional endoscopic therapies such as dilation and stenting remain challenging to manage. These refractory strictures can result in abdominal pain, jaundice, pancreatitis, and cholangitis. Furthermore, obstructing strictures precluding catheter advancement may not be amenable to standard endoscopic techniques. Within the chronic pancreatitis population, nearly 20 % of patients will develop main pancreatic duct (PD) strictures [1]. If symptomatic, treatment recommendations typically include pancreatic sphincterotomy in combination with dilation and stenting, preferably with a 10 Fr stent [2]. Refractory strictures are classically defined as those that persist or relapse 1 year after placement of a single stent, although in our practice, we often perform multiple side-by-side stenting across symptomatic strictures prior to considering them to be refractory [2]. Endoscopic measures for these refractory strictures entail placement of multiple side-by-side plastic stents or covered metal stents. Long-term data regarding multiple plastic stent placement, however, demonstrate recurrence of pain in 25 % of patients after stent removal [3]. Within this context, novel therapies are needed to treat refractory strictures in an effort to facilitate earlier resolution of strictures. This may permit a reduction in stent-associated stricture while avoiding repeated procedures and potentially pancreatic surgery for a



▶ **Fig. 1** Laser dissection of a pancreatic duct stricture (top panels) with improvement seen on pancreatogram (bottom panels).

benign condition that has multifactorial mechanisms for pain [4].

Lasers have been used for ablation purposes in urological indications, and preliminary studies in the biliary tract have demonstrated safety, therefore, this therapy potentially represents a novel endoscopic technique for dissection and ablation [5–8]. The aim of this study was to evaluate the safety and efficacy of laser dissection/ablation for refractory strictures in the pancreas and biliary tract.

Patients and methods

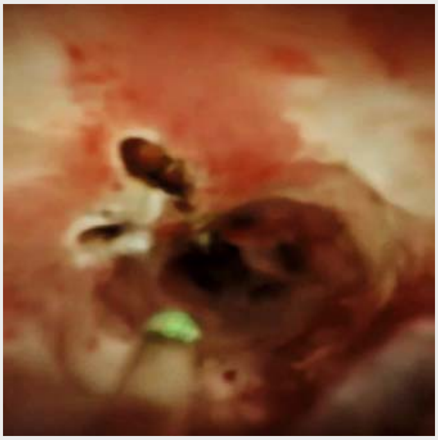
This study was approved by the Colorado Multiple Institutional Review Board.

Patients

This retrospectively identified case series included patients treated with laser dissection/ablation from February 2017 to September 2019 at a single tertiary medical center. All patients had non-malignant strictures with symptoms including abdominal pain, jaundice, and recurrent pancreatitis refractory to prior treatment with dilation and stenting. In regards to selection of patients for this treatment, those with strictures with concentric ring/band fibrosis or mucosal hyperplastic changes were considered amenable to laser dissection. Patients with extrinsic strictures or non-obstructive fibrotic bands or rings were not considered ideal candidates for laser therapy. Three patients had been previously described in case reports [5, 6]. All procedures were performed by a single endoscopist (RJS).

Technique

ERCP was performed using standard techniques with a side-viewing duodenoscope (Olympus, Center Valley, Pennsylvania, United States) in patients with normal anatomy or a pediatric colonoscope (Olympus) in a single patient status post-Whipple procedure. After deep cannulation, a 200- to 272-μm laser fiber (International Medical Lasers, Tualatin, Oregon, United States) was advanced into the desired duct. For intraductal strictures, direct visualization using a 10.5 Fr single-operator cholangiopancreatoscope (SpyGlass DS or DS2, Boston Scientific, Marlborough, Massachusetts, United States) guided placement of the fiber to the stricture location. Holmium (Litho, Quanta System, Italy) or thulium (Cyber TM, Quanta System, Italy) laser was applied (▶ **Fig. 1**) under saline immersion at the discretion of the endoscopist using lower power settings than lithotripsy (frequency of 8–10 Hz, energy of 0.5 Joules, and power of 5–

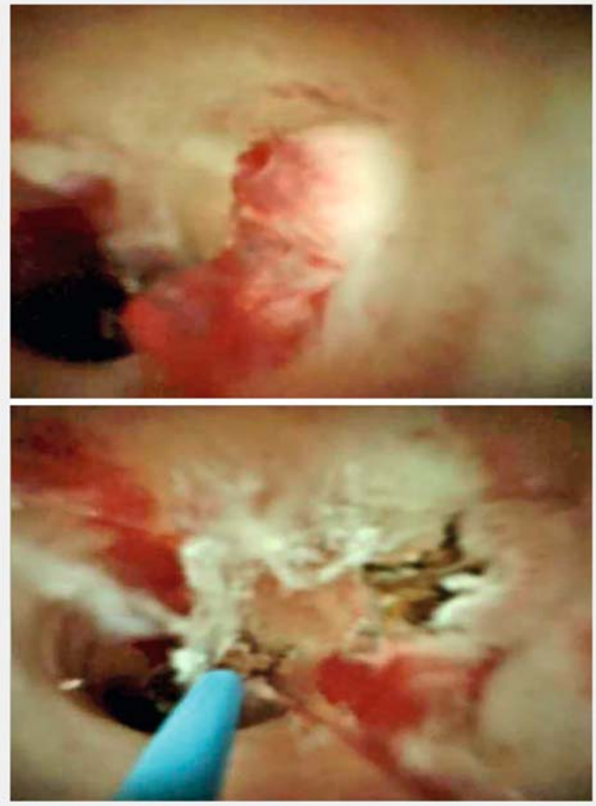


Video 1 Laser dissection of a pancreatic duct stricture.

▶ **Table 1** Patient characteristics (N = 11).

Variable	Mean (SD) or N (%)
Age	58 (12.2)
Female sex	10 (90.9 %)
Indication	
▪ Pancreatic duct stricture	8 (72.7 %)
▪ Pancreaticojejunostomy anastomotic stricture	1 (9.1 %)
▪ Intraductal papillary mucinous neoplasm ablation	1 (9.1 %)
▪ Bile duct stricture	1 (9.1 %)
▪ Prior number of ERCPs	3.6 (2.6)
Prior stricture dilations	9 (81.8 %)
▪ Maximum diameter of dilation (mm)	6 (1)
Prior stenting	10 (90.9 %)
▪ Maximum stent(s) total outer diameter (French)	14.2 (10.9)
Smoker	5 (45.5 %)
History of alcohol abuse	5 (45.5 %)
Disease duration (years)	5.5 (6.7)
Follow-up time (months)	12.1 (11.1)

20 Watts). Holmium enables lithotripsy of main pancreatic duct (PD) stones and was used simultaneously when stricture dissection was required to improve access to impacted stones upstream of PD strictures [9]. Compared to holmium, thulium provides a continuous wave that has a shallower depth of penetration and may be beneficial in dissection or ablation [10]. For stricture dissection, gentle strokes of the laser fiber using a "cut" setting from a distal to proximal approach was applied in three quadrants until improved luminal patency permitted



▶ **Fig. 2** Intraductal papillary mucinous neoplasm (left) and after laser ablation (right).

advancement of the cholangiopancreatoscope followed by balloon dilation and therapeutic stenting in all patients (▶ **Video 1**). For ablation, which was used to treatment an intraductal papillary mucinous neoplasm (IPMN), shorter strokes using both "cut" and "coagulation" were performed until obliteration of the tissue to the level of the mucosal surface was achieved.

Outcomes

Initial stricture measurements by pancreatography, after the previously placed stent had been removed and prior to CPL, used the diameter of the duodenoscope as a reference point. Immediate technical success was defined as the ability to traverse the stricture with the cholangiopancreatoscope after dissection or obliteration of the lesion and short-term technical success for strictures was defined as greater than 90 % resolution of the treated stenosis as seen on a subsequent pancreatography session compared to pre-treatment pancreatography. Adverse events (AEs) were defined in accordance to ERCP-related adverse events as outlined by the American Society for Gastrointestinal Endoscopy (ASGE) [11].

Results

A total of 11 patients (90.9 % female, mean age of 58 ± 12.2 years) underwent laser dissection/ablation (▶ **Table 1**). Nine patients had refractory PD strictures, one of whom had a concom-

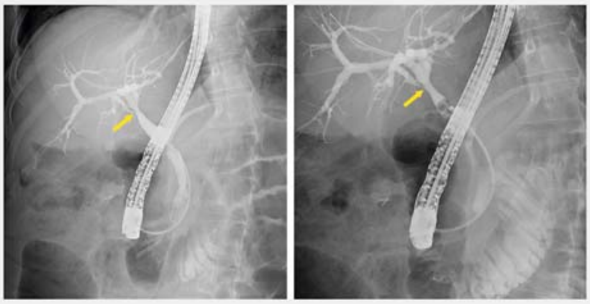
▶ **Table 2** Laser treatment details.

Patient	Location of laser treatment	Disease etiology	No. laser sessions	Type of laser	Total energy (Kilojoules)	Immediate technical success	Short-term technical success	Adverse events
1	1. Pancreaticojejunostomy Anastomosis 2. PD body stricture	Ampullary cancer s/p Whipple	2 (over 2 months)	1.Holmium 2.Thulium	1. 0.19 2. 1.69	1.Yes 2. No	1.Yes 2. No	None
2	PD body stricture	Idiopathic chronic pancreatitis	1	Holmium	7.82	Yes	Yes	None
3	Common hepatic duct	Cholecystectomy injury	1	Thulium	1.61	Yes	Yes	None
4	PD head stricture	Alcohol/smoking chronic calcific pancreatitis	1	Holmium	19.82	Yes	Yes	None
5	PD head stricture	Alcoholic chronic pancreatitis	2	Holmium (twice)	1. 25.56 2. 12.6	Yes	No	None
6	PD head stricture	Idiopathic chronic pancreatitis	1	Holmium	3.64	Yes	Yes	None
7	PD head stricture	Alcohol/smoking chronic calcific pancreatitis	1	Holmium	18.16	Yes	Yes	None
8	1. PD head stricture 2. PD body stricture	Idiopathic chronic pancreatitis	1	1. Thulium 2. Thulium	2.31	1. Yes 2. Yes	1.Yes 2. Yes	None
9	1. PD body stricture 2. PD genu stricture	Intraductal papillary mucinous neoplasm	3 (over 39 months)	1. Holmium 2. Holmium 3. Thulium	1. 0.33 2. 0.71 3. 0.28	1. Yes 2. Yes	1. Yes 2. Yes	None
10	PD body stricture	Alcohol/smoking chronic calcific pancreatitis	1	Holmium	9.25	Yes	Yes	Yes (pneumonia)
11	PD head stricture	Alcohol/smoking chronic calcific pancreatitis	3	1. Holmium 2. Holmium 3. Holmium	1. 16.26 2. 17.62 3. 9.90	Yes	Yes	None

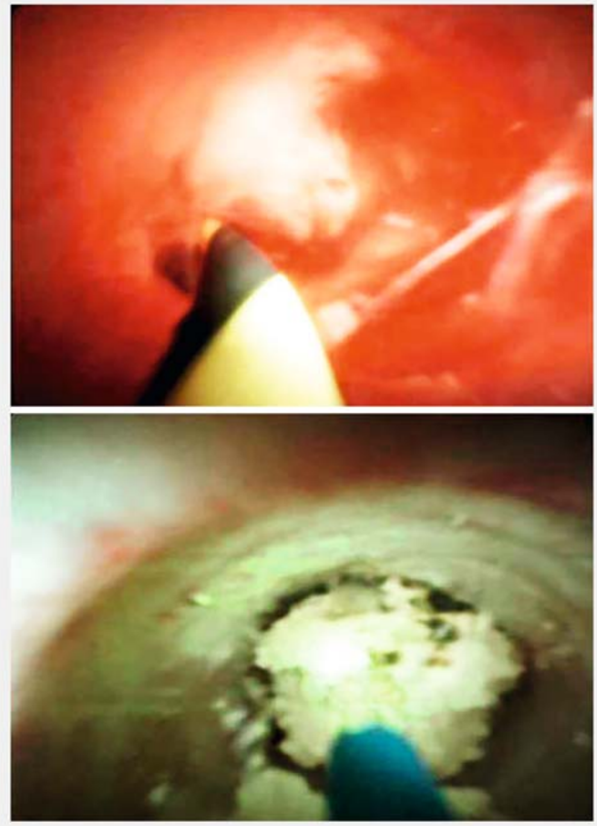
PD, pancreatic duct.

itant pancreaticojejunostomy anastomotic stricture. Three of these patients had two strictures along the PD treated with laser dissection. One patient had an inoperable intraductal papillary mucinous neoplasm (IPMN) (▶ **Fig. 2**) and recurrent episodes of pancreatitis despite therapeutic PD stenting and one patient had a refractory, symptomatic common hepatic duct/hilar stricture that did not improve with multiple side-by-side stents. Patients had a mean of 3.6 ERCPs prior to CPL with dilation/stenting and a mean total stent(s) outer diameter of 14.2 Fr for PD strictures.

In all, 17 (median 1, range 1–3) sessions of laser therapy were performed with holmium used most frequently (73.3 %) and a median energy delivered of 8.5 kJ (▶ **Table 2**). The cholangiopancreatoscope was unable to traverse the strictures prior to laser therapy. After laser therapy, immediate technical success (e. g. ability to traverse the stricture with the cholangiopancreatoscope) (▶ **Fig. 3**) was 94.1 % with the one failure being in a post-Whipple patient where laser dissection was successful in opening an anastomotic stricture that reoccurred despite prior needle-knife/balloon dilation stricturoplasty, but failed in improving lumen patency of a stricture in the body of the pancreas. In the case of IPMN ablation, the pancreatoscope was immediately able to be advanced past the ablated IPMN and subsequent ERCP with pancreatoscopy revealed minimal residual tumor with significantly less mucin identified. The short-term technical success (> 90 % resolution of the treated stenosis on subsequent ERCP) rate was 88.2 % (15/17 strictures) where in addition to the aforementioned post-Whipple patient, one patient with chronic pancreatitis secondary to alcohol did not have improvement in a stricture in the head of the pancreas despite two sessions of holmium therapy. Laser therapy also permitted access to downstream PD stones for concomitant lithotripsy (▶ **Fig. 4**) in seven patients (63.6 %) in whom stricture dilation alone due to balloon breakage or difficult fibrosis was insufficient. The patient with IPMN has had no further episodes of pancreatitis at 39 months since index laser ablation and contin-



▶ **Fig. 3** Common hepatic duct/hilar stricture before (left) and after (right) laser dissection.



▶ **Fig. 4** Stricture in the pancreatic duct (above) treated with laser dissection and permitted access to obstructing stone for lithotripsy (below).

ues to receive pancreatic duct stent exchanges at 6-month intervals to prevent pancreatic duct obstruction from gradual mucin accumulation. After laser therapy, patients underwent a mean of 2.7 ERCPs with stenting typically performed after pancreatoscopy-guided lithotripsy until complete clearance of stones was achieved. In patients who received further stenting on subsequent ERCP, stents with a larger diameter (mean increase of 3.9 Fr) were able to be placed. During a mean follow-up period of 12.1(± 11.1) months, there have been no stricture recurrences.

In terms of AEs, one episode of likely anesthesia-related pneumonia occurred and there were no endoscopy-related AEs such as pancreatitis or perforation.

Discussion

Refractory pancreatic and biliary strictures and inoperable neoplasms such as IPMNs can pose significant problems such as persistent pain, stent-dependency, or recurrent bouts of pancreatitis. While typically treated with numerous sessions of multiple plastic or fully-covered metal stents, these therapies may not provide an effective long-term solution and cause significant burden in the number of repeat procedures for these patients that may often render patients "stent-dependent." Given the morbidity of surgery and the multi-factorial mechanisms of pain of patients suffering from chronic pancreatitis, salvage endoscopic therapies such as laser dissection/ablation may provide an alternative, effective, and durable treatment modality.

In this case series, we demonstrate the potential efficacy of holmium or thulium laser therapy in treating refractory strictures. With regard to pancreatic duct strictures, the use of fully-covered metal stents may provide an effective long-term option, but in addition to cost, are subject to serious AEs including stent migration, stent-induced and non-traversable de novo strictures, and obstruction of the PD side branches, which may result in pancreatic sepsis [12, 13]. Furthermore, catheter access across the stenosis is required for dilation and placement of plastic or metal stents. With laser dissection, the stenosis can be treated with guidewire traversal of the stricture alone. In addition, in patients with symptomatic PD stones, laser dissection of downstream stenoses can improve access and allow for immediate lithotripsy of impacted stones, providing an efficient means of endoscopic therapy. Lastly, effective laser dissection may reduce the number of additional procedures associated with stent exchanges/upsizing while also reducing risk of development of stent-associated strictures.

Salvage methods for non-operable IPMN include radiofrequency ablation (RFA) or alcohol ablation performed via ERCP or under endosonographic guidance [14, 15]. Baughman et al detailed use of laser fulguration with a holmium laser fiber within a ureteroscope through a percutaneous biliary drain in a single patient with a biliary IPMN, but application of laser ablation endoscopically in the pancreatic duct under direct visualization as described in this study offers another treatment modality for IPMN [16]. While surgical resection remains the treatment of choice for main-duct IPMNs, further studies examining laser ablation are needed in non-surgical symptomatic patients.

Limitations of this study include its retrospective nature and lack of long-term follow-up data. In addition, as one expert endoscopist performed all laser dissection/ablation with patients selected at the discretion of the endoscopist, the generalizability remains limited at this time.

Conclusion

In summary, laser dissection/ablation is a feasible salvage therapy for treatment of refractory pancreaticobiliary strictures. To improve intraductal lithotripsy targeting of impacted stones with associated tight downstream strictures, dissection may be beneficial. Further, patients who have already had dilation and therapeutic stenting without appreciable improvement by pancreatography or in strictures where only the guidewire is able to traverse, may potentially benefit from this technique. We caution, however, that using this technique in patients with complete obstruction and inability to traverse the stricture with the guidewire as laser dissection may result in ductal perforation. If a smaller-diameter .025-inch wire is used to traverse the stenosis, a laser fiber may be passed in parallel through the cholangioscope working channel and serve as a "safety wire" to assure bridging the stenosis for stenting in case of transmural ductal injury. Larger multicenter studies with long-term follow-up, however, are required to demonstrate the safety, efficacy, and durability of this novel technique. In addition, given the cost associated with use of both the cholangioscopy and laser systems, randomized studies comparing this technique with other modalities are warranted to address cost-effectiveness but would need to be weighed with surgical alternatives and associated morbidity and mortality. Finally, while this technique should only be performed in expert hands with significant experience not only in therapeutic pancreatic ERCP but also with cholangiopancreatoscopy, laser therapy adds to the arsenal of tools available to the endoscopist.

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Competing interests

Dr. Shah is a consultant and advisory board member for Boston Scientific and a consultant for Cook Medical and Olympus.

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