

Treatment of hypertriglyceridemia-induced pancreatitis by pancreatic duct stenting: a retrospective study

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Abstract

Background

To evaluate the effectiveness and safety of pancreatic duct (PD) stenting under endoscopic retrograde cholangiopancreatography (ERCP) in the treatment of patients with hypertriglyceridemia-induced pancreatitis (HTGP).

Methods

The clinical data of 84 patients with HTGP admitted to General Hospital of Ningxia Medical University between January 1, 2017, and July 1, 2020, were retrospectively analyzed. Patients were divided into a conservative group (n = 51) and a stent group (n = 33). The complication rate, transfer rate to intensive care unit (ICU), acute physiological and chronic health APACHE II score at 48 h of admission, triglyceride level and duration of enzyme-inhibiting drug use were compared between the two groups.

Results

A total of 84 patients with HTGP were enrolled, 68 males and 16 females with a mean age of (38.55 ± 9.63) years. The median triglyceride level at admission was 16.40 (11.85–31.33) mmol/L. All 33 patients in the stent group had successful pancreatic duct stent placed, a large amount of **mucinous** material filling of the pancreatic duct was clearly observed in 16 patients (48%). The incidence of persistent organ failure was higher in patients with this substance in the pancreatic duct [31.25% (5/16) versus 0% (0/17), $P < 0.05$]. After the treatment, leukocytes, amylase, triglycerides and APACHE II scores of both in conservative and stent group were significantly lower than those before the treatment ($P < 0.05$). Patients in the stent group had significantly lower APACHE II scores after treatment than those in the conservative group [(4.65 ± 2.63) versus (2.94 ± 1.45), $P < 0.05$]. The number of days of fasting, length of hospital stay, and duration of enzyme inhibiting drug use were significantly lower in the stent group than in the conservative group ($P < 0.05$). The incidence of local complications in the stent group was lower than that in the conservative group [0% (0/33) versus 11.76% (6/51), $P < 0.05$], and the overall complication rate was also significantly lower than that in the conservative group [9.09% (3/33) versus 47.06% (24/51), $P < 0.05$].

Conclusion

PD stent implantation is a safe and effective treatment strategy, which can quickly relieve abdominal pain, reduce hospitalization time and improve prognosis in patients with HTGP.

Conclusion

Pancreatic duct stenting is a safe and effective treatment strategy as it can rapidly relieve the clinical symptoms, reduce the length of hospital stay and improve the prognosis of patients with HTGP.

Trial Registration:

This study was registered as a single-centre, retrospective case series at chictr.org.cn.

What Is Known

The effect of simple conservative treatment for severe HTGP patients is not good, and there are still high complications and mortality. Therefore, the treatment of HTGP is still a difficult problem.

what is new The innovation of this paper is to improve abdominal pain, reduce complications and shorten hospital stays by the early placement of pancreatic duct stents to alleviate PD obstruction and PD hypertension.

Introduction

Acute pancreatitis (AP) is an acute abdominal condition caused by an abnormal release of digestive enzymes, which can digest the pancreas and its surrounding organs. AP is characterized by local inflammation of the pancreas, and it can contribute to the early development of multiple organ dysfunction. The prevalence of pancreatitis is around (4.9 ~ 73.4)/100000 worldwide, and has increased significantly in the past decades [1–3]. Cholelithiasis, excessive drinking and hypertriglyceridemia are common causes of AP, hypertriglyceridemia accounting for up to 10% of all cases of AP [4]. In the past 16 years, the annual admission rate of HTGP patients in China has increased from 14.3–35.5% [5]. The incidence of HTGP tends to be younger, which is more serious and more prone to relapse than other types of pancreatitis [6]. 29% of HTGP patients had acute peripancreatic fluid collection and 35% had pancreatic necrosis. Most of these patients were more likely to be admitted to an ICU, result in susceptible to developing persistent organ failure, multiple organ failure, and persistent systemic inflammatory response syndrome(SIRS)[7, 8].

In addition to fluid resuscitation, pain control, and nutritional support, which several principal treatment, HTGP treatment also includes plasma exchange, insulin, heparin, and long-term anti-hypertriglyceridemia medications [9]. At present, there is no unified treatment guide. However, Previous studies have shown that the serum triglyceride level in patients is closely related to the HTGP severity, so, lipid-lowering treatment remains an essential component of HTGP management[10], but there is no clear evidence to indicate that early control of triglyceride levels might affect the incidence of complications and mortality of acute pancreatitis[11]. In addition, recent studies have shown that the rapid reduction of TG levels does not necessarily bring additional benefits to the overall outcome of treatment [12, 13]. Severe patients with poor efficacy of simple conservative treatment still have high complications and mortality. Therefore, the treatment of HTGP is still a difficult problem [14, 15].

It is necessary to master the pathogenesis of AP for treatment. Some studies believe that PD obstruction and acinar overstimulation play an important role in the early-stage, and PD pressure may play a key role in the onset and progression of the disease [16, 17]. Some studies also reported that early placement of PD stents can effectively alleviate PD obstruction, reduce mortality, and reduce the incidence of serious complications [16, 18].

Recently, we also reported that early endoscopic pancreatic stent implantation in AP patients within 48 hours after admission can effectively shorten fasting time and hospital stay, low complication rate [19, 20].

However, in our clinical work, we found that HTGP patients also suffered from PD obstruction, which resulted in poor pancreatic juice drainage. Smooth pancreatic juice drainage is of great significance for symptom relief and rapid recovery of HTGP patients. Based on the above clinical observations, this study will evaluate the clinical efficacy of PD stenting in the treatment of HTGP.

Materials And Methods

Patients

Retrospective analysis of clinical data of HTGP patients admitted to the General Hospital of Ningxia Medical University from January 1, 2017 to July 1, 2020. The inclusion criteria included (1) HTGP was the first seizure; (2) Stent placement within 24 hours of admission. Exclusion criteria included (1) pregnant and lactating women; (2) Acute fAttacks with Chronic Pancreatitis; (3) Patients with poor general condition can't tolerate ERCP; (4) Incomplete clinical data ; (5) Extramural hospital treatment > 72 hours. Finally, 84 patients with HTGP were enrolled and divided into two groups according to the treatment method: the conservative group (n = 51) and the stent group (n = 33). This study was approved by the Ethics Committee of the General Hospital of Ningxia Medical University (No. 2019 - 467). All patients volunteered to participate in this study and signed an informed consent form.

Diagnosis

The diagnosis of acute pancreatitis requires the presence of two of the following three criteria: (1) abdominal pain related to acute pancreatitis; (2) Serum amylase or lipase activity > 3 times the upper limit of normal value; (3) The imaging findings were consistent with those of acute pancreatitis. Diagnosis of HTGP: based on the diagnosis of acute pancreatitis, The diagnosis of hypertriglyceridemic pancreatitis is based upon the triglyceride > 1000 mg/dl (11.3 mmol/L) or triglyceride 500 ~ 1000 mg/dl (5.65 ~ 11.3 mmol/L) and serum is chylous [21].

Treatment

The standardized treatment offered to all the patient by the initial management guidelines for acute pancreatitis of the American Association of Gastroenterology[22] after admission. At the same time, patients who received lipid-lowering treatment were given the low molecular weight heparin combined

with insulin. Patients in the stent group received PD stent implantation with lipid-lowering treatment within 24 hours after admission. All catheter-guided endoscopic intubation procedures were performed by physicians with more than 10 years of experience. The endoscope reaches the descending segment of the duodenum through the gastric cavity. After reaching the duodenum, the duodenal papilla is found at the inner side of the duodenum. After successful intubation, the guide wire is confirmed to run along the direction of the PD through fluoroscopy, followed up with the duodenal papillary sphincter incision knife to draw the PD, until clear pancreatic juice is observed to flow out, and the PD stent is placed along the guide wire. Endoscopic papillotomy shall be performed during the operation if the duodenal papilla is obvious oedema, the opening is too small, or biliary tract angiography is expected to be performed before the operation.

Related indications

Indications for surgery and PD stent placement

1) Moderate and severe AP; 2) Necrotizing pancreatitis, especially large area necrosis, is suspected to damage the integrity of PD; 3) There are many peripancreatic effusion or local complications; 4) Patients at risk of post-ERCP pancreatitis; 5) Obstructions were found in PD during operation.

Indications for first oral intake

Functions of the gastrointestinal system recovered, abdominal pain and distension was significantly relieved. After drinking water, the abdominal symptoms did not increase significantly and the serum amylase did not elevate. When to start enteral feeding, type of fat consumed should be paid attention. Meanwhile, the changes of triglyceride, blood glucose and amylase were detected.

Discharge indication

The patients had regained complete oral intake without any supplemental nutrition; had no symptoms of infection, no obvious abdominal pain, and amylase returned to normal.

Indications of pancreatic stent removal

Repeated whole abdominal CT scan every 2 weeks after discharge showed the pancreas size and morphology returned to normal level without local complications, and the patient had no pancreatitis-related abdominal pain. The average stent retention time was 2 months.

Outcome indicators

Primary endpoints

The incidence of complications, mortality, incidence of new organ failure, Intensive Care Unit (ICU) admission rates, fasting days, hospitalization days, duration of pancreatic enzyme use, etc.

Secondary endpoints

The white blood cell count, serum amylase value, triglyceride value and APACHE II score were compared between the two groups before and after treatment (48 hours after admission).

Statistical analysis

The statistical analyses were performed using the Statistical Package for the Social Sciences version 20.0 (SPSS Inc., Chicago, IL, USA). Non-normally distributed metric variables were analyzed by the Kruskal–Wallis test and Mann–Whitney U-test. The same group (before and after the medical treatment) were analyzed by Wilcoxon's signed-rank test. The chi-square test or Fisher's exact probability method was employed to assess the classified data (%) for comparison between groups. $P \leq 0.05$ was considered statistically significant.

Results

A total of 84 patients were included in the study (68 males and 16 females). The average age was (38.55 ± 9.63) years old. The median serum amylase at admission was 479.00 (245.00-785.00) U / L, the white blood cell count was (14.55 ± 5.37) 10^9 / L, the median triglyceride was 16.40 (11.85–31.33) mmol / L, and the median time from onset to admission was 24 (24–48) h. There was no significant difference in gender, age and other general baseline data between the two groups ($P > 0.05$). As seen in Table 1 for details.

Table 1
Comparison of clinical data of two groups of patients at admission

Variable	Conservative group (n = 51)	Stent group (n = 33)	t/z/ χ^2 value	P value
Age (Y)	39.27 ± 9.60	37.42 ± 9.69	-0.859	0.393
Gender, case(%)			0.951	0.329
Male	43(84.31)	25(75.76)		
Female	8(15.69)	8(24.24)		
BMI	26.39 ± 3.92	26.36 ± 3.86	-0.034	0.973
Severe AP, case(%)	11(21.57)	5(15.15)	0.548	0.459
Organ failure, case(%)	30(58.82)	25(75.76)	2.542	0.111
Fatty liver, case(%)	42(82.35)	24(72.72)	1.006	0.316
Diabetes, case(%)	15(29.41)	8(24.24)	0.269	0.604
Time from admission to onset, h, (M)	24(24–48)	24(21–48)	-1.000	0.317
BalthazarCT score	6.49 ± 1.34	6.42 ± 1.80	-0.203	0.840

Comparison of laboratory indexes before and after treatment

The differences in detection indexes between the conservative group and stent group before and after treatment were compared. Intra-group comparison, compared with before treatment, white blood cells, amylase, triglycerides, and APACHE II score of conservative group and stent group were significantly lower after treatment ($P < 0.05$). Comparison between groups, after treatment, the APACHE II score of the stent group was lower than that of the conservative group, and the difference was statistically significant ($P < 0.05$). As seen in Table 2 for details.

Table 2
Comparison of clinical data between the two groups before and after treatment

variable	Conservative group (n = 51)		Stent group (n = 33)	
	Before treatment	After treatment	Before treatment	After treatment
Serum amylase, U/L(M)	504.00(247.00-883.20)	154.80(69.00-312.00) ^a	426.15(222.05-608.98)	133.25(70.35-183.43) ^a
White blood cell value, 10 ⁹ /L	15.13 ± 5.23	10.26 ± 3.40 ^a	13.65 ± 5.55	8.77 ± 3.41 ^a
Triglyceride, mmol/L, (M)	11.86(11.85–31.05)	5.89(3.93–8.73) ^a	19.83(11.85–39.18)	5.45(3.30–7.23) ^a
Blood glucose level, mmol/L, (M)	12.98(8.70-18.03)	8.85(7.12–10.98) ^a	12.51(6.28–17.88)	9.53(5.07–12.81) ^a
APACHEII score, score	8.73 ± 2.50	4.65 ± 2.63 ^a	8.30 ± 2.77	2.94 ± 1.45 ^{ab}
^a Compared with before treatment, P < 0.05; ^b Compared with the conservative group, P < 0.05				

Comparison of prognostic indicators

No death occurred in both groups. The fasting days, hospital stay and the use time of enzyme inhibitors in the stent group were lower than those in the conservative group (P < 0.05). In-stent group, 3 patients (15.0%) developed respiratory failure 48 hours post-operation, 1 of whom was transferred to ICU due to severe respiratory failure, disseminated intravascular coagulation and electrolyte disturbance. This patient was then transferred back to the general ward the next day after plasma exchange. After 48 hours of treatment, 19 patients in the conservative group developed new-onset organ failure, of which 10 patients were transferred to ICU for multiple organ failure and electrolyte disorder mainly caused by respiratory failure and renal failure. In-stent group, 2 patients were treated with plasma exchange due to renal failure and severe electrolyte disturbance, and 1 patient was treated with peritoneal puncture drainage due to ascites. In the conservative group, 6 patients were treated with plasma exchange, 1 patient was treated with thoracic puncture drainage, and 2 patients were treated with abdominal puncture drainage. The incidence of total complications and local complications in the stent group was lower than that in the conservative group (P < 0.05).As seen in Table 3 for details.

Table 3
Comparison of prognosis between two groups

variable	Conservative group (n = 51)	Stent group (n = 33)	t/z/ χ^2 value	P value
Fasting time,d,(M)	6(4–11)	3(2–5)	-4.598	<0.001
Hospitalization time,d,(M)	12(9–15)	5(3–9)	-5.747	<0.001
Duration of use of pancreatic enzymes, d,(M)	6.00(3.75-9.00)	1.00(0–1.00)	-4.092	<0.001
Transfer to ICU for treatment,case(%)	10(19.60)	1(3.03)	5.772	0.016
Total complications,case(%)	24(47.06)	3(9.09)	14.864	<0.001
New organ failure,case(%)	19(37.25)	3(9.09)	9.150	0.002
SIRS,case(%)	7(13.73)	2(6.06)	1.319	0.251
Local complications,case(%)	6(11.76)	0	6.284	0.012
Walled-off necrosis	4(7.84)	0		
Pancreatic pseudocyst	1(1.96)	0		
Infectious pancreatic necrosis	1(1.96)	0		

Operative observation

33 patients successfully underwent PD stent implantation. During the operation, 16 cases (48%) could be clearly observed that the PD was filled with a large amount of mucinous material, which was called PD protein thrombus (Fig). The incidence of PD protein thrombus in mild, moderate, and severe HTGP was 17% (2 / 12), 56% (9 / 16) and 100% (5 / 5), respectively. The blood glucose, Balthazar CT score and APACHE II score of HTGP patients with this substance in the PD were higher than those of patients without PD protein thrombus ($P < 0.05$). The incidence of persistent organ failure was higher in patients with this substance in the PD, but there was no significant difference in hospitalization time between the two groups after treatment (Table 4). After the duodenal sphincter incision knife suction to clean up the substance, clear pancreatic juice can be seen. Removal of white matter for cytological examination was irregular necrotic tissue, a small amount of inflammatory cell infiltration

Table 4
Comparison of patients with and without PD protein thrombus

variable	PD protein thrombus(n = 16)	without PD protein thrombus(n = 17)	t/z/ χ^2 value	P value
APACHEII score, score	8.88 ± 4.05	4.94 ± 3.15	3.098	0.004
Balthazar CT score, score	7.19 ± 1.75	5.60 ± 1.50	-2.693	0.012
Triglyceride(admission),mmol/L(M)	22.93(17.35–45.57)	11.90(8.87–29.14)	-1.821	0.069
Blood glucose (admission),mmol/L(M)	15.83(11.16–19.89)	6.93(5.77–13.78)	-2.882	0.004
persistent organ failure(n, %)	5(31.25)	0	7.475	0.006
hospitalization time, d(M)	5(4–9)	4(3–10)	-0.803	0.444

Adverse reactions associated with ERCP

No post-ERCP pancreatitis occurred in all patients, but 2 patients developed post-ERCP amylase elevation after stent placement. One patient with difficulty intubation was caused by intraoperative stimulation of the PD. Serum amylase returned to normal within 48 h in both patients without severe adverse events.

Discussion

The pathogenesis of HTGP is still unclear. At present, studies in animal models[23] believe that the free fatty acids produced by the hydrolysis of large amounts of TG cause pancreatic cell damage and ischemia. The increase of free fatty acids and chylomicrons also aggravates the disturbance of pancreatic microcirculation, leading to ischemia and necrosis in the pancreas [9]. Endoplasmic reticulum stress is also thought to be associated with the occurrence of HTGP [24]. Studies have shown that some specific genes are also associated with HTGP [25,26]. As the pathogenesis is not entirely clear, so there are no clear guidelines for HTGP treatment. Studies have pointed out apart from conventional fasting, rehydration, analgesia, and trypsin inhibitor treatment. In HTGP the earlier (within 48 h) to decrease triglyceride levels below 500mg/dl (5.65mmol/L), the less likely organ dysfunction occurs. Therefore, lipid-lowering has become first-line treatment for HTGP treatment.

According to the animal experiments of Harvey [28] and Markus [29] et al, whether biliary pancreatitis, alcoholic pancreatitis or obstructive pancreatitis, PD obstruction is considered to be key events. Many studies also believe that PD obstruction and hypertension are important factors in the development of AP [16, 30]. Therefore, HTGP patients may also have pancreatic duct obstruction. In our study, 48% of HTGP patients had white flocculent material in the pancreatic duct, of which 87% had moderate and severe HTGP. The APACHE II score and Balthazar CT score of patients with this substance were significantly

higher than those of other patients, and the incidence of persistent organ failure [31.25% (5 / 16) vs 0% (0 / 17), $P < 0.05$] and admission blood glucose were also higher ($P < 0.05$). However, persistent hyperglycemia may be a risk factor for early exacerbation of pancreatitis [31], but there was no significant difference in hospitalization time between the two groups after pancreatic duct stent implantation. the white flocculent substance in the pancreatic duct is related to the severity of the disease in patients with HTGP to a certain extent, which may hinder the excretion of pancreatic juice and induce or aggravate HTGP [32].

Based on my findings, PD stent placement as well as conservative treatment can drainage to relieve the potential obstruction of pancreatic juice in patients with HTGP. After unobstructed drainage of pancreatic juice, we found that the application timing of anti-enzyme drugs in the stent group was shortened by about 83% compared with the conservative group ($P < 0.05$). The reason may be that patient in the stent group have unobstructed drainage of pancreatic juice, weakened the reaction of enzymes and substrates, eliminated the risk factors of pancreatic enzyme damage, and reduced the dependence on pancreatic enzyme inhibitors in treatment. The fasting time of patients in the stent group was significantly shorter than that in the conservative group by about 50% ($P < 0.05$), demonstrated that pancreatic stent implantation can quickly relieve abdominal symptoms and accelerate gastrointestinal recovery compared with single conservative treatment to achieve early complete oral feeding. Early oral feeding in HTGP patients helps maintain normal intestinal flora and reduces the incidence of infection and organ failure [34]. The results of this study showed that the incidence of new organ failure in the stent group was significantly lower than that in the conservative group (9.09% vs 37.25%, $P < 0.05$), which was inevitably related to the shortened fasting time.

Previous studies have shown that rapid lipid-lowering can improve the prognosis of patients with HTGP [35]. The results of this study showed that there was no significant difference in serum triglyceride levels between two groups after the same lipid-lowering treatment, but the APACHE II score and hospitalization time of the stent group were significantly lower than the conservative group($P < 0.05$). Under the premise of consistent lipid-lowering degree, early unobstructed drainage of pancreatic juice has a positive effect on the prognosis of the disease. Acosta et al [36] also confirmed that the duration of PD obstruction is the main factor in determining the severity of pancreatic lesions. Severe pancreatic lesions in patient with obstruction duration of less than 48 h are rare; in contrast, almost all patients with PD obstruction for more than 48 hours have pancreatic necrosis. In our study, the hospital stay and fasting time of patients in the stent group were about 58% and 50% shorter than those in the conservative group ($P < 0.05$). We observed that the abdominal pain of patients was significantly relieved after placement of the PD stent, which may prompt patients in the stent group to quickly resume diet. Previous studies have also found that pancreatic duct obstruction can cause pain in patients, and that drainage of pancreatic juice can effectively relieve this pain [37]. Pain from pancreatic is main caused by obstruction of pancreatic duct dilatation, or inflammatory reaction, increased interstitial pressure, ischemia and other pain caused by obstruction of pancreatic duct dilatation. After unobstructed drainage of pancreatic juice, the pain caused by PD spasms is ameliorated [38]. Therefore, patients showed abdominal symptoms improved quickly following pancreatic duct stent implantation.

In this study, the incidence of complications in the stent group was significantly lower than that in the conservative group ($P < 0.05$), indicating that unobstructed drainage of pancreatic juice can further prevent pancreatic necrosis and infection. PD stent has a good decompression and drainage effect for pseudocysts which formed when disruption of the main pancreatic duct. Therefore, for patients with severe acute pancreatitis, early PD stenting can relieve PD obstruction, control disease progression, and reduce the occurrence of complications such as pancreatic pseudocysts. PD stent decompresses the pancreas, contributing to the absorption of peripancreatic exudates and the improvement of pancreatic morphology [39]. At the same time, the patient's abdominal symptoms are rapidly relieved, and the fasting time is greatly shortened to maintain intestinal physiological function and reduce the risk of systemic infection [40]. Studies have found that 31–44% of patients with acute necrotizing pancreatitis have PD rupture [41, 42]. For these patients, the PD drainage through the duodenal papilla can directly enter the necrotic effusion cavity through the ruptured PD, thereby achieving drainage without additional invasive procedures [43, 44]. PD stent implantation based on conservative treatment can achieve local to systemic symptom relief and disease reversal in HTGP patients.

The median value of serum amylase in both groups was low. In previous studies, the amylase level in HTGP patients was lower than that in biliary pancreatitis and even at normal levels, which was related to the higher serum triglyceride in HTGP patients affecting the determination of serum amylase [45]. There were 2 cases (6%) of elevated serum amylase related to ERCP in the stent group, which was considered hyperamylasemia, and the proportion was lower than that in previous studies [46]. No post-ERCP pancreatitis occurred in this study. In addition to the gentle and skilled operation, PD stent implantation also plays an important role [47]. PD stent placement under ERCP is difficult, even for the most experienced endoscopists, there is still a failure rate of 5–10% [48]. Therefore, the operation level of ERCP has a great influence on the effect of the operation and the prognosis of patients. Effective operation is the basic condition for the treatment of HTGP with a PD stent.

Our study found that HTGP patients may have potential PD obstruction. The protein suppository clearance and the PD stent implantation can relieve the obstruction of the PD and drain the pancreatic juice. The above results showed that combined treatment could relieve the symptoms of the patients faster, shorten the hospitalization time, and have fewer complications.

Conclusions

PD stent implantation as a treatment option in HTGP patients are safety and efficacy, Therefore, more indepth investigations of PD stent implantation will provide new ideas for the treatment of HTPG. This study is not a large sample randomized controlled trial, so there are some limitations.

Abbreviations

AP, Acute pancreatitis, **HTGP**, hypertriglyceridemia-induced pancreatitis, **ERCP**, Endoscopic retrograde cholangiopancreatography, **PD**, curve, Receiver operating characteristic, **BMI**, Body Mass Index, **OF**, Organ

failure, **SIRS**, systemic inflammatory response syndrome

Declarations

Availability of data and materials:

All data generated during this study are included in this published article.

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Contributions

Guarantor of integrity of the entire study: ZC, YW, WZ, CA; Study concepts: ZC, YW, WZ; Study design: ZC, CA, WZ; Definition of intellectual content: ZC, YW; Literature research: YW, WZ; Clinical studies: ZC, YW, WZ, CA; Data acquisition: ZC, YW; Data analysis: ZC, YW; Statistical analysis: WZ; Manuscript preparation: ZC; Manuscript editing: ZC, YW; Manuscript review: WZ. All authors reviewed and approved the manuscript.

Conflicts of Interest:

The authors have no conflicts of interest to declare.

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Ethics approval and consent to participate:

The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was approved by Ethics Committee of the General Hospital of Ningxia Medical University (No. 2019-467) and written informed consent was obtained from all patients. All procedures performed in this study involving human participants were by the Declaration of Helsinki (as revised in 2013). At chictr.org.cn, this study was recorded as a single-center, retrospective case-control study (ChiCTR1800017845).

Consent for publication:

Not applicable.

Competing interests:

The authors declare that they have no competing interests.

Authors' original submitted files for images:

Authors' original file for figure 1

References

1. Peery A F, Crockett S D, Barritt A S, et al. Burden of Gastrointestinal, Liver, and Pancreatic Diseases in the United States[J]. *Gastroenterology*, 2015,149(7):1731-1741.
2. Yadav D, Lowenfels A B. Trends in the epidemiology of the first attack of acute pancreatitis: a systematic review[J]. *Pancreas*, 2006,33(4):323-330.
3. Boxhoorn L, Voermans R P, Bouwense S A, et al. Acute pancreatitis[J]. *Lancet*, 2020,396(10252):726-734.
4. Valdivielso P, Ramírez-Bueno A, Ewald N. Current knowledge of hypertriglyceridemic pancreatitis[J]. *Eur J Intern Med*, 2014,25(8):689-694.
5. Jin M, Bai X, Chen X, et al. A 16-year trend of etiology in acute pancreatitis: The increasing proportion of hypertriglyceridemia-associated acute pancreatitis and its adverse effect on prognosis[J]. *J Clin Lipidol*, 2019,13(6):947-953.
6. Wang Q, Wang G, Qiu Z, et al. Elevated Serum Triglycerides in the Prognostic Assessment of Acute Pancreatitis: A Systematic Review and Meta-Analysis of Observational Studies[J]. *J Clin Gastroenterol*, 2017,51(7):586-593.
7. Wan J, He W, Zhu Y, et al. Stratified analysis and clinical significance of elevated serum triglyceride levels in early acute pancreatitis: a retrospective study[J]. *Lipids Health Dis*, 2017,16(1):124.
8. Zhang R, Deng L, Jin T, et al. Hypertriglyceridaemia-associated acute pancreatitis: diagnosis and impact on severity[J]. *HPB (Oxford)*, 2019,21(9):1240-1249.

9. Rawla P, Sunkara T, Thandra K C, et al. Hypertriglyceridemia-induced pancreatitis: updated review of current treatment and preventive strategies[J]. *Clin J Gastroenterol*, 2018,11(6):441-448.
10. Nawaz H, Koutroumpakis E, Easler J, et al. Elevated serum triglycerides are independently associated with persistent organ failure in acute pancreatitis[J]. *Am J Gastroenterol*, 2015,110(10):1497-1503.
11. Arvanitakis M, Ockenga J, Bezmarevic M, et al. ESPEN guideline on clinical nutrition in acute and chronic pancreatitis[J]. *Clin Nutr*, 2020,39(3):612-631.
12. He W H, Yu M, Zhu Y, et al. Emergent Triglyceride-lowering Therapy With Early High-volume Hemofiltration Against Low-Molecular-Weight Heparin Combined With Insulin in Hypertriglyceridemic Pancreatitis: A Prospective Randomized Controlled Trial[J]. *J Clin Gastroenterol*, 2016,50(9):772-778.
13. Miyamoto K, Horibe M, Sanui M, et al. Plasmapheresis therapy has no triglyceride-lowering effect in patients with hypertriglyceridemic pancreatitis[J]. *Intensive Care Med*, 2017,43(6):949-951.
14. de Pretis N, Amodio A, Frulloni L. Hypertriglyceridemic pancreatitis: Epidemiology, pathophysiology and clinical management[J]. *United European Gastroenterol J*, 2018,6(5):649-655.
15. Valdivielso P, Ramírez-Bueno A, Ewald N. Current knowledge of hypertriglyceridemic pancreatitis[J]. *Eur J Intern Med*, 2014,25(8):689-694.
16. Dubravcsik Z, Hritz I, Fejes R, et al. Early ERCP and biliary sphincterotomy with or without small-caliber pancreatic stent insertion in patients with acute biliary pancreatitis: better overall outcome with adequate pancreatic drainage[J]. *Scand J Gastroenterol*, 2012,47(6):729-736.
17. Wang G J, Li Y, Zhou Z G, et al. Integrity of the pancreatic duct-acinar system in the pathogenesis of acute pancreatitis[J]. *Hepatobiliary Pancreat Dis Int*, 2010,9(3):242-247.
18. Dubravcsik Z, Madácsy L, Gyökeres T, et al. Preventive pancreatic stents in the management of acute biliary pancreatitis (PREPAST trial): pre-study protocol for a multicenter, prospective, randomized, interventional, controlled trial[J]. *Pancreatology*, 2015,15(2):115-123.
19. Yao W, Wang Z, Yang Y, et al. Treatment of acute pancreatitis with early pancreatic stenting: a case series of 336 patients[J]. *Gland Surg*, 2021,10(9):2780-2789.
20. Yao W, Wang G, Wang Q, et al. Stenting of the pancreatic duct in the early phase of acute pancreatitis: a retrospective study[J]. *BMC Gastroenterol*, 2022,22(1):414.
21. Chinese Pancreatic Surgery Association C S O S. [Guidelines for diagnosis and treatment of acute pancreatitis in China (2021)][J]. *Zhonghua Wai Ke Za Zhi*, 2021,59(7):578-587.
22. Crockett S D, Wani S, Gardner T B, et al. American Gastroenterological Association Institute Guideline on Initial Management of Acute Pancreatitis[J]. *Gastroenterology*, 2018,154(4):1096-1101.
23. Garg R, Rustagi T. Management of Hypertriglyceridemia Induced Acute Pancreatitis[J]. *Biomed Res Int*, 2018,2018:4721357.
24. Zeng Y, Wang X, Zhang W, et al. Hypertriglyceridemia aggravates ER stress and pathogenesis of acute pancreatitis[J]. *Hepatogastroenterology*, 2012,59(119):2318-2326.
25. Chang Y T, Chang M C, Su T C, et al. Association of cystic fibrosis transmembrane conductance regulator (CFTR) mutation/variant/haplotype and tumor necrosis factor (TNF) promoter

- polymorphism in hyperlipidemic pancreatitis[J]. *Clin Chem*, 2008,54(1):131-138.
26. Ivanova R, Puerta S, Garrido A, et al. Triglyceride levels and apolipoprotein E polymorphism in patients with acute pancreatitis[J]. *Hepatobiliary Pancreat Dis Int*, 2012,11(1):96-101.
 27. Lu Z, Li M, Guo F, et al. Timely Reduction of Triglyceride Levels Is Associated With Decreased Persistent Organ Failure in Hypertriglyceridemic Pancreatitis[J]. *Pancreas*, 2020,49(1):105-110.
 28. Harvey M H, Wedgwood K R, Austin J A, et al. Pancreatic duct pressure, duct permeability and acute pancreatitis[J]. *Br J Surg*, 1989,76(8):859-862.
 29. Lerch M M, Saluja A K, Rünzi M, et al. Pancreatic duct obstruction triggers acute necrotizing pancreatitis in the opossum[J]. *Gastroenterology*, 1993,104(3):853-861.
 30. Lankisch P G, Apte M, Banks P A. Acute pancreatitis[J]. *Lancet*, 2015,386(9988):85-96.
 31. Zechner D, Spitzner M, Bobrowski A, et al. Diabetes aggravates acute pancreatitis and inhibits pancreas regeneration in mice[J]. *Diabetologia*, 2012,55(5):1526-1534.
 32. Wang Z, Wang Q, Song J, et al. Treatment of severe acute pancreatitis via endoscopic pancreatic stenting and nasopancreatic drainage: Case reports[J]. *Exp Ther Med*, 2019,17(1):432-436.
 33. Freeman M L. Pancreatic stents for prevention of post-ERCP pancreatitis: for everyday practice or for experts only?[J]. *Gastrointest Endosc*, 2010,71(6):940-944.
 34. Forsmark C E, Vege S S, Wilcox C M. Acute Pancreatitis[J]. *N Engl J Med*, 2016,375(20):1972-1981.
 35. Gavva C, Sarode R, Agrawal D, et al. Therapeutic plasma exchange for hypertriglyceridemia induced pancreatitis: A rapid and practical approach[J]. *Transfus Apher Sci*, 2016,54(1):99-102.
 36. Acosta J M, Rubio G O, Rossi R, et al. Effect of duration of ampullary gallstone obstruction on severity of lesions of acute pancreatitis[J]. *J Am Coll Surg*, 1997,184(5):499-505.
 37. Stone H H, Fabian T C, Dunlop W E. Gallstone pancreatitis: biliary tract pathology in relation to time of operation[J]. *Ann Surg*, 1981,194(3):305-312.
 38. Brescia F J, Portenoy R K, Ryan M, et al. Pain, opioid use, and survival in hospitalized patients with advanced cancer[J]. *J Clin Oncol*, 1992,10(1):149-155.
 39. Wang Z, Wang Q, Song J, et al. Treatment of acute pancreatitis with pancreatic duct decompression via ERCP: A case report series[J]. *Exp Ther Med*, 2020,20(3):2593-2598.
 40. Bakker O J, van Brunschot S, van Santvoort H C, et al. Early versus on-demand nasoenteric tube feeding in acute pancreatitis[J]. *N Engl J Med*, 2014,371(21):1983-1993.
 41. Lau S T, Simchuk E J, Kozarek R A, et al. A pancreatic ductal leak should be sought to direct treatment in patients with acute pancreatitis[J]. *Am J Surg*, 2001,181(5):411-415.
 42. Neoptolemos J P, London N J, Carr-Locke D L. Assessment of main pancreatic duct integrity by endoscopic retrograde pancreatography in patients with acute pancreatitis[J]. *Br J Surg*, 1993,80(1):94-99.
 43. Trevino J M, Tamhane A, Varadarajulu S. Successful stenting in ductal disruption favorably impacts treatment outcomes in patients undergoing transmural drainage of peripancreatic fluid collections[J]. *J Gastroenterol Hepatol*, 2010,25(3):526-531.

44. Shrode C W, Macdonough P, Gaidhane M, et al. Multimodality endoscopic treatment of pancreatic duct disruption with stenting and pseudocyst drainage: how efficacious is it?[J]. *Dig Liver Dis*, 2013,45(2):129-133.
45. Scherer J, Singh V P, Pitchumoni C S, et al. Issues in hypertriglyceridemic pancreatitis: an update[J]. *J Clin Gastroenterol*, 2014,48(3):195-203.
46. He Q B, Xu T, Wang J, et al. Risk factors for post-ERCP pancreatitis and hyperamylasemia: A retrospective single-center study[J]. *J Dig Dis*, 2015,16(8):471-478.
47. Kawaguchi Y, Ogawa M, Omata F, et al. Randomized controlled trial of pancreatic stenting to prevent pancreatitis after endoscopic retrograde cholangiopancreatography[J]. *World J Gastroenterol*, 2012,18(14):1635-1641.
48. García-Cano J, Viñuelas C M, Del M M M, et al. Pancreatic stent insertion after an unintentional guidewire cannulation of the pancreatic duct during ERCP[J]. *Rev Esp Enferm Dig*, 2018,110(7):416-420.

Figures

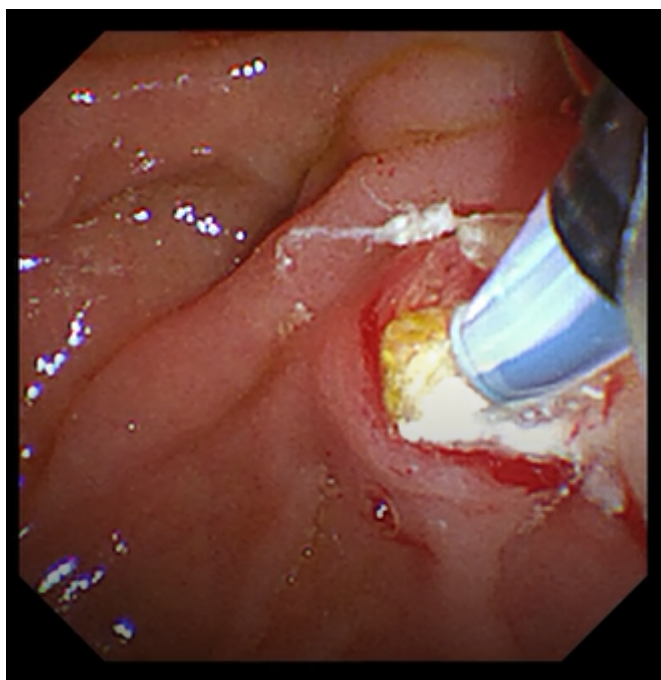


Figure 1

White obstruction in the pancreatic duct found during the operation