Systematic Review and/or Meta-analysis

INTERNATIONAL JOURNAL OF SURGERY

OPEN

Comparison of patency rates and complications with or without antithrombotic therapy following portal vein stent placement after pancreatic surgery: a systematic review and meta-analysis

Lin Chen, MD[a], Ziyan Wang, BSc[a,c], Liangbo Dong, MD[a], Zhiwei Wang, MD[b], Zehui Li, BSc[a,d], Weibin Wang, MD[a,e,f,*]

Background: Portal vein stent placement is used for portal vein stenosis. However, reports on postpancreatic surgery cases are rare. Whether antithrombotic therapy should be administered remains controversial. In this paper, the authors reviewed current data to evaluate the influence of antithrombosis on stent patency after pancreatic surgery.

Materials and methods: This systematic review and meta-analysis compared studies in which patients did or did not receive antithrombotic therapy after portal vein stent placement. The authors compared patency after stent placement and complication rate.

Results: There were 22 ($n = 207$) studies in which patients received antithrombotic therapy and 8 ($n = 61$) in which patients did not receive therapy. Antithrombotic agents, such as aspirin, clopidogrel, heparin, and warfarin, were used. The overall patency rates were similar between the groups (79.2% in the antithrombosis group vs. 88.0% in the nonantithrombosis group). Subgroup analyses included those for the etiology of stenosis, types of antithrombotic agents, acute or chronic stenosis, and causes of stent stenosis. None revealed a significant difference between the patency rates in the antithrombosis and nonantithrombosis groups. However, bleeding complications only occurred in patients who received antithrombotic therapy.

Conclusion: There is no significant benefit of antithrombotic therapy after portal vein stent placement following pancreatic surgery. Antithrombotic therapy should be performed with caution because it may cause complications, such as bleeding.

Keywords: antithrombosis, meta-analysis, pancreatic surgery, portal vein stenosis, stents, systematic review

Introduction

Portal vein stenosis is a rare complication of pancreatic surgery, particularly when the portal vein is resected and reconstructed[1,2]. Its etiology includes benign stenosis, such as postoperative changes or compression, and malignant stenosis, such as tumor recurrence[3]. Severe stenosis results in portal vein hypertension, and patients experience clinical manifestations, including ascites, gastrointestinal bleeding, abnormal liver function, and melena[3,4].

Percutaneous transhepatic stenting is the first-line treatment of stenosis[5]. Clinical efficacy and safety have been widely discussed, and almost all studies have reported high patency rates with few complications[6,7]. However, little is known about the detailed use of stents owing to the relatively few cases encountered in practice. When is the suitable time for stent placement? Should asymptomatic patients diagnosed with stenosis via radiology undergo stent placement? In most cases, the presence of

HIGHLIGHTS

- We reviewed current data to evaluate the influence of antithrombotic therapy on stent patency after pancreatic surgery.
- There was no significant benefit of antithrombotic therapy after portal vein stent placement following pancreatic surgery.
- Bleeding complications only occurred in patients who received antithrombotic therapy.
- Antithrombotic therapy should be performed with caution as it may cause complications such as bleeding.

[a]Department of General Surgery, Peking Union Medical College Hospital, Peking Union Medical College, Chinese Academy of Medical Sciences, [b]Department of Radiology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, [c]School of Medicine, Tsinghua University, [d]Plastic Surgery Hospital, Chinese Academy of Medical Sciences, [e]Key Laboratory of Research in Pancreatic Tumor, Chinese Academy of Medical Sciences and [f]National Science and Technology Key Infrastructure on Translational Medicine in Peking Union Medical College Hospital, Beijing, People's Republic of China

Lin Chen and Wang Ziyan contributed equally to this manuscript.

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

*Corresponding author. Address Department of General Surgery, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, No. 1 Shuaifuyuan Road, Wangfujing, Dongcheng District, Beijing 100730, China. Tel.: +86 010 6915 2620. fax: +86 010 6915 6007. E-mail: wwb_xh@163.com (W. Weibin).

International Journal of Surgery (2024) 110:5771–5780

Received 14 February 2024; Accepted 19 May 2024

Published online 29 May 2024

http://dx.doi.org/10.1097/JS9.0000000000001755

symptoms and stenosis on radiology are indications for stent placement and should be discussed further[3]. In one study, the influence of balloon pre-expansion was unclear, and the success and patency rates were not compared between patients with or without balloon pre-expansion[8]. However, one study reported venous rupture following balloon dilation, indicating the potential risk of balloon dilation[4]. Furthermore, whether antithrombotic therapy should be administered remains unclear[9]. Many believe that antithrombosis is necessary to avoid thrombosis-related stenosis[9]. However, side effects such as bleeding cannot be neglected. This controversy is due to the small number of cases in each study. Therefore, a systematic review is needed to summarize and reach a conclusion to guide stent placement.

Herein, we review current data to evaluate the influence of antithrombosis on stent patency after pancreatic surgery.

Methods

Study protocol

This meta-analysis was reported in line with PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses)[10] and AMSTAR (Assessing the Methodological Quality of Systematic Reviews)[11] guidelines. Two databases (Medline since 1985 and PubMed since 1970) were searched for studies published before July 2023. The search terms included 'anticoagulation OR antiplatelet', 'portal vein stenosis OR portal vein stent', and 'pancreatic surgery OR pancreatic operation OR pancreatoduodenectomy OR Whipple'. No search of unpublished literature was performed. Two reviewers independently extracted each full-text article and included the studies.

Study selection

We only included studies that described patients who underwent pancreatic surgery, including pancreatoduodenectomy, pancreatectomy, distal pancreatectomy, or total pancreatectomy, and at least one patient who underwent portal vein stent placement after surgery. Only studies that described the use of antithrombotic agents and patency information were included. A flowchart of the search process is shown in Figure 1.

Data collection, synthesis, and management

Data were collected using a standardized data collection form. The collected information included author, country, year of publication, study type, patient demographics, type of operation, portal vein resection/reconstruction information, symptoms after surgery, indications for stent placement, stenting information, including stent type, technical details, patency parameters, and complications. The meta-analysis was conducted in accordance with the methodology recommended by the PRISMA statement. The pooled effect was calculated using a common-effect model considering that the heterogeneity was low, except for a subgroup analysis of the nonantithrombosis group because there were too few studies to obtain an accurate estimate of the between-studies variance.

Sensitivity analysis and assessment of heterogeneity

We performed sensitivity analysis by conducting a leave-one-out analysis to address its influence on the effect estimate. The existence of heterogeneity among the effect sizes of individual studies was assessed using the I^2 statistic and defined as low (25–50%), moderate (50–75%), or high (> 75%).

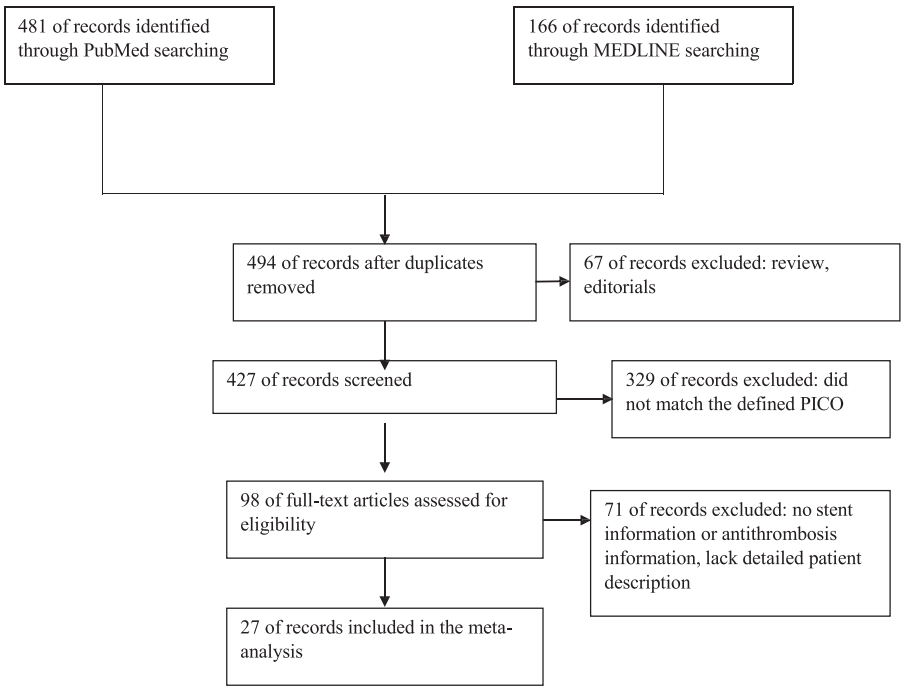


Figure 1. Flow chart of the search history for meta-analysis.

Table 1

Overview of characteristics of included studies.

Author	Year	Study type	*n*	Type of operation	Clinical manifestations	Indications for stent placement	Technical success	AT after stenting	Patency	Etiology for stent stenosis	Selection bias	Lost to follow-up	Information bias	Confounding bias	Overall bias
Khan[12]	2020	Retrospective study	8	PD-7, TP-1	GIB, Ascites	Enhanced CT: Stenosis > 50%, Doppler US	8/8	8/8	AT + :6/8	AT + : Thrombosis-1, Recurrence-1	Unclear	Low	Low	Low	Low
Ferral	2021	Retrospective study	12	PD-12	Abdominal pain, Ascites	Enhanced CT	12/12	5/12	AT + :2/5, AT-:4/7	AT + : Recurrence-3; AT-: Recurrence-3	Low	Low	Low	Low	Low
You[13]	2021	Retrospective study	15	PD-15	GIB, Ascites	Enhanced CT: Stenosis > 50%, Symptoms	14/15	11/14	AT + :9/11, AT-:2/3	AT + : Recurrence-2; AT-: Recurrence-1	Unclear	Unclear	Low	Low	Unclear
Beyer[14]	2015	Retrospective study	2	PD-2	Ascites	Enhanced CT: Stenosis > 90%	2/2	2/2	AT + :1/2	AT + : Thrombosis-1	Low	Unclear	Low	Unclear	Unclear
Kim[3]	2011	Retrospective study	9	PD-9	GIB, Ascites	Enhanced CT	9/9	0/9	AT-:6/9	AT-: Thrombosis-1, Recurrence-2	Low	Low	High	Low	Unclear
Mugu[4]	2020	Retrospective study	39	PD-24, DP-10, TP-5	GIB, Ascites	CT Volumetric Analysis, Symptoms	35/39	25/35	AT + :22/25, AT-:7/10	AT + : Thrombosis-1, Recurrence-2; AT-: Thrombosis-3	Low	Unclear	Unclear	Low	Unclear
Kato[6]	2017	Retrospective study	14	P-14	HE, GIB, Ascites	Enhanced CT	14/14	14/14	AT + :11/14	AT + : Recurrence-3	Low	Low	Unclear	High	Unclear
Miyazaki[15]	2017	Retrospective study	1	DP-1	N.A.	Enhanced CT, Doppler US	1/1	1/1	AT + :0/1	AT + : Thrombosis-1	Unclear	Unclear	High	Low	Unclear
Nio[16]	2009	Retrospective study	4	N.A.	GIB, Ascites	Enhanced CT	4/4	4/4	AT + :4/4	–	Low	Low	Unclear	Unclear	Unclear
Zhou[9]	2014	Retrospective study	35	N.A.	GIB, Ascites	Enhanced CT, Doppler US	35/35	35/35	AT + :24/35	AT + : Thrombosis-3, Recurrence-8	Unclear	Low	High	Unclear	Unclear
Hiyoshi[26]	2015	Retrospective study	5	PD-5	GIB	Enhanced CT, Symptoms	4/5	4/4	AT + :3/4	AT + : Recurrence-1	Low	Low	Low	Low	Low
Jeon[7]	2016	Retrospective study	22	PD-13, P-2	GIB, Ascites	Enhanced CT: Stenosis > 50%	21/22	0/21	AT-:20/21	AT-: Recurrence-1	Low	Unclear	Low	Low	Low
Hyun[27]	2017	Retrospective study	9	PD/PPPD-8, TP-1	GIB	Enhanced CT, Symptoms	9/9	0/9	AT-:8/9	AT-: Thrombosis-1	Low	Low	Low	Low	Low
Ohgi[28]	2019	Retrospective study	6	PD-6	GIB, Ascites	Enhanced CT: Shortest Diameter <3 mm	6/6	6/6	AT + :6/6	–	Unclear	Low	Low	Low	Low
Lee	2020	Retrospective study	60	N.A.	HE, GIB, Ascites	Enhanced CT, Symptoms	60/60	60/60	AT + :47/60	AT + : Thrombosis-11, Recurrence-2	Unclear	Low	High	Low	Unclear
Cao[31]	2013	Retrospective study	6	PD/PPPD-4, P-2	Abdominal pain, GIB, Ascites	Enhanced CT	5/6	5/5	AT + :4/5	AT + : Thrombosis-1	Low	Low	Low	Low	Low
Takao[8]	2021	Case report	1	PD-1	GIB	Enhanced CT	1/1	1/1	AT + :1/1	–	Unclear	Low	Low	Low	Low
Schellhammer[17]	2008	Case report	1	PD-1	Abdominal pain	Enhanced CT, Doppler US	1/1	1/1	AT + :1/1	–	Unclear	Unclear	Low	Low	Unclear
Ota[18]	2005	Case report	1	PD-1	GIB	Enhanced CT	1/1	1/1	AT + :1/1	–	Unclear	Low	Low	Low	Low
Sakai[19]	2005	Case report	1	N.A.	GIB	Enhanced CT	1/1	1/1	AT + :1/1	–	Unclear	Low	High	Low	Unclear
Hwang[20]	2007	Case report	1	PD-1	GIB	Enhanced CT	1/1	0/1	AT-:1/1	–	Unclear	Low	Low	Low	Low
Ichihara[21]	2007	Case report	1	PD-1	GIB	Angiography, Symptoms	1/1	1/1	AT + :1/1	–	Unclear	Low	Low	Low	Low
Tsuruga[22]	2013	Case report	3	PD-2, DP-1	Ascites	Enhanced CT, Symptoms	3/3	3/3	AT + :3/3	–	Low	Low	Low	Low	Low

Table 1

(Continued)

Author	Year	Study type	*n*	Type of operation	Clinical manifestations	Indications for stent placement	Technical success	AT after stenting	Patency	Etiology for stent stenosis	Selection bias	Lost to follow-up	Information bias	Confounding bias	Overall bias
Sakural[23]	2014	Case report	1	PD-1	GIB	Enhanced CT, Symptoms	1/1	1/1	AT + :1/1	–	Unclear	Low	Low	Low	Low
Sakamoto[24]	2018	Case report	1	PD-1	HE, GIB	Enhanced CT, Symptoms	1/1	0/1	AT-:1/1	–	Unclear	Low	Low	Unclear	Unclear
Sawai	2018	Case report	3	PD-3	N.A.	Enhanced CT	3/3	3/3	AT + :2/3	N.A.	Unclear	Low	Unclear	Low	Unclear
Zhang[30]	2014	Case report	1	PD-1	Abdominal pain, GIB	Enhanced CT	1/1	1/1	AT + :1/1	–	Unclear	Low	Low	Low	Low

AT + /AT-: with/without antithrombotic agent use; CT, computed tomography; DP, distal pancreatectomy; GIB, gastrointestinal bleeding; HE, Hepatic encephalopathy; N.A., not available; P, pancreatectomy; PD, pancreaticoduodenectomy; PPPD, pylorus preserving pancreaticoduodenectomy; TP, total pancreatectomy; US, ultrasonography.

Subgroup analysis

Subgroup analyses were performed for different etiologies of primary portal vein stenosis (thrombosis, postoperative changes, and recurrence), usage of anticoagulants/antiplatelet agents, acute or chronic stenosis, and causes of stent stenosis (thrombosis and recurrence).

Results

The meta-analysis included 268 patients in 27 studies[3–9,12–31], of whom 207 (77.2%) received antithrombotic therapy after portal vein stent placement, and 61 (22.8%) did not receive antithrombotic therapy after stent placement. Table 1 presents a summary of these studies.

There has been no randomized controlled trial on this topic, and 11 of the studies included were case reports with one to five cases of stent placement. In most studies, the choice of antithrombotic therapy was all or none for all patients. Therefore, the meta-analysis was one-armed, comparing the patency rates in the antithrombosis and nonantithrombosis groups after portal vein stent placement. We also assessed the quality of the included studies; the risk of bias analysis is presented in Table 1.

In general, the pooled patency rate was 79.2% (95% CI: 73.4–84.4%, $I^2 = 28\%$) for the antithrombosis group and 88.0% (95% CI: 80.1–96.0%, $I^2 = 7\%$) for the nonantithrombosis group (Fig. 2A and B). No significant differences were found between both groups. Funnel plots of the studies used in the meta-analysis are shown in Figure 2C and D and show a basic symmetric triangle distribution, excluding publication bias. Sensitivity analysis showed that the patency rates of the two groups were solid.

Next, we investigated why antithrombotic therapy did not significantly impact stent patency. First, we performed subgroup analyses for different etiologies of portal vein stenosis: thrombosis, postoperative changes or anastomotic stenosis, and tumor recurrence. Reports on portal vein stenosis caused by thrombosis after pancreatic surgery are scarce; only nine patients from three studies received antithrombotic therapy, and only three from a single study did not receive antithrombotic therapy (Fig. 3A). Among the nine patients who received antithrombotic therapy, six underwent stent placement within 1 month after surgery owing to acute thrombosis. Among these, stent placement failed in one patient, and stent patency was not maintained in two due to stent thrombosis, even after receiving antithrombotic therapy. The remaining three patients underwent stent placement after surgery for several months, and all exhibited stent patency. For the three patients who did not receive antithrombotic therapy, stent placements were all conducted within 1 month after surgery, and all exhibited stent patency. Owing to the limited reports and cases, we could not conclude on the impact of antithrombotic therapy in this subgroup; however, we believe that it is necessary to administer antithrombotic therapy if the patient's portal vein stenosis is caused by acute thrombosis unless contraindicated, such as during bleeding.

Regarding the postoperative change, anastomotic stenosis, or benign portal vein stenosis subgroup in many studies, the pooled patency rate was 90.9% (95% CI: 73.6–99.4%, $I^2 = 30\%$) in the antithrombosis group and 87.4% (95% CI: 64.9.6–99.2%, $I^2 = 87\%$) in the nonantithrombosis group (Fig. 3B). There was no significant difference, and the overall patency rate was higher,

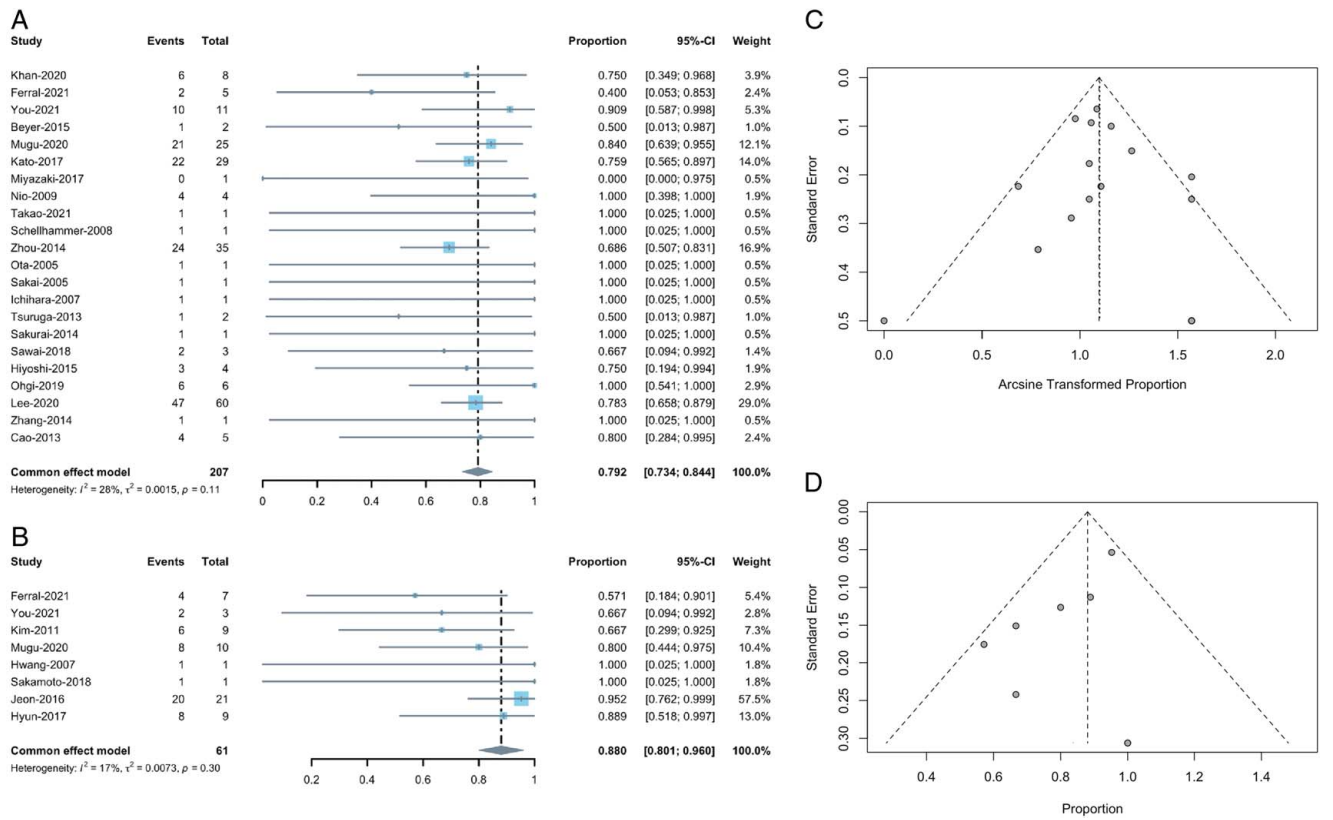


Figure 2. Forest and funnel plots examining the pooled proportions of the patency rate with or without antithrombotic agent use. A, B, Forest plots of the pooled proportions of the patency rate of included studies with (A) or without (B) antithrombotic agent use. C, D, Funnel plots of included studies with (C) or without (D) antithrombotic agent use.

indicating that portal vein stenosis caused by postoperative changes could be kept patent with stent placement. For the recurrence subgroup, the pooled patency rate was 85.5% (95% CI: 69.7–96.1%, $I^2 = 9\%$) for the antithrombosis group and 68.9% (95% CI: 39.9–91.5%, $I^2 = 53\%$) for the non-antithrombosis group (Fig. 3C). However, the difference was not statistically significant.

We next investigated whether the usage of anticoagulants or antiplatelet agents would influence stent patency. Patients receiving antithrombotic therapy after stent placement were divided into anticoagulant only, antiplatelet agent only, and anticoagulant combined with antiplatelet agent subgroups. Most patients in the anticoagulant only subgroup were administered heparin, low-molecular-weight heparin, or warfarin. Four patients were administered rivaroxaban. The pooled patency rate was 80.5% (95% CI: 69.1–89.8%, $I^2 = 47\%$) (Fig. 4A). Most patients in the antiplatelet only subgroup were administered aspirin and clopidogrel, and the pooled patency rate was 79.4% (95% CI: 69.3–88.0%, $I^2 = 0\%$) (Fig. 4B). Heparin and sequential aspirin was frequently administered to patients in the anticoagulant combined with antiplatelet agent subgroup, and the pooled patency rate was 78.8% (95% CI: 67.2–88.5%, $I^2 = 41\%$) (Fig. 4C). Overall, there was no significant difference among three subgroups, and the patency rates were also similar to those in the nonantithrombosis group (Figs. 2B and 4).

Acute and chronic stenoses differ in clinical practice. Therefore, we conducted a subgroup analysis of the interval between surgery and stent placement. Acute portal vein stenosis was defined as stenosis within 30 days of surgery, and chronic stenosis was defined as stenosis within 30 days after surgery. Notably, the acute portal vein stenosis subgroup was a subset of the thrombosis subgroup described previously, that is, six patients received antithrombotic therapy, and three did not receive antithrombotic therapy; their acute stenoses were all caused by thrombosis (Fig. 3A). This indicated that acute portal vein stenosis was frequently caused by thrombosis formation. Moreover, the chronic subgroup is similar to that shown in the general summary table. This contradicts the finding of a previous study that reported that 10/826 patients experienced postoperative portal vein stenosis/occlusion within the first month after surgery and that all stenosis cases were not due to thrombosis but occurred following postoperative changes[2]. Therefore, more detailed cases should be investigated to reach a reliable conclusion regarding acute stenosis of the portal vein.

The next analysis concerned the etiology of secondary stenosis after stent placement, which was caused by thrombosis or tumor recurrence. For the thrombosis-induced secondary stenosis subgroup, the pooled incidence rate was 2.6% (95% CI: 0.6–5.7%, $I^2 = 18\%$) for the antithrombosis group and 3.8% (95% CI: 0.5–9.9%, $I^2 = 44\%$) for the nonantithrombosis group (Fig. 5A). The incidence was higher in the nonantithrombosis group, although the difference was not significant, mainly because of the heterogeneity in the nonantithrombosis group. For the recurrence subgroup, the incidence rates were higher, that is, 14.2% (95%

A

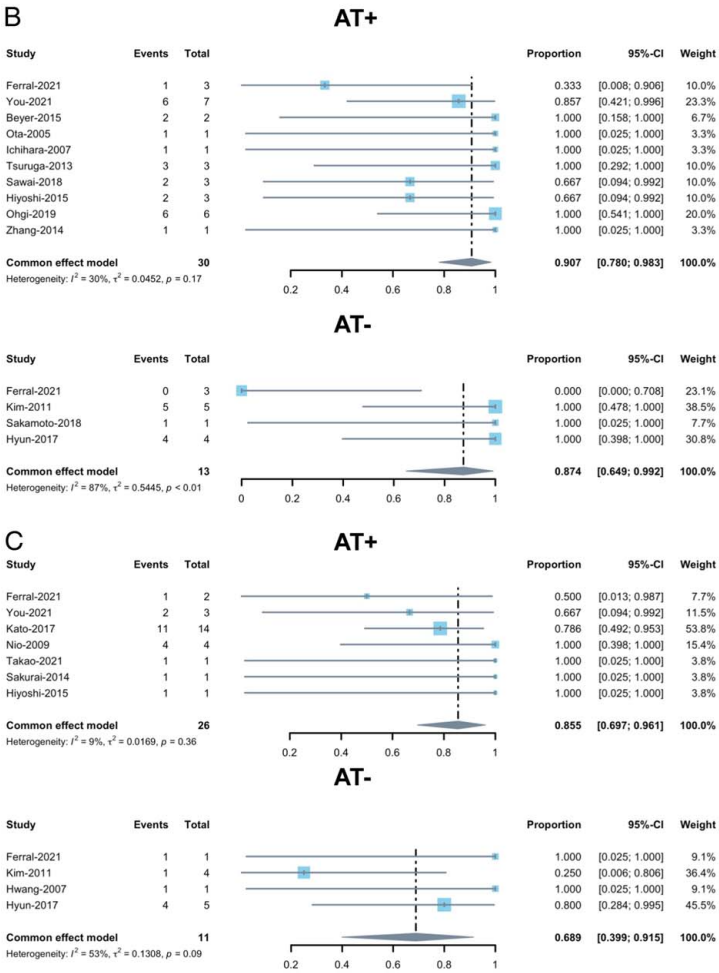
AT+

No.	Author-year	Primary disease	Surgery	Interval from surgery to stent placement	Etiology	Patency
1	Cao-2013	Pancreatic cancer	P,SP	8d	Thrombosis	Y
2	Cao-2013	Pancreatic cancer	PD	7d	Thrombosis	N, thrombosis
3	Cao-2013	Pancreatic cancer	PD	6m	Thrombosis	Y
4	Cao-2013	Pancreatic cancer	PD	2d	Thrombosis	Y
5	Cao-2013	Pancreatic cancer	PPPD	7d	Thrombosis	Y
6	Cao-2013	Pancreatic cancer	P,SP	5d	Thrombosis	-
7	Schellhammer-2008	Pancreatic cancer	PD	4m	Thrombosis	Y
8	Miyazaki-2017	N.A.	DP	27d	Thrombosis	N, thrombosis
9	You-2021	N.A.	N.A.	10m	Thrombosis	Y

AT-

No.	Author-year	Primary disease	Surgery	Interval from surgery to stent placement	Etiology	Patency
1	Ferral-2021	Pancreatic cancer	PD	6d	Thrombosis	Y
2	Ferral-2021	Pancreatic cancer	P	4d	Thrombosis	Y
3	Ferral-2021	Pancreatic cancer	PD	18d	Thrombosis	Y

B



C

Figure 3. Subgroup analysis of different etiologies of portal vein stenosis. A, Case of portal vein stenosis after pancreatic surgery due to thrombosis. B-C, Forest plots of the pooled proportions of the patency rate with etiologies of portal vein stenosis being postoperative changes (B) or tumor recurrence (C) with or without antithrombotic agent use. AT + /AT-: with/without antithrombotic agent use, DP, distal pancreatectomy; NA, not available; P, pancreatectomy; PD, pancreaticoduodenectomy; PPPD, pylorus-preserving pancreaticoduodenectomy; SP, splenectomy.

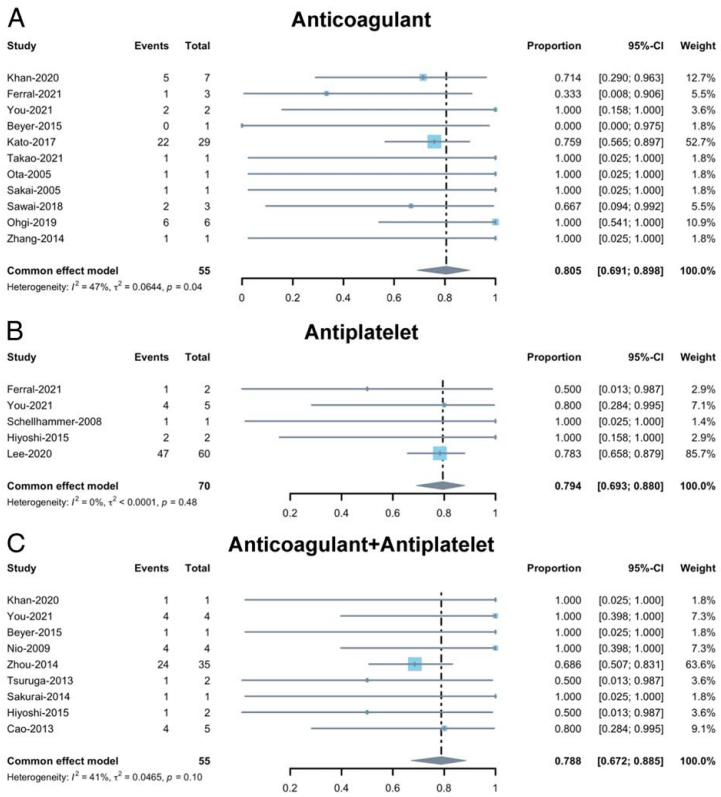


Figure 4. Subgroup analysis of usage of anticoagulants/antiplatelet agents. A-C, Forest plots of the pooled proportions of the patency rate with the usage of antithrombotic drugs after stent placement being anticoagulants only (A), antiplatelet agents only (B), and anticoagulants combined with antiplatelet agents (C).

CI: 8.8–20.6%, $I^2 = 29\%$) in the antithrombosis group and 12.1% (95% CI: 5.2–21.4%, $I^2 = 51\%$) in the non-antithrombosis group, with no significant difference (Fig. 5B).

The abovementioned analysis showed no significant difference between the antithrombosis and nonantithrombosis groups, even after subgroup analysis for the etiology of portal vein stenosis, interval between surgery and stent placement, and etiology of secondary stent stenosis. We inferred that the etiology of portal vein stenosis and secondary stent stenosis rarely involved thrombosis. Therefore, antithrombotic therapy did not significantly prevent stenosis. Most patients experience stenosis owing to postoperative changes or tumor recurrence. As a result, the impact of antithrombotic therapy after stent placement is limited unless portal vein stenosis occurs shortly after pancreatic surgery due to acute thrombosis, and this requires further research.

We summarized the stent-related complications (Table 2). Complications included bleeding, acute thrombosis, and infection or fever. Bleeding complications only occurred in the antithrombosis group, with three studies reporting five cases of bleeding. Bleeding was not observed in the nonantithrombosis group. This finding suggests that bleeding should be considered when deciding on antithrombotic therapy.

Overall, we systematically reviewed studies on the use of antithrombotic agents after portal vein stent placement. Our findings showed that antithrombotic therapy did not significantly influence stent patency, although it introduced potential bleeding risks.

Discussion

Portal vein stenosis/occlusion is a rare complication of pancreatic surgery[28]. However, it can cause severe complications, including bleeding, ascites, hematochezia, and melena[12]. Percutaneous transhepatic stent placement has been reported in many studies and has proven safe and useful in resolving clinical manifestations. However, this procedure is rarely performed, and its technical details remain unknown; therefore, whether antithrombotic therapy should be adopted is controversial. This review systematically summarized studies on stent placement after pancreatic surgery and focused on the use of antithrombotic agents. In most studies, antithrombotic therapy was administered to prevent stent thrombosis[28,29]. However, many researchers have mentioned concerns about the side effects of antithrombosis, such as bleeding, and some have not used antithrombotic therapy after stent placement[4]. It was reported that antithrombosis did not increase stent patency for benign superior vena cava syndrome[32]. However, reports on stent placement after pancreatic surgery are rare, and this should be independently discussed because the situation after surgery differs. Some studies with relatively large postpancreatic surgery sample sizes reported

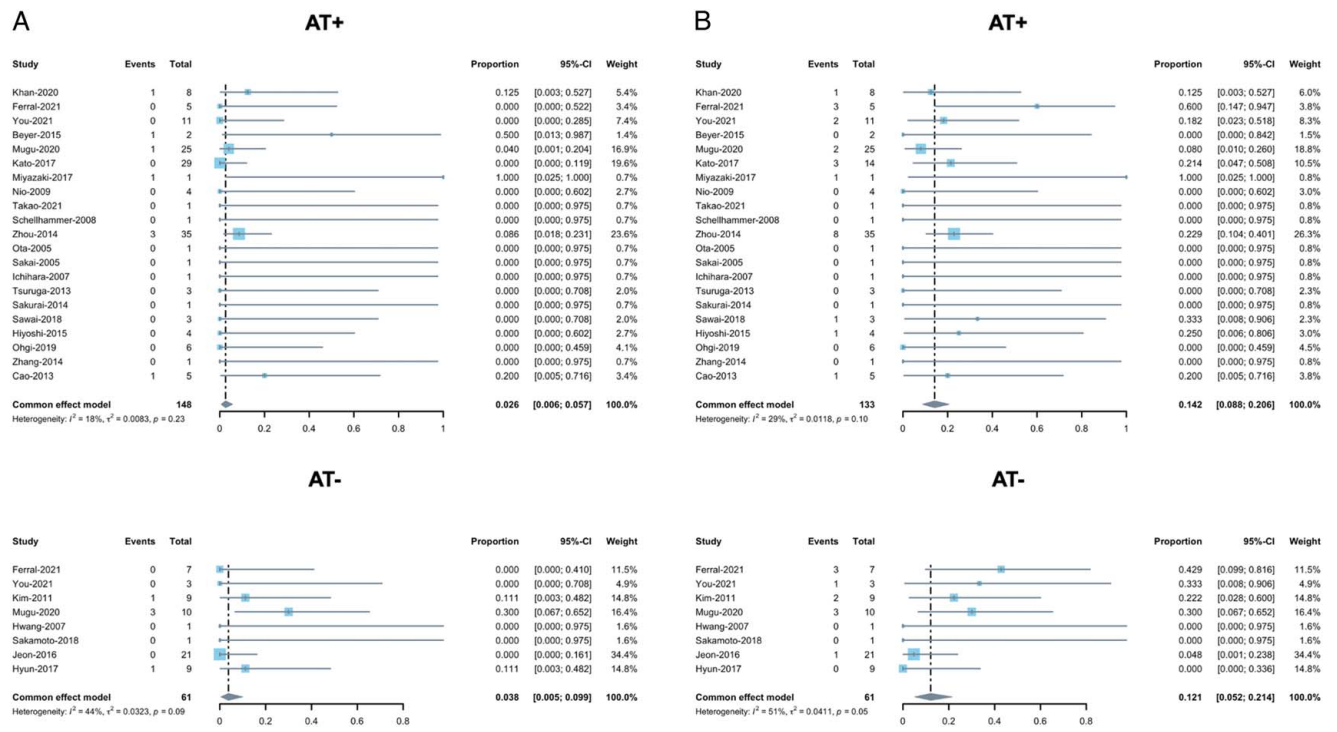


Figure 5. Subgroup analysis of pooled incidence rates of different causes of stent stenosis. A-B, Forest plots of the pooled incidence rates of thrombosis (A) or tumor recurrence (B) causing stent stenosis with or without antithrombotic agent use. AT + /AT-: with/without antithrombotic agent use.

that stent patency was unrelated to antithrombosis agent use[4,6], although none confirmed this conclusion.

To the best of our knowledge, our study is the first to summarize previous studies and find that stent patency did not differ significantly with or without antithrombosis agent use. Studies varied in the usage of antithrombotic agents owing to the lack of standard protocols in the literature[14]; therefore, we wondered whether the patency rates would be influenced by the use of different types of drugs. Anticoagulants inhibit the coagulation cascade and fibrin formation, whereas antiplatelet agents primarily inhibit platelet activation and aggregation[33]. Venous thrombosis is rich in fibrin and is usually without damage to the vessel wall[33]. Therefore, the use of anticoagulants is crucial for managing portal vein thrombosis (PVT)[34] and is suggested to be related to PVT improvement, recanalization, and decreased all-cause mortality in patients with PVT[35]. Direct oral anticoagulants are also favored in the treatment of PVT and are preferred to warfarin because of better patient compliance and its safety profile[36]. Four patients from two studies were administered rivaroxaban[8,13], and all retained patent stents in the follow-up without complication. Stent placement would possibly cause damage to the vessel wall, and the platelets would be recruited and aggregated; hence, the use of antiplatelet agents is justifiable. Therefore, anticoagulants and antiplatelet agents work at different stages of PVT formation and would likely help in the patency rates. We performed the subgroup analysis and found no significant difference in the use of different types of antithrombotic agents (Fig. 4). This piqued our interest in why antithrombotic therapy seemed ineffective. In most cases, stents maintain their patency during further evaluation. Only 10–15% of patients experience stent stenosis/occlusion; most occlusions are caused by tumor recurrence or progression. Thrombosis accounted for only a small portion of occlusions. Therefore, antithrombotic therapy may not prevent stenosis. Furthermore, antithrombotic therapy may be ineffective when a shunt is created[6] owing to decreased blood flow in the portal vein. The presence of a collateral vein was reportedly related to the development of stent occlusion because of which antithrombosis was not very effective.

What types of patients can benefit from antithrombotic therapy? We presumed that patients with PVT, especially acute thrombosis, could benefit after stent placement. However, only nine patients who underwent stent placement due to acute PVT after pancreatic surgery had been reported in previous studies (Fig. 3A). Among them, six patients received antithrombotic therapy after stent placement; two of these six patients had thrombosis after stent placement and experienced clinical failure (Fig. 3A AT + No. 2, 8). Their experience emphasizes the importance of antithrombotic therapy in treating patients with previous thrombosis. However, it is strange that all patients who underwent stent placement within 1 month of surgery had PVT, which contradicts the results of previous incidence studies[2]. Therefore, we could not conclude on the use of antithrombotic agents if the patient's stenosis occurred shortly after surgery or was likely caused by thrombosis. More retrospective studies are needed.

Complications are a major concern during stent placement. There are several types of stent-related complications. The first is infection; some patients experience transient fever, although others may experience septicemia or liver abscess and require antibiotics. Second, thrombosis did not cause stent occlusion.

Table 2

Summary of reported complications of stent placement.

	n	Complication	Bleeding	Acute thrombosis	Infection/ Fever
			AT+		
Khan-2020[12]	8	3	2	1	
Ferral-2021[5]	5	0			
You-2021[13]	11	1	1		
Beyer-2015[14]	2	0			
Mugu-2020[4]	25	0			
Kato-2017[6]	14	3			3
Miyazaki-2017[15]	1	0			
Nio-2009[16]	4	0			
Takao-2021[8]	1	0			
Schellhamm-2008[17]	1	0			
Zhou-2014[9]	35	11/59			11
Ota-2005[18]	1	0			
Sakai-2005[19]	1	0			
Ichihara-2007[21]	1	0			
Tsuruga-2013[22]	3	0			
Sakurai-2014[23]	1	0			
Sawai-2018	3	0			
Hiyoshi-2015[26]	4	2	2		
Ohgi-2019[28]	6	0			
Lee-2020	60	0			
Zhang-2014[30]	1	0			
Cao-2013[31]	5	1		1	
			AT-		
Ferral-2021[5]	7	0			
You-2021[13]	3	0			
Kim-2011[3]	9	3		1	2
Mugu-2020[4]	10	0			
Hwang-2007[20]	1	0			
Sakamoto-2018[24]	1	0			
Jeon-2016[7]	21	0			
Hyun-2017[27]	9	0			

AT+/AT-: with/without antithrombotic agent use.

Third, bleeding was only reported in the antithrombosis group. As patients with portal vein stenosis usually have manifestations of portal vein hypertension, they tend to experience bleeding owing to varices and abnormal liver function. Therefore, antithrombotic therapy should be considered after carefully evaluating the potential benefits and risks. Our results suggest that unless explicit stenosis is caused by thrombosis, antithrombosis cannot improve the stent patency rate but could cause bleeding. Therefore, antithrombotic therapy should be considered carefully.

This study has some limitations. First, since portal vein stent placement after pancreatic surgery is relatively rare in clinical situations, there were no prospective studies or randomized control trials; we could only enroll retrospective studies and case reports. However, the use of antithrombotic agents is important in clinical decisions because of which prospective studies with more cases are needed in the future. Second, there is no standard indication for portal vein stent placement, and we hope that future studies could investigate this further.

Conclusion

This study suggests that there is no significant benefit of antithrombotic therapy after portal vein stent placement following pancreatic surgery. Antithrombotic therapy should be performed with caution because it may cause complications, such as bleeding.

Ethical approval

Not applicable.

Consent

Not applicable.

Source of funding

Wang, Weibin received the support from the National Natural Science Foundation of China (No. 82173074), the Beijing Natural Science Foundation (No. 7232127), the National High Level Hospital Clinical Research Funding (No. 2022-PUMCH-D-001, No. 2022-PUMCH-B-004), and the CAMS Innovation Fund for Medical Sciences (CIFMS) (No. 2021-I2M-1-002). Lin, Chen received the support from the Fundamental Research Funds for the Central Universities (No. 2019-PUMCH-3332019025).

Author contribution

C.L. and W.W.: designed the research; C.L. and Z.W.: collected the data, performed data analysis, and interpretation; C.L. and Z.W.: wrote the paper. All authors discussed the manuscript.

Conflicts of interest disclosure

The authors declare no competing interests.

Research registration unique identifying number (UIN)

We had registered our research on Prospero, with ID: CRD42024501888, https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42024501888

Guarantor

Wang, Weibin and Lin, Chen.

Data availability statement

The data generated in this study are available upon reasonable request.

Provenance and peer review

Not commissioned, externally peer-reviewed.

References

[1] Dua MM, Tran TB, Klausner J, *et al*. Pancreatectomy with vein reconstruction: technique matters. HPB 2015;17:824–31.

[2] Kang MJ, Jang JY, Chang YR, *et al*. Portal vein patency after pancreatoduodenectomy for periampullary cancer. Br J Surg 2014;102:77–84.
[3] Kim KR, Ko GY, Sung KB, *et al*. Percutaneous transhepatic stent placement in the management of portal venous stenosis after curative surgery for pancreatic and biliary neoplasms. AJRAm J Roentgenol 2011;196: W446–50.
[4] Mugu VK, Thompson SM, Fleming CJ, *et al*. Evaluation of technical success, efficacy, and safety of portomesenteric venous intervention following nontransplant hepatobiliary or pancreatic surgery. J Vasc Interv Radiol 2020;31:416–424.e2.
[5] Ferral H, Alonzo MJ, Datri J, *et al*. Endovascular management of portal vein obstruction in hepatobiliary cancer patients. J Surg Oncol 2022;125:392–8.
[6] Kato A, Shimizu H, Ohtsuka M, *et al*. Portal vein stent placement for the treatment of postoperative portal vein stenosis: long-term success and factor associated with stent failure. BMC Surg 2017;17:11.
[7] Jeon UB, Kim CW, Kim TU, *et al*. Therapeutic efficacy and stent patency of transhepatic portal vein stenting after surgery. World J Gastroenterol 2016;22:9822.
[8] Takao S, Hirakawa M, Takeishi K, *et al*. Portal vein stenting for jejunal variceal bleeding after recurrence of pancreatic adenocarcinoma: a case report and review of the literature. Interv Radiol (Higashimatsuyama) 2021;6:44–50.
[9] Zhou ZQ, Lee JH, Song KB, *et al*. Clinical usefulness of portal venous stent in hepatobiliary pancreatic cancers: usefulness of PV stent in hepatobiliary pancreatic cancers. ANZ J Surg 2014;84:346–52.
[10] Page MJ, McKenzie JE, Bossuyt PM, *et al*. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. Int J Surg 2021;88: 105906.
[11] Shea BJ, Reeves BC, Wells G, *et al*. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. BMJ 2017;358:j4008.
[12] Khan A, Kleive D, Aandahl EM, *et al*. Portal vein stent placement after hepatobiliary and pancreatic surgery. Langenbecks Arch Surg 2020;405:657–64.
[13] You Y, Heo JS, Han IW, *et al*. Long term clinical outcomes of portal vein stenting for symptomatic portal vein stenosis after pancreaticoduodenectomy. Medicine (Baltimore) 2021;100:e27264.
[14] Beyer LP, Wohlgemuth WA, Uller W, *et al*. Percutaneous treatment of symptomatic superior mesenteric vein stenosis using self-expanding nitinol stents. Eur J Radiol 2015;84:1964–9.
[15] Miyazaki M, Shimizu H, Ohtuka M, *et al*. Portal vein thrombosis after reconstruction in 270 consecutive patients with portal vein resections in hepatopancreatobiliary (HPB) surgery. Am J Surg 2017;214:74–9.
[16] Nio Y, Iguchi C, Itakura M, *et al*. Placement of an expandable metallic stent improves the efficacy of chemoradiotherapy for pancreatic cancer with malignant portal vein stenosis or obstruction. Anticancer Res 2009; 29:3329–35.
[17] Schellhammer F, Esch JSA, Hammerschlag S, *et al*. Surgical access to jejunal veins for local thrombolysis and stent placement in portal vein thrombosis. Cardiovasc Intervent Radiol 2008;31(S2):185–7.
[18] Ota S, Suzuki S, Mitsuoka H, *et al*. Effect of a portal venous stent for gastrointestinal hemorrhage from jejunal varices caused by portal hypertension after pancreatoduodenectomy. J Hepatobiliary Pancreat Surg 2005;12:88–92.
[19] Sakai M, Nakao A, Kaneko T, *et al*. Transhepatic portal venous angioplasty with stenting for bleeding jejunal varices. Hepatogastroenterology 2005;52:749–52.
[20] Hwang S, Sung KB, Park YH, *et al*. Portal vein stenting for portal hypertension caused by local recurrence after pancreatoduodenectomy for periampullary cancer. J Gastrointest Surg 2007;11:333–7.
[21] Ichihara T. Stent placement is effective on both postoperative hepatic arterial pseudoaneurysm and subsequent portal vein stricture: a case report. World J Gastroenterol 2007;13:970–2.
[22] Tsuruga Y. Portal vein stenosis after pancreatectomy following neoadjuvant chemoradiation therapy for pancreatic cancer. World J Gastroenterol 2013;19:2569–73.
[23] Sakurai K, Amano R, Yamamoto A, *et al*. Portal vein stenting to treat portal vein stenosis in a patient with malignant tumor and gastrointestinal bleeding. Int Surg 2014;99:91–5.
[24] Sakamoto T, Arai Y, Morimoto M, *et al*. Portal vein stenting for portal vein stenosis after pancreatoduodenectomy: a case report. Yonago Acta Med 2018;61:182–6.
[25] Sawai Y, Kokudo T, Sakamoto Y, *et al*. Stent placement for benign portal vein stenosis following pancreaticoduodenectomy in a hybrid operating room. Biosci Trends 2019;12:641–4.
[26] Hiyoshi M, Fujii Y, Kondo K, *et al*. Stent placement for portal vein stenosis after pancreaticoduodenectomy. World J Surg 2015;39: 2315–22.
[27] Hyun D, Park KB, Cho SK, *et al*. Portal vein stenting for delayed jejunal varix bleeding associated with portal venous occlusion after hepatobiliary and pancreatic srgery. Korean J Radiol 2017;18:828–34.
[28] Ohgi K, Sugiura T, Yamamoto Y, *et al*. Benign portal vein stenosis after pancreaticoduodenectomy. World J Surg 2019;43:2623–30.
[29] Lee JH, Yoon CJ, Choi WS. Transhepatic stent placement for portal vein obstruction after hepatobiliary and pancreatic surgery: long-term efficacy and risk factor for stent failure. Eur Radiol 2021;31:1300–7.
[30] Zhang WG, Liu DM, Li Z, *et al*. Endovascular treatment for extrahepatic portal vein bifurcation stenosis after a whipple procedure using the kissing stents technique. Ann Vasc Surg 2014;28:264.e13–6.
[31] Cao G, Ko GY, Sung KB, *et al*. Treatment of postoperative main portal vein and superior mesenteric vein thrombosis with balloon angioplasty and/or stent placement. Acta Radiol 2013;54:526–32.
[32] Haddad MM, Thompson SM, McPhail IR, *et al*. Is long-term anticoagulation required after stent placement for benign superior vena cava syndrome? J Vasc Interven Radiol 2018;29:1741–7.
[33] Tsoumani ME, Tselepis AD. Antiplatelet agents and anticoagulants: from pharmacology to clinical practice. Curr Pharm Des 2017;23: 1279–93.
[34] Boccatonda A, Gentilini S, Zanata E, *et al*. Portal vein thrombosis: state-of-the-art review. J Clin Med 2024;13:1517.
[35] Yao C, Zhao M, Ibrahim B, *et al*. Anticoagulation for the treatment of portal vein thrombosis in cirrhosis: a systematic review and meta-analysis of comparative studies. J Clin Exp Hepatol 2023;13:404–13.
[36] Van Es N, Coppens M, Schulman S, *et al*. Direct oral anticoagulants compared with vitamin K antagonists for acute venous thromboembolism: evidence from phase 3 trials. Blood 2014;124:1968–75.