

Original Article

Anticoagulation after pancreatic surgery with venous resection (TIGRESS): What should we do? Results from an international survey

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Backgrounds/Aims: Patients who undergo pancreatic surgery with venous resection have high rates of morbidity/mortality. Also, they are high-risk for postoperative venous thromboembolism. Whether this group should be routinely anticoagulated is unknown. This study aimed to establish current anticoagulation practices.

Methods: A survey (<https://form.jotform.com/220242489107048>) was sent out to pancreatic surgeons. Questions covered center volume, venous resection/reconstruction techniques and anticoagulation policies.

Results: Sixty-five centers from 17 countries responded. Following a “side-bite” venous resection with a patch repair, 40% used an autologous vein patch, 27% used peritoneum, and 27% used a bovine patch. After formally resecting a segment of vein, 17% of centers used an interposition graft (IG). Left renal vein (41%) and polytetrafluoroethylene (73%) grafts were the most commonly used autologous and prosthetic IGs, respectively. Following a prosthetic IG, an autologous IG, and a “side-bite” resection, 59%, 28%, and 19% of centers provided therapeutic anticoagulation, respectively (66% used low molecular-weight heparin). The duration of therapy provided varied from inpatient stay only (14%) to six months (32%).

Conclusions: Our global survey indicates that anticoagulation practices are highly variable. Centers do not agree on when to anticoagulate, how to anticoagulate, or the duration of therapy. A robust trial is required to provide clarity.

Key Words: Anticoagulants; Pancreaticoduodenectomy; Venous thromboembolism; Veins

INTRODUCTION

Resectional surgery remains the only curative treatment for patients with pancreatic ductal adenocarcinoma (PDAC). This is only possible in fit patients who present early with resectable disease. Since PDAC most commonly affects the pancreatic

head, most surgical patients are treated with pancreatoduodenectomy (PD). Due to the aggressive nature of PDAC, around one in eight PD patients will undergo concomitant resection of a named vein [1]. This correlates with higher morbidity and mortality rates, and an increased risk of postoperative venous thromboembolism (VTE) [2]. There are currently no guidelines outlining how these patients should be managed to reduce their VTE risk and optimise their perioperative outcomes. Thus, the objective of this survey study was to establish current practice by surveying hepatopancreatobiliary (HPB) surgeons around the world.

MATERIALS AND METHODS

A JotForm.com survey (the anTI coaGulation aEftEr vEnous reSection survey) was emailed to members of various HPB societies. In addition, surgeons could respond via an advertise-

Received: May 18, 2023, **Revised:** June 7, 2023,
Accepted: June 8, 2023, **Published online:** October 17, 2023

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ment on Twitter. Volunteers were asked to respond on behalf of their HPB units (no more than one response per unit) to clarify how they typically managed elective PD patients. The survey (<https://form.jotform.com/220242489107048>) contained 19 questions. It was designed to take less than three minutes to complete. Questions (Supplementary Fig. 1) covered center volume, reconstruction techniques, postoperative management and anticoagulation therapy. Responses were fully anonymised. Data are presented as frequency counts and associated percentages. Our study adhered to the Declaration of Helsinki. It was approved by University Hospitals Plymouth NHS Trust Research and Development Department and was endorsed by the European-African Hepato-Pancreato-Biliary Association (E-AHPBA).

RESULTS

We obtained responses from 65 centers (Table 1). Responders were not required to provide their institution or country. Responses were received from small (< 50 pancreatic resections per year, 28%), medium (50–100 pancreatic resections per year, 43%) and large (> 100 pancreatic resections per year, 29%) HPB centers in the UK, Italy, Spain, India, the Netherlands, France, the USA, Norway, Costa Rica, Germany, Turkey, Indonesia, Brazil, Australia, Greece, South Africa, and Switzerland. A quarter of these units performed less than five pancreatic resections per year where a named vein was also resected and 46% performed more than ten.

Two-thirds of the centers routinely used a patch to repair a “side-bite” venous resection (VR). Of these, autologous vein patches, peritoneum and bovine pericardial patches were used by 40%, 27%, and 27%, respectively. When formally resecting a segment of vein, most (83%) units routinely performed an end-to-end reconstruction with no graft while the remainder (17%) used an interposition graft (IG). The most commonly used

grafts were autologous vein (48%) and cadaver grafts (25%). Among centers that frequently used autologous grafts, the most common harvest site was the left renal vein (41%), followed by the internal jugular vein (21%). Among centers that frequently used prosthetic grafts, the most commonly used material was polytetrafluoroethylene (73%), followed by polyethylene terephthalate (Dacron, 23%).

Before starting a venous reconstruction, 66% of units administered a heparin bolus while 34% did not. When fashioning a venous anastomosis, just 12% routinely occluded the superior mesenteric artery inflow to prevent congestion and intestinal oedema. Following a venous reconstruction, just 26% of units routinely performed a computed tomography scan in the post-operative phase. Among those that did, the timing of this was highly variable. These units also differed in when they provided therapeutic dose anticoagulation (TAG). Just over half provided this for patients who received a prosthetic IG. Just over a quarter provided this for patients who received an autologous IG. A fifth of the centers anticoagulated patients who underwent a “side-bite” resection with a patch repair. A third of the centers did not provide TAG in any of these scenarios. Among those that did provide TAG, most (66%) used low molecular weight heparin (LMWH), followed by an oral anticoagulant. The duration of TAG also differed between units: 41% provided TAG for three months, 32% provided TAG for six months and 14% provided TAG for the inpatient stay only.

Two-thirds of the surveyed units switched from routine prophylactic anticoagulation to TAG if a patient was diagnosed with portal vein (PV)/superior mesenteric vein (SMV) thrombosis following VR/reconstruction. However, 20% did not alter management at all. The final question asked responders if they (and their institution) would be interested in participating in a randomized controlled trial comparing routine TAG to no anticoagulation following VR/reconstruction. Over 80% declared an interest.

Table 1. Selected results from the TIGRESS survey (percentages in brackets are rounded to nearest whole number)

Question	Responses received (n = 65)
How many pancreatic resections would you estimate your unit performs each year?	Less than 50: 18 (28) 50–100: 28 (43) More than 100: 19 (29)
How many pancreatic resections would you estimate your unit performs each year where a venous resection is also performed?	Less than 5: 17 (26) 5–10: 18 (28) More than 10: 30 (46)
If you routinely perform “side-bite” resections, which type of patch would you typically use?	Autologous vein patch: 18 (40) Peritoneum: 12 (27) Bovine pericardial patch: 12 (27) Synthetic patch: 2 (4) Cadaveric vein graft: 0 (0) Other: 1 (2) We do not routinely use patches: 20*
At your unit, when you formally resect a segment of vein, how do you typically perform the reconstruction?	End-to-end reconstruction with no graft: 54 (83) End-to-end reconstruction with interposition graft: 11 (17)

Table 1. Continued

Question	Responses received (n = 65)
Which type of graft would you most commonly use when performing a reconstruction?	Autologous vein: 25 (48) Cadaver graft: 13 (25) Synthetic graft: 11 (21) Bovine patch: 0 (0) Peritoneal segment: 1 (2) Other: 2 (4) We do not typically use grafts: 13*
When an autologous venous graft is required, which harvest site would you most commonly use?	Left renal vein: 17 (41) Internal jugular vein: 9 (21) Gonadal vein: 5 (12) Other: 11 (26) We do not routinely use autologous venous grafts: 23*
When using a prosthetic graft, which material would you most commonly use?	PTFE: 19 (73) Dacron: 6 (23) Other: 1 (4) We do not routinely use prosthetic grafts: 39*
Do you routinely administer a heparin bolus before starting a venous reconstruction?	Yes: 43 (66) No: 22 (34)
Do you routinely occlude SMA inflow whilst fashioning a venous anastomosis in order to prevent congestion and intestinal oedema?	Yes: 8 (12) No: 57 (88)
Following a venous resection and reconstruction, do you routinely perform a CT scan in the postoperative phase?	Yes: 17 (26) 24 h post-surgery: 1 24 h and 72 h post-surgery: 2 24 h and 1 wk post-surgery: 1 48 h post-surgery: 1 72 h post-surgery: 3 Within 1 wk of surgery/prior to discharge: 6 Not specified: 3 No: 48 (74)
In which of these scenarios would you routinely provide therapeutic dose anticoagulation therapy? Select all that apply	A patient who has received a prosthetic interposition graft: 38 (59) A patient who has received an autologous interposition graft: 18 (28) A patient who has undergone a "side-bite" resection with a patch repair: 12 (19) A patient who has undergone an end-to-end anastomosis without graft: 9 (14) A patient who has undergone a "side-bite" resection with primary closure: 3 (5) None of these scenarios: 21 (32)
Which of these anticoagulant therapies would you typically provide?	LMWH followed by an oral anticoagulant: 29 (66) IV heparin followed by an oral anticoagulant: 7 (16) Oral anticoagulant alone (with or without "bridging" therapy): 2 (5) Other: 6 (14) Nb excludes the 21 units that would not provide anticoagulation therapy
How long would you typically provide anticoagulation therapy for?	3 mon: 18 (41) 6 mon: 14 (32) For the duration of the hospital stay only: 6 (14) Other: 6 (14) Nb excludes the 21 units that would not provide anticoagulation therapy
If you identify PV/SMV thrombosis in a patient who has undergone pancreatic surgery with venous resection, how would your management plan change?	The patient would be on prophylactic anticoagulation so I would switch this to a therapeutic dose: 42 (65) The patient would already be on anticoagulation therapy so I wouldn't change anything: 13 (20) The patient would already be on anticoagulation therapy but I would switch to a different anticoagulant: 2 (3) Other: 8 (12)
Would you be interested in participating in a randomized controlled trial which compares therapeutic anticoagulation to no anticoagulation following pancreatic surgery with venous resection?	Yes: 53 (82) No: 12 (19)

Values are presented as number (%) or number only.

TIGRESS, antiCoagulation after pancreatic surgery with venous resection; LMWH, low molecular weight heparin; PTFE, polytetrafluoroethylene; PV, portal vein; SMA, superior mesenteric artery; SMV, superior mesenteric vein.

*Excluded from percentages.

DISCUSSION

Pancreatic cancer is an aggressive malignancy. It commonly invades into the retroperitoneal space where it can infiltrate the PV and SMV. Whilst this is no longer an absolute contraindication for resection, the benefits of a concomitant VR remain controversial [3]. In a recent systematic review of 41 non-randomized studies that compared the outcomes of PD patients who underwent VR ($n = 1,921$) to those who did not ($n = 5,646$), the former were found to have longer operation times and increased intraoperative blood loss [4]. This group also had higher rates of postoperative haemorrhage, delayed gastric emptying (DGE), reoperation and 30-day mortality, although overall morbidity rates were similar [4]. One-, three-, and five-year survival rates were shorter in the VR patients. However, the impact of disease stage was not studied [4]. The authors concluded that VR is safe and feasible in PD patients and that, given the survival benefits of a complete resection, it may be necessary to achieve a radical resection. Indeed, some studies have shown that when a radical resection is performed, a survival benefit of almost two years (median) is obtained [5].

In a recent meta-analysis of 30 retrospective cohort studies, VR was found to correlate with longer operation times, increased intraoperative blood loss, larger tumour size and lower complete resection rates [6]. Although overall morbidity rates were similar, VR was associated with higher rates of postoperative haemorrhage, bile leak, DGE, reoperation and perioperative mortality [6]. The authors concluded that VR can result in additional risk and that it is only indicated in selected cases. Further, they suggested that VR was associated with reduced overall survival (OS), possibly due to tumour/disease factors, rather than intraoperative factors. Additional studies have suggested that the length of resected vein is an important variable. Pan et al. found that VR did not affect OS. However, patients who had > 3 cm of a named vein resected had worse OS than those who had ≤ 3 cm of a named vein resected [7].

In some instances, a VR might be necessary to obtain a complete resection, which is known to have survival benefits [8]. The amount of vein that needs to be resected depends on both tumour factors and the experience of the operating surgeon. In some scenarios, performing a "side-bite" resection is possible rather than formally resecting a vein segment. This less aggressive approach may or may not require reconstruction with a patch. Primary repair of a vein is associated with better one-year patency rates compared to end-to-end anastomoses or IGs [9]. Most surgeons who responded to our survey stated that they used a patch following a "side-bite" resection. However, the type of patch used varied hugely. When a segment of PV/SMV is formally resected, either an end-to-end anastomosis or an IG is required. The latter is associated with the lowest one-year patency rates [9]. Depending on the length of the vein resected and the skillset of the operating surgeon, this can be performed with or without an IG. Most of the surgeons sur-

veyed stated that they did not typically use IGs. The type of IG used was also highly variable.

Following a VR, the risk of VTE is higher than in those who undergo a standard pancreatic resection. Indeed, over 20% of those who undergo PD with a PV resection experience a postoperative VTE [5]. In contrast, compared to all patients who have a HPB malignancy resected, the incidence is 5% in those who undergo extended VTE prophylaxis and 12% in those who receive prophylaxis only as an inpatient [10]. Whilst no recent studies have been performed, a meta-analysis from 2013 highlighted the high degree of heterogeneity in the use of anticoagulation after VR/reconstruction [11]. Currently, there are no guidelines to advise how this group of patients should be managed to minimise this risk. This is reflected in our survey results, e.g., around half of the centers routinely provided TAG to patients who had received a prosthetic IG while the remainder did not. Similarly, around a quarter of units provided patients who had received an autologous IG with TAG whilst the remainder did not.

The type of TAG given is also a point of disagreement. Whilst most units stated their standard of care was LMWH (followed by an oral anticoagulant), many centers provided intravenous heparin, an oral anticoagulant alone, or an entirely different therapy. It seems that guidelines are required for clarity, yet there is currently no evidence to guide these. A further source of disagreement was the duration of TAG. Whilst most centers provided this for three to six months, some only treated patients for the duration of their inpatient stay. This is a huge discrepancy. Data from a robust study would ensure that practice is evidence-based.

Our study has several limitations. Although we received a response from 65 units, these responses may not accurately reflect all HPB centers. Secondly, our results were based on survey responses rather than hard data. Therefore, they might have been affected by biases typical of survey studies. Since the responses were fully anonymised, we did not know the demographics of the responders (e.g., age, level of experience, etc.). When designing the TIGRESS (anTIcoagulation after pancreatic surgery with vEnouS reSection) survey we did not consider that a vascular surgeon might be involved in venous reconstruction. Therefore, the questions did not reflect this. Finally, formal statistical analyses were not possible due to the small sample size.

In summary, the results from our international survey of HPB centers suggest that the management of patients who undergo a VR/reconstruction is highly variable. In particular, centers disagree on when to provide TAG, how to provide TAG and the duration of therapy. Data from robust studies are required so that consensus guidelines can be produced and perioperative outcomes can be optimized.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found at <https://doi.org/10.14701/ahbps.23-065>.

ACKNOWLEDGEMENTS

We would like to thank those who took the time to complete the TIGRESS survey.

The results outlined in this paper were presented as an oral presentation at ASGBI Congress 2023 (Harrogate, UK) and as a poster presentation at E-AHPBA Congress 2023 (Lyon, France).

FUNDING

None.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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Conceptualization: All authors. Data curation: TBR. Methodology: All authors. Visualization: All authors. Writing - original draft: TBR. Writing - review & editing: DC, SA.

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