Graft type for superior mesenteric and portal vein reconstruction in pancreatic surgery
– A systematic review

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ABSTRACT

Background: Contemporary practice for superior mesenteric/portal vein (SMV-PV) reconstruction during pancreatectomy with vein resection involves biological (autograft, allograft, xenograft) or synthetic grafts as a conduit or patch. The aim of this study was to systematically review the safety and feasibility of the different grafts used for SMV-PV reconstruction. **Methods:** A systematic search was performed in PubMed and Embase according to the PRISMA guidelines (January 2000-March 2020). Studies reporting on ≥ 5 patients undergoing reconstruction of the SMV-PV with grafts during pancreatectomy were included. Primary outcome was rate of graft thrombosis. **Results:** Thirty-four studies with 603 patients were included. Four graft types were identified (autologous vein, autologous parietal peritoneum/falciform ligament, allogeneic cadaveric vein/artery, synthetic grafts). Early and overall graft thrombosis rate was 7.5% and 22.2% for synthetic graft, 5.6% and 11.7% for autologous vein graft, 6.7% and 8.9% for autologous parietal peritoneum/falciform ligament, and 2.5% and 6.2% for allograft. Donor site complications were reported for harvesting of the femoral, saphenous, and external iliac vein. No cases of graft infection were reported for synthetic grafts. **Conclusion:** In selected patients, autologous, allogenic or synthetic grafts for SMV-PV reconstruction are safe and feasible. Synthetic grafts seems to have a higher incidence of graft thrombosis.

INTRODUCTION

Pancreatectomy with superior mesenteric/portal vein (SMV-PV) resection is considered standard of care in patients with pancreatic and periampullary tumours with involvement of the SMV-PV and a reconstructable vein. Several studies have been published on pancreatectomy with SMV-PV resection, but results related to technical aspects of the vascular resection and the rate of graft thrombosis are often not reported as the key outcomes of these studies. For patients with pancreatic cancer, Ravikumar et al showed that the type of venous reconstruction did not affect long-term survival^[1]. Thus, the optimal method for venous reconstruction is the one that provides the greatest chance of a safe R0/R1 resection of the tumour^[1, 2]. Several different approaches are reported, and centres have different preferences. Primary end-to-end anastomosis and venorrhaphy are reportedly used in 20–83% and 15–56% of patients, respectively^[3]. When primary anastomosis is difficult to achieve due to tension and the risk of stenosis, different types of grafts have been used. No consensus exists on the optimal graft for SMV-PV reconstruction^[4]. Contemporary practice involves biological (autograft, allograft, xenograft) or synthetic grafts as a conduit or patch for segmental or partial vein wall reconstructions. Some centres advocate that a graft may be avoided in most cases^[5, 6]. Comparative trials are scarce, and daily decisions are often made using low-quality evidence.

Surgery with venous resection for pancreatic cancers has been proven comparable to surgery without venous resection in terms of perioperative outcome and long-term survival. The major concerns with SMV-PV resection and reconstruction with a graft are graft thrombosis and long term patency. Even though there are no large studies available some specific concerns have been raised. Synthetic grafts are anticipated to have a higher risk of thrombosis and infection, the use of autologous venous grafts is at risk of complications related to the donor site, and cadaveric allografts may be in risk of rejection^[5]. The aim of this

study was to assess the safety and feasibility of the different grafts used for SMV-PV reconstruction during pancreatic surgery and to determine potential benefits of the different types of grafts considering the rate of graft thrombosis as primary outcome.

METHODS

Systematic literature search and selection

Adhering to the 2009 PRISMA guidelines, a systematic search was performed in PubMed and Embase for articles published from January 2000 to March 2020^[7]. First author screened articles by title and abstract and, if applicable, the full articles for eligibility based on predefined inclusion and exclusion criteria. The search was restricted to studies on humans and studies published in languages other than English were excluded. Reference lists of all included papers and related articles were screened manually to identify missed but relevant studies. If there was any doubt about the suitability of the studies after reading the titles and abstracts, the full articles were obtained for detailed evaluation, and all eligible studies were included. The following search terms were used^[8]: (pancreatoduodenectomy OR pancreaticoduodenectomy OR duodenopancreatectomy OR pancreatectomy OR pancreatic resection) AND (vein resection OR vascular resection OR vein reconstruction OR vascular reconstruction) AND (vein grafts OR vascular grafts OR grafts).

Eligibility criteria

Included were studies concerning reconstruction of SMV-PV reporting on the incidence of graft thrombosis. Excluded were studies with fewer than 5 relevant patients, review articles, meta-analysis, and published conference abstracts.

Data extraction

All selected studies were evaluated for relevant patients, defined as patients undergoing pancreatic resection with SMV-PV resection and reconstruction with a graft. Study design, sample size and data on early and late graft thrombosis, graft patency, graft infection, morbidity, mortality, complications related to donor site, radiological surveillance modality and anticoagulation policy were extracted. Mortality was defined as death within 30-days of surgery or as in-hospital mortality.

Quality assessment

The methodological quality of the included non-randomized studies was assessed by using the Newcastle–Ottawa Scale (NOS)^[9]. NOS includes three domains ‘selection of patients’, ‘comparability of study groups’ and ‘assessment of outcome’. In this systematic review, the parts of the NOS score (‘selection of the non-exposed’=S2, and ‘comparability’=C1+C2) were not applicable, because of its descriptive nature. For studies with no relevant data accordingly to NOS items S2 and C1+C2 for appraisal, we noted them as “not relevant” (NR). Thus, each study could not be evaluated and rated on the NOS 0–9 scale, but was ranked with a maximum of 6 points.

Statistical analysis

Results and outcomes in tables are expressed as they were originally reported. No meta-analysis was performed because of heterogeneity between studies. Hence, no statistical analysis was done owing to variation in the outcomes reported and variation of treatments used.

RESULTS

The systematic search identified 34 studies, all retrospective cohort studies, comprising 603 patients undergoing pancreatectomy with SMV-PV resection and

reconstruction with a graft. No randomized trials were available. A PRISMA flow diagram is shown in Figure 1. Many of these retrospective studies failed to provide a detailed description of how graft thrombosis was assessed by means of radiological surveillance strategy (modality, time intervals) (Table 1-4). This produced an overall assessment of moderate quality according to NOS (Table S1, supporting information).

Four hundred and fifty-five patients underwent pancreatoduodenectomy, 19 patients total pancreatectomy, 20 patients distal pancreatectomy, and in 109 patients the type of pancreatectomy was not specified. Type of graft used for SMV-PV reconstruction was autologous vein in 239 patients (left renal vein 39, saphenous vein 44, femoral vein 38, internal jugular vein 32, external iliac vein 50, and other veins 36 (gonadal, inferior mesenteric, splenic vein or not specified), synthetic graft in 158 patients (polytetrafluoroethylene (PTFE): 150, polyester: 8), cadaveric allografts in 161 patients (vein: 150, artery: 11), falciform ligament in 27 patients, and parietal peritoneum in 18 patients. Interposition graft was performed in 435 patients, patch in 123 patients, and details about the procedure were not specified in 45 patients (Table 1- 4).

The incidence of early graft thrombosis (< 30 days) was 7.5 % for synthetic grafts, 5.6 % for autologous veins, 6.7 % for parietal peritoneum/falciform ligament, and 2.5 % for cadaveric allografts. The overall incidence of graft thrombosis was 22.2 % for synthetic grafts, 11.7 % for autologous veins, 8.9 % for parietal peritoneum/falciform ligament, and 6.2 % for cadaveric allografts. If patients with locoregional recurrence and concomitant late graft thrombosis were excluded the overall incidence of graft thrombosis was 16.4 % for synthetic grafts, 11.7 % for autologous veins, 8.9 % for parietal peritoneum/falciform ligament, and 4.3 % for cadaveric allografts. The postoperative surveillance strategy varied between studies. The radiological follow up most often consisted of Doppler ultrasound during the first postoperative days and CT in case of symptoms during hospital stay and during post-

discharge follow up. In some cases MR venography was used. There was no consistent definition of graft patency. Terms as "patent", "no occlusion", "no stenosis" or "no thrombosis" were commonly used to define graft patency. Some studies defined patency as grade of stenose (%) comparing the diameter of the reconstructed SMV-PV with the preoperative diameter.

In-hospital/30-days mortality was 2.7 % for synthetic grafts, 2.7 % for autologous veins, 0 % for parietal peritoneum/falciform ligament, and 3.2 % for cadaveric allografts. Overall 30-day/in-hospital mortality was 2.7 % (13/489). Only three postoperative deaths were reported to be caused by acute, early SMV-PV thrombosis (3/27, 11.1 %). Morbidity was classified according to the Clavien-Dindo if applicable, and are presented in Table 1-4. There were no reports of graft infection with the use of synthetic grafts. Two studies reported transient elevated serum creatinine levels during postoperative day 1-3 after left renal vein harvest. Four studies reported postoperative edema, deep venous thrombosis or chronic pain in ipsilateral leg after external iliac vein or femoral/saphenous vein harvest.

Antiplatelet and anticoagulant protocols varied extensively between studies, and in some cases within the same study as choice of therapy was at surgeons discretion. Six studies reported that postoperative anticoagulation was not routinely recommended. Fourteen studies recommended LMWH, heparin or oral warfarin during hospital stay, and in some centres anticoagulation was continued after discharge. Fourteen studies recommended daily acetyl salicylic acid for 3-6 months.

DISCUSSION

This systematic review of 603 patients undergoing pancreatectomy with SMV-PV resection has shown that the use of autografts, allografts or synthetic grafts for SMV-PV reconstruction appears to be safe and feasible in selected patients. Graft thrombosis do occur with all types of grafts (early 2.5 % -7.5%, overall 6.2 - 22.2 %), but synthetic grafts seems to have a higher incidence of graft thrombosis. The studies had a substantial risk of selection bias, and the choice of graft are most likely made on basis of surgeon and/or centre preferences. No uniform definition of long term graft patency was found. The studies varied extensively regarding the postoperative follow-up imaging and anticoagulation protocols.

Some authors prefer to avoid synthetic grafts due to an anticipated higher risk of thrombosis and infection compared with native grafts^[5]. The data from this review indicate that graft thrombosis is more likely after synthetic graft reconstruction, but an association with increased mortality was not shown. None of the 10 studies reported any cases of graft infection with synthetic grafts. Only three of the 10 studies made specific comments on how to avoid graft infection. Administration of perioperative antibiotics, graft immersion in antibiotic solution, avoidance of enteric and biliary spillage, placement of an omental wrap, and use of antibiotic irrigant, albeit unquantitated in efficacy, were all suggested as potential means of minimizing infection^[10-12].

Overall 30-day/in-hospital mortality in this systematic review was 2.6 % (13/494). Most studies reported all-cause mortality as opposed to venous reconstruction type or early SMV-PV thrombosis associated mortality. Chandrasegaram et al showed that the overall mortality associated with early SMV-PV thrombosis after pancreatectomy with or without grafts was 40% (8/20) compared to 11.1 % (3/27) in this systematic review after pancreatectomy with grafts^[11, 13-15]. Kantor et al analyzed 640 patients undergoing

pancreatoduodenectomy with venous resection in the American College of Surgeons National Surgical Quality Improvement Project from 2006 to 2013^[16]. Of these 224 patients had a graft repair that was associated with increased overall morbidity (58.7 %, $p < 0.01$) and 30-day mortality rates (21 of 229, 7.7 %, $p < 0.01$)^[16]. Although based on small study samples, SMV-PV graft thrombosis seems to be a significant event and is associated with a mortality of > 10 %.

A recent survey showed that most surgeons prefer a segmental resection with primary anastomosis or a partial venous excision with direct closure, and thought that SMV-PV reconstruction with a conduit carries the highest risk of complications^[4]. This systematic review shows that studies on the use of autologous veins and synthetic grafts were published from 2006 to 2019, whereas studies on cadaveric allografts and parietal peritoneum/falciform ligament were published from 2013 to 2019 and 2015 to 2019, respectively. During the last ten years several centres have also advocated that a graft may be avoided in most cases^[5, 6]. Thus, there seems to have been some reconsiderations of type of graft and reconstruction methods during time. Over the last decade, advancements in preoperative chemotherapy and radiation therapy in pancreatic cancer have led to expansion of indications for surgical resection in patients with borderline resectable and locally advanced pancreatic cancer. Whether this will affect the choice of SMV-PV reconstruction remains to be established. Of note, recently a novel approach with SMV-PV resection without reconstruction has been introduced in patients with significant venous collaterals^[17].

The stability of the patient may play a role, and more urgent clinical conditions may lead to the use of prosthetic grafts or cadaveric allografts to decrease the operative time^[3, 18]. Cadaveric allografts are easy available in some centres, and is likely to save operative time. In a recent study, donor-specific allosensitization after allogeneic venous reconstruction of the SMV-PV has been documented^[19]. Moreover, PV transplantation in mice have revealed full

thickness infiltration of the vascular wall with mononuclear cells and moderate destruction of the endothelium and tunica media at postoperative week 1 with significantly reduced luminal diameter and intimal thickening on the 4th postoperative week^[20]. Thus, an immune mediated phenomenon in reconstruction with cadaveric vein allografts cannot be excluded. The nine studies on the use of cadaveric allografts had similar rate of graft thrombosis and as good long term graft patency as other biological grafts, and no studies reported any kind of immunosuppression or steroid therapy. Short term low level immunosuppression could possibly be of value after SMV-PV reconstruction with allogenic grafts to mitigate the allogeneic immuneresponse. The level and duration of immunosuppression has to be balanced against the risk of side effects and possible impact on complications like pancreatic fistula. One possible strategy could be a course of corticosteroids with or without mycophenolate mofetil with gradual weaning in the course of a few weeks, but no data are available with regards to the routine use of immunosuppressants, specific agents or duration in this particular setting.

Autologous vein harvesting is associated with an additional surgical procedure carried out at another site of the body, disruption of the main operation, and prolonged operative time. Left renal vein is easily exposed during the abdominal dissection, and an additional incision is not required to access it^[21]. Two studies reported transient elevated serum creatinine levels during postoperative day 1-3 after left renal vein harvest^[21, 22]. Two studies reported no increase in creatinine levels, and demonstrated collateral venous drainage from the left kidney by CT^[23, 24]. Thus, the left renal vein may be excised without compromising venous return from the left kidney if the adrenal and gonadal veins are preserved. Several studies reported postoperative edema or deep venous thrombosis in ipsilateral leg associated with external iliac vein or femoral/saphenous vein harvest^[25-28]. Some centres have even presented reconstruction techniques of the external iliac vein to overcome this

complication^[29]. In addition, there were some reports of seroma and wound dehiscence in the groin associated with harvesting of femoral/saphenous vein^[25, 30].

The parietal peritoneum is considered as a rapidly available option for vascular reconstruction, especially for unplanned lateral reconstruction of the SMV-PV with the need of a patch, whereas the falciform ligament has been suggested as an option in case of the need of an interposition graft^[31-34]. Other types of reconstruction revealed during the search was xenografts (bovine pericardium) or recanalized umbilical vein (Mesorex), but the reports in the literature were based on case reports or small case series^[35, 36].

Song et al performed a metaanalysis of relevant trials comparing vein grafts versus no vein grafts during pancreatoduodenectomy with venous resection and found 14 studies including 257 patients with vein grafts and 570 patients without vein grafts^[8]. They found a lower long-term vein patency rate in patients with vein grafts indicating that interposition grafts may be more likely to lose function. However, there are no randomized controlled trials and only a few comparative trials designed to compare different reconstruction techniques. Kleive et al showed that reconstruction of the SMV-PV with allograft was associated with longer operative time and more perioperative bleeding compared with primary end-to-end anastomosis^[19]. Preoperative CT images revealed that allograft reconstruction was performed in patients in whom a longer segment of the vein was affected by tumor (2.4 cm versus 1.8 cm, $p=0.02$), and a higher proportion of patients had >180 -degree tumour-vein interface (35.7 % versus 21.1 %, $p=0.01$). Zhang et al showed that patients undergoing reconstruction with allograft had a significant longer vein segment resected compared with patients undergoing primary end-to-end anastomosis (3 cm versus 2 cm, $p>0.001$). Liao et al also showed that patients receiving PTFE grafts for SMV-PV reconstruction had a longer vein segment resected (4 cm versus 2.9 cm, $p<0.001$), and in addition a larger tumour diameter (3.4 cm versus 2.9 cm, $p=0.016$) than patients undergoing primary end-to-end anastomosis^[12].

Moreover, PTFE graft was associated with longer operative time and more perioperative bleeding. These studies suggest that resection and reconstruction in patients receiving grafts are technically more challenging, which may account for the longer operative time and more extensive perioperative bleeding. Moreover, the longer vein segment resected and the larger tumour diameter in patients receiving a graft may reflect the fact that the patients requiring interposed allograft had more locoregional advanced tumours. Thus, comparing patients receiving interposition grafts with a primary end-to-end anastomosis may not be justified. It is only recently, that a standardized radiology reporting template has been proposed for pancreatic ductal adenocarcinoma^[37]. Although planned SMV-PV resections for pancreatic cancer were associated with higher rates of postoperative morbidity than unplanned resections, R0 resection rates were better^[38]. The use of proper preoperative imaging would likely aid in peroperative planning, in particular regarding the SMV-PV resection part of the procedure.

This systematic review confirms that there is a lack of consensus on the definition and reporting of long term graft patency after pancreatic surgery with SMV-PV resection and reconstruction. Patency rates may be overestimated when using only occlusion and/or thrombosis as a definition for failed late graft patency. However, the need for long term evaluation of the SMV-PV reconstruction may be debated as several studies report disease recurrence as the most common cause of late graft thrombosis and stenosis^[3, 11, 28, 39]. Snyder et al found that 76 % (19/25) of the cases of late SMV-PV thrombosis after vein resection with or without graft occurred in the setting of locoregional recurrence^[40]. Thus, late SMV-PV thrombosis is likely due to tumor biology causing tumor in-growth or compression on the area of previous vein resection, and less likely due to technical issues or graft type. Moreover, imaging findings of local recurrence can be difficult to distinguish from post-operative changes after SMV-PV reconstruction^[41]. Some authors advocate that long-term patency of

the SMV-PV should be examined, because long-term survivors who experience SMV-PV stenosis/occlusion may develop portal hypertension^[42]. However, the therapeutic consequence of detecting an asymptomatic SMV-PV stenosis/occlusion is under debate. Due to increased risk of complications, the indication for percutaneous PV stent placement after pancreatectomy with venous resection and reconstruction is recommended to be limited to patients with clinical symptoms^[42, 43]. Most patients are asymptomatic, whereas others present with the typical clinical signs of portal hypertension, including gastrointestinal hemorrhage, ascites and splenomegaly^[42]. Glebova et al showed that tumor recurrence played the dominant role in ascites development in cases of an associated SMV-PV thrombus^[18]. However, ascites may also be the first sign of early postoperative SMV-PV occlusion and thrombus^[11, 32].

Antiplatelet and anticoagulant protocols varied extensively between studies. This is in line with a systematic review showing that there is a significant heterogeneity in the use of anticoagulation/antiplatelet therapy after SMV-PV resection and reconstruction, with aspirin being a common minimum therapy for prophylaxis^[15]. Chandrasegaram et al performed a systematic review on studies with an anticoagulation policy to no anticoagulation policy after venous resection during pancreatectomy and showed that early SMV-PV thrombosis rate was similar in the two groups (7 % vs 3 %)^[15]. Kleive et al found no difference in the rate of early SMV-PV thrombosis (4.4% vs 4.2%) or postpancreatectomy hemorrhage (13.3% vs 16.7%) between patients receiving low- or high-dose low-molecular-weight heparin after pancreatoduodenectomy with venous resection and reconstruction^[44]. Given the technical complexity and heterogeneity of these operations and the consequences of thrombosis, it would be difficult to standardize practice in the absence of a randomized prospective trial^[45]. As suggested by Chandrasegaram, we agree that ideally the effects of antiplatelets or anticoagulants on graft patency should be investigated further in the context of a multicentre randomized controlled trial, and that such a study should include standardized definitions to

describe the types of vascular resection and type of graft used. However, it may be difficult to elucidate whether the most important factor for graft thrombosis is type of graft, technical factors or anticoagulation policy.

The results of this systematic review should be interpreted in light of several limitations. Only retrospective cohort studies were identified, and no randomized trials were available. Moreover, the quality of included studies were moderate according to NOS. Despite these limitations, the presented results and outcomes of all available literature on the use of grafts for SMV-PV reconstruction during pancreatectomy allow for a better understanding and critical evaluation of this approach. In order to achieve high-level evidence regarding anticoagulation policy, optimal reconstruction technique and follow-up, future research must be established in a multicentre platform with standardized definitions and predefined selection criterias.

Prisma flowchart, search 31th of March 2020

TABLES

Table 1 Cadaveric vein or arterial allografts (9 studies)

Author/Year	Graft type/ Number of patients	Morbidity	Mortality	Graft thrombosis	Graft patency (% or n)/Modality	Follow up	Anticoagulation
Zhang 2013 ^[46]	Cadaveric portal vein allograft 3/Cadaveric iliac artery allograft 6 (interposition)	3 (CD 1-3)	0	0	100 % Doppler US, CT or MRI	Median 18.1 months	None
Mascoli 2015 ^[47]	Cadaveric artery allograft 5 (aorta 3, femoral artery 2) (interposition)	2 (CD 3)	0	0	100 % Doppler US	Median 10 months	LMWH twice a day POD 1-30 according to weight and blood clotting tests. If platelets >400x10 ³ /ul, antiplatelet therapy was also administered.
Kleive 2016 ^[3]	CIVA 45 (interposition 37, patch 8)	16 (CD ≥3)	2 (in-hospital)	2 (<30 days) 3 (>30 days, concomitant with locoregional recurrence)	Severe stenosis (>70 % stenosis vs preoperative diameter, occlusion or thrombus): 26 (of whom 23 had signs of locoregional recurrence). Doppler US, CT	Median 13 months	LMWH 200 IU/kg first month, 100 IE/kg the following two months. Lifelong ACA 75 mg daily at the surgeon's discretion.
Zhao 2016 ^[48]	CIVA 21 (interposition)	6 (CD 1-5)	1 (in-hospital)	0 (<30 days) 2 (>30 days)	NS Doppler US, CT	Mean 18.2 months	LMWH 2850 IU twice daily first week, then ACA 100 mg daily for up to 6 months.
Meniconi 2016 ^[13]	CIVA 11 (interposition 7, patch 4)	5 (CD 1-5)	1 (30 days)	1 (<30 days, died) 0 (>30 days)	No stenosis. Doppler US, CT	Median 9 months	LMWH (enoxaparin 4000 IU) daily for 30 days.
Yamamoto 2017 ^[49]	Cadaveric portal and femoral vein allograft 18 (interposition 11, patch 7)	5 (CD 1+2) 0 (CD ≥3)	0	0 (<30 days) 1 (>30 days)	Clinically relevant stenosis (>50% stenosis vs preoperative diameter): 8 (pseudo-intimal hyperplasia in 5, local recurrence in 3). Doppler US, CT or MRI	Median 18 months	NS
Zhang 2018 ^[50]	CIVA 42 (interposition)	13 (CD 1-3)	0 (in-hospital)	0	NS Doppler US, CT	NS	Nodroparin calcium 0.4 mLx1 POD 2-7, then daily ACA for 1 month.
Dumitrascu 2018 ^[51]	CIVA 5 (interposition)	NS	NS	0	NS	Median 10.5 months	NS
Procikievicz 2019 ^[14]	CIVA 5 (interposition)	3 (CD ≥2)	1 (30 days)	1 (<30 days, died) 0 (>30 days)	No graft thrombosis or stenosis in remaining 4 patients. Doppler US, CT	NS	LMWH started 24 hours postoperatively to prevent DVT (depending on the Caprini score). ACA 100 mg daily from POD 7.
Overall	161		3.2 % (5/156)	Early 2.5 % (4/161) Late 3.7 % (6/161) Overall 6.2 % (10/161) Overall 4.3 % (locoregional recurrences excluded; 7/161)			

ACA: acetyl salicylic acid, CIVA: cadaveric iliacal vein allograft, CD: Clavien Dindo, CT: computer tomography, DVT: deep venous thrombosis, LMWH: low molecular weight heparin, MR: magnetic resonance imaging, NS: not specified, POD: postoperative day, US: ultrasound

Table 2 Parietal peritoneum and falciform ligament (4 studies)

Author/Year	Graft type/ Number of patients	Morbidity	Mortality	Graft thrombosis	Graft patency (n)/Modality	Follow up	Anticoagulation
Dokmak 2015 ^[31]	Parietal peritoneum 18 (patch 15, near total 2, tube made 1)	12 (CD 1-4)	0	1 (<30 days, tube made) 0 (>30 days)	No-mild stenosis (0-25 %): 15 Moderate stenosis (25-75 %): 2 Severe stenosis/ (> 75 %): 0 Thrombosis: 1 CT	Mean 14 months	LMWH 0.4 mL (0.6 mL if body mass index > 35 kg/m2) for 4 weeks.
Zhiying 2017 ^[33]	Falciform ligament 10 (patch 6, interposition 4)	5 (CD 1-3)	0	0 (<30 days) 1 (>30 days, occlusion)	Complete patency: 3 Moderate stenosis: 6 Occlusion: 1 Doppler US, CT	Mean 2 months	None
Shao 2018 ^[34]	Falciform ligament 6 (patch)	2 (CD 2-3)	0	0	Moderate stenosis: 1 Doppler US, CT	Mean 12 months	None
Malinka 2018 ^[32]	Falciform ligament 11 (patch 9, interposition 2)	6 (CD 2-3)	0	2 (<30 days, occlusion) 0 (>30 days)	All patent grafts on discharge (n=9) revealed persistent patency. Doppler US, CT	Median 64 days (range 18-147)	Unfractionated heparin (goal: partial thromboplastin time of 40-50 seconds) for 5 days, followed by LMWH to prevent DVT during hospital stay.
Overall	45		0	Early 6.7 % (3/45) Late 2.2 % (1/45) Overall 8.9 % (4/45)			

CD: Clavien Dindo, CT: computer tomography, DVT: deep venous thrombosis, LMWH: low molecular weight heparin, US: ultrasound

Table 3 Autologous venous grafts (14 studies)

Author	Graft type/ Number of patients	Morbidity	Mortality	Graft thrombosis	Graft patency (% or n)/ Modality	Donor site	Follow up	Anticoagulation
Suzuki 2006 ^[24]	Left renal vein 7 (type NS)	NS	0	0	100 % CT	Creatinine levels were not increased, collateral venous drainage from the left kidney was well demonstrated by CT	Median 18 months	NS
Smoot 2007 ^[22]	Left renal vein 9 (interposition 8, patch 1)	3 (CD 1-3)	0	0	89 %	Creatinine levels transiently increased, normalized by discharge	Mean 6.8 months	Clopidogrel: 1 Daily ACA: 8
Ohwada 2007 ^[23]	Left renal vein 6 (type NS)	3 (CD 1-5)	1 (in-hospital) (hepatopancreato- duodenectomy)	2 intraoperatively (treated with thrombectomy/ reanastomosis)	100 %	Creatinine levels were not increased	Mean 22.5 months	Heparin, followed by warfarin or ACA
Kaneoka 2008 ^[27]	External iliac vein 15 (interposition)	NR	2 (in-hospital)	0	Occlusion: 1 (received intraoperative radiation therapy)	Edema of the right leg present for 1-3 months	Mean 32 month	None
Stauffer 2009 ^[10]	7 (gonadal or inferior mesenteric vein) (type NS)	NS	NS	1 (<30 day)	86 % Doppler US, CT or MRI	NS	Median 13.8 months	Standard thromboprophylaxis (NS)
Lee 2010 ^[25]	Femoral vein 19 Saphenous vein 15 (interposition 15, patch 19)	3 DVT	0 (<30 days)	2 (<30 days, occlusion)	88 % CT	3 FV: seroma drainage 2 FV: minor wound dehiscence 8 FV+1 SV: minimal transient edema in ipsilateral leg	Mean 5 months	NS
Turley 2012 ^[28]	Femoral vein interposition 9 External iliac/Inferior mesenteric/ Saphenous patch 25	Overall NS	2 (<30 days)	1 (<30 days, occlusion)	91.7 % Occlusion: 2 (concomitant with locoregional recurrence). Partial narrowing or occlusion: 7 CT	FV/EIV: edema in ipsilateral leg, severe venous insufficiency 1, no permanent disability DVT in 7 patients with FV interposition	> 6 months	Routine thromboprophylaxis (NS) and ACA
Krepline 2014 ^[52]	Saphenous vein patch 9 Internal jugular vein interposition 14	NS	NS	Early 0 Late 1 Early 1 Late 1	Patent 8 Patent 12 Modality NS	NS	Median 12 months	Daily ACA: 6 LMWH: in selected cases if indication
Hirono 2014 ^[26]	External iliac vein 10 Internal jugular vein 4 (interposition)	6 (CD 1-4)	2 (in-hospital)	0	No occlusions Doppler US, CT	3 EIV: DVT ipsilateral leg 1 EIV: leg edema/chronic pain	Mean 28.2 months	NS
Glebova 2015 ^[18]	11 (internal jugular 4, left renal 4, splenic 2, saphenous 1) (interposition)	NS	0	1 (<30 day)	Patent 10 CT	NS	Median 7 months	None
Dua 2015 ^[45]	24 (gonadal 2, internal jugular 4, left renal 2, saphenous 6 and femoral vein 10) (type NS)	NS	NS	8 (time NS)	NS Doppler US, CT or MRI	NS	Median 8.7 months	70% of patients daily ACA
Loveday 2019 ^[21]	Left renal vein 11 (interposition)	5 (HPB complica tions)	0	4 (thrombus or complication requiring revision of the anastomosis)	Patency NS Modality NS	Acute kidney injury: POD 1=5, POD 3=3, resolved within the first week, no long-	Median 12.9 months	NS

				(time NS)		term sequelae on renal function		
Pantoja 2019 ^[30]	Saphenous vein 13 Internal jugular vein 6 (interposition)	4 0	0	2 (<30 days), 1(>30 days) 2 (<30 days)	85 % 80 % Doppler US, CT	Seroma drainage + wound dehiscence	Mean 17.1 months Mean 8.2 months	Daily ACA
Terasaki 2019 ^[53]	External iliac vein 25 (interposition)	3 (CD >=3)	0	1 (time NS)	84 % Doppler US, CT	NS	12 months	5000 heparin POD 0, 10 000 U heparin POD 1+2
Overall	239		2.7 % (5/185)	Early 5.6 % (10/179) Late 1.7 % (3/179) Time NS 21.7 % (13/60) Overall 11.7% (28/239)				

ACA: acetyl salicylic acid, CD: Clavien Dindo, CT: computer tomography, DVT: deep venous thrombosis, LMWH: low molecular weight heparin, NS: not specified, POD: postoperative day, UL: ultrasound

Table 4 Synthetic (polytetrafluoroethylene) grafts (10 studies)

Author/Year	Graft and N	Morbidity	Mortality	Graft infection	Graft thrombosis	Graft patency (% or n)/ Modality	Follow up	Anticoagulation
Smoot 2006 ^[39]	PTFE 18 (patch 2, interposition 16)	NS	0	0	1 (<30 days) 5 (>30 days, associated with, locoregional recurrence)	NS Intraoperative US, CT	Mean 12.2 months	Surgeon preference. ACA, warfarin, or clopidogrel.
Stauffer 2009 ^[10]	PTFE 10 (patch 1, interposition 9)	NS	NS	0	1 (<30 days) 0 (>30 days)	100 % Doppler US, CT or MRI	Median 13.8 months	Standard thromboprophylaxis (NS) plus 1–2 mg warfarin daily once oral intake was tolerated for 3 months.
Chu 2010 ^[11]	PTFE 33 (patch 9, interposition 24)	15 (CD 1-5)	2 (30 d)	0	3 (<30 days, 1 died) 5 (>30 days, 4 associated with concomitant locoregional recurrence)	77.3% at 6 months (n=22) 64.3% at 12 months (n=14) 75.8 % at last follow up Doppler US, CT or MRI	Mean 14 months	ACA or LMWH initiated by the time of discharge, continuation for 3 to 6 months.
Liao 2014 ^[12]	PTFE 34 (interposition)	10 (CD 1-5)	1	0	1 (<30 days) 5 (>30 days)	87.9% at 6 months 83.5% at 12 months Doppler US, CT or MRI	Median 14 months	11 patients > 70 years: ACA for 3 months
Glebova 2015 ^[18]	PTFE or Dacron 6 (interposition)	NS	0	0	3 early/late NS	Patent: 3 CT	Median 7 months	None
Flis 2016 ^[54]	Dacron 8 (interposition)	NS	NS	0	0	NS	NS	NS
Gao 2016 ^[55]	PTFE 7 (interposition)	6	0	0 (encapsulated effusion around graft 1, edema around graft 1)	2* (<30 days) 4* (>30 days) (*one patient both early and late)	Stenosis (> 50%) 2 (< 30 days), 3 (> 30 days) Doppler US, CT	Median 12 months	LMWH for 2 weeks after surgery, followed by oral warfarin for 6 months
Dumitrascu 2018 ^[51]	PTFE 19 (interposition)	NS	NS	NS	3 early/late NS	NS	Median 10.5 months	NS
Wang 2019 ^[56]	PTFE 10 (interposition)	4 (CD 1+2)	0	0	2 (<30 days) 0 (>30 days)	100 % at 2 months CT	NS	LMWH for 7 days after surgery, followed by oral warfarin (INR 1.5-2)
Tsitos 2019 ^[57]	PTFE 13 (interposition)	NS	NS	0	0	100 % Doppler US	2 months Doppler US	
Overall	158		2.7 % (3/108)	0	Early 7.5 % (10/133) Late 14.3 % (19/133) Time NS 24 % (6/25) Overall 22.2 % (35/158) Overall 16.4 % (locoregional recurrences excluded; 26/158)			

ACA: acetyl salicylic acid, CD: Clavien Dindo, CT: computer tomography, INR: international normalized ratio, LMWH: low molecular weight heparin, MRI: magnetic resonance imaging, NS: not specified, POD: postoperative day, PTFE: Polytetrafluoroethylene, UL: ultrasound

Table S1

Quality assessment of included articles based on the Newcastle-Ottawa Scale (NOS)

Study	Year	Selection		Comparability				Exposure			No. of stars
		S1	S2	S3	S4	C1	C2	E1	E2	E3	
<u>Cadaveric vein or arterial allografts</u>											
Zhang	2013	*	NR	*	*	NR	NR	*	*	*	6
Mascoli	2015	*	NR	*	*	NR	NR	*	*	*	6
Kleive	2016	*	NR	*	*	NR	NR	*	*	-	5
Zhao	2016	*	NR	*	*	NR	NR	*	*	-	5
Meniconi	2016	*	NR	*	*	NR	NR	*	*	*	6
Yamamoto	2017	*	NR	*	*	NR	NR	*	*	*	6
Zhang	2018	*	NR	*	*	NR	NR	*	*	*	6
Dumitrascu	2018	*	NR	*	*	NR	NR	-	*	-	4
Procikievicz	2019	*	NR	*	*	NR	NR	*	*	*	6
<u>Parietal peritoneum and falciform ligament</u>											
Dokmak	2015	*	NR	*	*	NR	NR	*	*	*	6
Zhiying	2017	*	NR	*	*	NR	NR	*	*	*	6
Shao	2018	*	NR	*	*	NR	NR	*	*	*	6
Malinka	2018	*	NR	*	*	NR	NR	*	*	-	5
<u>Autologous venous grafts</u>											
Suzuki	2006	*	NR	*	*	NR	NR	*	*	*	6
Smoot	2007	*	NR	*	*	NR	NR	-	*	*	5
Ohwada	2007	*	NR	*	*	NR	NR	-	*	-	4
Kaneoka	2008	*	NR	*	*	NR	NR	-	*	-	4
Stauffer	2009	*	NR	*	*	NR	NR	*	*	*	6
Lee	2010	*	NR	*	*	NR	NR	-	*	-	4
Turley	2012	*	NR	*	*	NR	NR	-	*	*	5
Krepline	2014	*	NR	*	*	NR	NR	*	*	*	6
Hirono	2014	*	NR	*	*	NR	NR	*	*	*	6
Glebova	2015	*	NR	*	*	NR	NR	*	*	*	6
Dua	2015	*	NR	*	*	NR	NR	*	*	*	6
Loveday	2019	*	NR	*	*	NR	NR	-	*	-	4
Pantoja	2019	*	NR	*	*	NR	NR	-	*	*	5
Terasaki	2019	*	NR	*	*	NR	NR	*	*	*	6
<u>Synthetic grafts</u>											
Smoot	2006	*	NR	*	*	NR	NR	*	*	*	6
Stauffer	2009	*	NR	*	*	NR	NR	*	*	*	6
Chu	2010	*	NR	*	*	NR	NR	*	*	-	5
Liao	2014	*	NR	*	*	NR	NR	*	*	*	6
Glebova	2015	*	NR	*	*	NR	NR	*	*	*	6
Flis	2016	*	NR	*	*	NR	NR	-	*	*	5
Gao	2016	*	NR	*	*	NR	NR	*	*	*	6
Dumitrascu	2018	*	NR	*	*	NR	NR	-	*	-	4
Wang	2019	*	NR	*	*	NR	NR	-	*	*	5
Tsitos	2019	*	NR	*	*	NR	NR	-	*	-	4

*No. of stars given= relevant score possibility; S1, How representative is the exposed cohort?; S2, Selection of the non-exposed cohort?; S3, Ascertainment of exposure?; S4, Outcome not present at start of study?; C1, Comparability of outcome?; C2, Comparability of the design?; E1, Assessment of outcome?; E2, Sufficiently long follow-up for outcome to occur?; E3, Adequacy of follow-up?; NR=Not relevant

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