



What to expect with major vascular reconstruction during Whipple procedures: a single institution experience and literature review

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Background: Major vascular reconstruction during a pancreaticoduodenectomy (PD), also known as a Whipple procedure, leads to controversial postoperative outcomes compared to conventional Whipple. Discussion with the patient regarding postoperative expectations is a crucial component of holistic surgical healthcare. The aim of this study was to report our 8-year experience of Whipple procedures involving vascular reconstruction and to review relevant literature to further evaluate expectant outcomes, therefore leading to more accurate discussion.

Methods: A retrospective review of patients undergoing Whipple procedures from January 2010, through December 2017 was performed. Patch, graft, and primary anastomosis during Whipple procedures were considered major vascular reconstruction. Literature on the current understanding of the outcomes associated with vascular reconstruction during Whipple procedures was reviewed.

Results: Twenty-nine from a total of 405 patients that met inclusion criteria had a Whipple procedure that involved major vascular reconstruction. Twelve patients were male and 17 were female (mean age, 65.2 years). Median hospital and intensive care unit (ICU) stay [range] of patients with vascular reconstruction was 12 [5–92] days and 3 [0–59] days, respectively. Thirty-day survival and 1-year survival of patients with vascular reconstruction was 93.1% and 55.2%, respectively, compared to non-vascular reconstruction patients 96.0% and 83.5%, respectively ($P=0.35$, $P<0.001$). Ninety-day readmission for vascular reconstruction patients was 31.0% compared to 14.6% in non-vascular reconstruction patients ($P=0.03$). The 1-year survival of those who had patch reconstruction, graft reconstruction, and primary anastomosis was 50.0%, 62.5%, 53.8%, respectively.

Conclusions: Compared to conventional Whipple procedures, those requiring major vascular reconstruction are associated with decreased survival. When vascular reconstruction is a valid option patients should be well aware of the associated outcomes.

Keywords: Whipple; vascular reconstruction; survival; pancreatic cancer

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Introduction

Pancreatic adenocarcinoma is a highly lethal disease that has a 5-year survival as low as 6% in the United States (1,2). Most patients with pancreatic cancer are asymptomatic until the disease has reached an advanced stage often limiting potential curative resection (2). In addition, the tumor biology of pancreatic adenocarcinomas leads to early recurrence and metastasis with resistance to conventional neo-adjuvant and adjuvant therapies (chemotherapy, radiotherapy) (1). Early surgical resection remains to be regarded as the only treatment that potentially leads to increased patient survival, and cure (3-8). A common surgery for resection of pancreatic head adenocarcinoma is a pancreaticoduodenectomy (PD), or Whipple procedure (3-8), which involves resecting the head of the pancreas, duodenum, gallbladder, and bile duct (9). However, when the surgical margin is positive for cancer (R1 resection); survival rates remain very poor, thus putting an emphasis on accurate preoperative diagnosis and surgical interventions that fully removes the disease (10). In order to achieve a negative margin (R0 resection), resection of vessels [superior mesenteric vein (SMV), portal vein (PV), and hepatic artery] may be deemed necessary. Because the PV, SMA, and hepatic arteries may be involved a vascular resection during PD often requires secondary vascular reconstruction of the resected vessels. Literature has debated the feasibility of vascular resection and the secondary reconstruction during Whipple procedures. Multiple single-center series reports argue that vascular resection/reconstruction is a safe and feasible procedure during PD in an attempt to obtain negative margins (10-22). However, multiple studies, including those arguing for the feasibility and safety of the procedure, have data showing that vascular reconstruction secondary to resection leads to decreased survival rates (1-, 3-, 5-year) and increased postoperative complications compared to PD without vascular intervention (3,12,16,23,24). These inconsistencies call for further analysis of the outcomes associated with PD involving vascular reconstruction, and their impact on patient care. The ability to accurately inform a patient with pancreatic carcinoma during the decision making process is critical to holistic, patient-orientated healthcare. Additionally, the process of engaging with the patient, and discussing treatment options and postoperative expectations, is especially critical for older patients undergoing high-risk surgeries (i.e., PD with vascular reconstruction) (25).

The aim of this study is to report our 8-year experience of Whipple procedures involving vascular reconstruction and to review relevant literature to further evaluate expectant outcomes of the surgery in order to increase patient awareness during the decision making progress.

Methods

A retrospective review of the patients who underwent PD, pylorus-preserving pancreaticoduodenectomy (PPPD), and total pancreatectomy (TP) after Whipple procedures, between January 2010 and December 2017 at the Mayo Clinic Jacksonville, Florida, was performed using data collected from a Mayo Clinic Institutional Review Board (IRB)-approved prospective database (IRB 09-00-3940). Informed consent was waived by the IRB as this study was deemed minimal risk to patients. Patients with clinical, radiologic, and final pathologic confirmation of pancreatic adenocarcinomas, who underwent surgical intervention involving an open or laparoscopic (including intraoperative conversion) Whipple procedure, were included in the study. Patient information, including demographics, clinical history, symptoms, previous surgeries, and tumor pathologies, was collected.

Patients were divided into two separate groups: those who underwent additional major vascular reconstruction following resection of vessels (SMV, PV, and hepatic artery) during a Whipple procedure, and those who did not require additional vascular manipulation. The two groups were compared in terms of demographics, intraoperative characteristics (estimated blood loss, amount of blood transfused, operative time, vascular surgeon involvement, resection margins) type of major vascular reconstruction [primary anastomosis, interposition polytetrafluoroethylene (PTFE) graft, patch, and complex], type of vessel resected/reconstructed (PV, SMV, hepatic artery, etc.) and postoperative outcomes (hospital stay, intensive care unit (ICU) stay, readmission rates, 30-day survival, 1-year survival). The patients were followed postoperatively to determine if readmission was due to complications involved with the vascular reconstruction (thrombosis, etc.) and if continued treatment/follow-up was required for those complications. Lateral renorrhaphy was not considered a major vascular reconstruction in this study.

Statistical analysis was performed using both a two-sided Fisher's exact test and an unpaired *t*-test for categorical data. Statistical significance was defined as a P value of less than 0.05.

Table 1 Preoperative characteristics

Characteristics	Whipple+ (n=29, %)	Whipple- (n=376, %)	P value
Age (\pm SD)	65.2 \pm 12.5	64.0 \pm 11.9	0.62
Sex			
Male	12 (41.4)	205 (54.5)	0.18
Female	17 (58.6)	171 (45.5)	0.18
Preoperative main symptoms			
Jaundice	15 (51.7)	151 (40.2)	0.24
Weight loss	17 (58.6)	173 (46.0)	0.25
Nausea/vomiting	9 (31.0)	67 (17.8)	0.09
Abdominal pain	16 (55.2)	180 (47.9)	0.56
Asymptomatic	2 (6.9)	57 (15.2)	0.28
Comorbidities			
HTN	12 (41.4)	234 (62.2)	0.03
DM	10 (34.5)	106 (28.2)	0.52
Cardiac disease	8 (27.6)	97 (25.8)	0.83
ASA			
I	0 (0.0)	1 (0.27)	1.00
II	3 (10.3)	65 (17.3)	0.44
III	24 (82.8)	294 (78.2)	0.81
IV	2 (6.9)	16 (4.3)	0.37
Type of surgery			
PD	5 (17.2)	41 (10.9)	0.22
PPPD	18 (62.1)	289 (76.9)	0.11
TP	6 (20.7)	46 (12.2)	0.24

Whipple+, Whipple procedure with additional vascular reconstruction; Whipple-, Whipple procedure without additional vascular reconstruction; HTN, hypertension; DM, diabetes mellitus; ASA, physical status classification system used preoperatively to indicate a patient's operative risk. As the number increases, as does the risk. PD, pancreaticoduodenectomy; PPPD, pylorus-preserving pancreaticoduodenectomy; TP, total pancreatectomy.

Results

Preoperative characteristics

Demographics, symptoms, and comorbidities of patients undergoing conventional Whipple (-) and Whipple involving vascular reconstruction (+) data are presented in *Table 1*. Of the 29 patients who underwent Whipple with vascular reconstruction, 12 (41.4%) were male and 17 (58.6%) were female, with a mean age of 65.2 years. A majority of Whipple+ patients presented to the clinic with weight loss (58.6%), abdominal pain (55.2%), and/or

jaundice (51.7%). When comparing Whipple+ to Whipple-, 31.0% of patients presented with nausea/vomiting compared to 17.8%, respectively (P=0.09). Twelve (41.4%) patients who underwent Whipple+ had a history of hypertension, compared to 234 (62.2%) patients who underwent Whipple- (P=0.03). A majority of Whipple+ patients (82.8%) had an ASA score of III, with only 2 (6.9%) having a score of IV.

Perioperative characteristics

Perioperative characteristics of Whipple+ and Whipple-

Table 2 Perioperative characteristics

Variables	Whipple+ (n=29)	Whipple- (n=376)	P value
Operative time (min)	553 (\pm 167)	384 (\pm 139)	<0.0001
Estimated blood loss (mL)	2,100 (\pm 3,869)	362 (\pm 725)	<0.0001
Perioperative blood transfusion (units)	6.3 (\pm 11.8)	2.0 (\pm 7.8)	0.0064

Whipple+, Whipple procedure with additional vascular reconstruction; Whipple-, Whipple procedure without additional vascular reconstruction. Units, one unit of blood is approx. 300 mL.

Table 3 Postoperative characteristics

Variables	Whipple+ (n=29)	Whipple- (n=376)	P value
Median hospital stays (days)	12 [5–92]	7 [2–302]	–
Median ICU stay (days)	3 [0–59]	0 [0–144]	–
30-day survival	27 (93.1%)	361 (96.0%)	0.35
1-year survival	16 (55.2%)	314 (83.5%)	<0.001
90-day readmission	9 (31.0%)	55 (14.6%)	0.03

Whipple+, Whipple procedure with additional vascular reconstruction; Whipple-, Whipple procedure without additional vascular reconstruction; ICU, intensive care unit.

are presented in *Table 2*. The average operative time of Whipple+ and Whipple- was 553 (SD \pm 167) and 384 (SD \pm 139) min, respectively (P <0.0001). The average estimated blood loss of patients who underwent Whipple+ was 2,100 (SD \pm 3,869) mL compared to 362 (SD \pm 725) mL for patients who underwent Whipple- (P <0.0001).

Postoperative characteristics

Postoperative characteristics including hospital stay, ICU stay, 30-day survival, 1-year survival, and 90-day readmission are presented in *Table 3*. Patients who underwent Whipple+ had a median [range] hospital and ICU stay of 12 [5–92] and 3 [0–59] days, respectively. Readmission rates of patients who underwent Whipple+ and those who underwent Whipple- was 31.0% and 14.6%, respectively (P =0.03). Survival rates were lower for patients who underwent Whipple+ compared to Whipple- patients. The 30-day survival rate for Whipple+ and Whipple- was 93.1% and 96.0%, respectively (P =0.35). The 1-year survival rates for the same groups was 55.2% and 83.5%, respectively (P <0.001).

Vascular reconstruction characteristics

One-year survival varied based on certain preoperative, perioperative, and postoperative characteristics. Ten (34.5%)

patients had neo-adjuvant therapy with a 1-year survival rate of 40.0%, compared to 19 (65.5%) without neo-adjuvant therapy with a 1-year survival rate of 63.2%. In terms of the vessel resected/reconstructed and the type of reconstruction, a majority of the vascular reconstructions involved the PV (65.5%), with a 1-year survival rate of 52.6%, and were reconstructed via primary anastomosis (44.8%), with a 1-year survival rate of 53.8%. The 1-year survival of those who had interposition graft placement (27.6%) was 62.5%. The lowest survival rates were seen in reconstruction involving the PV (52.6%) and patch reconstruction (50.0%). Vascular surgeon assistance was utilized in 4 (13.8%) patients, with a 1-year survival rate of 75%. Overall, 4 (13.8%) patients were readmitted for complications involving the reconstruction. Of these 4, only 1 (3.4%) required re-intervention, and 2 (6.9%) required continued treatment for the complications and follow-up with vascular surgery.

Discussion

Preoperative discussion concerning treatment options and the associated postoperative outcomes are vital to any patient-orientated healthcare model. A study by Steffen *et al.* argued that engaging in preoperative discussion with patients focusing on treatment options and postoperative

Table 4 Literature review of survival outcomes of Whipple procedures involving additional vascular reconstruction

Study, publication year	Inclusion period	Number of patients	30-day survival (%)	1-year survival (%)
Harrison <i>et al.</i> , 1996 (13)	1983–1995	58	94.8	NA
Bachelier <i>et al.</i> , 2001 (10)	1990–1999	31	96.8	48.4
Tseng <i>et al.</i> , 2004 (21)	1990–2002	110	97.9	NA
Martin II <i>et al.</i> , 2009 (22)	1999–2007	36	NA	41.7
Chakravarty <i>et al.</i> , 2010 (26)	1996–2006	87	100	49.4
Castleberry <i>et al.</i> , 2012 (3)	2005–2009	281	94.3	60.1
Gong <i>et al.</i> , 2013 (23)	2006–2011	119	93.3	30.3
Cheung <i>et al.</i> , 2014 (17)	2001–2012	32	96.9	70.6
Beltrame <i>et al.</i> , 2015 (19)	1998–2012	64	96.9	42.0
Zakaria <i>et al.</i> , 2017 (12)	1995–2014	601	NA	55.1
Present study, 2018	2010–2017	29	93.1	55.2
Survival between studies (survival/total #), (SD)			92.4 (749/811) ±2.16	52.7 (674/1,280) ±11.1

SD, standard deviation; NA, not available.

outcomes is crucial; especially for older patients undergoing high-risk procedures (25). This pertains directly to Whipple procedures involving vascular reconstruction, for the average patient is over 65 years of age (*Table 1*) and the surgery is associated with high mortality (*Table 3*).

Although a small number of patients undergoing a Whipple procedure for attempted resection of a pancreatic adenocarcinoma required additional major vascular resection and secondary reconstruction (7.2%), the results of the procedures reveal significant differences compared to those not requiring vascular reconstruction. The majority of these patients were female (58.6%) and had an ASA score of III (82.6%). Jaundice, weight loss, and abdominal pain were the most prevalent symptoms in both groups of patients, which is consistent with advanced pancreatic adenocarcinoma (2).

Compared to Whipple- procedures, Whipple+ procedures result in significantly increased operation time, estimated blood loss intraoperatively, and perioperative blood transfusion (*Table 2*). An increase in each of these characteristics of surgery are associated with increased odds of complications postoperatively (27,28). A study by Seykora *et al.* showed that increasing intraoperative blood loss during a PD was significantly correlated with poor perioperative outcomes, and that a main factor of increased blood loss was vascular resection (28). Therefore, this supports our findings that a Whipple+ procedure results in poor perioperative outcomes associated with increased operation time and intraoperative blood loss. This is

supported by the results seen in *Table 3*, where 90-day readmission rate of Whipple+ procedures were significantly higher than that of Whipple- procedures. Nine (31.0%) of Whipple+ patients were readmitted within the first 90 days postoperatively, compared to 55 (14.6%) of Whipple- patients ($P=0.03$). Additionally, median ICU and hospital stay were both longer for Whipple+ patients compared to Whipple- patients (2 and 12 *vs.* 7 and 0, respectively). The 1-year survival rate of patients who underwent Whipple+ procedures was significantly less than those who received a Whipple- procedure (55.2% and 83.5%, respectively) ($P<0.001$). Interestingly, the 30-day survival was not significantly different between the two groups; however, the 30-day and 1-year survival rates were similar to those described previously in literature (*Table 4*). This may suggest that the vascular reconstruction has no significant short-term effect on patient outcome, but significantly affects the patient's long-term recovery.

As for the characteristics of the vascular reconstruction, the majority of reconstructions involved the manipulation of the PV (65.5%), reconstruction via primary anastomosis (44.8%), no neo-adjuvant therapy (65.5%), no vascular surgeon assistance (86.2%), and negative margins of cancer (93.1%) (*Table 5*). Patients receiving neo-adjuvant therapy had a lower 1-year survival compared to those who were not (40.0% and 63.2%, respectively). In terms of the type of vessel resected and type of reconstruction, the 1-year survival was the lowest for PV resection (52.6%) and

Table 5 Vascular reconstruction characteristics

Characteristics	Patient number (n=29) [n (%)]	1-year survival [n (%)]
Preoperative		
Neo-adjuvant therapy	10 (34.5)	4 (40.0)
No neo-adjuvant therapy	19 (65.5)	12 (63.2)
Perioperative		
Type of repair		
Patch	8 (27.5)	4 (50.0)
PTFE graft	8 (27.6)	5 (62.5)
Primary anastomosis	13 (44.8)	7 (53.8)
Type of vessel reconstructed		
PV	19 (65.5)	10 (52.6)
SMV	9 (31.0)	6 (66.7)
Hepatic artery	5 (17.2)	3 (60.0)
Vascular surgeon assistance	4 (13.8)	3 (75.0)
Postoperative		
R1 margins	2 (6.9)	2 (100.0)
Readmission for complication	4 (13.8)	2 (50.0)
Re-intervention for complication	1 (3.4)	1 (100.0)
Continued treatment for complications	2 (6.9)	1 (50.0)

PTFE, polytetrafluoroethylene; PV, portal vein; SMV, superior mesenteric vein.

patch reconstruction (50.0%). The 1-year survival rates were highest for resection of the SMV (66.7%) and graft reconstruction (62.5%). Interestingly, Tee *et al.* further investigated the impact of the type of resection, arterial type, and use of neoadjuvant therapy in 111 patients who require a pancreatectomy with vascular reconstruction and found that none had a significant impact on long-term survival (29). Reconstructions performed by vascular surgeons (13.8%) had a 1-year survival of 75%. This suggests that vascular surgeon assistance during major vascular reconstruction may lead to a better chance of survival. Of the 29 patients who underwent a Whipple+ procedure, only 4 (13.8%) were readmitted due to complications associated with the reconstruction. Of these 4, 1 (3.4%) required re-intervention and 2 (6.9%) required continued follow-up with vascular surgery. An analysis of a larger number of Whipple+ patients would allow for a

better understanding of the impact specific intra-operative characteristics have on patient outcomes.

To this day, there is a debate regarding the feasibility and safety of the procedure. Many studies argue for feasibility of the procedure (10-22), while some, like this study, report data suggesting that vascular reconstruction during Whipple procedures result in significantly lower survival rates and increased complications (3,12,16,23,24). This present study utilizes the arguing studies' results, along with the results of this study, to develop a clearer image of the postoperative outcomes associated with Whipple procedures involving vascular reconstruction. As seen in *Table 4*, a majority of studies report relatively similar 30-day survival rates (SD \pm 2.16%), while 1-year survival rates had more variation (SD \pm 11.1%). Of note, Cheung *et al.* reported 70.6% 1-year survival rate for patients receiving vascular reconstruction. The higher value is likely due to the group excluding patients with unresectable adenocarcinoma of the pancreas, who were deemed physically unfit for major PD, were considered to have long-segment arterial encasement of the tumors, or received only bypass graft operations, from analysis. In order to develop a better representation of expectant survival following Whipple procedure involving vascular reconstruction, the combination of the total number of patients with 30-day survival and 1-year survival in each study were divided by the total number of patients in the study. The 30-day and 1-year survival rates were 92.4% (749/811) and 52.7% (674/1,280), respectively (*Table 4*). Therefore, vascular reconstruction during Whipple procedures has just over 90% of 30-day survival, and just over 50% of 1-year survival. The present study increases the body of evidence in the field of Whipple procedures involving vascular resection with secondary reconstruction, while also analyzing previous and recent evidence in order to generate a more accurate postoperative expectation that can be relayed to the patient preoperatively.

Conclusions

Compared to conventional Whipple procedures, those requiring additional major vascular reconstruction are associated with decreased survival and increased readmission. When vascular reconstruction is a valid option, patients should be well aware of the associated outcomes prior to making their decision regarding treatment.

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None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: This study was performed using data collected from a Mayo Clinic Institutional Review Board (IRB)-approved prospective database (IRB 09-00-3940). Informed consent was waived by the IRB as this study was deemed minimal risk to patients.

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