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Vascular resection in distal cholangiocarcinoma: Review of the literature

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ABSTRACT

Vascular resection including portal vein resection and/or hepatic artery resection has rarely been reported in distal cholangiocarcinoma. This review aimed to elucidate the safety and oncological outcomes of surgery with vascular resection in patients with distal cholangiocarcinoma. The following data were extracted from the identified studies: type of vascular resection, surgical outcome, pathological findings, recurrence-free survival (RFS), and overall survival (OS). Six studies were identified, and patients were classified into the vascular resection (VR) group and non-VR group according to the presence or absence of vascular resection in each study. The vascular resection ratios ranged from 6.8% to 20.0% in the surgical cases. The most frequent tumor location in the VR group was the extrapancreatic common bile duct and the most frequent sites of vascular resection were portal vein and right hepatic artery. The ratios of T3 or T4 tumor were significantly higher in the VR group. The ratios of severe complications and postoperative mortality were not significantly different between the VR and non-VR groups. The median RFS time and OS time in the VR group were shorter than 1 year and 2 years, respectively, in all studies. In conclusion, the patients with distal cholangiocarcinoma in the VR group tended to show early recurrence and shorter survival, although vascular resection could be performed safely.

Key words: *Distal cholangiocarcinoma*, *Vascular resection*, *Hepatic artery resection*, *Portal vein resection*

INTRODUCTION

Cholangiocarcinoma is an aggressive tumor, and most patients have advanced disease at presentation, and surgical resection is the only curative treatment option for this tumor[7]. However, the clinical significance of vascular resection (VR) with pancreaticoduodenectomy (PD) remains unclear in patients with distal cholangiocarcinoma, because only a few reports has investigated this issue so far. In hilar cholangiocarcinoma, several reports have described the safety and efficacy of VR concomitant with major hepatectomy[8]. Nagino et al.[8] reported that major hepatectomy and hepatic artery resection (HAR) in hilar cholangiocarcinoma was technically demanding; however, this surgery could be performed with acceptable mortality rate and offers a better chance of long-term survival in selected patients. Regarding pancreatic ductal adenocarcinoma (PDAC), PD is the standard surgery similar to distal cholangiocarcinoma, and the concept of borderline resectability has been used for the treatment of patients with vascular invasion[1]. This review aimed to elucidate the safety and oncological outcomes of surgery with VR in patients with distal cholangiocarcinoma.

MATERIALS AND METHODS

Eligibility criteria and literature search

Observational studies published in English were eligible for inclusion. Only full-text articles were included, whereas abstracts for workshops or conferences were excluded. A literature search was conducted using the following terms: “distal cholangiocarcinoma and portal vein resection”, “distal cholangiocarcinoma and hepatic artery resection” and “distal cholangiocarcinoma and vascular resection”. The MEDLINE database was searched. Studies in the reference lists of retrieved articles were also searched. Studies that only partially mentioned VR were excluded.

Data collection and assessment

The following data were extracted from the identified studies: type of vascular resection, surgical outcome, pathological findings, recurrence-free survival (RFS), overall survival (OS), and the correlation between radiological finding and vascular resection. The pathologic tumor stage was determined according to the tumor staging system based on the American Joint Committee on Cancer Staging Manual, 7th or 8th edition criteria. Vascular resection cases or histologic vascular invasion cases were classified into the VR group in each study, and

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other cases were classified into the non-VR group. The extracted data were compared between the two groups.

RESULTS

Literature review

Six eligible articles were identified from the electronic database search[2,4–6,9,10], and 99 patients in the VR group and 946 patients in the non-VR group were included in this review (Table 1).

Type of vascular resection

The type of vascular resection was portal vein resection (PVR) in 3 studies[4–6], HAR in 2 study[2,9], and both HAR and PVR in 1 study[10] (Table 1). The vascular resection ratios ranged from 6.8% to 20.0% in each study. The tumor location was described in two studies, and extrapancreatic common bile duct was the most frequent tumor location in the VR group. The location of PVR was described in 3 studies[4,6,10]. Portal vein (PV) was the most frequent site, and superior mesenteric vein (SMV) resection was rare. The location of HAR was described in three studies. Right hepatic artery (RHA) or replaced right hepatic artery (rRHA) were the most frequent sites for HAR.

Surgical outcome and pathological finding

Surgical outcome and pathological findings are summarized in Table 2. Operation time was investigated in five studies, and was significantly longer in the VR group in 3 studies. Blood loss and the ratio of blood transfusion were greater in the VR group than in the non-Vascular group in all studies. The length of hospital stay did not differ significantly between the two groups. The ratios of severe complication and postoperative mortality showed no significant differences between the two groups in all studies. The ratios of pathological vascular invasion in the VR group ranged from 30.0% to 100% in each study. R0 resection rate was lower in the VR group than in the non-VR group in all studies. The ratios of advanced T3 or T4 tumor and lymph node metastasis were higher in the VR group in all studies.

Recurrence-free survival and overall survival

The RFS and OS times are summarized in Table 3. The recurrence pattern was investigated in three studies, and Shizuoka Cancer Center Group reported that the local recurrence ratios were comparable between the two groups (VR group *vs.* non-VR group: 8.0% *vs.* 10.7%, $p > 0.999$), but distant recurrence tended to be observed more frequently in the VR group (64.0% *vs.* 41.5%, $p = 0.053$)[10]. Similarly, Hiroshima University Group reported that the local recurrence ratios showed no significant differences; however, the peritoneal disseminations were significantly more common in the VR group (37.5% *vs.* 1.9%, $p < 0.01$)[9]. The median RFS time was shorter than 1 year in the VR group in all investigated studies, and was significantly shorter in the VR group (Table 3). The median OS time was shorter than 2 years in the VR group in all investigated studies. Five-year OS rates ranged from 0% to 16.7% in the VR group and from 35% to 50.7% in the non-VR group.

Radiological vascular invasion and surgical vascular resection

The radiologic criteria for vascular invasion are described in three studies (Table 4). The criteria included radiological vascular narrowing[6], tumor contact over 180°[9,10], or contact under 180° with contour irregularity[10]. The Nagoya Surgical Oncology Group reported that 11 patients showed radiological vascular narrowing before surgery and all of them underwent PVR[6]. However, the remaining 20 (64.5%) patients with PVR did not show radiological vascular narrowing before the surgery. The Shizuoka Cancer Center Group reported that 19 (63.3%) of 30 patients with preoperative radiological tumor abutment > 180° underwent VR, and six (8.0%) of 75 patients with tumor abutment < 180° underwent VR[10].

DISCUSSION

VR has rarely been reported in distal cholangiocarcinoma and little is known about this procedure. Only six previous studies have reported this procedure[2,4–6,9,10]. However, the VR cases were not very rare and the ratios ranged from 6.8% to 20.0%. Regarding tumor location in the VR group, the extrahepatic CBD was the most frequent location, and tumors in the intrapancreatic CBD were less likely to require VR. Therefore, PV is the frequent site of VR, and cases of SMVR are rare. For HAR, the most frequent site was RHA or rRHA, followed by PHA. Anatomically, RHA and rRHA cross with the extrahepatic bile duct and they can be invaded by distal cholangiocarcinoma. Arterial reconstruction is necessary in PHA resection and it may be unnecessary in RHA or rRHA resection. Burasakarn et al.[2] reported that 10 patients who underwent PD and RHAR without arterial reconstruction had no postoperative liver abscesses. However, in Hiroshima University[9], one patient who underwent rRHA resection without reconstruction developed postoperative liver infarction. Therefore, further investigation is necessary to determine the indications for arterial reconstruction in RHA resection.

Concerning the safety of VR in distal cholangiocarcinoma, the ratios of severe complication and mortality were not significantly different between the VR and non-VR groups. In patients who underwent RHAR without reconstruction[2], these results might be natural, because the difficulty level of surgery might be equivalent for conventional PD without VR. However, patients who had undergone highly difficult PD with vascular reconstruction were included in other studies, and their complication and mortality ratios showed no significant differences between the VR and non-VR groups.

Furthermore, the local recurrence rates were similar between the two groups, which may indicate successful local tumor removal in the VR group. These surgical outcomes in the VR group were acceptable; however, the tumors in this group were significantly more advanced

Table 1 Type of vascular resection

No.	Year	Author	Patients (*n*)	VR (*n*, %)	Tumor location	PVR location (*n*)	HAR location (*n*)
1	2015	Miura[4]	Histologic PV invasion (8)	10 (7.8%)			
			non-invasion (121)				
2	2017	Maeta[5]	PVR (31)	31 (6.8%)	**Extra 58.0%, Intra 42.0%**	PV (25), PV-SMV (3), SMV (3)	
			non-PVR (422)		**Extra 30.3%, Intra 69.7%**		
3	2021	Burasakarn[6]	RHAR* (10)	10 (20.0%)			RHA (10)
			non-RHAR (40)				
4	2021	Lyu[7]	Histologic PV invasion (17)	21 (17.1%)		PV (6), PV-SMV (7), SMV (4)	
			non-invasion (106)				
5	2022	Yamamoto[8]	PVR and/or HAR (25)	25 (10.9%)		PV (9), PV-SMV (3), RPV-PV (1), LPV-PV (1), RAPV-PV (1)	RHA-RHA (8), RHA-GDA (3), RHA-PHA (1), RPHA-RHA (1)
			non-VR (205)				
6	2023	Sumiyoshi[9]	HAR (8)	8 (13.3%)	Extra 75.0%, Extra-Intra 25.0%, Intra 0%		RHA (2), rRHA (3), PHA (3)
			non-HAR (52)				

The gray parts indicate the vascular resection (VR) group and white parts indicate the non-VR in each study. PV, portal vein; PVR, portal vein resection; RHAR*, right hepatic artery resection without reconstruction; HAR, hepatic artery resection; Extra, extrapancreatic common bile duct; Intra, intrapancreatic common bile duct; Extra-Intra, extra- and intrapancreatic common bile duct; SMV, superior mesenteric vein; RPV, right portal vein; LPV, left portal vein; RAPV, right anterior portal vein; RHA, right hepatic artery; GDA, gastroduodenal artery; PHA, proper hepatic artery; RPHA, right posterior hepatic artery; rRHA, replaced right hepatic artery. **Bold numbers indicated statistical significances between the VR and non-VR groups ($p < 0.05$).**

Table 2 Surgical outcome and pathological finding

No.	Patients (*n*)	Operation time	Blood loss*	BT	Hospital Stay	Morbidity*	Mortality	Pathological invasion*	R0	T3 or 4	N1 or 2
1[4]	PV invasion (8)						25.0%	8 (100%)	75.0%	**100%**	**87.5%**
	non-invasion (121)						5.8%		81.0%	**59.5%**	**37.2%**
2[5]	PVR (31)	**510 min**	1330 mL	**48.4%**	37 days	61.0%	6.5%	21 (67.7%)	**67.7%**	**97.0%**	**81.0%**
	non-PVR (422)	**427 min**	1111 mL	**30.7%**	42 days	69.1%	3.3%		**88.2%**	**54.0%**	**39.8%**
3[6]	RHAR* (10)	317.5 min	1050 mL		31.5 days	40.0%	10.0%	3 (30.0%)	**30.0%**	60.0%	40.0%
	non-RHAR (40)	364 min	955 mL		31.5 days	32.5%	0%		**85.0%**	57.5%	37.5%
4[7]	PV invasion (17)	708 min		**58.8%**	21 days		5.9%	17 (100%)	94.1%	100%	
	non-invasion (106)	573 min		**31.1%**	21 days		4.7%		95.3%	85.8%	
5[8]	PVR and/or HAR (25)	**669 min**	**1501 mL**	24.0%		96.0%	0%	15 (60.0%)	#92.0%/88.0%	72.0%	52.0%
	non-VR (205)	**467 min**	**927 mL**	13.0%		70.0%	2.0%		#97.6%/93.2%	67.0%	41.0%
6[9]	HAR (8)	**460.5 min**	655.5 mL	25.0%		12.5%	0%	3 (37.5%)	62.5%	**87.5%**	75.0%
	non-HAR (52)	**339.5 min**	610 mL	19.2%		42.3%	1.92%		90.4%	**17.3%**	42.3%

Blood loss*, median amount of intraoperative blood loss; BT, blood transfusion; Morbidity*, postoperative severe complication with Clavien Dindo grade 3 to 5;
Pathological invasion*, pathological vascular invasion; PV, portal vein; PVR, portal vein resection; RHAR*, right hepatic artery resection without reconstruction; HAR, hepatic artery resection; #, ductal margin/radial margin. **Bold numbers indicated statistical significances between the VR and non-VR groups ($p < 0.05$).**

Table 3 Recurrence-free survival and overall survival

No.	Patients (*n*)	Recurrence pattern	RFS	1y RFS%	3y RFS%	5y RFS%	OS	1y OS%	3y OS%	5y OS%
1[4]	PV invasion (8)						**3m**	**17%**	**17%**	**0%**
	non-invasion (121)						**39m**	**82%**	**50%**	**39%**
2[5]	PVR (31)	NSD								**15%**
	non-PVR (422)	NSD								**42.4%**
3[6]	RHAR (10)		**11m**	**50.0%**	**30.0%**	**10.0%**	21m*	70%	30%	10%*
	non-RHAR (40)		**34m**	**77.5%**	**47.5%**	**35.0%**	40m*	87.5%	55%	35%*
4[7]	PV invasion (17)		**8m**	**31.3%**	**0%**		**12m**	**48.6%**	**0%**	
	non-invasion (106)		**27m**	**73.3%**	**40.5%**		**33m**	**79.7%**	**42.2%**	
5[8]	PVR and/or HAR (25)	Local 8.0%, Distant 64.0%#								**16.7%**
	non-VR (205)	Local 10.7%, Distant 41.5%#								**50.7%**
6[9]	HAR (8)	Local 12.5%, **Peritoneal 37.5%**	**7.4m**	**58.3%**						
	non-HAR (52)	Local 11.5%, **Peritoneal 1.9%**	**34.2m**	**88.4%**						

RFS, recurrence-free survival (median months); y, year; RFS%, recurrence-free survival rate; OS, overall survival (median months); OS%, overall survival rate; 6*, our institutional cases; PV, portal vein; PVR, portal vein resection; RHAR, right hepatic artery resection; HAR, hepatic artery resection; VR, vascular resection; NSD, not significant difference; #$p = 0.053$; Local, local recurrence; Distant, distant metastasis; Peritoneal, peritoneal dissemination; m, month; *$p = 0.051$. **Bold numbers indicated the statistical significances between the VR and non-VR groups ($p < 0.05$).**

Table 4 Radiological finding and vascular resection

No.	Patients (*n*)	Radiologic criteria for vascular invasion	Radiological finding (*n*)/Vascular resection in surgery [*n*]
2[5]	PVR (31)	Narrowing, stenosis, or obstruction	Radiologically unilateral narrowing (10)/Vascular resection [10] Radiologically bilateral narrowing (1)/Vascular resection [1]
4[7]	Histologic PV invasion (17)	Tumor contact of > 180° or contact of < 180° with contour irregularity	Radiologically invasion (21)/Vascular resection [21]
5[8]	PVR and/or HAR (25)	Tumor abutment angle > 180°	Radiologically abutment of ≥ 180° (30)/Vascular resection [19] Radiologically abutment of < 180° (75)/Vascular resection [6] Radiologically no abutment (125)/Vascular resection [0]

PVR, portal vein resection; PV, portal vein; HAR, hepatic artery resection; [], number of patients who actually underwent vascular resection.

than those in the non-VR group. The RFS and OS were significantly shorter in the VR group than in the non-VR group in almost all studies, and VR was deemed a poor prognostic factor in distal cholangiocarcinoma. One unsolved problem is that whether both cases with pathological vascular invasion and vascular resection without invasion equally show poor prognosis, because the ratios of pathological vascular invasion differed in each study. The ratios of pathological vascular invasion were low as 30.0% and 37.5% in two studies[2,9]; however, the median RFS times were shorter than 1 year in both studies. Further investigation focused on this issue is necessary.

The early recurrence and short survival in the VR group may suggest the concept of "borderline resectable distal cholangiocarcinoma". This concept of borderline resectable cancer has been widely accepted and is used clinically for PDAC. PDAC with remarkable invasion to surrounding vascular is regarded as borderline resectable cancer. Accumulating evidence indicates that the prognosis after upfront surgery is poor in borderline resectable PDAC, although the tumor is technically resectable by vascular resection[3]. Regarding distal cholangiocarcinoma, only one previous study reported that PV invasion should be regarded as borderline resectable[5]. To adapt the concept of borderline resectability to distal cholangiocarcinoma with vascular invasion, preoperative radiological assessment of vascular invasion is requisite.

Only three previous reports described the criteria for radiological vascular invasion in distal cholangiocarcinoma[4,6,10]. The Nagoya Surgical Oncology Group demonstrated that all patients with radiological vascular narrowing underwent VR, which was highly indicative of VR[6]. However, 64.5% of the VR cases did not show radiological vascular narrowing before surgery. The other criterion for radiological vascular invasion was tumor contact > 180°[4,10]. This criterion has originally been used in borderline resectable PDAC. It remains unclear whether the criterion of borderline resectability in PDAC can be adapted to distal cholangiocarcinoma.

This study had a crucial limitation. The number of included studies was small, and many unsolved problems remains unclear. Further investigation including a large-scale multicenter study is necessary to elucidate the real clinicopathological features of VR in distal cholangiocarcinoma.

In conclusion, patients with distal cholangiocarcinoma in the VR group tended to show early recurrences and shorter survival, although VR could be performed safely.

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