 doi:10.20944/preprints202108.0378.v1

*Article*

# Vascular Resection in Perihilar Cholangiocarcinoma

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**Abstract:** Perihilar cholangiocarcinoma (phCC) is the most common type of cholangiocarcinoma, accounting for approximately 60 % of cases, followed by the distal and then the intrahepatic forms. There is not a staging system that allows comparation of all series and extract some conclusions to increase the long-survival rate in this dismal disease. The extension of the resection, which theoretically dependes on the type of phCC, is not closed subject. As surgery is the only known way to achieve a cure, many aggressive approachs have been adopted. Despite extended liver resections and even vascular resections, margins are positive in around one third of patients. In the past two decades, with advances in diagnostic and surgical techniques, the surgical outcomes and survival rates have gradually improved, although variability is the rule, with morbidity and mortality rates ranging from 14% to 76% and from 0% to 19%, respectively. Extended hepatectomies and portal vein resection even right hepatic artery reconstruction for the left side tumors are frequently needed. Salvage procedures when arterial reconstruction is not feasible, as well as hepatopancreatoduodenectomy, are still under evaluation too. In this article, we discuss the aggressive surgical approach to phCC focused on vascular resection. Disparate results on the surgical treatment of phCC made it impossible to reach clear-cut conclusions.

**Simple Summary:** Advance perihilar cholangiocarcinoma usually involves portal and hepatic arteries and, therefore most of them are unresectables but in the recent decades, not without controversy, several groups have published aggressive procedures with moderately good results in comparation to not surgical therapies. There are very important different among series and between Eastes and Westerns coutries too. In this article, we discuss the aggressive surgical approach to phCC focused on vascular resection. Disparate results on the surgical treatment of phCC made it impossible to reach clear-cut conclusions

**Keywords**: perihilar cholangicarcinoma; advance perihilar cholangiocarcinoma, perihilar cholangiocarcinoma vascular involvement; biliary cancer.

## 1. Introduction

Altemeier in 1957 and Gerald Klatskin in 1965 were the first surgeons who described cholangiocarcinoma [1,2]. Between 50% and 70% of all colangiocarcinomas are perihilars (phCC) or Klatskin tumors [3,4,5,6]. PhCC is a highly unresectable malignancy because, despite being a slow growing tumor, its proximity to hepatic hilar structures leads to early vascular involvement, complicating surgical resection. Thus, most patients are diagnosed in an advanced stage of the disease which includes major vascular involvement. Surgical resection is the standard therapy for phCC and provides the only chance for cure in this disease. An aggressive surgical approach increases the number of resectable tumors that

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are initially regarded as unresectable [7], with 5-years survival rates (5-y SR) of 25-45% in R0 resections and of 0-23 % in R1 resections [3,4,8,9]. Vascular resections (VR) of the portal vein (PV) or the hepatic artery (HA) or both add postoperative morbidity and mortality, although they achieve a higher R0 resection rate (i.e., microscopically negative margin), which is the most important factor to get increasing overall survival [3,9].

The aims of surgery in phCC are (1) to achieve the macroscopic removal of the tumor (VR increases the number of resected patients), (2) to restore satisfactorily the bile flow to the gut; and (3) minimize the postoperative liver failure or death. There are several surgical techniques to perform in these cases, since the extension of the resection depend on the radial extension of the tumor (leading to VR of PV and/or HA), the longitudinal extension (forcing to do a hepatopancreatoduodenectomy) or both (VR and hepatopancreatoduodenectomy) [3].

Advanced phCC requires extended liver resection and often VR, although margins may be affected in about one third of the patients [7]. Right-sided tumors are likely to need extended right hepatectomy and PV resection, best served by an *en-bloc* hilar resection or Rex-recess approach. Left-sided tumors often involve contralateral blood vessels and require extended left hepatectomy with possible right PV or right HA reconstruction. Right HA involvement is more frequent due to its proximity to the biliary bifurcation. Arterial infiltration of the contralateral side of the planned hepatic resection is a contraindication of surgical treatment, though not in all centers. (Figure 1). Histological portal involvement is present in 20%-30% of patients with R0 resections and its preoperative identification is achieved with a precision of 85%.[10-16]

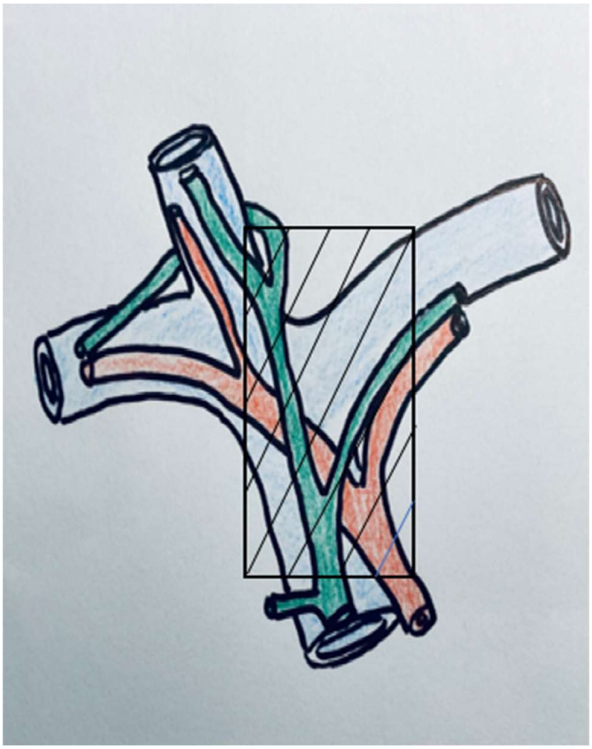

**Figure 1.** Hilar anatomy (Klatskin tumor area).

The conventional surgical technique for the treatment of phCC is right or left hepatectomy, plus segment 1 resection, plus biliary duct resection, plus hilar lymphadenectomy. To this technique, a PV resection alone, a HA resection alone, both (HA resection may be followed or not by a HA reconstruction or a PV arterialization), or a pancreatoduodenectomy can be added. Liver transplantation is a also a possible treatment considered as a drastic vascular resection (Fig 2).[3, 18, 19]

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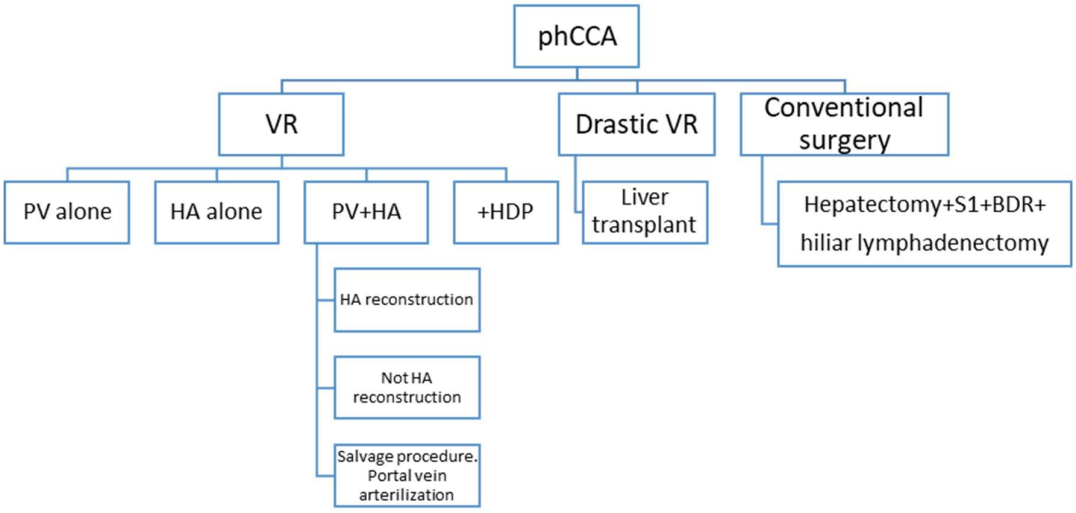


**Figure 2.** Vascular resections options. HPD: hepatopancreatectoduodenectomy; BDR: biliary duct resection.

If we could not achieve a consensus on the surgical treatment of colorectal liver metastases, in the case of the treatment of pHCC the final photo is even more complex [20]. Controversies arise in PV resection "on demand" or "elective", in HA resection in the remnant liver, in left or right extended hepatectomy in Bismuth type IV, and in liver transplant. The difficulties to analyze the available data and draw clear conclusions on the efficacy of these treatments are due to the use of different classifications, both surgical (Bismuth and Corlette, 1975) and oncological (extension of tumor within the biliary tree, vascular invasion, lobar atrophy, and metastatic disease); the heterogeneity of data and series, since many large series are limited to very specific areas; the number of different preoperative, postoperative, and histological staging classifications; the large differences in the range of results; the differences in the neoadjuvant chemotherapies and radiotherapies protocols used in the last decades, and the significant differences between Western and Eastern countries (even within the same country) in the management of the vascular involvement.

Several limitations should be considered when interpreting data, according to Liang's study. Although we only selected high-quality studies, all of them were predominantly retrospective in nature and, as such, there may be inherent selection bias. Also, the heterogeneity in the selection of patients may have led to selection bias. Finally, some prognostic factors were with significant heterogeneity [21].

There are notable differences between Western and Eastern countries in the use of PV embolization, PV resection, HA resection and even in the future remnant liver volumne (FRL). All of them, except FRL, are more frequently performed in Eastern countries, with reported morbidities and mortalities lower than in Western ones [22]. Even in the same zone there are several differences too. Fig. 3 shows wide differences between two European hospitals.

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 18 August 2021 doi:10.20944/preprints202108.0378.v1



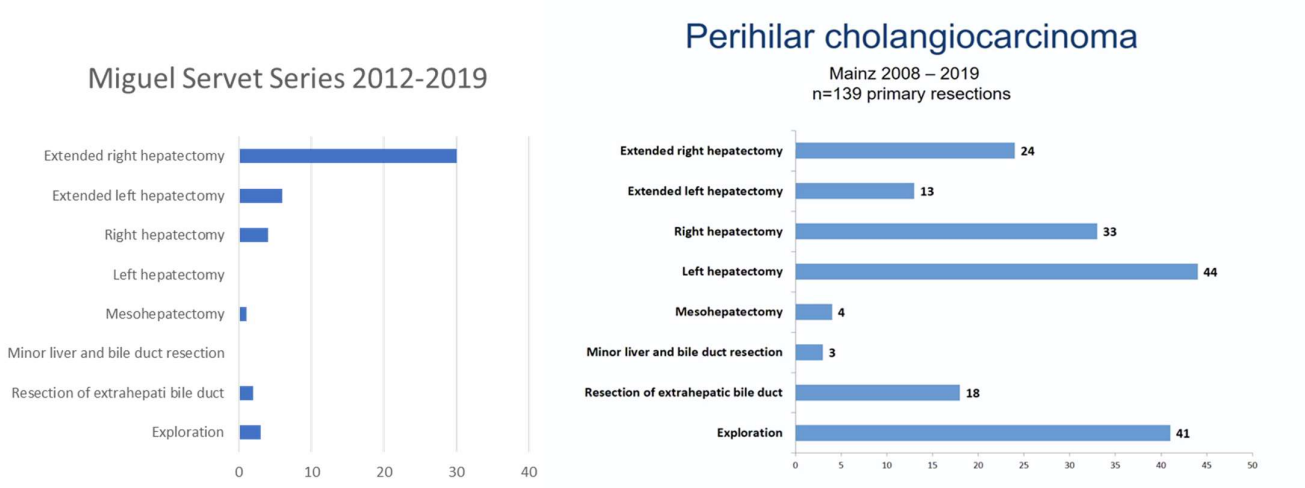


**Figure 3.** Miguel Servet/Mainz Series.

**Table 1.** Vascular resection in phCC.

| STUDY | Year | PATIENTS n | Vascular resection, n | Morbidity % | Mortality % | 5 y SV | R0 % | R1 % | R0 with VR% |
|---|---|---|---|---|---|---|---|---|---|
| Lygidakis et al | 1988 | 13 | 7 | NA | 15 | NA | NA | NA | 46 |
| Edmond et al | 1989 | 13 | 5 | 69 | 15 | NA | NA | NA | 46 |
| Klempnauer et al. | 1997 | 125 | 41 | 29,8 | 9,9 | 28 | 26 | 6,8 | 73 |
| Magriaga et al. | 1998 | 28 | 9 | 32 | 14 | 8 | 11 | 0 | 50 |
| Neuhaus et al | 1999 | 66 | 23 | 56 | 3 | 22 | 42 | 9 | 61 |
| Lee *et al* | 2000 | 111 | 29 | 22 | 6,3 | 24 | NA | NA | 77 |
| Nimura et al | 2000 | 142 | 43 | 48,6 | 9 | 25 | 26 | 16 | 61 |
| Nagino et al | 2001 | 105 | 33 | 81 | 9,5 | NA | NA | NA | NA |
| Muñoz *et al* | 2002 | 28 | 10 | 25 | 3 | 23 | NA | NA | NA |
| Neuhaus et al | 2003 | 133 | NA | NA | NA | NA | 38 | 18 | NA |
| Ebata et al | 2003 | 160 | 52 | 84 | 9,6 | 37 | NA | NA | NA |
| Shimada et al | 2003 | 39 | 15 | 71 | 6,7 | 56 | 50 | 10 | 50 |
| Kondo et al | 2004 | 42 | 14 | 48 | 0 | NA | NA | NA | 95 |
| Hemming et al | 2005 | 53 | 23 | 40 | 9 | 35 | 45 | 0 | 80 |
| Baton et al | 2007 | 59 | 5 | 42 | 5 | 20 | 28 | 6 | 67 |
| Miyazaki *et al* | 2007 | 161 | 43 | 39 | 7 | NA | 36 | 0 | 36 |
| Hidalgo et al. | 2008 | 44 | 17 | 66 | 6,8 | 41 | 45 | 26 | 45 |
| Song *et al* | 2009 | 259 | 51 | 54 | 9,6 | 29,3 | 29,3 | 17 | 71,8 |
| Igami *et al* | 2010 | 298 | 111 | 43 | 2 | 42 | 52 | 32 | 66 |
| Young et al | 2010 | 51 | 21 | 75 | 8 | 20 | 40 | 2 | 57 |
| Miyazaki et al | 2010 | 107 | 25 | NA | 2 | NA | 33 | 21 | 59 |
| Nagino et al | 2010 | 261 | 50 | 54 | 2 | 30 | 40,7 | 0 | 54 |
| Hemming et al | 2011 | 95 | 42 | 36 | 5 | 43 | 50 | 0 | 84 |
| **ALL** | **24 years** | **2393** | **30.4** | **50.8** | **7.2** | **30.2** | **37** | **10.2** | **62** |

The 90-day postoperative mortality is up to 10% in experienced centers in Europe, with most of the patients (around 48%) dying from post-hepatectomy liver failure [41,42]. In the largest center in Asia, the overall mortality was 4.7% for the period 1977–2010, decreasing sharply from 11.1% to 1.4% for the periods 1977–1990 and 2006–2010, respectively, even after including patients with more locally advanced disease during the last period [7]. The presence of Bismuth type IV phCC (involving both the right and left intrahepatic ducts) is no longer an absolute contraindication for complete resection since it is associated with an overall survival (OS) similar to that of patients with less extensive biliary extension [43]. Moreover, resection and reconstruction of the PV and HA are increasingly performed [9,10].

In an Australian study there were a higher mortality and morbidity in the VR patients' group and these two rates increased when HA resection was performed [10]. The overall series had a 50.8% morbidity and a 7.2% mortality, but VR was done only in 29.6%

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of the cases. The authors concluded that PV invasion did not preclude the curative resection and that it should be performed in case of PV involvement.

**2. Portal Vein Resection**

True PV invasion in phCC is difficult to determine preoperatively. On computed tomography, loss of a clear plane, constriction of the vessel and occlusion are regarded as evidence of venous invasion.

Left PV resection is not a technically complex procedure. Usually, end-to-end anastomosis is possible with or without graft interposition, autologous or not. The graft is necessary when the length of resection is more than 5cm but, since the left PV has a long extrahepatic path and there is an easy access to the vein into the umbilical fissure, it is almost always possible to avoid the grafting [44,45]. Generally, there is not much difference in diameter between both ends and it is possible to perform a standard anastomosis.

The right PV is short and bifurcates early in its course. The limits of the right PV resection depend on whether the first branches can be controlled with clamps. A Y graft may be necessary. There are discrepancies in the diameters of the main PV and the right branches (specially between the right posterior sector branch and the main PV) [44,46]. The Rex recess approach includes a right hepatectomy with *en-bloc* resection of the hepatoduodenal ligament and PV reconstruction to the left portal vein at the Rex recess [44,45].

In general, PV bifurcation should be resected only when tumor adherence or infiltration has been detected or when it seems invaded. The Nehaus' team practice of PV resection *a priori* has not been yet validated. Higuchi et al in 2019 found that the absence of neoplastic invasion of the vein in histological analysis was a good prognostic factor compared with the presence of high dysplasia or *in situ* tumor [47]. van Vugt et al in 2018 concluded that both unilateral and main HA involvement are independent poor prognostic factors for overall survival, whereas PV involvement is not [47]. Actual rates of venous invasion on histopathological examination after resection vary from 21% to 80% according to Abbas's metaanalysis [10].

The point of controversy regarding portal vein resection is whether it is performed systematically or on demand, based on the radiological and intraoperative findings [49]. Nehaus in 2012 compared two groups of 50 patients each, one with *en-bloc* resection of the PV and other with only major hepatectomy. The first group had better survival rate than the second group. Although an evaluation of short-term results failed to reveal any association between combined PV resection and a high postoperative complication rate, a correlation between PV resection and a higher mortality was identified [49]. The mean mortality rate of combined PV resection is lower in the studies with larger sample sizes, and it was also lower in studies published after 2008. Liver failure was and is the main cause of postoperative mortality, although the management of jaundice with percutaneous drainage and improvements in anesthesia management have decreased the mortality in the last decade.

Ebata et al. found that macroscopic portal vein invasion was a poor prognostic factor [13]. In the Netherland group, Rassam et al in 2018 showed that 20% of their cases had PV resection, with a 44.3% 5-y SR, alike the 43% in the Berlin group of R0 resections using unconditional *en-bloc* resection [51].

We can conclude that, currently, PV resection on demand has the same survival rate that resection *en-bloc*, so that the decision whether to resect or not the PV should be made in the operating theatre. PV resection increases the survival rates but at the cost of significant high rates of morbidity and mortality. De Jong et al analyzed 305 patients, with PV resection performed in 16.7% of them. Thirty and 90-day mortality was more that 4-fold higher in this group, compared with the non-vascular resected group [9].

**3. Hepatic Artery Resection**

The right hepatic artery, vital for preservation of the liver remnant after left-sided resection, is intimately related to the posterior surface of the biliary confluence and is often

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involved by tumour. Complete tumour clearance may require *en-bloc* resection and reconstruction of an involved artery, a procedure traditionally associated with high morbidity and mortality [10]. This does not apply to right-sided resections because the left hepatic artery lies well away from the biliary confluence, enters the umbilical fissure at the extreme left of the hilum, and is rarely involved by tumour. The rate of positive involvement in the resected hepatic artery is lower than in the resected portal vein (PV 47.1% and HA 40%) [46].

Arterial resection and reconstruction are usually performed in a left-side resection (IIIb) for anatomical reasons. Most reports show dismal results: Gerhads et al reported a 55.6% mortality; Ota et al stated a 46.9% mortality, but their series was about HPD; Yamanaka et al informed a 10% mortality but a 90% morbidity; Shimada et al reckoned a mortality with HA resection and reconstruction of 13.3% vs 8.3% without it; Sakamoto et al report 0% mortality, and Miyazaki at al stated a 33% mortality and a 0% 3-y SR in patients with HA resection [31,35,52-55].

The inflection point of the current improvement in surgical techniques lies in the knowledge derived from the living donor liver transplant techniques, since they have been key to improve these data. After 2010, outcomes began to be better than before (Table 2).

**Table 2.** Arterial Resection in phCC.

| Author | Year | Cases | Hepatic Left Trisectionectomy | Hepatic Right Trisectionectomy | Simultaneous PVR | Morbidity (%) | Mortality (%) | 5y-SV |
|---|---|---|---|---|---|---|---|---|
| Nagino M et al 15 | 2010 | 50 | 26(52%) | 0 | 50 (100%) | 54 | 2 | 30 |
| Wang ST et al 56 | 2015 | 24 | 0 | 0 | 18 (75%) | 42 | 4 | 25 |
| Matsuyama R et al 57 | 2016 | 44 | 22 (50%) | 0 | 24 (55%) | 66 | 9 | 22 |
| Noji T el at 58 | 2016 | 28 | 7 (25%) | 0 | 23 (82%) | 57 | 4 | 26 |
| Peng C et al 59 | 2016 | 26 | 0 | 0 | 2 (8%) | 19 | 8 | 31 |
| Hu HJ et al 60 | 2018 | 63 | 12 (19%) | 3 (1%) | 35 (56%) | 19 | 3 | 22 |
| Schimizzi GV et al 61 | 2018 | 12 | 0 | 1 (8%) | 2 (17%) | 67 | 8 | - |
| Higuchi R et al 47 | 2018 | 19 | 1 (5%) | 0 | 12 (63%) | 47 | 16 | 16 |
| Kotenko O et al 62 | 2019 | 13 | NA | NA | 13 (100%) | NA | 9.3 | 18.8 |
| Mizuno T et al 63 | 2020 | 146 | 86 (59%) | 1 (1%) | 100 (68%) | 51 | 4 | 27 |
| ALL | | 425 | 154 (37.4%) | 5 (1.2%) | 277 (65.1%) | 0.47 | 7.5% | 27.2% |

In the series from 2010 to 2020, with 425 patients, 37.4% had an extended left hepatectomy, 1.2% an extended right hepatectomy and 65.1 % a combined PV resection. Morbidity was 47%, mortality was 7.5% and the 5-y SR was 27.2%. All these good data come from the higher quality Asian groups.

Nagino et al did not find statistically significant differences associating VR or pancreatoduodenectomy. But despite these aggressive procedures, the circumferential margin was positive in 34% of the patients and 50% of them had nodal involvement, although they got a 1, 3 and 5-y SR of 78.9, 36.3 and 30.3%, respectively [63,64]. They defended the HA resections when they analyzed the unresected patients in comparation with arterial and/or portal vein resected.

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Some surgical refinements have been proposed. De Santibañes et and Iida et al groups gave the surgeon the possibility of creating a satisfactory anastomosis before the resection began and the possibility of abandoning the procedure if it was not feasible [65,66]. As Bismuth type IIIB often requires a major left hepatic resection and the invasion of the right HA usually contraindicates the procedure, they proposed to perform an HA reconstruction between the posterior branch of the right HA and the left HA as the first surgical step, before the transection of the parenchyma and the hilar resection. Uchiyama et al, in an excellent technical article, tried to standardize the PV resection and HA resection in extended left hepatectomy although perhaps this complex surgery should be centralized in specific groups [67].

We can decide not to perform a right HA reconstruction. This is possible when the right HA or one of the right hepatic arteries come from the superior mesentery artery or when, in patients undergoing left-sided resections involving RHA, the liver is minimally mobilized to preserve the collaterals. Some surgeons prefer to embolize the proper HA, or the left or right HA, to stimulate the growth of collateral arteries, but this procedure carries a great risk of ischemia [68,69].

van Vugt et al concluded that the HA involvement (one or both) was a poor prognostic factor but that the PV involvement was not [48]. Govil et al concluded that the ability to perform a safe arterial resection increases the ability to perform potentially curative laparoscopic liver resections for phCC [70]. This in turn increases the resectability rate for pHCC, particularly for Bismuth-Corlette Type IV tumors.

When both the PV and HA are involved, resection and reconstruction of both can be performed. When both are resected, the PV anastomosis is performed first [63].

**4. Vascular Resection and Hepatopancreatoduodenectomy**

We can find deep different results between Eastern and Western countries regarding survival rate. Nagino et al in 2021 showed a 5-y SR of 37% but Souza et al in 2021 reported a lower SR and a 17% 90-days mortality [64,71,72].

In Nagino's series, patients were an mean of 60 years old. Most of combined VR and HPD were performed with extended left hepatectomy [64]. PV reconstruction was performed with external iliac venous graft and HA reconstruction with end-to-end anastomosis except in two cases (one with portal vein arterialization and one using the radial artery). Despite this huge surgical *tour de force*, R1 resection was presented in 45% of the cases, although the 5-y SR was 37%. In Ebata study in 2014, hepaticopancreatoduodenectomy combined with VR was a poor prognostic factor, together with the histological status [18].

Due to the complexity of the surgery and its high morbidity and mortality, in addition to the dispersion of the data and the concentration of the series in a few centers, no conclusion can be drawn.

**5. Portal Vein Arterialization (PVA)**

PV arterialization has been used as a salvage procedure when the arterial reconstruction fails during surgery, with around a 60% of success. In the series from the Paul Brousse Hospital there were 4 intrahospital deaths and 10 deaths between 2 and 30 months of follow-up out of 16 patients. Complications related with this procedure are hyperbilirubinemia and hemorrhage due to portal hypertension. Sometimes we have needed to embolize urgently this shunt for uncontrolled hemorrhage [73]. We performed this procedure during extended left hepatectomy with curative intention except in one patients (25%) in whom the shunt was performed during the postoperative course as an emergency surgery, with a mortality of 50%. Table 3.

Making conclusions in this setting are very difficult because PV arterialization is usually an unplanned approach, even a rescue procedure and, although it is a technique that hepato-pancreato-biliary surgeons must know, its results are difficult to predict.

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**Table 3.** Portal vein arterialization.

| Hospital | Age/sex | Hepatobiliary Surgery | | Portal vein arterialization | | | |
|---|---|---|---|---|---|---|---|
| | | Indication for surgery | Primary procedure | Indication for PVA and timin | Timing | Type | Interposed vein/prosthesic |
| Paul Brousse | 61/M | Hilar cholangiocarcinoma (Klatskin type IIIB) | Left extended hepatectomy (including segments I, V, VIII) | For curative resection (RHA involvement) | During LR | CHA to PV | No |
| Miguel Servet | 56/M | Hilar cholangiocarcinoma (Klatskin type IIIB) | Left extended hepatectomy (including segments I, V, VIII) | For HA thrombosis (LHA to RPHA). Savage procedure | 20th POD | PHA to PV | No |
| Miguel Servet | 71/F | Hilar cholangiocarcinoma (Klatskin type IIIB) | Left extended hepatectomy (including segments I, V) | For curative resection (RHA involvement) | During LR | PHA to PV | No |
| Miguel Servet | 68/F | Hilar cholangiocarcinoma (Klatskin type IIIB) | Left extended hepatectomy (including segment I) | For curative resection (RHA involvement) | During LR | PHA to PV | No |
| Miguel Servet | 74/F | Hilar cholangiocarcinoma (Klatskin type IIIB) | Left extended hepatectomy (including segments I, V, VIII) | For postoperative complication with pseudoaneurima 21 POD. Rescue after hepatic art reconstruction | 21st POD | CHA to PV | No |
| Shiuzoka General | 64/M | Hilar cholangiocarcinoma (Klatskin type IIIB) | Extended left LR + PD with RHA excision/ reconstruction | Post op HAT in reconstructed artery | 1 POD | Mesenteric vascular branches (ileal) | No |
| Shiuzoka General | 72/F | Hilar cholangiocarcinoma (Klatskin type IIIa) | Extended right LR | Postoperative ligation of CHA following HAP rupture (day 6) causing massive liver necrosis | 7th POD | First PVA –mesenteri c vascular branches (ileocecal) | No |
| Shiuzoka General | 65/M | Hilar cholangiocarcinoma (Klatskin type IIIB) | PD, extended left LR, excision of anterior branch RHA | For curative surgery (pre-emptive shunt) | 5 days before major resection | Mesenteric vascular branches (ileal) | No |
| Tsuruga National Hospita | NA | Hilar cholangiocarcinoma | Left extended LR with HAP excision | For curative surgery | During LR | GDA to PV | No |
| Hokkaido University | 56-81 | Hilar cholangiocarcinoma (6) | Major liver resection with en bloc HA resection | For curative surgery | During LR | GDA or CHA to PV | No |
| St James's University | 54/M | Hilar cholangiocarcinoma | LR | For curative surgery | During LR | GDA to PV | No |
| St James's University | 51/F | Hilar cholangiocarcinoma | LR | For curative surgery | During LR | RHA to PV | No |
| General Hospital of Chinese People's Liberation Army | 50-54 | Hilar cholangiocarcinoma (3) | LR | For curative surgery | During LR | HA to PV (wirth calibration) | No |
| West China Hospital | 55/M | Hilar cholangiocarcinoma | LR | For curative surgery | During LR | GDA to PV | No |

### 6. Liver Transplantation (LT)

Liver transplantation is the most radical procedure in terms of vascular resections. Under strict conditions LT can be offered in unresectable phCC in patients with (1) a malignant appearing stricture and, at least, one of the following: malignant cytology or histology, CA-19.9 > 130 U/mL without cholangitis, polysomy on fluorescence in situ hybridization, a mass on cross-sectional imaging ≤3 cm and no extrahepatic disease, (2) a cancer located primarily above the cystic duct, and (3) an unresectable cancer de novo phCCA or cancer arising in the setting of a primary sclerosing cholangitis [74].

Loveday B, et al reported one and two year post transplant overall survival of 83.3% and 55.6%, respectively, in intent-to-treat patients [75]. In the European Liver Transplant Register experience, Mantel HT et al reported a 59% 5 years-SR in patients within the

Mayo Clinic criteria and only a 21% in those beyond it. Therefore, the authors advocated that the selection criteria should be within the Milan protocol [76].

In 2018, Ethun CG, argued that the premise that patients with resectable phCC may derive superior survival from hepatic resection as opposed to liver transplant has been challenged . Conducting a prospective observational study, these investigators sought to validate outcomes following chemoradiotherapy and orthotopic LT for technically 'unresectable disease' as outlined by the Mayo Clinic, and compare them with outcomes following hepatectomy for 'resectable' phCCA [77]. Despite having disease which prohibited upfront resection, the transplantation group fared much better, with 5-y SR of 64% compared to 18% in the group that was resected ($p < 0.001$) [77].

In the Transplant Oncology Consensus Conference 2020, the agreed conclusions were that LT for phCC is an acceptable indication, that patients should undergo neoadjuvant chemoradiation prior to LT, that the inclusion criteria for LT should be based on the Mayo Clinic criteria, and that, due to organ allocation issues, living donor liver transplant, if possible, is the preferred option.

## 7. Conclusions

We can conclude (1) that advanced pHCC needs an extended hepatic resection and frequently a vascular resection too, (2) that extended right hepatectomy in right-side tumors is likely to need PV resection with an end-to-end anastomosis or a Rex recess approach, (3) that PV resection increases morbidity and mortality but achieves R0 resection more frequently and should be performed "on demand", (4) that extended left hepatectomy in left-side tumors is likely to need PV resection as well as HA resection to get an R0 resection, (5) that arterial reconstruction causes more morbidity and mortality and its oncological benefits are unclear, (6) that HPD with VR should be performed in high level centers and in very selected patients, (7) that PV arterialization is a salvage procedure with uncertain outcomes, and (8) that liver transplant could be key to rescue more patients with vascular involvement within Mayo-Clinic/Toronto Protocol.

**Author Contributions:** Conceptualization, Serrablo A.; methodology, Serrablo A; software, Serrablo A, Serrablo L.; validation, Serrablo A, Serrablo L, Alikhanov R, Tejedor L.; formal analysis, Serrablo A, Serrablo L; writing—original draft preparation, Serrablo A, Serrablo L.; writing—review and editing, Alikhanov R, Tejedor L. All authors have read and agreed to the published version of the manuscript."

**Funding:** No economic support.

**Conflicts of Interest:** "The authors declare no conflict of interest.".

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