

# Positive circumferential resection margin and outcome in patients with hilar cholangiocarcinoma

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# Background

- Hilar cholangiocarcinoma is a malignant tumor with poor prognosis.
- Surgical resection is the gold standard of treatment with 5-year survival rates of 20-45%.<sup>1-3</sup>
- Tumor differentiation, positive resection margin and node status have been identified as negative prognosticators in patients who undergo surgical resection.<sup>1</sup>
- In addition to the surgical resection margin, the ductal circumferential resection margin is assessed upon histopathological investigation of the resected specimen.
- At present, the influence of a positive circumferential margin on clinical outcome is unclear.

1. Matsuo et al. The Blumgart preoperative staging system for hilar cholangiocarcinoma: analysis of resectability and outcomes in 380 patients. *J Am Coll Surg* 2012;215(3):343-355.
2. van Gulik et al. Multidisciplinary management of hilar cholangiocarcinoma (Klatskin tumor): extended resection is associated with improved survival. *Eur J Surg Oncol* 2011;37(1):65-71.
3. Nagino et al. Evolution of surgical treatment of perihilar cholangiocarcinoma: a single-center 34-year review of 574 consecutive resections. *Ann Surg* 2013;258(1):129-140.

# Patients and Methods

- Ninety-eight (59 male/39 female) patients with resected de novo hilar cholangiocarcinoma enrolled
- Two European hepatobiliary centres (Medical University of Vienna and Aintree University Hospital, 2006-2016)
- Classification according to resection margin status (all negative, surgically positive, circumferentially positive) and investigation with respect to overall survival (OS).
- **Margin definitions:**
  - Surgical margin: transection sites at the bile duct (proximally and distally) and the liver parenchyma
  - Circumferential margin: interface of the extrahepatic bile duct and the surrounding lymphatic/fatty tissue of the hepatoduodenal ligament
- **Group definitions:**
  1. “Negative margin group”: negative surgical (duct and liver parenchyma) and circumferential margins
  2. “Surgically positive margin group”: positive surgical margin (+/- positive circumferential margin)
  3. “Circumferentially positive margin group”: positive circumferential but negative surgical margin

# Results

Median follow-up: 21.3 months (range 0.3-92.4)

Variable	Negative n=43	Surgically positive n=23	Circumferential ly positive n=32	P value
Age, years	61.5 (11.0)	63.4 (10.4)	63.9 (10.0)	0.58
Sex ratio (M:F)	25:18	14:9	20:12	0.93
Tumour grade G1 G2 G3	8 24 11	3 12 8	4 21 7	0.75
Tumor classification T1 T2 T3 T4	8 25 8 2	4 11 7 1	0 21 9 2	0.25
Node classification N0 N1 Missing	28 15 0	13 10 0	17 14 1	0.63
Lymphovascular invasion Present Absent Missing	21 21 1	10 13 0	17 14 1	0.71
Perineural invasion Present Absent Missing	8 31 4	4 19 0	3 27 2	0.50
Portal vein resection Yes No	8 35	8 15	11 21	0.54

Table 1. Patient and tumor characteristics

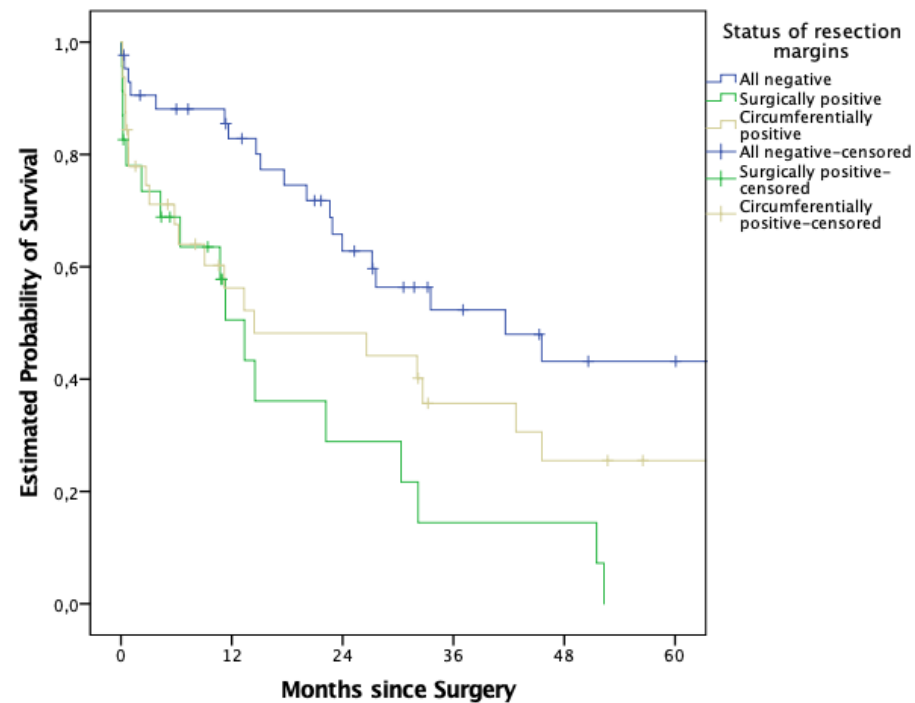


Figure 1. Resection margin status and OS (log rank,  $P=0.003$ ;  
**Median OS:** All negative 41.6 months, Circumferentially positive 14.4 months, Surgically positive 13.4 months;  
**5-year OS:** All negative 43%, Circumferentially positive 26%, Surgically positive 0%)

# Results and Conclusions

Variable	Univariable		Multivariable	
	HR (95% CI)	P value	HR (95% CI)	P value
Age >70 years ≤70 years	0.94 (0.49, 1.81) 1 (Reference)	0.86		
Sex Female Male	1.01 (0.60, 1.70) 1 (Reference)	0.96		
Tumour grade G3 G1, G2	1.33 (0.75, 2.36) 1 (Reference)	0.33		
Tumor classification T3, T4 T1, T2	1.80 (1.07, 3.04) 1 (Reference)	0.027	n.a.	0.15
Node classification N1 N0	2.66 (1.55, 4.54) 1 (Reference)	<0.001	2.97 (1.66, 5.31) 1 (Reference)	<0.001
R status R1 R0	1.90 (1.12, 3.21) 1 (Reference)	0.017	n.a.	0.41
Lymphatic vessel invasion Present Absent	1.45 (0.86, 2.45) 1 (Reference)	0.16		
Perineural invasion Present Absent	2.89 (1.14, 7.34) 1 (Reference)	0.026	n.a.	0.07
Portal vein resection Yes No	1.45 (0.83, 2.54) 1 (Reference)	0.19		
Status of resection margins Surgically positive Circumferentially positive Negative	2.97 (1.55, 5.68) 1.71 (0.94, 3.10) 1 (Reference)	0.004	3.43 (1.74, 6.78) 1.42 (0.74, 2.72) 1 (Reference)	0.002

Table 2. Univariable and multivariable Cox regression of factors associated with OS (not applicable, n.a.)

- Our data show that a positive circumferential resection margin is associated with better clinical outcome than a positive surgical margin.
- This margin status should therefore be routinely assessed upon histopathological investigation of the resected specimen and may therefore serve as a new prognostic biomarker.