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Original Research

Extended resection of intrahepatic cholangiocarcinoma: A retrospective single-center cohort study

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ABSTRACT

Background: For complete removal of intrahepatic cholangiocarcinoma (ICC), extended resection is often necessary. Information on the influence of visceral or vascular extension, extended resection, or postoperative morbidity on survival is scarce. The aim of this study was to show the impact of an aggressive surgical attitude on morbidity, mortality, and long-term outcome.

Materials and methods: All explorations at a high volume tertiary center between January 2008 and June 2018 with histological proof of ICC were included in this retrospective cohort study. The primary outcome was the extent of resection, secondary outcomes were postoperative morbidity, and their influence on overall survival (OS) and recurrence-free survival (RFS).

Results: Out of 210 patients, 150 underwent curative intended resection. A total of 87 extended, 26 major, and 37 minor resections were performed.In-hospital morbidity occurred in 46% of patients, with a 90-daymortality of 8%. Severity and frequency of morbidity did not differ significantly in the extended, major, or minor resection groups. If minor or major resections with visceral and/or vascular extensions were included in the extended resection group, minor ($p = 0.005$) and major ($p = 0.042$) resection had significantly better OSthan the extended resection group. All groups had significantly better OS than the exploration group. Comparing the different extended resection groups (segmental extended resection, segmental extended resection with visceral/vascular extension, minor/major resection with visceral/vascular extension), no difference was found ($p = 0.977$). Regarding RFSand the extent of resection, minor resection benefitted RFS, though not significantly ($p = 0.051$). Morbidity had no influence on RFS ($p = 0.649$).

Conclusion: Extended resection results in worse OS in patients with ICC than major or minor liver resection. Minor and major resection with visceral or vascular extension should be classified as extended resection. Despite worse OS, extended resection offers a chance for long-term survival and performs significantly better than the exploration group with manageable accompanied risks.

1. Introduction

Intrahepatic cholangiocarcinoma (ICC) is rare and often diagnosed at an advanced stage, with poor long-term outcome [1–3]. Major or extended resections are commonly necessary to achieve complete removal, which offers the only chance of cure [4]. Due to visceral or vascular infiltration, resection and reconstruction may be required to achieve this goal [5,6]. Different studies have addressed the feasibility and postoperative and long-term outcome of extended resections, especially in the case of ICC [3,4,6]. All of the studies conclude that extended resection is a reasonable procedure offering the chance of long-term survival with acceptable morbidity and mortality. Even major vascular resection for ICC is feasible and not associated with a higher risk of any or major complications [7,8], and additional visceral resection can be appropriate in select cases if infiltration is suspected [5]. Severe morbidity influences the long-term outcome of patients suffering from ICC, independently predicting overall survival and the time to recurrence [9].

The present study was conducted in a single-center collective with a very high number of extended resections with or without vascular and visceral extensions in order to show the impact of an aggressive attitude concerning resection on morbidity, mortality, and long-term outcome.

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Table 1
Patient characteristics.

Groups	All	Resection groups				
		Segmental extended	Seg. extended + visc/vasc[e]	Min/maj + visc/vasc[f]	Major	Minor
	n = 210	Extended resection group			Major	Minor
Resections	**n = 150**	**n = 21**	**n = 40**	**n = 26**	**n = 26**	**n = 37**
Median age, years	64.2	60.1	61.5	70.4	64.9	64.5
Interquartile range	56–73.7	51.7–69.9	50.7–71.6	63–80.3	58.4–73.1	59.2–73
Range	32.3–84.4	34.5–83.4	32.3–79	47.3–84.4	35.9–84	38.1–81.5
Gender (women/men)	77/73	11/10	10/30	16/10	15/11	21/16
ASA classification						
ASA I	2	–	2	–	–	–
ASA II	62	13	18	7	12	12
ASA III	83	8	20	18	14	23
ASA IV	3	–	–	1	–	2
Comorbidities						
Cardiac[a]	36	4	4	5	10	13
Renal[b]	6	2	2	–	1	1
Pulmonary[c]	12	4	1	1	3	3
Diabetes	24	2	5	6	4	7
Nicotine abuse	33	6	7	4	5	11
Alcohol abuse	7	1	1	–	2	3
Right trisectionectomy	26	5	21	–	–	–
Left trisectionectomy	22	9	13	–	–	–
Right hepatectomy	25	–	–	11	14	–
Left hepatectomy	19	–	–	7	12	–
Mesohepatectomy[d]	7	3	4	–	–	–
ALPPS	6	4	2	–	–	–
Monosegmentectomy	9	–	–	1	–	8
Bisegmentectomy	25	–	–	6	–	19
Resection of 3 liver seg.	9	–	–	1	–	8
Atypic/wedge resection	2	–	–	–	–	2
T Status						
T1a	23	2	–	2	4	15
T1b	31	8	6	5	4	8
T2	62	10	18	8	13	13
T3	13	1	3	4	4	1
T4	21	–	13	7	1	–
N Status						
N0	90	16	21	14	18	21
N1	42	4	18	8	6	6
N2	1	–	–	–	1	–
Nx	17	1	1	4	1	10
R Status						
R0	131	18	32	23	25	33
R1	19	3	8	3	1	4
Irresectability	**n = 60**	-	-	-	-	-

[a] s/p myocardial infarction, s/p stenting, cardiac arrhythmia.
[b] Kidney insufficiency (no patient with renal failure and dialysis).
[c] Chronic obstructive pulmonary disease (COPD), chronic bronchitis, bronchial asthma.
[d] Resection of ≥3 central liver segments.
[e] Segmental extended resection group with additional visceral and/or vascular extension.
[f] Minor or major resection group with additional visceral and/or vascular extension.

2. Methods

All liver resections between January 2008 and June 2018 at a high volume tertiary medical center were collected in a prospective institutional database.The records of all patients with histologically proven ICC were isolated for further analysis in this retrospective cohort study. Patients with hepatocellular carcinoma, perihilar cholangiocarcinoma, gallbladder carcinoma, or any kind of liver metastasis were excluded. Patients with a centrally located tumor mass with contact or infiltration of the liver hilum exceeding a diameter of 3 cm and obviously originating in the secondary or tertiary order bile ducts were included as ICC.

This work is fully compliant with the STROCSS criteria (www.strocssguideline.com) and reported in accordance with the criteria [10]. This study is registered with Research Registry under unique identifying number (UIN) researchregistry4768. All patients provided written consent for their data to be collected anonymously.

2.1. Preoperative work-up, surgical procedure, and follow-up

Most patients were referred from secondary centers with the suspicion of or histologically proven ICC. If metastatic disease had not been ruled out, we performed gastroscopy and colonoscopy to eliminate the possibility of a gastrointestinal primary malignancy. Computed tomography (CT) or magnetic resonance imaging (MRI) of good quality was necessary to assess the extent of disease and for surgical planning.

All procedures were performed by experienced hepato-pancreaticobiliary surgeons. Minor resections were classified as ≤ 3 resected segments and major resections as 4 resected segments. Extended resections were defined as ≥ 5 resected segments, mesohepatectomy, associating liver partition and portal vein ligation for staged hepatectomy (ALPPS), or minor or major resection with additional vascular and/or visceral extension.

Follow-up was conducted every 3 months for at least 2 years after resection, with ultrasound, CT, or MRIevery 6 months. Some patients were not able to perform follow-up at our center due to distance. In these cases, we contacted the referring physician to obtain all of the necessary information.

2.2. Data analysis

Data analysis focused on patient demographics, surgical procedure, vascular and visceral extensions, postoperative outcome, morbidity, mortality, recurrence, and survival. For histological classification, we used the 8th edition of the AJCC/UICC classification [11].Morbidity was classified according to the Dindo and Clavien classification [12]. All in-hospital deaths are included in mortality, which is provided as 30- and 90-day mortality. Recurrence-free survival (RFS) was defined according toPunt et al. [13].

2.3. Statistical analysis

For statistical analysis, only patients with complete datasets were included and the data transferred into SPSS 23 (SPSS Inc. Released 2014, IBM SPSS Statistics for Windows, Version 23.0, IBM Armonk, NY, USA). Categorical data were processed by the χ^2-test. Overall survival and RFS were analyzed using the Kaplan-Meier model, and the log rank test was used for factorial comparison.

3. Results

Out of 210 patients, 150 underwent curative intended resection, including 60 patients who had irresectable tumors. Reasons for irresectability were peritoneal carcinomatosis (n = 23), multifocal tumor dissemination (n = 15), advanced tumor extension/infiltration (n = 11), and cirrhosis/impaired liver function of the liver (n = 11). Details of the patients' demographic, surgical, and histological characteristics are shown in Table 1.

3.1. Extended resections

The distribution of patients and their distinct categorization regarding extended resections are shown in Fig. 1. A total of 87 extended resections (58% of resection group) were performed with 8 initial minor and 18 initial major resections that became extended resections because of vascular or visceral extension. Details about the vascular and visceral extensions are given in Table 2. Vascular (p = 0.003) and visceral extensions (p < 0.001) were performed significantly more often in patients who underwent extended resections classified according to the segmental extent.

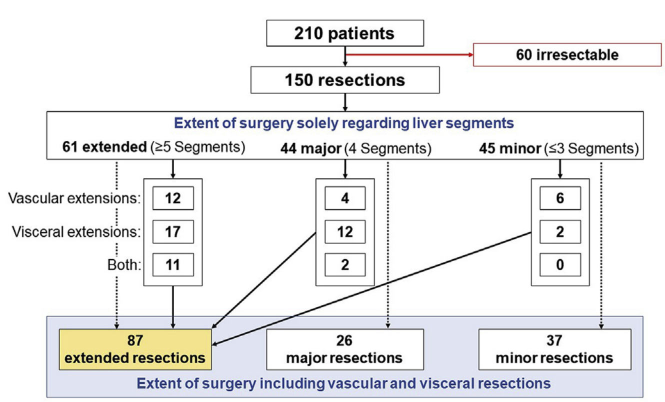


Fig. 1. Flow chart of patient enrollment and resections. The resections are grouped after segmental extent by additional vascular, visceral, or both extensions.

3.2. Morbidity

In the resection group, 69 patients (46%) suffered from any kind of morbidity, including mortality. Table 3 offers a detailed overview of morbidity and mortality categorized by the extent of surgery. Most common were major complications (IIIa n = 28, IIIb n = 3), followed by minor (grade I + II n = 17) and severe complications (IVa n = 6, IVb n = 2). Twenty grade IIIa patients received percutaneous drainage, and three patients received an ERCP because of bile leakage. A pleural catheter was used twice because of effusion, gastroscopy performed twice because of gastrointestinal bleeding, and a cardiac catheter used twice. In one patient, massive ascites was drained. Thirty interventions are listed instead of 28 as in Table 3, because one patient underwent percutaneous drainage and received a cardiac catheter, and another underwent percutaneous drainage and received a pleural catheter. Reasons for grade IIIb complications were bile duct stenosis (n = 1) and bile leakage (n = 2). Treated grade IVa and b complications were bleeding (n = 3), respiratory insufficiency (n = 2), and portal vein thrombosis, bradycardia with resuscitation, and colon perforation (n = 1 each).

A comparison of extended, major, minor resections regarding the appearance and severity of morbidity or mortality revealed no significant difference (p = 0.142). In a comparison of the three different extended resection groups (segmental extended resection with additional visceral/vascular extension [n = 40], segmental extended resection without extension [n = 21], and minor/major resections with visceral/vascular extension [n = 26]), no significant difference in the appearance or severity of postoperative morbidity was detected (p = 0.818).

3.3. Mortality

Thirteen patients died postoperatively, resulting in a mortality of 8.7% (30-day n = 12; 90-day n = 1). Multi-organ failure was the most common cause of death (n = 6), followed by liver failure (n = 4) and sepsis (n = 3). In these patients, 11 extended resections were performed (7x segmental extended resection with visceral/vascular extension, 3x without extension, and 1x major resection with visceral/vascular extension; see Table 3). One patient died after each minor and major resection. No significant difference in mortality was detected for extended resection (p = 0.125).

3.4. Influence on survival

Median overall survival in the resection group (intention to treat) was 21.6 months (IQR: 7.5–32.1) with a consecutive 1-, 3-, and 5-year overall survival of 72%, 29%, and 16%, respectively.

3.4.1. Influence of extent of surgery

For analyses of overall survival regarding the extent of surgery, we performed statistical analysis in two different group sets, always excluding the exploration group from the log rank test (even if illustrated in Figs. 2 and 3). First, we analyzed extended resections on the basis of segmental extent (p = 0.030), with comparable overall survival for the extended and major resection groups and a clear benefit from minor resections (Fig. 2). If visceral and vascular extensions in minor and major resections were included as extended resections, significance was reached (p = 0.006) with a benefit of minor over major over extended resections (Fig. 3). In a comparison of the different extended resection groups (segmental extended resection with/without additional visceral/vascular extension vs. minor/major resections with visceral/vascular extension), the outcome was comparable (p = 0.977; Fig. 4).

Table 2
Vascular and visceral extensions.

Vascular extensions	Total	Infiltration[k]	Segmental extent of resection			p-value
			Extended	Major	Minor	
	n = 52[a]	n = 10[b]	n = 36[c]	n = 6[d]	n = 10[e]	0.003
Hepatic artery	0	0	0	0	0	–
Portal vein	18	4	11	3	4	0.163
Major hepatic vein	21	4	16	2	3	**0.002**
Vena cava inferior	13	2	9	1	3	0.069
Visceral extensions	n = 50[f]	n = 21[g]	n = 33[h]	n = 15[i]	n = 2[j]	< 0.001
Diaphragm	10	2	4	5	1	0.224
Adrenal gland	4	1	3	1	0	0.294
Hilar bifurcation	32	14	24	8	0	**< 0.001**
Pericardium	1	1	1	0	0	0.480
Duodenum	1	1	0	1	0	0.297
Colon	1	1	0	0	1	0.309
Stomach	1	1	1	0	0	0.480

Patients with visceral infiltration (n = 19) and infiltration of the inferior vena cava (n = 2) are classified as T4 using the 8th edition of TNM classification [11]. The number of patients differs because some patients underwent multiple extensions:
[a] n = 35.
[b] n = 9.
[c] n = 23.
[d] n = 6.
[e] n = 6.
[f] n = 44.
[g] n = 19.
[h] n = 28.
[i] n = 14.
[j] n = 2.
[k] Histologically proven infiltration; all other patients had suspected infiltration or needed extension for technical reasons.

Table 3
Relationships between extent of surgery, morbidity, and mortality.

Morbidity groups	n = 150	No/minor			Major			Severe			Mortality	
Dindo-Clavien classification [12]		no	I + II	%	IIIa	IIIb	%	IVa	IVb	%	V	%
Complete resection group		81	17	65.3	28	3	20.7	6	2	5.3	13	8.7
All extended resections	**n = 87**	**37**	**12**	**56.3**	**20**	**1**	**24.1**	**4**	**2**	**6.9**	**11**	**12.6**
+ visceral/vascular extension	40	15	6	52.5	8	1	22.5	2	1	7.5	7	17.5
- visceral/vascular extension	21	11	1	57.1	5	0	23.8	0	1	4.8	3	14.3
minor/major + visc/vasc ext.	26	11	5	61.5	7	0	26.9	2	0	7.7	1	3.8
Major resection	**n = 26**	**18**	**2**	**76.9**	**4**	**1**	**19.2**	**0**	**0**	**0**	**1**	**3.8**
Minor resection	**n = 37**	**26**	**3**	**70.3**	**4**	**1**	**13.5**	**2**	**0**	**5.4**	**1**	**2.7**

Median overall survival (OS) for all extended resections was 21.2 months (IQR: 4.9–30.2), for major resections 29.7 months (IQR: 12.2–37), and for minor resections 29.3 months (IQR: 11.2–39). Consecutive 1-, 3-, and 5-year OS was 74%, 25%, and 8% for extended resections, 91%, 41%, and 14% for major resections, and 80%, 41%, and 41% for minor resections, respectively.

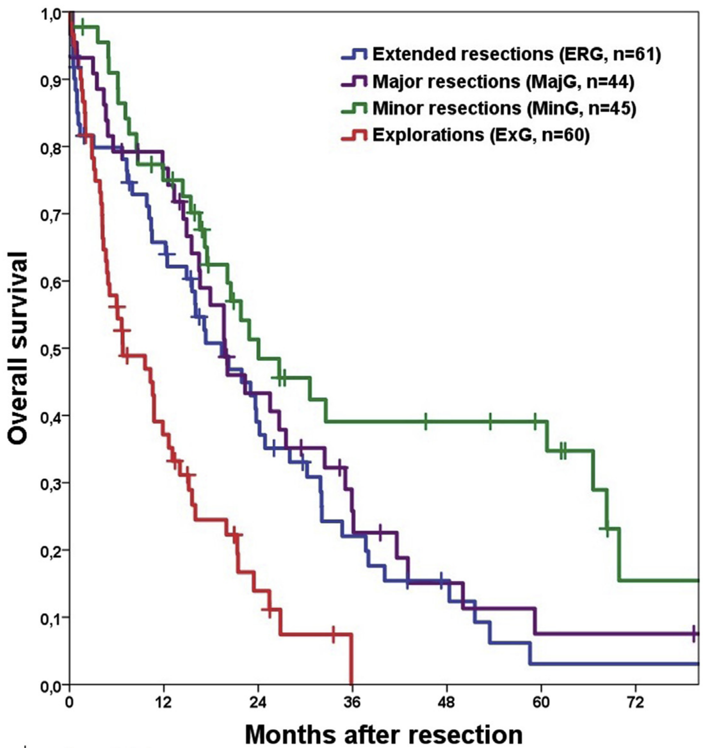
The extended resection group including minor or major resections with vascular or visceral extensions included patients with different UICC stages. A comparison of patients with T4 and/or N1 and/or M1 status (≥UICC IIIB) versus all patients with UICC ≤ IIIA within this group revealed a significant influence on OS (p = 0.045; Fig. 5).

Recurrence-free survival (RFS) did not reach significance when comparing all extended resections vs. major and minor resections (p = 0.051), but showed a benefit for the minor resection group. Median RFS for the extended resection group was 8.8 months (IQR: 2.1–11.8), for the major resection group 11.8 months (IQR: 4.7–18.7), and for the minor resection group 10.1 months (IQR: 5.1–25.1). Consecutive 1-, 3-, and 5-year RFS was 32%, 8%, and 6% for the extended resection group, 49%, 15%, and 10% for the major resection group, and 41%, 34%, and 29% for the minor resection group, respectively.

3.4.2. *Influence of morbidity*

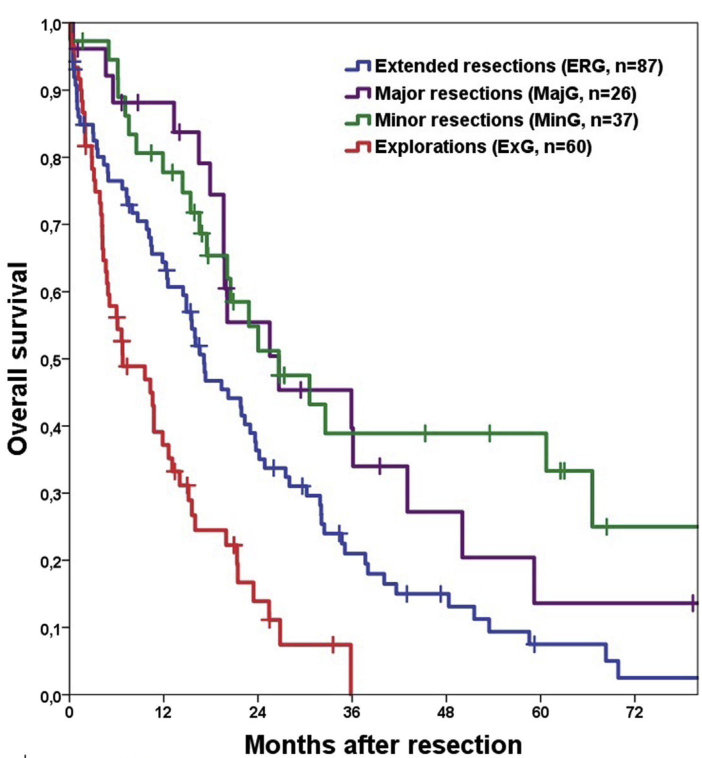
For overall survival, no difference was shown for morbidity groups ≥ major (Dindo grade III + IV) vs. ≤ minor complications (Dindo grade 0 + I + II; p = 0.353). The median OS for the ≥major complication group was 23.8 months (IQR: 8.7–30.2), with a consecutive 1-, 3-, and 5-year OS of 71%, 38%, and 29%, respectively. For the ≤ minor complication group, the median OS was 23.6 months (IQR: 12.4–34.8), with a consecutive 1-, 3-, and 5-year OS of 82%, 30%, and 13%, respectively.

No significant difference in RFS was shown for ≥ major vs. ≤ minor groups (p = 0.649). The median RFS for the ≥major complication group was 9.8 months (IQR: 4.6–17.7), with a consecutive 1-, 3-, and 5-year RFS of 39%, 23% and 19%, respectively. For the ≤minor complication group, the median RFS was 9.5 months (IQR: 4.9–15.9), with a consecutive 1-, 3-, and 5-year OS of 37%, 13%, and 9%, respectively.



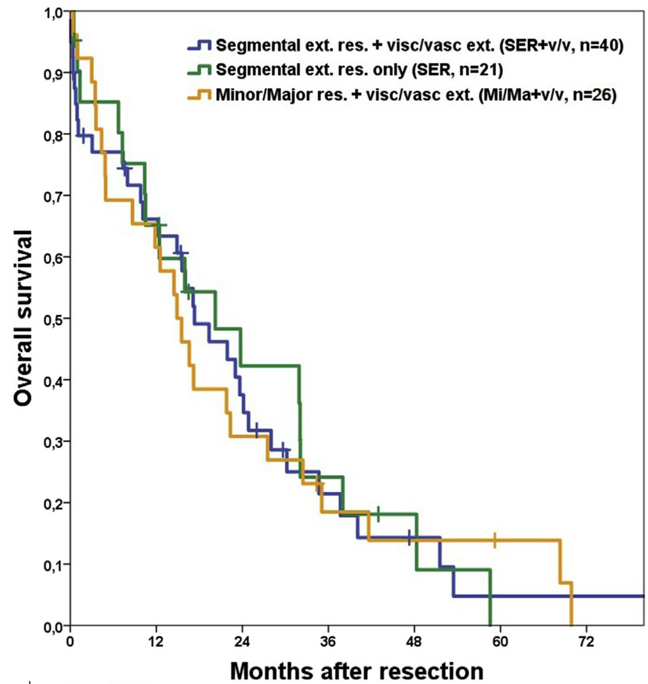
	number at risk						
Extended resections	61	37	20	10	5	1	1
Major resections	44	31	16	8	4	2	2
Minor resections	45	32	18	12	11	9	2
Explorations	60	19	5	-	-	-	-

Fig. 2. Kaplan-Meier curve of overall survival comparing the segmental extent of resections without recognition of vascular or visceral extension ($p = 0.030$ excluding exploration group). Subgroup comparison: ERG vs. MajG, $p = 0.410$; ERG vs. MinG, $p = 0.010$; ERG vs. ExG, $p < 0.001$; MajG vs. MinG, $p = 0.101$; MajG vs. ExG, $p < 0.001$; MinG vs. ExG, $p < 0.001$.



	number at risk						
Extended resections	87	53	28	14	8	3	1
Major resections	26	20	11	7	4	2	2
Minor resections	37	27	15	9	8	7	2
Explorations	5	4	2	-	-	-	-

Fig. 3. Kaplan-Meier curve of overall survival comparing the extent of resections when including minor/major resections with visceral and/or vascular extension ($p = 0.006$ excluding exploration group). Subgroup comparison: ERG vs. MajG, $p = 0.042$; ERG vs. MinG, $p = 0.005$; ERG vs. ExG, $p < 0.001$; MajG vs. MinG, $p = 0.599$; MajG vs. ExG, $p < 0.001$; MinG vs. ExG, $p < 0.001$.



	number at risk						
Segmental ext. res. + visc/vasc ext.	40	24	13	6	3	1	1
Segmental extended resection	21	13	7	4	2	-	-
Major/Minor + visc/vasc ext.	26	16	8	4	3	2	-

Fig. 4. Kaplan-Meier curve of overall survival comparing the different extended resection groups (p = 0.977). Subgroup comparison: SER + v/v vs. SER, p = 0.739; SER + v/v vs. Mi/Ma + v/v, p = 0.868; SER vs. Mi/Ma + v/v, p = 0.933.

4. Discussion

In this study, we analyzed the influence of extended resections, visceral and vascular extensions, and consequential morbidity on survival. Morbidity was not influenced by the extent of resection. Minor resections, in particular, had favorable overall survival with significant benefit compared to the extended resection groups. No significant influence on RFS was shown. Postoperative morbidity and its severity had no influence on overall survival and RFS in our cohort. Extended resection still offers a chance of long-term survival and performed significantly better than exploration.

The extent of liver resection has evolved over the last few decades and, currently, extended resections and more advanced approaches, such as ALPPS, are accepted as safe and feasible procedures in select patients [3–6,14,15]. In addition, the influence of major vascular resections (most often defined as resection of the inferior vena cava, the portal vein, or both) on patient outcomes has been investigated for ICC. The authors concluded that major vascular resections are feasible and do not lead to worse postoperative or oncological outcomes [7,8]. Regarding visceral extensions, data are scarce. Our own data show the feasibility of these procedures, but visceral infiltration is a strong negative predictor of overall survival [5]. Vascular and/or visceral extensions were most often performed after segmental extended resection. This is understandable as advanced ICC, which necessitates segmental extended resection, is more likely to infiltrate major vessels or adjacent organs/structures. Furthermore, our results suggest that even minor or major resections that require vascular and/or visceral extension should be considered as extended resections. If only the segmental extent of resection is considered, major and extended resections have comparable overall survival (see Fig. 2). However, if minor and major resections with visceral and/or vascular extension are considered extended resections, a more obvious and significant difference is observed in overall survival between these groups (see Fig. 3).

In the course of advances in perioperative management and technical finesse, extended hepatic resections for primary or secondary haptic malignancies have been performed more frequently since the 1990s. Vauthey et al. questioned the rationality of extended liver resection in 127 patients with different malignancies and were able to show the safety and feasibility with an impressive mortality rate of 0.8% [16]. The first focused analysis of extended resections for ICC by Lang et al. showed thatR0 resections in particular offer patients with advanced ICC a chance of long-term survival [4]. In that study, postoperative morbidity was 36% with a mortality rate of 6%. The authors concluded that palliative resections are not justified, but if R0resection can be achieved there is a role for extended resections for ICC. Recent studies took up the reasonableness of extended resections for ICC. Bergeat et al. analyzed 107 patients, including 27 who underwent extended resections [6]. Extended resection was an independent risk factor for major complications, but overall survival and disease-free survival were not influenced by the extent of resection. Spolverato et al. [3] reported on a high proportion of extended resections (> 30%) in an analysis of 557 patients with large or multifocal ICC; morbidity occurred in 50.4% and the postoperative mortality rate was 2.7%. Severe morbidity was more frequent in the group of patients with larger or multifocal tumors who underwent major or extended resections more often. Comparing our data is difficult because we have a large number of extended resections (58%) and, thus, we analyzed a unique single-center cohort. Extent of resection significantly influenced overall survival with a benefit of minor and major resections over extended resections. Nevertheless, extended resections had a strong significant benefit over exploration. For RFS, significance was barely not reached, but showed a benefit for the minor resection group. That extended resections perform worse than major or minor resections is understandable, as tumor extent and biology is expected to be worse in patients who need extended resections to achieve complete tumor removal; therefore, overall survival is influenced by the extent of surgery.

We showed that, within the extended resection group, different AJCC/UICC stages significantly influence survival. This study did not aim to analyze the influence of different factors on overall survival and

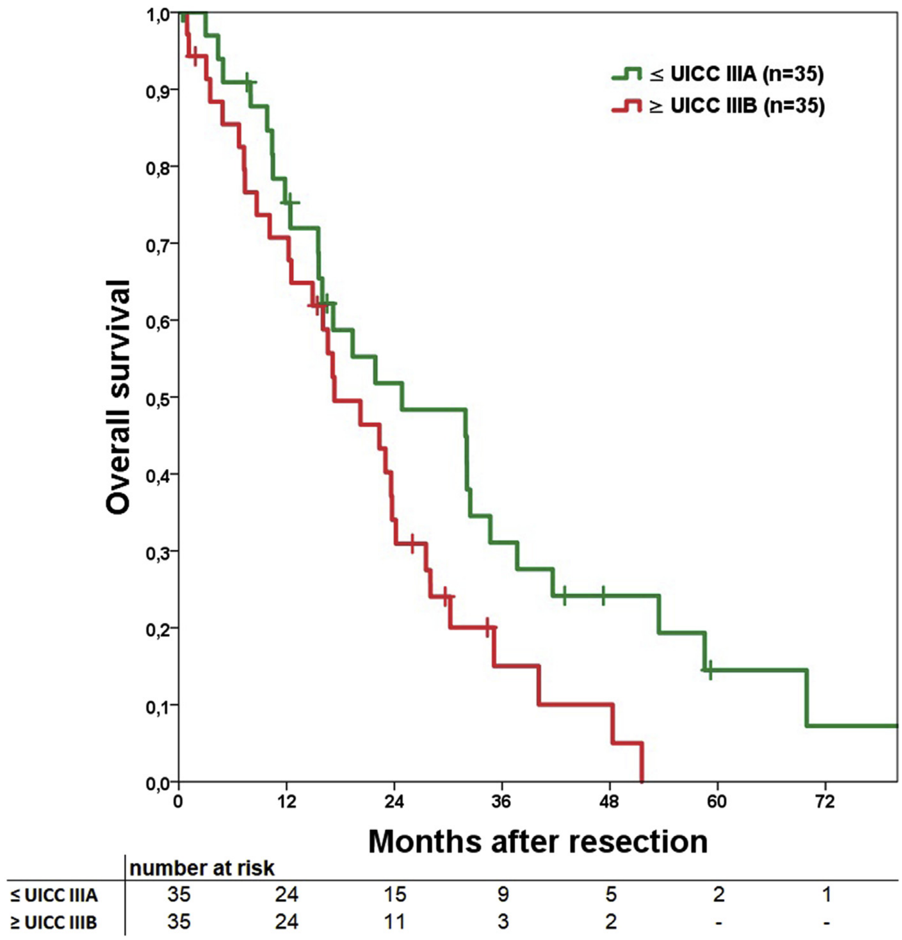


Fig. 5. Kaplan-Meier curve of overall survival comparing the influence of the UICC stage in the extended resection group. The extended resections include minor/major resections with visceral and/or vascular extension. UICC stages IIIB and IV had significantly worse overall survival than the ≤ UICC IIIA group ($p = 0.045$).

RFS or to find independent predictors. However, this result was expected. In particular, the ≥ UICC IIIB group included only patients with T4 and/or N+ and/or M1 disease, a cohort with expected worse survival. Other groups already showed an influence of the AJCC/UICC stage on survival [17,18], as well as our own data [5].

Morbidity is a common problem in liver surgery, and rates vary between 22.6% and 44% for ICC [9,19,20]. Focused data on morbidity for resection of ICC are scarce. Doussot et al. analyzed the impact of morbidity and mortality on survival after resection of ICC in a multicenter study of 522 patients [9]. Morbidity occurred in 42.5% with severe morbidity (Dindo-Clavien grade III-IV) in 21.6% of patients. Severe morbidity was one of the different independent predictors of overall survival, whereas major hepatectomy and intraoperative blood transfusion were independent predictors of severe morbidity. These findings are different from our results. Though the frequency of morbidity was comparable (46% in our cohort), the extent of resection had no significant influence on appearance and severity of morbidity. Furthermore, we were not able to show a significant influence on overall survival or RFS. Interestingly, our group of patients with major complications had slightly better overall survival compared to the minor/no complication group, especially at 5 years (29% vs. 13%). This is difficult to explain and maybe due to the effects of a limited subgroup size.

This study has some limitations. The analysis was performed retrospectively, which reduces its validity. There is no real standard definition of what to call an extended liver resection. Our approach was that every complex visceral or vascular extension makes even a minor or major resection an extended liver resection. This definition can be discussed because most articles use the segmental extent. Therefore, it maybe difficult to compare studies with different classifications of extent of resection, but our data demonstrate that minor or major liver resection with visceral or vascular extension should be counted as an extended resection. The number of patients, especially in subgroups, is limited in a single-center study and the power of statistical tests decreased. Further data from single- or multi-center studies are necessary to confirm our results and conclusions.

In conclusion, extended resection has worse overall survival in patients with ICC compared to major or minor liver resection. The severity and frequency of morbidity does not differ significantly between extended, major, or minor resection. Furthermore, minor and major resections with visceral or vascular extensions should be classified as extended resections because they have comparable overall survival as the segmental extended resections. Nevertheless, extended resections offer a chance for long-term survival and perform significantly better than exploration, with manageable accompanied risks.

Ethical approval

All patients gave informed consent for anonymous collection of data and follow-up.

Sources of funding

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Author contribution

Bartsch: Study design, data collection,analysis, writing.
Tripke: Data collection.
Baumagart: Data collection.
Hoppe-Lotichius: Data collection, follow-up.
Heinrich: Study design, data analysis, writing.
Lang: Study design, data analysis, writing.

Conflicts of interest and financial disclosure

There are no conflicts to declare or financial relationships to disclose. No funding.

Research registration number

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Guarantor

Fabian Bartsch
Hauke Lang

Provenance and peer review

Not commissioned, externally peer reviewed.

Data statement

Data will not be available due to data protection of involved patients. All patients signed informed consent that data and follow-up will be collected anonymously. We do not want to enable the possibility that patients are identified about date of resection, date of death or other details.

CRediT authorship contribution statement

Fabian Bartsch: Conceptualization, Data curation, Formal analysis, Methodology, Writing - original draft. **Verena Tripke:** Data curation. **Janine Baumgart:** Data curation. **Maria Hoppe-Lotichius:** Data curation, Investigation, Resources. **Stefan Heinrich:** Supervision, Writing - review & editing. **Hauke Lang:** Conceptualization, Supervision, Writing - review & editing.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.ijsu.2019.05.006.

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