

## ORIGINAL ARTICLE

# Hospital variation and outcomes after repeat hepatic resection for colorectal liver metastases: a nationwide cohort study

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## Abstract

**Background:** Approximately 70% of patients with colorectal liver metastases (CRLM) experiences intrahepatic recurrence after initial liver resection. This study assessed outcomes and hospital variation in repeat liver resections (R-LR).

**Methods:** This population-based study included all patients who underwent liver resection for CRLM between 2014 and 2022 in the Netherlands. Overall survival (OS) was collected for patients operated on between 2014 and 2018 by linkage to the insurance database.

**Results:** Data of 7479 liver resections (1391 (18.6%) repeat and 6088 (81.4%) primary) were analysed. Major morbidity and mortality were not different. Factors associated with major morbidity included ASA 3+, major liver resection, extrahepatic disease, and open surgery. Five-year OS after repeat versus primary liver resection was 42.3% versus 44.8%,  $P = 0.37$ . Factors associated with worse OS included largest CRLM >5 cm (aHR 1.58, 95% CI: 1.07–2.34,  $P = 0.023$ ), >3 CRLM (aHR 1.33, 95% CI: 1.00–1.75,  $P = 0.046$ ), extrahepatic disease (aHR 1.60, 95% CI: 1.25–2.04,  $P = 0.001$ ), positive tumour margins (aHR 1.42, 95% CI: 1.09–1.85,  $P = 0.009$ ). Significant hospital variation in performance of R-LR was observed, median 18.9% (8.2% to 33.3%).

**Conclusion:** Significant hospital variation was observed in performance of R-LR in the Netherlands reflecting different treatment decisions upon recurrence. On a population-based level R-LR leads to satisfactory survival.

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## Introduction

Up to fifty percent of colorectal cancer (CRC) patients presents with colorectal liver metastases (CRLM) either at the time diagnosis of the primary tumour or during follow-up. Only 20–30% of patients are deemed eligible for resection with curative intent.<sup>1–3</sup> Approximately 50–70% will develop recurrent intra-hepatic metastases after resection.<sup>4</sup> Repeat liver resection (R-LR) emerges as a potential salvage option in patients with recurrent CRLM.

In patients who underwent R-LR, low mortality and morbidity rates have been described previously.<sup>5,6</sup> Despite these results, R-LR appears to be an underused treatment option. The potential to opt for repeated resection may have increased due to the increased use of minimally invasive resections at the index operation and integration of thermal ablation as an adjunct to resection. However, the cohort of patients eligible for R-LR remains highly selected as R-LR is only performed in 6%–30% of patients with recurrent disease.<sup>5–8</sup> Alternatives for other patients may include percutaneous thermal ablation or stereotactic radiotherapy or systemic therapy.

The selection of patients for R-LR is based on the same criteria applied for primary resection, including factors such as the absence of extra-hepatic disease and considerations regarding the function and size of the future liver remnant. Although these factors are consistent, access may vary due to impact of previous interventions. Research on treatment plans in patients with CRLM showed considerable undertreatment in primary liver resection. This is also likely in the context of resection of recurrent CRLM. The probability of resection depends on the assessment of the multidisciplinary team.<sup>9</sup> However, little is known about variation in patient selection for R-LR between hospitals and oncological networks, where variation unrelated to patient or tumour characteristics is unwarranted.

The aim of this study was to investigate outcomes of R-LR on a national scale and to assess variation in utilisation of R-LR among hospitals and oncological networks in the Netherlands.

## Methods

All consecutive patients registered in the Dutch Hepato Biliary Audit (DHBA) who underwent liver resection for CRLM between 2014 and 2022 were eligible in this study. Patients were excluded when essential data on date of birth and surgery were missing. Patients who only received thermal ablation or underwent a two-stage procedure were also excluded from analysis. Patients were divided into two groups, patients who underwent liver resection with or without thermal ablation for the first time, or patients with a history of liver resection treated with an R-LR or R-LR combined with thermal ablation.

The DHBA was established in 2013 as a clinical audit for hepatobiliary surgery. Registration in the audit has been

mandatory for all patients undergoing liver resection or a combination of resection and ablation since January 2014.<sup>10</sup> Since 2018 it has been possible to register (percutaneous and surgical) thermal ablations without liver resection in the DHBA. Registration of percutaneous ablations has not been obligatory until 2023. Data verification of resections in 2017 showed 97% data completeness.<sup>11</sup> Previous studies used DHBA data to give insight into practice variation and outcomes.<sup>12–16</sup>

In the Netherlands, each hospital should perform a minimum of 20 liver resections per hospital per year, which resulted in some centralisation of liver surgery in the last decade. Among the required 20 liver resections there is no specification in either minor or major resections, or indications (i.e., primary or secondary liver tumour) or primary or repeat hepatectomy. Additionally, oncological networks have been formed to improve referral patterns between hospitals.<sup>13</sup> Networks consist of at least one tertiary referral centre and several regional hospitals. Ideally, oncological networks minimise hospital variation and improve patient outcomes, yet using these networks is optional. Distribution of oncological networks is described previously.<sup>13</sup>

Since the DHBA is a clinical audit with data until 30 days postoperatively or discharge overall survival is not registered. Therefore, the DHBA was linked to two other datasets (Vektis and GBP), which contain survival status due to any cause of death. Data linkage has been described earlier.<sup>16,17</sup> The linking percentage was 92.8% between 2014 and 2018. However, this percentage decreased after the introduction of the General Data Protection Regulation (GDPR) law in 2018. Overall survival was therefore only assessed in the cohort operated on between 2014 and 2018.

No ethical approval was needed for this study since audit data is anonymised under the Dutch Law. Permission for data analyses was obtained from the DHBA scientific committee.

## Variables

Collected patient characteristics included sex, age (in years), American Society of Anaesthesiologists (ASA) classification, Charlson Comorbidity Index (CCI), body mass index (BMI), history of liver resection and history of liver disease. Tumour characteristics included the number of CRLM, diameter of the largest CRLM before any form of treatment, and location of primary tumour (colon/rectal). Treatment characteristics included: resection or combined resection/ablation for primary and R-LR, minimally invasive or open approach for primary and repeat resection, major or minor liver resection, type of hospital where treatment was performed, the oncological network where treatment was performed, and surgical margins as reported by the pathologist. Positive tumour margins were defined as R1 (surgical margin within 1 mm of tumour) and R2 (macroscopic residual disease). Major liver resection was defined as resection of  $\geq 3$  adjacent liver segments.

## Outcomes

Postoperative outcomes included length of stay (in days), overall morbidity rate, major morbidity rate, 30-day or in-hospital mortality rate and overall survival. Major morbidity was defined as a complication graded Clavien-Dindo grade 3a or higher within 30 days of surgery or before discharge if this was later than 30 days postoperatively. Mortality was defined as death within 30 days from date of surgery or mortality during initial hospitalisation. Secondary surgical-specific outcomes included intra-abdominal infection, liver failure, bile leakage (defined according to the international study group of liver surgery),<sup>18</sup> pneumonia, and cardiac complications. Overall survival was calculated from the date of surgery to the date of death of any cause.

## Statistical analysis

Baseline characteristics and outcomes were compared between primary and R-LR. For categorical variables, chi-squared or Fisher exact test and for continuous variables, students t-test were used. Multivariable logistic regression analysis was performed to investigate the association of potential patient, tumour and treatment characteristics with 30-day major morbidity. Missing data on predictive variables in this model was handled by performing multiple imputations using a fully conditional imputation method, assuming data were missing at random.

The influence of patients, tumour and treatment factors was expressed as an adjusted odds ratio (aOR) with 95% confidence intervals (CI). Statistical significance was defined as a two-sided p-value of <0.05 in the multivariable model. The variance inflation Factor (VIF) was used to test multicollinearity; multicollinearity was assumed when VIF was higher than 2. Overall survival was estimated using the Kaplan–Meier method. Association of patient and tumour characteristics with overall survival after repeat resection was analysed using a univariable and multivariable cox regression analysis. Patients with missing data on follow-up time or status of being alive were excluded. If the association in the univariable model was positive p-value of p < 0.10, variables were entered in the multivariable model. The influence of different factors was expressed as adjusted hazard ratios (aHR) with 95% confidence intervals (CI). A P-value of p < 0.05 in the imputed multivariable Cox regression model was deemed statically significant. The proportional hazard assumption was evaluated with scaled Schoenfeld residuals.

Unadjusted hospital and oncological network variation in performing R-LR were assessed as the proportion of R-LR of all liver resections. No adjustment for case-mix factors was performed to compare hospital and network variation since this was not meaningful in treatment groups that were not identical per definition. All analysis were performed in R version 4.2.3<sup>®</sup> (R-core team (2018) R Foundation for Statistical Computing, Vienna, Austria).

## Results

In total, 7479 liver resections were included between 2014 and 2022, of which 1391 (18.6%) were R-LR and 6088 (81.4%) were primary liver resections. **Table 1** displays all baseline characteristics of patients who underwent R-LR compared to patients who underwent primary resection. Patients who underwent R-LR had higher ASA scores, ASA  $\geq 3$ , 22.8% vs. 25.7% (P = 0.030), and fewer and smaller CRLM. Patients who underwent R-LR, were less often treated with chemotherapy, both preoperative (28.2% vs. 23.9%, P = 0.006) and adjuvant 6.1% vs. 3.7%, P < 0.001). Surgical approach for R-LR was more often an open approach (65.3% vs. 78.8%, P < 0.001). Major liver resection was performed in 18.2% of all patients who underwent R-LR.

## Postoperative outcomes

Short-term postoperative outcomes are shown in **Table 2**. Length of stay of patients who underwent R-LR was shorter. Overall morbidity (28.6% vs. 26.8%), major morbidity (10.1% vs. 10.0%) and 30-day mortality (1.2% vs. 1.8%) were not different between groups. ASA-score III (aOR 1.95, 95% CI 1.33–2.87, P = 0.001), major liver resection (aOR 2.61, 95% CI 1.73–3.93, P < 0.001), and extrahepatic disease (aOR 1.58, 95% CI 1.01–2.47, P = 0.047) were associated with increased major morbidity. A minimally invasive approach was associated with decreased major morbidity, data is shown in **Supplementary Table 1**. Multicollinearity was assessed and not observed in this model.

## Overall survival

In total, 4239 patients (treated between 2014 and 2018) were included in the overall survival analysis, of whom 737 (17.3%) underwent R-LR. Median follow-up of all patients was 67 months IQR (41.6–86.5). Five-year overall survival rate after R-LR *versus* primary resection was 42.3% (95% CI 38.8–46.1) versus 44.8% (95% CI 43.2–46.5) P (log-rank) = 0.37 (**Fig. 1**).

In **Table 3** factors associated with a lower overall survival after R-LR are shown. These factors included largest CRLM >5 cm (aHR 1.58, 95% CI: 1.07–2.34, p = 0.023), >3 CRLM (aHR 1.33, 95% CI: 1.00–1.75, P = 0.046), extrahepatic disease (aHR 1.60, 95% CI: 1.25–2.04, P = 0.001), positive tumour margins (aHR 1.42, 95% CI: 1.09–1.85, p = 0.009).

## Between-hospital and oncological network variation

In total, the percentage of patients who underwent R-LR among all patient who underwent liver resection was 18.6%. Significant hospital variation was present reflected by a different proportion of performed R-LR among all liver resections across different hospitals in the Netherlands. The uncorrected percentage of R-LR ranged between 8.2% and 33.3%, nine hospitals fell outside the 95% confidence interval. Six hospitals performed R-LR significantly less often and three performed R-LR significantly more often compared to the median R-LR rate in the Netherlands (**Fig. 2a–b**, **Supplementary Fig. 1A–B**).

**Table 1** Baseline characteristics of patients after primary resection and repeat resection for colorectal liver metastases between 2014 and 2022 in the Netherlands

Factor	Primary resections N (%)	Repeat resections N (%)	P-value
<b>Total</b>	6088	1391	
<b>Patient characteristics</b>			
<b>Sex</b>			0.642
Male	3842 (63.1)	904 (65.0)	
Female	2227 (36.6)	484 (34.8)	
Missing	19 (0.1)	3 (0.2)	
<b>Age (median, IQR)</b>			0.020
	67 [59–74]	66 [58–73]	
<b>BMI (mean, SD)</b>			<0.001
	25.6 [23.3, 28.4]	26.3 [23.6, 29.4]	
<b>ASA score</b>			0.020
I/II	4640 (76.2)	1013 (72.8)	
≥III	1386 (22.8)	358 (25.7)	
Missing	62 (1.0)	20 (1.4)	
<b>CCI</b>			0.245
0/1	4507 (74.0)	1008 (72.5)	
≥2	1581 (26.0)	383 (27.5)	
<b>Tumour characteristics</b>			
<b>Origin primary tumour</b>			0.492
Colon	3995 (65.6)	929 (66.8)	
Rectum	2082 (34.2)	458 (32.9)	
Missing	11 (0.2)	4 (0.3)	
<b>Number of CRLM</b>			<0.001
1	2600 (42.7)	733 (52.7)	
2	1248 (20.5)	284 (20.4)	
3	683 (11.2)	137 (9.8)	
4	424 (7.0)	89 (6.4)	
5	350 (5.7)	56 (4.0)	
>5	612 (10.1)	60 (4.3)	
Missing	171 (2.8)	32 (2.3)	
<b>Size in mm</b>			<0.001
<20	1657 (27.2)	447 (32.1)	
20–30	1526 (25.1)	340 (24.4)	
31–40	930 (15.3)	199 (14.3)	
41–50	514 (8.7)	93 (6.7)	
>50	835 (13.7)	123 (8.8)	
Missing	937 (10.3)	189 (13.6)	
<b>Extrahepatic disease</b>			<0.001
No	5143 (84.5)	1100 (79.1)	
Yes	729 (12.0)	233 (16.8)	
Missing	216 (3.5)	58 (4.2)	
<b>CEA (median IQR)</b>			<0.001
Missing	1339 (21.9)	284 (20.3)	

Table 1 (continued)

Factor	Primary resections N (%)	Repeat resections N (%)	P-value
<b>Histopathology liver parenchyma</b>			<0.001
Normal liver	4056 (66.6)	870 (62.5)	
Liver disease	1238 (20.3)	283 (20.3)	
Missing	794 (13.1)	238 (17.1)	
<b>Treatment characteristics</b>			
<b>Preoperative imaging</b>			<0.001
MRI	2592 (42.6)	507 (36.4)	
PET-CT	778 (12.8)	218 (15.8)	
MRI + PET-CT	1683 (27.6)	379 (27.2)	
No additional imaging	807 (13.3)	213 (15.3)	
<b>Preoperative chemotherapy</b>			0.006
No	4014 (65.9)	975 (70.1)	
Yes	1715 (28.2)	333 (23.9)	
Missing	359 (5.9)	83 (6.0)	
<b>Adjuvant chemotherapy</b>			<0.001
No	5510 (90.5)	1276 (91.7)	
Yes	372 (6.1)	52 (3.7)	
Missing	206 (3.4)	63 (4.5)	
<b>Extend of liver resection</b>			0.042
Minor	4830 (79.3)	1138 (81.8)	
Major	1258 (20.7)	253 (18.2)	
<b>Surgical treatment</b>			<0.001
Open	3976 (65.3)	1096 (78.8)	
Laparoscopic	1819 (29.9)	245 (17.6)	
Robotic	266 (4.4)	40 (2.9)	
Missing	27 (0.4)	10 (0.7)	
<b>Type of local treatment</b>			0.002
Resection only	4716 (77.5)	1130 (81.2)	
Resection + ablation	1372 (22.5)	261 (18.8)	
<b>Type of hospital</b>			0.048
Regional	3268 (53.7)	788 (56.6)	
Tertiary referral centre	2820 (46.3)	603 (43.4)	
<b>Annual hospital volume</b>			0.016
<20	560 (9.2)	115 (8.3)	
21–39	2122 (34.9)	509 (36.6)	
40–59	2451 (40.3)	592 (42.6)	
60–79	566 (9.3)	95 (6.8)	
>80	383 (6.3)	78 (5.6)	
<b>Resection margins</b>			<0.001
R0	5298 (87.0)	1132 (81.4)	
R1	656 (10.8)	218 (15.7)	
R2	45 (0.7)	8 (0.6)	
Missing	89 (1.5)	33 (2.4)	

**Table 2** Postoperative outcomes of patients after primary resection and repeat resection for colorectal liver metastases between 2014 and 2022 in the Netherlands

Factor	Primary resection N (%)	Repeat resection N = (%)	P-value
<b>Total</b>	6088	1391	
<b>Length of stay in days (median IQR)</b>	6 [4, 8]	5 [4, 7]	<b>&lt;0.001</b>
<b>Bloodloss (ml, median, IQR)</b>	300 [100, 600]	400 [150, 700]	<b>&lt;0.001</b>
<b>Postoperative complications</b>			0.285
No	4335 (71.4)	1007 (73.2)	
Yes	1731 (28.6)	368 (26.8)	
Missing	32	16	
<b>Complicated course</b>			0.717
No	5293 (86.9)	1215 (87.3)	
Yes	795 (13.1)	176 (12.7)	
<b>Pneumonia</b>			0.015
No	5280 (94.8)	1215 (96.6)	
Yes	298 (4.7)	43 (3.1)	
Missing	519 (8.5)	133 (9.6)	
<b>Liver failure</b>			0.024
No	5975 (99.0)	1346 (98.3)	
Yes	60 (1.0)	24 (1.8)	
Missing	53	21	
<b>Biliary leakage</b>			0.275
No	5868 (97.2)	1324 (96.6)	
Yes	167 (2.8)	46 (3.4)	
Missing	53	21	
<b>Cardiac complications</b>			0.426
No	5868 (97.2)	1330 (96.7)	
Yes	171 (2.8)	45 (3.3)	
Missing	64	21	
<b>30-day major complications</b>			0.957
No	5474 (89.9)	1252 (90.0)	
Yes	614 (10.1)	139 (10.0)	
Missing			
<b>30-day mortality</b>			0.097
No	5952 (97.8)	1344 (98.2)	
Yes	71 (1.2)	25 (1.8)	
Missing	81	26	

For oncological networks, the percentage of R-LR ranged between 13.9% and 24.6%, one network performed R-LR significantly less often.

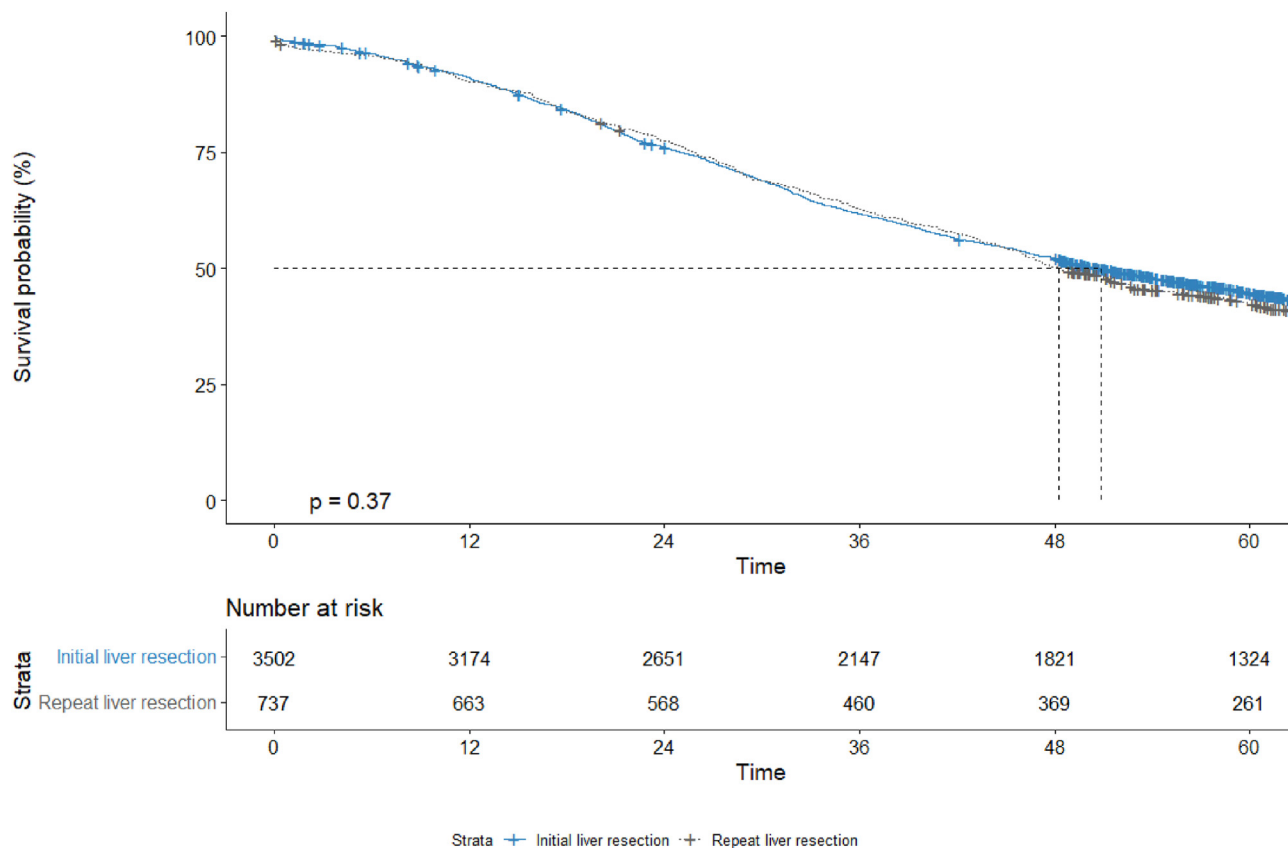
## Discussion

Postoperative outcomes and OS of patients who underwent R-LR were not inferior to those who underwent primary liver resection for CRLM. In this study, significant between hospital and

between oncological network variation in performance of R-LR was observed.

Overall morbidity rate was consistent with the rate reported in a recent meta-analysis on R-LR, which showed a mean overall morbidity rate of 23% (8–71%).<sup>19</sup> Major morbidity rate in this study was also in line with previous reports.<sup>20</sup> The comparable short-term postoperative outcomes between R-LR and primary liver resection for CRLM could partly be explained by distinct patient selection criteria.<sup>21</sup> This is evident in the lower tumour





**Figure 1** Overall survival of patients who underwent primary resection versus repeat hepatic resection for colorectal liver metastases between 2014 and 2018

burden seen for R-LR, reflected by less and smaller CRLM, and the absence of the need for simultaneous resection of the primary tumour. This study did not observe a difference in OS after R-LR versus primary liver resection. This is consistent with previous reported results.<sup>21–24</sup> However, it is essential to acknowledge the wide variability in reported five-year OS rates ranging from 21% to 73%.<sup>25</sup> Multiple studies have reported survival benefits for patients who underwent local treatment for recurrent metastases compared to those who did not receive<sup>26</sup> any treatment or chemotherapy only.<sup>26–29</sup> In this study, patients who underwent R-LR received less preoperative and adjuvant chemotherapy in comparison to those who underwent primary resection. These findings are in contrast with other studies, which demonstrate a higher frequency of chemotherapy administration in patients who underwent R-LR.<sup>5,6</sup> This may be the result of some reluctance among medical oncologists in the Netherlands to administer systemic therapy to patients with resectable metastases. For primary liver resections for CRLM this is included in the guideline and chemotherapy should be reserved for patients with unresectable metastases or patients with a very high risk of recurrence i.e. multiple resectable metastases). For recurrent CRLM it is at the discretion of the hepatobiliary surgeon and medical oncologist, but they still may favour local treatment if feasible.<sup>30</sup>

This study explored several patient, tumour and treatment-related factors associated with major morbidity and OS. Observed factors were in line with previous studies reporting tumour size, number of CRLM, surgical margins, and extrahepatic disease were associated with worse OS after R-LR.<sup>19,25,31,32</sup> Other studies reported contrasting results on the prognostic value of disease-free interval (DFI), were a DFI of less than 6 months has been identified as a poor prognostic factor.<sup>19</sup> However, other studies have also reported no influence of early recurrence on OS in patients with liver only metastases or limited extrahepatic disease.<sup>6,33</sup> In the current study detailed data on recurrence were missing. In particular, no data was available on possible other treatments before the R-LR, such as time of chemotherapy, non-surgical intervention, and watchful waiting. In selection of patients for R-LR, factors associated with morbidity and OS should be considered, yet patient factors alone should not deny a patient from treatment.

All liver surgery centres in the Netherlands performed R-LR. Significant variation among hospitals and networks in the performance of R-LR was observed. The observed variability in practice could be concerning if it leads to undertreatment of patients. Several potential explanations could be proposed which may contribute for the observed practice variation. Patients with

**Table 3** Multivariable (imputed) Cox regression to assess factors associated with overall survival in patients who underwent repeat liver resection for colorectal liver metastases between 2014 and 2018 in the Netherlands

Factor	N	Multivariable		P-value
		aHR	95% CI	
<b>Sex</b>				
Male	475	1		
Female	258	0.82	0.67–1.00	0.052
<b>Charlson Comorbidity Index</b>				
CCI 0/1	557	1		
CCI 2+	178	1.15	0.93–1.43	0.201
<b>ASA score*</b>				
ASA 1/2	576	1		
ASA 3+	141	1.27	1.00–1.62	0.050
<b>Number of lesions</b>				
1–3	607	1		
>3	106	1.33	1.00–1.75	<b>0.046</b>
<b>Diameter of largest CRLM</b>				
<2 cm	241	1		
2–3 cm	184	1.20	0.95–1.52	0.128
3–4 cm	92	1.15	0.82–1.60	0.407
4–5 cm	42	0.92	0.58–1.44	0.697
≥5 cm	63	1.58	1.07–2.34	<b>0.023</b>
<b>Location of primary tumour</b>				
Colon	478	1		
Rectal	254	1.21	1.00–1.46	0.052
<b>Early recurrence</b>				
No	330	1		
Yes	125	1.11	0.81–1.52	0.496
<b>Extrahepatic disease</b>				
No	614	1		
Yes	104	1.60	1.25–2.04	<b>&lt;0.001</b>
<b>Major liver resection</b>				
No	596	1		
Yes	139	1.21	0.89–1.64	0.220
<b>Tumour margins</b>				
Negative	603	1		
Positive	95	1.42	1.09–1.85	<b>0.009</b>
<b>Tumour margins primary resection</b>				
Negative		1		
Positive		0.91	0.51–1.62	0.730

Variables were included when  $P < 0.10$  in univariate cox regression analysis. Variables not included in multivariate regression because  $P > 0.10$  were age, histopathological liver disease, type of hospital where treatment took place.

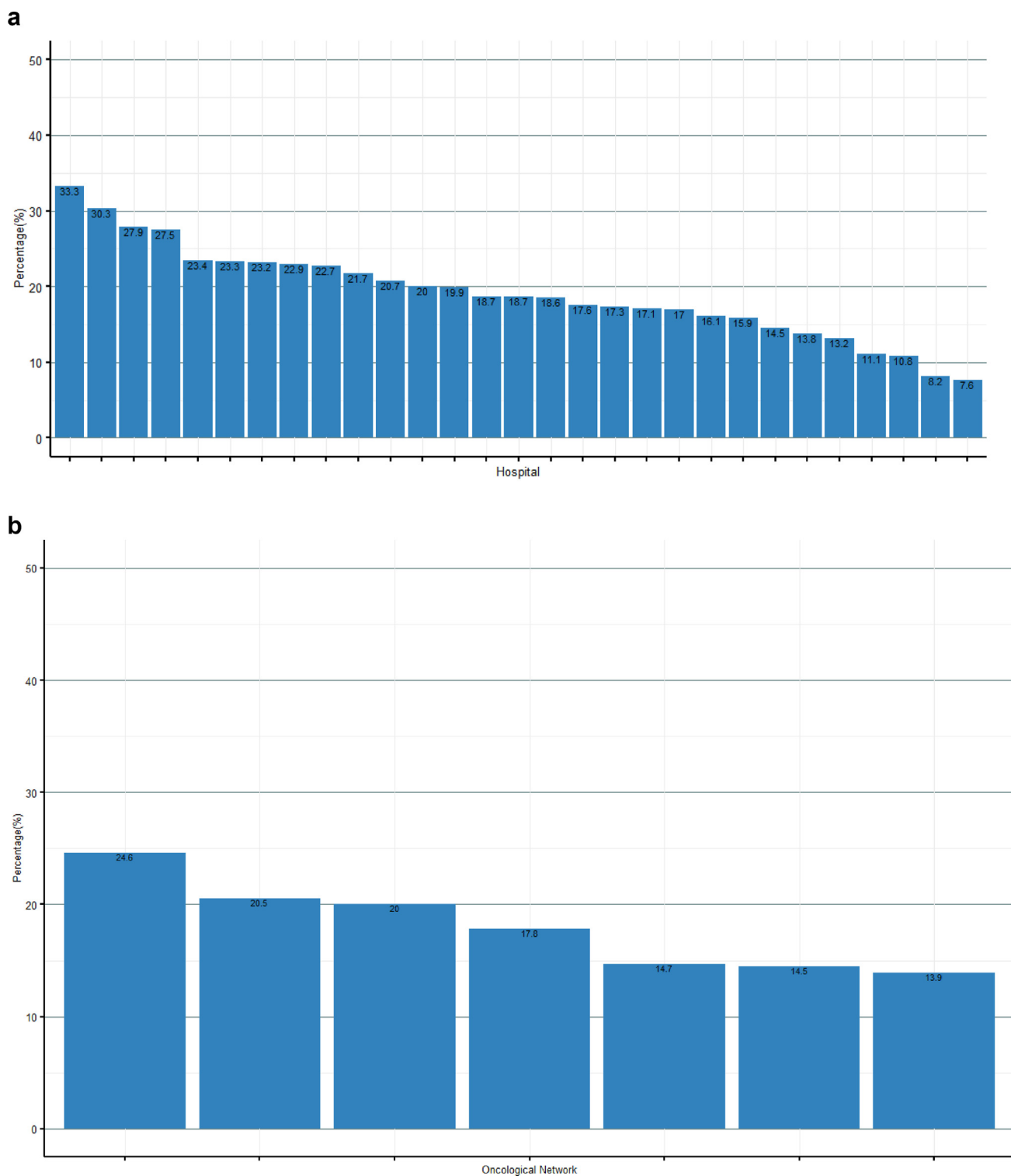
\* American Society of Anaesthesiologists (ASA) classification.

recurrent disease may receive alternative, non-surgical interventions such as percutaneous ablation and stereotactic radiotherapy.<sup>22,34</sup> Radiotherapy is not included in the current audit and registration of thermal ablation has only become mandatory since 2023. Consequently, it is possible that hospitals who proportionally undertake R-LR less frequently may lean towards performing more percutaneous thermal ablations for recurrent liver metastases. A prior study of our group highlighted significant hospital variation in the utilisation of combined liver resection and ablation, which may reflect different perspectives or availability of thermal ablation as a viable local treatment of (recurrent) colorectal liver metastases.<sup>35</sup> Additionally, parenchymal sparing approaches may allow for increased options for R-LR in case of recurrence.<sup>36</sup> Also, hospitals could refer patients who need R-LR to other hospitals within their oncological network. This does not explain the observed oncological network variation, assuming that most patients are referred within a network. Outcomes are discussed with almost all hospitals in an annual evaluation of the DHBA. In this session, it was concluded that further investigating the variability in repeat resection is warranted to offer all patients the best chances of long-term survival. In this session a future snapshot study was proposed which should address which patients were denied for liver surgery and whether other non-surgical local treatment options, such as thermal ablation and stereotactic radiotherapy may offer similar results.

Due to the absence of clear guidelines on resectability, treatment decisions for liver resection, in general, exhibit a considerable variability in decisions made by multidisciplinary teams (MDT). In the CAIRO V study significant disagreement was noted among members of the online expert panel with regard to resectability in patients with perceived unresectable CRLM in a single procedure.<sup>9</sup> The authors postulate that variability increases when MDTs have to decide on the preferred treatment for patients with recurrent liver metastases after primary resection. These MDTs vary in experience and preference, and patients may have less accessible metastases. The latter may lead to more non-surgical management. Availability of studies such as the PUMP-3 trial (NL71691.078.19), a phase 2 trial with hepatic artery infusion pump chemotherapy for recurrent liver-only metastases, may further increase variability in management. The most important message of the current study is that R-LR is has comparable postoperative results and is beneficial in selected patients and probably underused. It is important that all patients with recurrent metastases are discussed in an MDT and local treatment is considered and MDTs are trained to better understand recurrence and the potential treatment options and outcomes.

This study should be interpreted with several limitations. Data were obtained from a nationwide retrospective database, primarily used for auditing the quality of liver surgery. Therefore,





**Figure 2** (a) Hospital variation in performance of repeat liver resection for patients with colorectal liver metastases between 2014 and 2022. (b) Oncological network variation in performance of repeat liver resection for patients with colorectal liver metastases between 2014 and 2022

some specific patient variables or detailed information regarding the perioperative period were lacking. Furthermore, due to the GDPR limitations, it is currently impossible to link patient data when treated in different hospitals. Missing data on the timing of recurrent disease could bias results. Referral patterns for R-LR between centres (or even regions) could not be studied. Information about the primary colorectal tumour is captured in a separate audit, the Dutch Colorectal Cancer Audit (DCRA) and is also not linkable with data from the DHBA.

In conclusion, in patients selected for repeat hepatectomy short- and long-term outcomes are comparable to the initial liver resection. Repeat hepatectomy should be discussed as important therapeutic option for patients with recurrent liver metastases. Hospital and oncological network variability remain an important point of attention. Since repeat resection is a powerful tool to prolong survival in selected patients, the questions whether all eligible patients are currently considered for repeat resection and whether non-surgical alternatives lead to similar results remain and should be addressed.

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#### Conflicts of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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#### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.hpb.2024.02.014>.