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ORIGINAL ARTICLE

Factors associated with failure to rescue after liver resection and impact on hospital variation: a nationwide population-based study

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Abstract

Background: Failure to rescue (FTR) is defined as postoperative complications leading to mortality. This nationwide study aimed to assess factors associated with FTR and hospital variation in FTR after liver surgery.

Methods: All patients who underwent liver resection between 2014 and 2017 in the Netherlands were included. FTR was defined as in-hospital or 30-day mortality after complications Dindo grade ≥3a. Variables associated with FTR and nationwide hospital variation were assessed using multivariable logistic regression.

Results: Of 4961 patients included, 3707 (74.4%) underwent liver resection for colorectal liver metastases, 379 (7.6%) for other metastases, 526 (10.6%) for hepatocellular carcinoma and 349 (7.0%) for biliary cancer. Thirty-day major morbidity was 11.5%. Overall mortality was 2.3%. FTR was 19.1%. Age 65–80 (aOR: 2.86, CI:1.01–12.0, $p = 0.049$), ASA 3+ (aOR:2.59, CI: 1.66–4.02, $p < 0.001$), liver cirrhosis (aOR:4.15, CI:1.81–9.22, $p < 0.001$), biliary cancer (aOR:3.47, CI: 1.73–6.96, $p < 0.001$), and major resection (aOR:6.46, CI: 3.91–10.9, $p < 0.001$) were associated with FTR. Postoperative liver failure (aOR: 26.9, CI: 14.6–51.2, $p < 0.001$), cardiac (aOR: 2.62, CI: 1.27–5.29, $p = 0.008$) and thromboembolic complications (aOR: 2.49, CI: 1.16–5.22, $p = 0.017$) were associated with FTR. After case-mix correction, no hospital variation in FTR was observed.

Conclusion: FTR is influenced by patient demographics, disease and procedural burden. Prevention of postoperative liver failure, cardiac and thromboembolic complications could decrease FTR.

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Introduction

Major complications after liver surgery may lead to postoperative mortality and therefore adequate and early detection and management of these complications is essential.[1,2] Mortality after experiencing a major surgical complication has been called failure to rescue (FTR).[3–7] FTR is seen as a quality indicator that focusses on management of complications rather than on complications itself. For this reason, it is an important outcome to address when searching for measures to improve quality of care.

While some studies have reported on FTR after liver surgery, most studies focus on mortality, which is dependent of factors like pre-existing liver disease and extent of surgery. Postoperative mortality among patients who undergo liver resection for colorectal liver metastases (CRLM) or liver metastases from other tumour types has been described to be near 5%.[8–10] Mortality among patients with primary liver cancers such as hepatocellular carcinoma (HCC) and biliary cancer have been reported to be even higher, approximately 5–10% and 10–20% respectively.[11–14]

Improving complication management could lead to reducing postoperative mortality. Also, hospital and oncological network or regional variation has been associated with worse outcomes and higher costs.[15,16] Several studies on FTR have been performed but nationwide analysis of FTR rates and hospital variation in FTR after liver surgery are lacking. Also, it is unclear which patient demographics, disease burden and postoperative complications associated with occurrence of FTR. These leads can be a used to improve quality of care in liver surgery.

The aim of this study was to assess patient and disease characteristics as well as complications associated with FTR and to address possible existence of nationwide hospital variation in FTR.

Methods

This was a nationwide population-based study performed in the Netherlands. Several structural requirements for performing oncological care are established by SONCOS and endorsed by the Dutch Government and insurance companies.[17] These structural requirements for liver surgery include 24/7 availability of an interventional radiologist, two hepatobiliary surgeons, minimal procedural hospital volume requirements for liver resection (at least 20 liver resections per centre have to be performed annually for any indication) and participation in the Dutch Hepato Biliary Audit (DHBA). All patients should be assessed in a preoperative multidisciplinary team meeting before proceeding to surgery. Data was collected from the DHBA, the mandatory audit in which all hospitals in the Netherlands performing liver surgery register all liver resections.[18] Data verification was performed to provide insight in completeness and accuracy of the DHBA when compared to the Dutch Cancer Registry.[19] No ethical approval was needed under Dutch law as the DHBA is part of the Dutch Inspectorate of health care and the dataset is anonymized.

Patient selection

All patients who underwent liver resection for primary or secondary liver tumours between the 1st of January 2014 and the 31st of December 2017 in the Netherlands were included. Patients were excluded if no date of birth, date of surgery or type of tumour could be obtained. Patients who underwent thermal ablation only were also excluded from the study.

All hospitals performing liver resection in the Netherlands were included in the between hospital variation analysis of FTR. Oncological network variation in FTR was assessed. Oncological networks are regional collaborations between hospital performing oncological care in the Netherlands.[20]

Outcomes

Main outcome was Failure to Rescue (FTR). Failure to rescue was defined as in-hospital or 30-day mortality after first experiencing 30-day major morbidity. The nominator was defined as all patients who died after experiencing a major complication. The denominator includes all patients who experienced major morbidity. Major morbidity was defined as a complication grade 3a or higher according the Dindo classification, within 30 days of the surgical procedure.[21] Mortality was defined as death during hospitalization or within 30 days of the surgical procedure.

Surgical complications (bile leakage, postoperative haemorrhage, liver failure defined according the International Study Group of Liver Surgery, deep and superficial surgical site infections). Thromboembolic and cardiopulmonary complications were also scored according the Dindo classification within 30 days of the surgical procedure.[22]

Variables

Several variables were assessed that influenced occurrence of FTR using multivariable logistic regression. These included sex, age, American Society of Anesthesiologist (ASA) classification, Body Mass Index (BMI), comorbidity scores classified according to the Charlson Comorbidity Score (CCI), classification of liver parenchyma, earlier liver surgery and diameter of the largest tumour before the initiation of tumour-specific treatment. Treatment characteristics included use of preoperative chemotherapy, major liver resection, and hospital where treatment took place which was either a tertiary referral center or regional hospital. Major liver resection was defined as resection of three or more Couinaud segments.[23] Annual hospital volume was calculated as total number of liver resections per hospital per year and categorized <20, 20–39, 40–59, 60–79 and > 80.

Statistical analysis

Distribution of data was assessed using histograms and box plots. Normally distributed continuous data were presented as mean with standard deviation. Non-normally distributed data were presented as median with interquartile ranges (IQR). Categorical data were presented as frequency accompanied by percentage.

Table 1 Baseline characteristics for patients who underwent liver resection between 2014 and 2017 in the Netherlands

Factor		Overall	30-day morbidity	30-day mortality	FTR
		N = 4961 (%)	N = 570 (%)	N = 113 (%)	N = 109 (%)
Sex					
	Male	2986 (60)	388 (68)	79 (70)	77 (71)
	Female	1959 (40)	182 (32)	34 (30)	32 (29)
	Missing	16 (0)	0 (0)	0 (0)	0 (0)
Age in years					
	<50	415 (8)	32 (6)	3 (3)	3 (3)
	50–64	1706 (35)	181 (32)	30 (27)	30 (28)
	65–80	2500 (51)	314 (55)	72 (64)	70 (64)
	≥80	328 (7)	43 (8)	8 (7)	6 (6)
	Missing	12 (0)	0 (0)	0 (0)	0 (0)
Charlson comorbidity index (CCI)					
	0/1	3791 (76)	401 (70)	75 (66)	72 (66)
	2+	1170 (24)	159 (30)	38 (34)	37 (34)
American Society of Anesthesiology (ASA) classification					
	I/II	3863 (78)	387 (68)	64 (57)	61 (56)
	III+	952 (19)	167 (29)	39 (43)	48 (44)
	Missing	146 (3)	16 (3)	0 (0)	0 (0)
Body mass index (BMI)	Mean (sd)	26.2 (4.4)	26.2 (4.3)	26.8 (4.5)	26.9 (4.5)
Liver resection in the past					
	No	4085 (82)	476 (84)	94 (83)	90 (83)
	Yes	718 (15)	80 (14)	19 (17)	19 (17)
	Missing	158 (3)	14 (3)	0 (0)	0 (0)
Histological diagnosis of liver parenchyma					
	Normal	2983 (60)	324 (57)	55 (49)	53 (49)
	Steatosis	748 (15)	102 (18)	24 (21)	24 (22)
	Steato-hepatitis	111 (2)	21 (4)	5 (4)	5 (5)
	Cirrhosis	163 (3)	27 (5)	13 (12)	13 (12)
	Sinusoidal dilatation	49 (1)	8 (1)	2 (2)	2 (2)
	Missing	907 (18)	88 (15)	14 (12)	12 (11)
Type of tumour					
	CRLM	3707 (75)	359 (63)	52 (46)	49 (45)
	Other liver metastases	379 (8)	38 (7)	5 (4)	4 (4)
	HCC	526 (11)	81 (14)	27 (24)	27 (25)
	Biliary cancer	349 (7)	92 (16)	29 (26)	29 (27)
Preoperative chemotherapy					
	No	3341 (67)	395 (69)	88 (78)	85 (78)
	Yes	1120 (23)	123 (22)	21 (19)	20 (18)
	Missing	500 (10)	52 (9)	4 (4)	4 (4)
Maximum diameter of largest tumour (mm)					
	<20	1235 (25)	111 (20)	17 (15)	15 (14)
	20–34	1387 (28)	126 (22)	19 (17)	17 (16)
	35–54	780 (16)	89 (16)	18 (16)	18 (17)
	>55	632 (13)	97 (17)	22 (20)	22 (20)

(*continued on next page*)

Table 1 (*continued*)

Factor		Overall N = 4961 (%)	30-day morbidity N = 570 (%)	30-day mortality N = 113 (%)	FTR N = 109 (%)
	Missing	927 (19)	147 (26)	37 (33)	37 (34)
Major liver resection					
	No	3565 (72)	295 (52)	30 (27)	27 (25)
	Yes	1235 (25)	257 (45)	80 (71)	79 (73)
	Missing	161 (3)	18 (3)	3 (3)	3 (3)
Surgical approach					
	Open	3747 (75)	478 (84)	102 (90)	98 (90)
	Laparoscopic	1027 (21)	73 (13)	8 (7)	8 (7)
	Missing	187 (4)	19 (3)	3 (3)	3 (3)
Type of hospital[a]					
	Regional hospitals	2317 (47)	211 (37)	30 (26)	27 (25)
	Tertiary referral centre	2644 (53)	359 (63)	83 (74)	82 (75)
Annual hospital volume					
	<20	125 (3)	11 (2)	0 (0)	0 (0)
	20–39	944 (19)	81 (14)	14 (12)	13 (12)
	40–59	804 (16)	83 (15)	12 (11)	12 (11)
	60–79	732 (15)	85 (15)	8 (7)	7 (6)
	≥80	2356 (48)	310 (54)	79 (70)	77 (71)

Percentages may not add up to 100% as they are rounded to the nearest full number.
[a] Type of hospital: tertiary referral center are defined as hospitals with highest expertise on oncologic surgery.

The chi-square test or fisher exact test were used to compare categorical data as appropriate.

Rates of FTR, 30-day major morbidity and 30-day mortality were assessed separately for hospital mortality quartiles. Hospitals were ranked based on mean mortality and then divided into quartiles.

Factors associated with FTR were assessed using univariable and multivariable logistic regression. All variables available were entered in the multivariable logistic regression. Backward selection was performed based on a $p < 0.100$ if necessary. Outcomes of both univariable and multivariable logistic regression were reported as adjusted odds ratios (aOR) with corresponding 95% confidence intervals (CI). Two-sided p-value <0.05 were considered statistically significant. Patient and tumour characteristics in the multivariable model were classified as case-mix factors.

Uncorrected hospital and oncological network variation in FTR were assessed and visualised using histograms. Case-mix corrected hospital and oncological network variation in FTR were assessed using funnel plots displaying Observed/Expected (O/E) Ratios. The case-mix represents patient demographics and disease burden of the population surgically treated in a hospital.[9] For case-mix correction, the expected FTR per hospital was calculated per patient using multivariable logistic regression with all case-mix variables available. All patients in a hospital or oncological network compose the expected number of FTR. The O/E Ratio was calculated by dividing the true number of FTR through the expected number of FTR. An O/E Ratio above 1 indicates a performance worse regarding FTR than expected and an O/E ratio below 1 indicates a better performance regarding FTR than expected. The 95% confidence intervals (CI) were calculated to indicate statistical significance in the case-mix corrected funnel plot.

Annual hospital volume was included in the analysis and was calculated as total number of liver resections for all indications in a hospital. Missing categories were included in the analyses if this exceeded 5% of the total included cohort.

Multicollinearity was assessed using the Variance Inflation Factor (VIF). A VIF of 2 or lower indicated that there was no multicollinearity. All analyses were performed in R version 3.2.2® (R Core Team (2018): A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria).

Results

In total 4961 patients were included of whom 3707 (74.4%) underwent liver resection for CRLM, 379 (7.6%) underwent liver resection of other metastases, 526 (10.6%) underwent liver resection for HCC and 349 (7.0%) underwent liver resection for

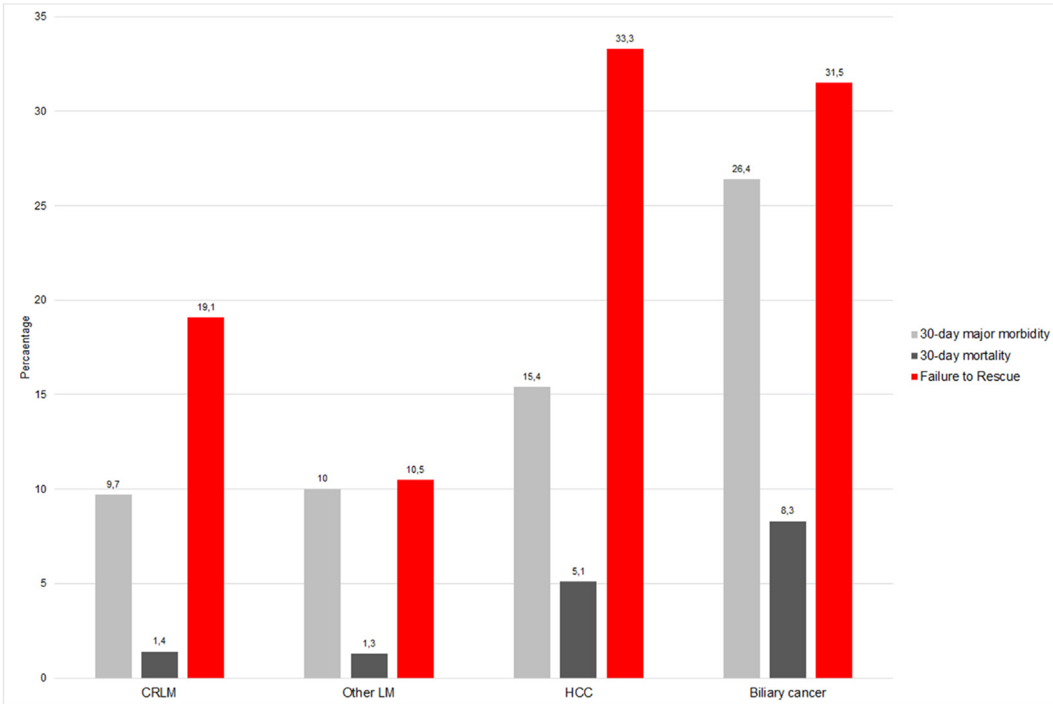

Figure 1 Thirty-day major morbidity, 30-day mortality and Failure to Rescue for primary and secondary liver tumours between 2014 and 2017 in the Netherlands.

biliary cancer (Table 1). Of patients who underwent liver resection for biliary cancer, 123 (35.2%) patients underwent resection of perihilar cholangiocarcinoma, 98 (28.1%) patients underwent resection of intrahepatic cholangiocarcinoma and 109 (31.2%) patients of gallbladder carcinoma. Biliary cancer locations of 19 patients were unknown.

Outcomes

Of all patients, 113 (2.3%) died in-hospital or within 30 days of surgery. Thirty-day major morbidity was observed in 570 (11.5%) patients. FTR occurred in 109 (19.1%) patients who experienced 30-day major morbidity. FTR was different between CRLM, other metastases, HCC and biliary cancer ($p < 0.001$) (Fig. 1, Supplementary Table 1).

Patient and tumour characteristics, and complications associated with FTR

Factors independently associated with FTR were age 65–80 (aOR 2.86, CI 1.01–12.0, $p = 0.049$), ASA classification 3 or higher (aOR 2.59, CI 1.66–4.02, $p < 0.001$), histopathological cirrhosis (aOR 4.15, CI 1.81–9.22, $p < 0.001$), biliary cancer as indication for liver resection (aOR 3.47, CI 1.73–6.96, $p < 0.001$), and major liver resection (aOR 6.46, CI 3.91–10.9, $p < 0.001$) (Table 2). No influence of annual hospital volume on FTR was observed.

Postoperative liver failure (aOR 26.9, CI 14.6–51.2, $p < 0.001$), cardiac complications (aOR 2.62, CI 1.27–5.29, $p = 0.008$) and thromboembolic complications (aOR 2.49, CI 1.16–5.22, $p = 0.017$) were independently associated with occurrence of FTR (Table 3).

Hospital and oncological network variation in FTR

Uncorrected FTR ranged from 0% to 50.0% between hospitals but after case-mix correction no hospitals performed significantly better or worse than expected (Fig. 2a & b). Uncorrected FTR ranged from 4.2% to 24.2% between oncological networks but after case-mix correction no oncological networks performed significantly better or worse than expected (Fig. 3a & b).

Discussion

This study found that FTR after liver resection is considerable in the Netherlands. Several patient and tumour characteristics were associated with FTR such as higher age, ASA classification 3, histopathological cirrhosis, liver resection for biliary cancer and major liver resection. Also, occurrence of postoperative liver failure, cardiac and thromboembolic complications were associated with FTR. The observed uncorrected variation in FTR between hospitals was attributable to patient demographics, disease burden and extent of resection in those hospitals and vanished after case-mix correction.

FTR rates using in hospital mortality after liver resection in the USA were described to vary between 11.8% and 16.8% in a cohort

Table 2 Univariable and multivariable logistic model of patient, tumour and surgical factors associated with Failure to Rescue in patients who underwent liver resection for primary and secondary liver tumours between 2014 and 2017 in the Netherlands

Factor		N	Univariable analysis			Multivariable analysis		
			OR	CI (95%)	p-value	aOR	CI (95%)	p-value
Sex					0.028			0.235
	Male	2986	1			1		
	Female	1959	0.63	0.41–0.94		0.76	0.47–1.19	
	Missing[a]	16						
Age in years					0.001			**0.048**
	<50	415	1			1		
	50–64	1706	2.46	0.87–10.3	0.139	1.95	0.67–8.33	0.281
	65–80	2500	3.96	1.47–16.2	0.020	2.86	1.01–12.0	**0.049**
	≥80	328	2.56	0.67–12.2	0.186	3.03	0.74–15.2	0.137
	Missing[a]	12						
Charlson comorbidity index (CCI)					0.011			0.243
	0/1	3791	1			1		
	2+	1170	1.69	1.12–2.50		1.32	0.83–2.06	
Body mass index			1.04	0.99–1.08	0.092	1.03	0.99–1.08	0.177
American Society of Anesthesiology (ASA) classification					<0.001			**<0.001**
	I/II	3863	1			1		
	III+	952	3.31	2.24–4.86		2.59	1.66–4.02	
	Missing[a]	146						
History of liver resection					0.463			
	No	4085	1					
	Yes	718	1.21	0.71–1.95				
	Missing[a]	158						
Histopathological liver disease[b]					<0.001			**0.016**
	Normal	2893	1			1		
	Steatosis	748	1.83	1.11–2.95	0.015	1.53	0.89–2.58	0.114
	Steato-hepatitis	111	2.61	0.89–6.06	0.055	2.54	0.81–6.59	0.076
	Cirrhosis	163	3.79	2.46–8.72	<0.001	4.15	1.81–9.22	**<0.001**
	Sinusoidal dilatation	49	2.35	0.38–7.88	0.245	1.85	0.27–7.21	0.441
	Missing	907	0.74	0.38–1.34	0.352	0.85	0.37–1.75	0.682
Type of tumour					<0.001			**0.003**
	CRLM	3707	1			1		
	Other LM	379	0.80	0.24–1.97	0.663	0.86	0.25–2.25	0.783
	HCC	526	4.04	2.47–6.47	<0.001	1.25	0.63–2.44	0.524
	Biliary cancer	349	6.77	4.17–10.8	<0.001	3.47	1.73–6.96	**<0.001**
Preoperative chemotherapy					0.013			0.057
	No	3341	1			1		
	Yes	1120	0.70	0.41–1.12	0.150	0.94	0.51–1.68	0.827
	Missing	500	0.31	0.09–0.74	0.022	0.16	0.01–1.10	0.074
Maximum diameter of largest tumour (mm)					<0.001			0.818
	<20	1235	1			1		
	20–34	1387	1.01	0.50–2.05	0.979	1.00	0.43–1.86	0.745
	35–54	780	1.92	0.96–3.89	0.064	1.18	0.57–2.48	0.656

Table 2 (*continued*)

Factor		N	Univariable analysis			Multivariable analysis		
			OR	CI (95%)	p-value	aOR	CI (95%)	p-value
	>55	632	2.83	1.52–5.81	0.001	1.27	0.63–2.63	0.521
	Missing	927	3.38	1.88–6.39	<0.001	1.27	0.64–2.61	0.401
Major liver resection					<0.001			**<0.001**
	No	3565	1			1		
	Yes	1235	8.95	5.83–14.2		6.46	3.91–10.9	
	Missing[a]	161						
Surgical approach					<0.001			0.118
	Open	3747	1			1		
	Laparoscopic	1027	0.29	0.13–0.57		0.56	0.24–1.15	
	Missing[a]	187						
Type of hospital[c]					<0.001			0.929
	Regional hospitals	2317	1			1		
	Tertiary referral hospital	2644	2.71	1.78–4.28		1.04	0.49–2.29	
Annual hospital volume					<0.001			0.210
	0–39	1069	1			1		
	40–59	804	1.23	0.55–2.73	0.607	0.81	0.32–1.96	0.636
	60–79	732	0.78	0.29–1.92	0.606	0.58	0.19–1.61	0.312
	≥80	2356	2.74	1.57–5.19	<0.001	1.31	0.51–3.31	0.569

Bold p-values indicate statistical significance (p<0.05)
Differences in outcomes between tumour types all had p-values <0.001.
[a] Missing not included in analyses based on relatively small group.
[b] History of liver disease containing liver cirrhosis, esophageal variceal disease, hepatorenal syndrome, liver failure, alcoholic liver disease, toxic liver disease (mild), (chronic) hepatitis or liver fibrosis.
[c] Type of hospital: tertiary referral center are defined as hospitals with highest expertise on oncologic surgery.

including 9874 patients from 2000 to 2010.[24] A recent study from Italy focussing on FTR within 90 days after resection of HCC observed an overall FTR rate of 19.2% which ranged between 28.6% in low volume centres and 5.1% in high volume centres.[25] In a German study using invoice data including 18,849 patients from 2009 to 2015 the in-hospital FTR rate was 28.9%.[26] Overall FTR rates of 19.1% in the Netherlands are therefore concordant with the literature. In these earlier studies a relationship between hospital volume and FTR was observed while no relationship between hospital volume and FTR was found in the current study. An earlier Dutch study on hospital volume and outcomes did not show any relationship. This may be explained by the fact that centralisation of liver surgery has taken place in the Netherlands.[8] This included both introduction of a required minimal annual hospital volume of 20 resections, centralisation of extended resections and resection of HCC in cirrhotic livers and biliary cancers in tertiary centres. FTR rates after HCC and biliary cancer resection in the Netherlands are high although literature is scarce regarding FTR in groups that underwent liver resection for these indications. It shows that these indications are different regarding disease and treatment characteristics than for example CRLM. However, improvement of FTR rates should be pursued as they are still considerable and during improvement focus should be on patients that undergo liver resection for HCC or biliary cancer.

In search of improvement of FTR rates, several prognostic factors were observed to be associated with FTR in the current study. Structural hospital characteristics such as hospital staffing and (surgeon) volume have been described to be associated with lower FTR.[27,28] In this study these factors could not be assessed due to lacking of these variables in the DHBA. However, patient demographics, disease burden and complications leading to FTR were assessed in the current study. In the USA, low hospital volume, age above 70, high comorbidity scores, primary hepatic malignancy and major liver resection were independently associated with FTR.[24] No influence of specific complications on FTR was assessed in the American study. In the Italian study on FTR after HCC resection only low centre volume was associated with FTR.[25] The current study confirms that patient factors such as higher age, ASA classification 3, histopathological cirrhosis and disease demographics such as liver resection for biliary cancer and major liver resection are risk factors for occurrence of FTR.

It should be stressed that in the current study occurrence of postoperative liver failure, cardiac and thromboembolic complications were precursors for FTR. Infectious complications

Table 3 Univariable and multivariable logistic model of complications associated with failure to rescue in patients who underwent liver resection for primary and secondary liver tumours between 2014 and 2017 in the Netherlands

Complication		N	Univariable analysis			Multivariable analysis		
			OR	CI (95%)	p-value	aOR	CI (95%)	p-value
Bile leakage					0.350			0.321
	No	4649	1			1		
	Yes	210	0.76	0.41–1.32		0.68	0.31–1.42	
	Missing[a]	102						
Postoperative haemorrhage					<0.001			0.072
	No	4793	1			1		
	Yes	60	4.30	1.99–9.25		2.61	0.90–7.37	
	Missing[a]	108						
Postoperative liver failure					<0.001			**<0.001**
	No	4760	1			1		
	Yes	101	29.1	16.6–52.8		26.9	14.6–51.2	
	Missing[a]	100						
Intra-abdominal infection					<0.001			**0.002**
	No	4518	1			1		
	Yes	339	0.37	0.23–0.57		0.39	0.21–0.71	
	Missing[a]	104						
Surgical site infection					0.005			**0.047**
	No	4671	1			1		
	Yes	186	0.29	0.11–0.64		0.37	0.13–0.92	
	Missing[a]	104						
Pneumonia					0.826			0.721
	No	4572	1			1		
	Yes	291	0.93	0.48–1.69		1.15	0.51–2.44	
	Missing[a]	98						
Cardiac complication					<0.001			**0.008**
	No	4692	1			1		
	Yes	166	2.64	1.50–4.53		2.62	1.27–5.29	
	Missing[a]	103						
Thromboembolic complication					<0.001			**0.017**
	No	4741	1			1		
	Yes	118	4.29	2.46–7.48		2.49	1.16–5.22	
	Missing[a]	102						

Bold p-values indicate statistical significance (p<0.05).
Differences in outcomes between tumour types all had p-values <0.001.
[a] Missing not included in analyses based on relatively small group.

such as intra-abdominal infection and surgical site infection were observed to be associated with a decreased FTR rate in this study. This was probably a result of selection-bias as patients without infectious complications more often had postoperative liver failure, cardiac complications and thromboembolic complications resulting in a negative association of infectious complications with FTR. Surgical teams should focus on preoperative patient selection as well as aggressive management of postoperative complications to prevent FTR and consider referral of high-risk patients to centres with the best pathways in place to treat complications adequately. This is particularly true for patients at risk for postoperative liver failure as in this study this proves to be the complication that poses greatest risk of FTR, most likely due to no effective treatment for liver failure apart from supportive measures. Risk assessment of potential liver failure should include preoperative volumetric assessment of the

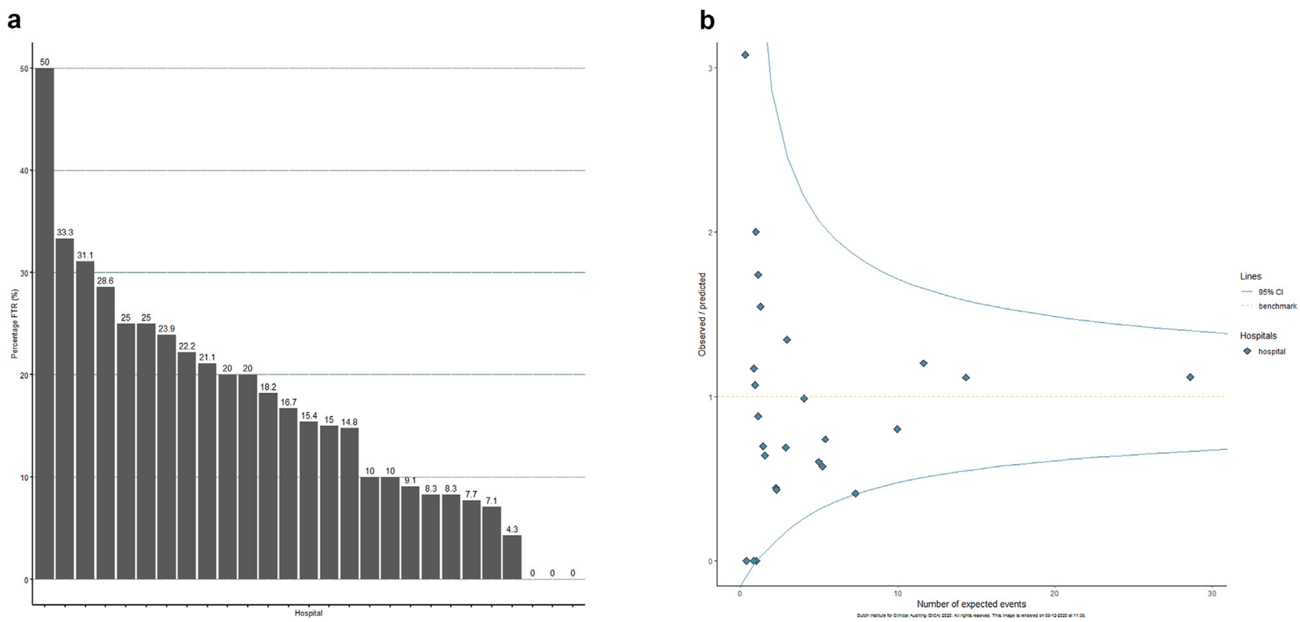

Figure 2 a. Unadjusted hospital variation in Failure to Rescue after liver surgery in the Netherlands between 2014 and 2017. b. Case-mix corrected hospital variation in Failure to Rescue after liver surgery in the Netherlands between 2014 and 2017.
Case-mix adjusted for these variables: sex, age, CCI, ASA classification, BMI, history of liver disease, preoperative chemotherapy, type of tumour, diameter of largest tumour, surgical approach, major liver resection, type of hospital and hospital volume

liver, hepatobiliary scintigraphy and liver biopsy of the future liver remnant in patients with extended resections and/or cirrhosis.[29,30] Patients' selection using these modalities and selection for preoperative portal vein embolization may decrease postoperative liver failure.[29,31] Also, aggressive management of complications in patients who are at risk of postoperative liver failure should be focussed on by screening for infections and subsequent aggressive management. Cardiac complications might be improved using preoperative patient optimalization through prehabilitation focussing on cardiopulmonary complications.[32,33] Decreasing thromboembolic complications after liver surgery can be achieved by using pharmacological and non-pharmacological prophylaxis and by early mobilisation.[34] Together, these measures can help surgical teams in decreasing complication and FTR rates.

Hospital and oncological network variation in uncorrected FTR were observed in the current study. However, this variation vanished after case-mix correction for patient demographics and disease burden.[9] This probably reflects the earlier described centralisation in the Netherlands with most patients with a high risk of complications treated in tertiary referral centres. However, further centralisation of patients who undergo extensive liver resection who are at risk of postoperative liver failure such as HCC patients with cirrhotic liver disease and perihilar cholangiocarcinoma patients could further decrease this specific complication leading to FTR. It has also been described that higher FTR rates are associated with higher costs.[35–37] Both reasons should encourage surgical teams to improve quality of care by decreasing FTR rates in the future. Several measures have been described in the current study to decrease FTR rates.

Limitations of this study include the use of the nationwide audit database for analysis. Most important were the lacking of 90-day morbidity and 90-day mortality in the DHBA as 90-day outcomes have been described a better proxy for true morbidity and mortality rates.[38–40] Also, use of the audit database might influence results of the study as this means absence of specific detailed information regarding preoperative, operative and postoperative outcomes. This includes detailed surgical information during surgery regarding vascular and biliary reconstructions. Specific grading, treatment of independent complications and primary cause of death and impact on mortality could not be assessed. This was particularly true for patients who experienced liver failure as no information was available regarding preoperative and postoperative pathway leading to liver failure. The benefit of the national audit data is, that the data includes all liver resections in the Netherlands and the data is reflective of true clinical practice.

In conclusion, FTR after liver resection is different between Dutch hospitals and is explained by patient demographics, disease burden and procedural type in those hospitals. Comparing FTR between hospitals therefore warrants case-mix correction. Surgical teams should focus on decreasing mortality after liver resection by

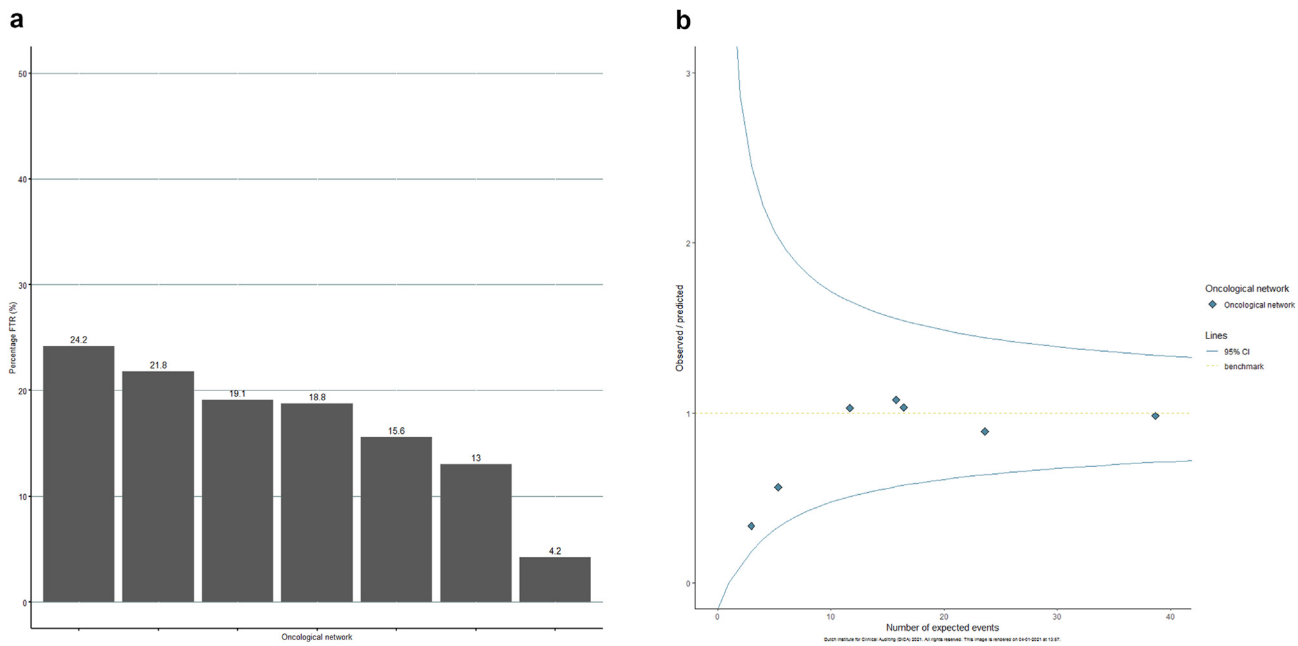

Figure 3 a. Unadjusted oncological network variation in Failure to Rescue after liver surgery in the Netherlands between 2014 and 2017. b. Case-mix corrected oncological network variation in Failure to Rescue after liver surgery in the Netherlands between 2014 and 2017. Case-mix adjusted for these variables: sex, age, CCI, ASA classification, BMI, history of liver disease, preoperative chemotherapy, type of tumour, diameter of largest tumour, surgical approach, major liver resection, type of hospital and hospital volume

decreasing FTR. This could be achieved through better patient selection by cardiopulmonary exercise with preoperative prehabilitation, preoperative liver function tests and improving postoperative care in patients that have higher risk for FTR.

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Declaration of interests

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.

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Appendix B. Supplementary data

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