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ORIGINAL SCIENTIFIC REPORT

Possible Preventable Causes of Unplanned Readmission After Elective Liver Resection, Results from a Non-academic Referral HPB Center

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Abstract

Introduction Unplanned readmission is a common event after liver resection, and it is a burden for both patients and healthcare policy makers. This study evaluates the incidence of and reasons for unplanned readmission after liver resection, in order to identify possible preventable causes.

Methods In this single-center cohort study, data from patients who underwent liver resection for both malignant and benign indications from 2001 to 2016 at our institute were collected from a database with prospective data. Readmissions were analyzed for their reasons and risk factors. Patients with general complaints with no specific complications were categorized as *failure to thrive*.

Results In 406 patients, the readmission rate was 11.6%. Most patients were readmitted because of failure to thrive (35%), deep and superficial surgical site infection (28%), or cardiopulmonary complications (15%). A multivariate analysis revealed that unplanned readmission was associated with the occurrence of complications during index admission—with an odds ratio of 4.69 (CI 2.41–9.12, $p < 0.001$).

Conclusion Readmission occurs in more than 1 in 10 patients after liver resection, and it is associated with a complicated course during index admission. One-third of readmissions occur because of failure to thrive and might be preventable. Future research in strategies to reduce readmission rates should focus on both the prevention of complications during index admission and programs at the interface between primary and secondary care.

Introduction

Reported unplanned hospital readmission rates after liver resection are between 6 and 19% [1–7]. Unplanned readmission is a significant burden for patients, their families, and their caregivers. Moreover, readmissions are a burden in terms of healthcare costs and capacity because most of the readmissions pass through the emergency department, and laboratory tests and diagnostic imaging tests are often performed. Also, as readmissions have been associated with established hospital surgical quality indicators, the readmission rate may serve as an underlying surrogate marker of quality of care [8].

Enhanced recovery programs are common practice in liver surgery nowadays, and they have resulted in reduced length of stay in hospital. The median length of stay differed from 5 days in enhanced recovery after surgery (ERAS) programs to 7.5 days in non-ERAS programs [9]. However, unplanned readmissions might be a downside, since complications may emerge only after the discharge.

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Enhanced recovery after surgery for liver resection patients is presumed to be safe and not associated with an increase in readmissions [10–12], although this increase is incidentally reported [13].

This single-center cohort study analyzed the readmission rate after liver resection in a Dutch non-academic regional referral center for hepato-pancreato-biliary surgery that introduced an ERAS program in 2011. The objective is to review readmission rates and to identify related risk factors and possible preventable causes of readmission in our center.

Methods

Study Design

This study analyzed all patients undergoing liver resection in the period from 2001 to 2016, and both malignant indications (primary tumors and metastasis) and benign indications were included. Furthermore, patients who underwent radiofrequency ablation (RFA) in the same procedure were also included. The following patients were excluded from the study: Those who received adjuvant therapy within 30 days after discharge (because readmission could be related to adjuvant therapy instead of the liver resection), trauma-related liver resections, and radical resection of gallbladder carcinoma and liver-invasive growth of extra hepatic tumors, as well as patients with planned readmission.

Data Collection and Analysis

Data were collected from a database containing prospectively collected patient, treatment, and outcome data from hospital and emergency room files. Patient characteristics included sex, age, diagnosis, and pathological results, and surgical details included resection type (wedge excision, segmental resection, and hemi-hepatectomy), open or laparoscopic surgery, operative time, blood loss, need for blood transfusion, and use of inflow occlusion. Furthermore, postoperative course included length of stay, the occurrence of a variety of complications, the occurrence of unplanned readmission, 30-day mortality, and 90-day mortality. Data collected on readmissions included discharge interval, length of stay of readmission, indication for readmission, and course of readmission. In addition, indications for readmission were categorized. Patients with no specific complication and without the need for invasive treatment were categorized as “failure to thrive.” In this category, patients may have one or more of the following symptoms: pain, nausea, vomiting, nutrition deficiency, dehydration, diarrhea, constipation, and general discomfort. In case of multiple readmissions, the cumulative readmission length was used. Readmissions and length of stay were also analyzed for changes over time within the cohort.

Morbidity was scored according to the Clavien–Dindo score [14]. Major morbidity was defined by a score of 3 or more. Moreover, in case of unplanned readmission, morbidity was scored for index admission (i.e., the primary or initial admission) and readmission separately.

Statistical Analysis

Continuous values were described as median and interquartile range (IQR) or range. Discrete data were described as total and frequency. A univariate analysis of factors with possible association with readmission was performed using the Mann–Whitney U test (continuous variables) and the chi-square test (discrete variables). Furthermore, logistic regression was used to identify independent risk factors for unplanned readmission. Readmissions were analyzed over time by dividing the study population in four quartiles of equal numbers of patients, which means the time frames of the quartiles are not necessarily equal, because of increasing volumes. Groups were compared by chi-square and Kruskal–Wallis test. p values under 0.05 were considered to be significant. For statistical analysis, SPSS version 24 (IBM, Armonk, NY) was used.

Ethical Approval

According to the Central Committee on Research involving Human Subjects (CCMO), this type of study does not require approval from an ethics committee in the Netherlands.

Results

For this analysis, 414 unique patients were eligible from a total of 462 primary liver resections performed at our institute between 2001 and 2016 (Fig. 1). Mortality during primary admission occurred in eight patients (1.9%), leaving 406 patients for possible readmission. Demographic, clinical, operative, and pathologic determinants are listed in Table 1.

Unplanned readmission occurred in 46 cases (11.3%). The median time from discharge to readmission was 7.5 (IQR 9) days, and 90% of readmissions occurred within 14 days after discharge (Fig. 2). Furthermore, the median length of readmission was 5 days, with a range of 1–50 days. No mortality occurred during readmission.

The reasons for readmission are presented in Table 2 and Fig. 3. The categories were failure to thrive (35%, $n = 16$); surgical deep and superficial site infection (28%,

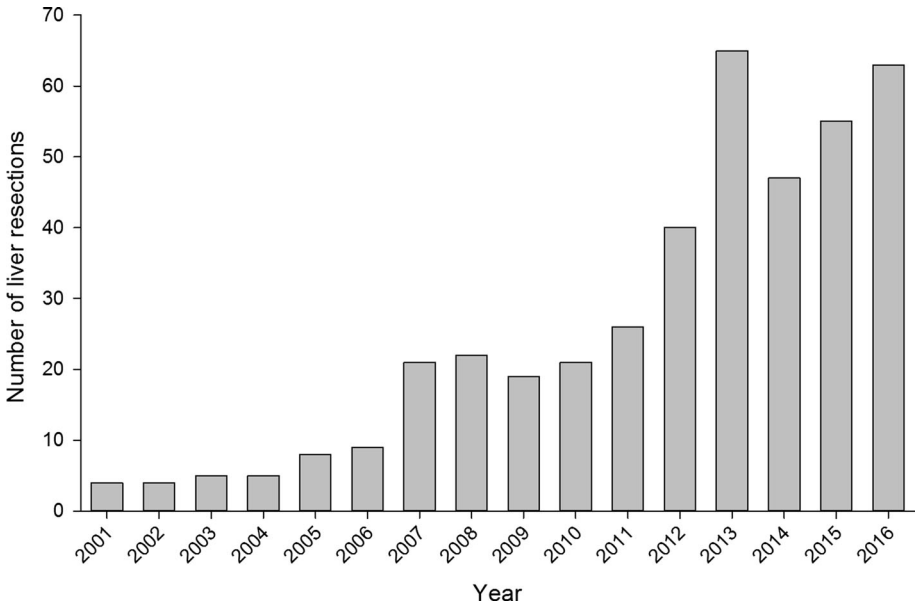

Fig. 1 Number of liver resections performed in our center from 2001 to 2016

Table 1 Demographic, clinical, operative, and pathologic determinants in patients with readmission and no readmission. *CRLM* colorectal liver metastasis, *C–D* Clavien–Dindo score. *p* values represent significance of difference between groups, and bold values indicate statistical significance

	Total $N = 406$	Readmission $N = 46$, 11,3%	No readmission $N = 360$	*p* value
Patient factors				
Male sex (*N* [%])	254 (62%)	29 (63%)	214 (59%)	0.639
Age (mean [SD])	62.5 (12.6)	62.7 (12.0)	62.5 (12.7)	0.922
Indication				0.580
CRLM	298 (73%)	30 (65%)	268 (74%)	
Metastasis other primary	30 (7%)	4 (8%)	26 (7%)	
Primary liver carcinoma	22 (5%)	3 (7%)	19 (5%)	
Benign	56 (14%)	9 (20%)	47 (13%)	
Operative factors				
Laparoscopic resection	46 (11%)	10 (22%)	35 (10%)	**0.018**
Operative time	120 (75)	120 (83)	120 (75)	0.967
Blood loss	400 (600)	400 (675)	400 (600)	0.907
Need for blood transfusion	50 (12%)	6 (13%)	44 (12%)	0.614
Major resection	149 (36%)	19 (41%)	130 (36%)	0.617
Use of inflow occlusion	186 (45%)	19 (41%)	173 (48%)	0.351
Morbidity index admission				
No complications (C–D 0–1)	334 (82%)	26 (56%)	308 (86%)	**< 0.001**
Complication C–D 2	26 (6%)	9 (20%)	17 (5%)	
Complication C–D 3	31 (7%)	8 (17%)	23 (6%)	
Complication C–D 4	10 (2%)	2 (4%)	8 (2%)	
Index hospitalization > 7 days	268	34 (74%)	234 (65%)	0.320
Index hospitalization > 10 days	357	27 (59%)	144 (40%)	**0.018**

$n = 13$); cardiopulmonary complications (15%, $n = 7$); bile leakage (9%, $n = 4$); complication associated with simultaneous procedure (7%, $n = 3$); other (4%, $n = 2$), which included unknown and early malignant progression; and cerebrovascular events (2%, $n = 1$). Patients with failure to thrive were generally treated with symptom relief, for

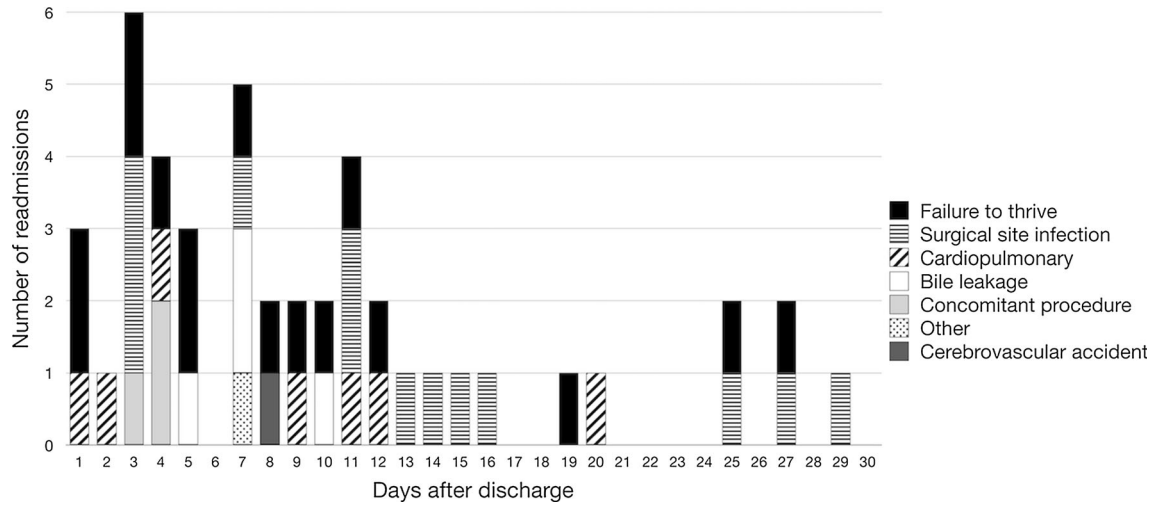

Fig. 2 Distribution of unplanned readmission in days after discharge and divided by indication for readmission

Table 2 Indications for readmission and the course of being readmitted, described as median and range

	Length of stay	Length of discharge	Readmission length of stay
Failure to thrive (n = 16)	8 (4–20)	7.5 (1–27)	3 (1–11)
Surgical site infection (n = 13)	11 (6–35)	13 (3–29)	7 (4–50)
Cardiopulmonary (n = 7)	16 (8–21)	9 (1–20)	9 (2–29)
Bile leakage (n = 4)	11 (9–20)	7 (7–10)	7 (2–22)
Complication associated with concomitant procedure (n = 3)	7 (7–10)	4 (3–4)	4 (2–16)
Other (n = 2)	16	7	10
Cerebrovascular accident (n = 1)	13	8	12

instance with pain medication, antiemetic medication, or laxatives.

The median length of stay of readmission of patients with failure to thrive was 3 days, compared to 8.5 days for patients with identified complications (p = 0.002). Cardiopulmonary complications were pneumonia, pulmonary embolism, cardiac decompensation, pleural effusion, and non-specified dyspnea. Simultaneous procedures included a hemi-colectomy and a gastrostomy because of nutrition problems in a case of a primary thyroid gland tumor. The characteristics of patients readmitted for failure to thrive and identified complication are displayed in Table 3.

The univariate analysis found no baseline characteristics significantly associated with unplanned readmission (Table 1). However, the occurrence of complications during index admission was different for the readmission group than for the non-readmission group (41% vs. 16%, $p < 0.001$). Of the readmitted patients, 59% had no complication during index admission, and of these patients, 62% had complications at or during readmission. Moreover, an index hospitalization of 10 days or more was more frequent in readmitted patients compared to non-readmitted patients (p = 0.018). Index hospitalization as a continuous variable was not correlated with readmission, nor was shortened hospitalization associated with readmission. Also, patients with laparoscopic resection had a higher incidence of unplanned readmission, compared to open resections (p = 0.005), without a difference in complication rate (26% vs. 31%, p = 0.40). Stepwise logistic regression with the parameters age, operative time, laparoscopy, blood loss, length of stay, and postoperative complications demonstrated that postoperative complication was the strongest independent predictive factor for readmission. In addition, laparoscopic resection was an independent predictor. The occurrence of complications was associated with unplanned readmission with an odds ratio of 4.69 (CI 2.41–9.12, $p < 0{,}001$). Moreover, major morbidity occurred more often during index admission in the group with readmission than in the group without readmission (32% vs. 11%, p = 0,006). Throughout the total period of admission and readmission, readmitted

Table 3 Readmissions for patients with identified complication and patients with failure to thrive. Bold values indicate statistical significance

	Defined complication $N = 30$	Failure to thrive $N = 16$	p value
Patient factors			
Male sex (N [%])	21 (70%)	8 (50%)	0.181
Age (mean [SD])	64.3 (10.4)	59.7 (14.8)	0.249
Indication			0.466
CRLM	19	11	
Metastasis other primary	4	0	
Primary liver carcinoma	2	1	
Benign	5	4	
Operative factors			
Laparoscopic resection	4 (13%)	6 (38%)	0.058
Operative time	125 (74)	110 (90)	0.474
Blood loss (mL)	500 (725)	125 (65)	**0.026**
Need for blood transfusion	5 (17%)	2 (13%)	0.708
Major resection	17 (57%)	2 (13%)	**0.004**
Use of inflow occlusion	12 (40%)	7 (44%)	0.975
Simultaneous colorectal resection	4 (13%)	4 (25%)	0.320
Morbidity index admission			0.201
Clavien–Dindo 0 to 1	17	10	
Clavien–Dindo 2	4	4	
Clavien–Dindo 3	7	1	
Clavien–Dindo 3	2	0	
Median index hospitalization	10 (6)	8 (8)	**0.042**
Index hospitalization > 7 days	26 (83%)	8 (50%)	**0.007**
Index hospitalization > 10 days	20 (65%)	7 (44%)	0.133
Length of readmission	8.5 (11)	3 (3)	**0.002**

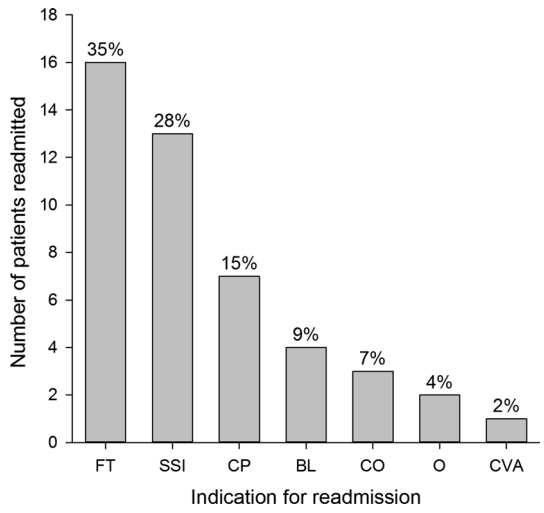

Fig. 3 Indications for readmission. *FT* failure to thrive, *SSI* (deep) surgical site infection, *CP* cardiopulmonary complications, *BL* bile leakage, *CO* complication associated with concomitant procedure, *O* other, and *CVA* cerebrovascular accident

patients had overall more major morbidity, compared to non-readmitted patients (50% vs. 8.6%, $p < 0.001$).

During the study period, the median length of stay decreased (Table 4): It was 11 days in the first quartile, 9 days in the second quartile, and 7 days in the third and fourth quartile ($p < 0.001$). In the fourth quartile, the readmission rate was the highest (18%). Moreover, in this quartile, the complication rate was similar to other quartiles, the amount of major liver resection was lower, and failure to thrive was the reason for readmission in 9 out of 18 patients.

Discussion

This study demonstrates that unplanned readmission after liver resection occurs in more than 1 in 10 patients (11.3%) and is associated with a complicated course during the index admission. One-third of the readmissions were because of failure to thrive, and this category is potentially preventable.

Table 4 Differences in various clinical characteristics between the four quartiles of the cohort. *p* values represent significance of difference between quartiles, and bold values indicate statistical significance

	Quartile 1 2001–2010 (n = 102)	Quartile 2 2010–2013 (n = 102)	Quartile 3 2013–2015 (n = 101)	Quartile 4 2015–2016 (n = 101)	p value
Readmission rate	13%	11%	4%	18%	**0.019**
Median index LOS (IQR)	10 (5)	9 (6)	7 (5)	7 (3)	**< 0.001**
Median total LOS (IQR)	11 (6)	10 (7)	8 (6)	8 (4)	**< 0.001**
Median total LOS readmitted patients (IQR)	25 (23)	18 (13)	14.5 (18)	13 (15)	0.073
Clavien–Dindo $\geq$ 3	18%	14%	12%	10%	0.378
Major resection	45%	42%	40%	27%	0.055
Simultaneous colorectal resection	5%	12%	6%	11%	0.228
Laparoscopy	1%	9%	15%	20%	**< 0.001**
Failure to thrive	1/13 (6%)	5/11(31%)	1/4 (6%)	9/18 (56%)	0.080
Invasive treatment during readmission	7/13	4/11	2/4	6/18	0.412

Several aspects of failure to thrive indicate that these readmissions might be avoidable. First, management requires, by definition, no invasive measures; however, patients were readmitted because their symptoms exceeded the capacity to thrive at home. Second, the length of readmission was short—significantly shorter than for patients with identified complications. Patients were managed with symptom relief, and most patients recovered in a few days. Finally, the length of stay of index admission in the failure-to-thrive group was shorter, possibly resulting in a longer interval to the first outpatient follow-up. Perhaps the management of this category of patients could be handled at home, but early identification is needed. The crucial issue is to distinguish complications from failure to thrive by adequate follow-up interventions. Narula et al [5] found a decrease in unplanned readmission from 14.5 to 6.5% after introducing a proactive outreach strategy consisting of contact by phone within 72 h after discharge. Complication rates did not differ; this supports the idea that some readmissions can in fact be prevented.

Previously, established factors associated with readmission are as follows: major hepatectomy, major postoperative complications, an index hospitalization longer than 7 days, greater blood loss, a blood transfusion within 72 h, and longer operative time [1–4, 15, 16]. Also, patient-related factors associated with readmissions were identified, and they include a higher American Society of Anesthesiologists (ASA) class and higher model for end-stage liver disease (MELD) score. Egger et al [17] developed a readmission risk score that includes these factors. We were only able confirm that the occurrence of (major) complications during index admission is associated with readmission. Furthermore, prolonged index hospitalization was associated with readmission, whereas the multivariate analysis indicated no independent relation.

Surprisingly, performing a laparoscopic resection was associated with readmission in this analysis. Laparoscopic liver surgery was introduced in our hospital in 2011, and in 5 years, only 46 patients underwent a laparoscopy. Given that this procedure was relatively new, the threshold for readmission in case of possible problems after discharge might have been lower. This is in line with the fact that most of the readmissions after laparoscopy were because of failure to thrive.

An important limitation of this study is that we did not record preoperative conditions and comorbidity. Preexistent comorbidity obviously cannot be ruled out as an important factor in readmission, as other studies were able to demonstrate comorbidity as a predictive factor [3]. Another limitation was the retrospective nature of our cohort. It is unlikely that readmissions were missed, because follow-ups were carried out with all patients at least once in our hospital.

Furthermore, the cohort covers a relatively long period. Our data did not demonstrate an evident trend in readmission over time; however, in the last quartile, a notable high readmission rate appeared. Interestingly, this is not accompanied by a higher rate of complications, and less major liver resections were performed. It can be argued that the high readmission rate in the fourth quartile is related to the implementation of ERAS in 2011 (the second quartile). However, the readmission rate in the third quartile, also after implementation of ERAS, is notably low. Furthermore, this study is not designed to evaluate the

ERAS protocol, and studies that were designed to review ERAS largely revealed no increase in readmission after implementation [10–12]. What stands out is that readmission caused by failure to thrive is high in this period: 9 out of 18 readmissions, which is 56% of total failure to thrive. This may be explained by more patients from other regions being treated in this period, who are more likely to be readmitted in case of failure to thrive, because of the longer traveling distance to our hospital. Finally, an explanation might be an increasing rate of laparoscopic procedures in the last quartile, and increased readmission rates might represent an early learning curve in laparoscopic liver surgery.

Future research should focus on possible preventive measures for readmission. A reduction in the complication rate would likely lead to a decrease in the readmission rate, possibly by centralization, higher caseloads for surgeons, prehabilitation programs, and strict ERAS implementation. In addition, it might be feasible to prevent readmission because of failure to thrive using adequate and proactive follow-up interventions. Proactive outreach strategies require a transmural approach. An intensive follow-up within the first week after discharge might reveal early signs of complications or failure to thrive, and this provides opportunities to take action before readmission occurs. Primary care providers could be trained to detect postoperative problems early after discharge. These strategies require close cooperation between surgery departments and primary care or home care providers. Patients should preferably not be discharged just before weekend days. During weekends, it might be harder to reach a specialist in case of problems after discharge, and patients may thus present themselves at the emergency department instead.

In conclusion, unplanned readmission is a common event after liver resection and is associated with a complicated course during index admission. Failure to thrive, surgical site infections, and cardiopulmonary complications account for 78% of readmissions. Failure to thrive after discharge might be—at least partly—prevented by introducing early follow-ups after discharge by transmural care arrangements.

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