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Graaff, M.R. de; Elfrink, A.K.E.; Buis, C.I.; Swijnenburg, R.J.; Erdmann, J.I.; Kazemier, G.; ... ; Dutch Hepato Biliary Audit Grp

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Defining Textbook Outcome in liver surgery and assessment of hospital variation: A nationwide population-based study

Michelle R. de Graaff [a, b, *], Arthur K.E. Elfrink [c], Carlijn I. Buis [b], Rutger-Jan Swijnenburg [c], Joris I. Erdmann [c], Geert Kazemier [c], Cornelis Verhoef [d], J. Sven D. Mieog [e], Wouter J.M. Derksen [f, g], Peter B. van den Boezem [h], Ninos Ayez [i], Mike S.L. Liem [j], Wouter K.G Leclercq [k], Koert F.D. Kuhlmann [l], Hendrik A. Marsman [m], Peter van Duijvendijk [n], Niels F.M. Kok [l], Joost M. Klaase [b], Cornelis H.C. Dejong [o], Dirk J. Grünhagen [d, 1], Marcel den Dulk [o, 1], for Dutch Hepato Biliary Audit Group, Collaborators

[a] Dutch Institute for Clinical Auditing, Scientific Bureau, Leiden, the Netherlands
[b] Department of Hepato-Pancreato-Biliary Surgery and Liver Transplantation, University Medical Center Groningen, Groningen, the Netherlands
[c] Department of Surgery, Cancer Centre Amsterdam, Amsterdam UMC, University of Amsterdam, Amsterdam, the Netherlands
[d] Department of Surgical Oncology, Erasmus MC Cancer Institute, Rotterdam, the Netherlands
[e] Department of Surgery, Leiden University Medical Center, Leiden, the Netherlands
[f] Department of Surgery, University Medical Center Utrecht, Utrecht, the Netherlands
[g] Department of Surgery, St Antonius Hospital, Nieuwegein, the Netherlands
[h] Department of Surgery, Radboud Medical Center, Nijmegen, the Netherlands
[i] Department of Surgery, Amphia Medical Center, Breda, the Netherlands
[j] Department of Surgery, Medical Spectrum Twente, Enschede, the Netherlands
[k] Department of Surgery, Máxima Medical Center, Veldhoven, the Netherlands
[l] Department of Surgery, Antoni van Leeuwenhoek – Dutch Cancer Institute, Amsterdam, the Netherlands
[m] Department of Surgery, OLVG, Amsterdam, the Netherlands
[n] Department of Surgery, Isala, Zwolle, the Netherlands
[o] Department of Surgery, Maastricht University Medical Center, Maastricht, the Netherlands

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ABSTRACT

Introduction: Textbook outcome (TO) is a composite outcome measure covering the surgical care process in a single outcome measure. TO has an advantage over single outcome parameters with low event rates, which have less discriminating impact to detect differences between hospitals. This study aimed to assess factors associated with TO, and evaluate hospital and network variation after case-mix correction in TO rates for liver surgery.

Methods: This was a population-based retrospective study of all patients who underwent liver resection for malignancy in the Netherlands in 2019 and 2020. TO was defined as absence of severe postoperative complications, mortality, prolonged length of hospital stay, and readmission, and obtaining adequate resection margins. Multivariable logistic regression was used for case-mix adjustment.

Results: 2376 patients were included. TO was accomplished in 1380 (80%) patients with colorectal liver metastases, in 192 (76%) patients with other liver metastases, in 183 (74%) patients with hepatocellular carcinoma and 86 (51%) patients with biliary cancers. Factors associated with lower TO rates for CRLM included ASA score ≥3 (aOR 0.70, CI 0.51–0.95 p = 0.02), extrahepatic disease (aOR 0.64, CI 0.44–0.95, p = 0.02), tumour size >55 mm on preoperative imaging (aOR 0.56, CI 0.34–0.94, p = 0.02), Charlson Comorbidity Index ≥2 (aOR 0.73, CI 0.54–0.98, p = 0.04), and major liver resection (aOR 0.50, CI 0.36–0.69, p < 0.001). After case-mix correction, no significant hospital or oncological network variation was observed.

* Corresponding author. Scientific Bureau, Dutch Institute of Clinical Auditing, 2333, AA, Leiden, the Netherlands.
E-mail address: m.degraaff@dica.nl (M.R. de Graaff).
[1] Equal author contribution (Senior).

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Conclusion: TO differs between indications for liver resection and can be used to assess between hospital and network differences.

1. Introduction

Clinical auditing is considered an essential instrument for quality assessment and improvement of care [1]. The Dutch Hepato Biliary Audit (DHBA) is a mandatory registry assessing the Dutch quality of liver surgery or thermal ablation using quality indicators [2]. Using DHBA-data, practice variation in treatment modalities is described previously [3,4].

Quality indicators typically focus on single outcome parameters, such as mortality and morbidity. While analysis of single outcome parameters enabled targeted interventions, it does not necessarily provide insight into the multidimensional aspects of the surgical care processes [5,6]. Furthermore, event rates of single outcome parameters can be low. For example, mortality after liver resection for colorectal liver metastases (CRLM), as registered in the DHBA, was 1.4% [7]. Consequently, single outcome parameters with low event rates have less discriminating impact to detect differences between hospitals and lack power to encourage improvements [7].

A multidimensional composite outcome indicator covering the entire surgical care process in a single indicator is 'Textbook outcome' (TO) [6,8,9]. TO is already implemented to evaluate certain other surgical procedures [6,8–12]. Multiple outcome parameters are combined in TO. When all predetermined conditions are achieved TO is accomplished and reflecting the chance for an uneventful hospitalisation. TO can provide comprehensive additional information for health professionals and patients [10,13]. Traditionally, TO has higher event rates and provides more power to detect differences between hospitals [6,12].

Several studies on TO in liver surgery have been performed. Still, a nationwide analysis of TO rates and hospital and oncological network variation with a validated case-mix model after liver resection for CRLM is lacking [14]. Case-mix adjustment seems obligatory to produce a reliable and valid comparisons, as a wide variety in localization of tumours within the liver exist and is accompanied by their own technical difficulties and postoperative outcomes. The aim of this study was to identify patient, disease, and treatment characteristics associated with TO, investigate the necessity of case-mix correction, and address the possible existence of nationwide hospital and oncological network variation in TO rates.

2. Methods

For this nationwide population-based study, data was retrieved from the DHBA. This mandatory audit registers all patients undergoing surgery with the intent for liver resection or thermal ablation in the Netherlands since 2013 [2]. For Dutch hospitals, a minimum required annual volume of 20 liver resections per centre is determined [15]. Seven oncological networks, formed by at least one tertiary referral centre and several regional hospitals, are established to optimize regional collaborations and decrease variation in treatment and outcomes [15,16].

Data verification for the DHBA was performed in 2017 to gain insight in completeness and accuracy of the data by comparing coverage to the number of registered liver resections in external data registry of the Dutch Cancer registry [17]. As data is registered anonymous, no ethical approval or informed consent was needed under the Dutch law.

2.1. Patient selection

All patients who underwent liver resection for CRLM, other liver metastases, hepatocellular carcinoma (HCC), and biliary cancer between January 1, 2019 and December 31, 2020 and registered in the DHBA were eligible for this study. Patients with missing essential data (date of surgery, date of discharge, date of birth, severe complications, mortality, readmission, resection margins, or tumour type) were considered lack of reporting and therefore excluded. Patients who underwent thermal ablation without surgical resection were also excluded.

2.2. Definitions

Severe complications were defined as complications within 30 days after primary surgery grade $\geq$3a according to the Clavien-Dindo classification [18]. Mortality was defined as death during hospitalisation or within 30 days after primary surgery. Readmission was defined as unplanned readmission within 30 days after discharge. For this manuscript R0 (microscopically negative) or R1 (microscopic residual tumour located <1 mm at resection margin) were considered adequate surgical resection margins.

2.3. Outcome

Main outcome in this study was TO. Relevant parameters for TO were nominated based on previous literature describing outcome parameters after liver surgery [19–21], previously published definitions of TO [5,22,23], and expert opinion. Relevant parameters were subsequently discussed in the scientific committee of the DHBA, consisting of 23 Dutch liver surgeons and interventional radiologists. According to the expert opinion of the scientific committee, TO was achieved when there was absence of severe postoperative complications, mortality, readmission, or prolonged length of stay (LOS) and when adequate surgical resection margins were obtained. Additionally, for the definition of prolonged LOS different cut-off values were calculated using the 50th, 75th, 85th, and 90th percentile of the total cohort for each indication of liver surgery (Table SC1). For each cut-off value an alternative TO was determined (Table SC1). After discussion in the scientific committee, prolonged LOS was defined as LOS > P_{90}.

2.4. Variables

Case-mix factors are non-modifiable patient and tumour characteristics, representing patient demographics and disease burden of the population treated in a hospital. Patient characteristics included sex, age, comorbidity scores according to the Charlson Comorbidity Index (CCI), American Society of Anesthesiologist (ASA) classification, Body Mass Index (BMI), histological classification of liver parenchyma, and history of liver surgery. Tumour characteristics included diameter of the largest tumour on preoperative imaging before tumour specific treatment, number of lesions, presence of extrahepatic disease or bilobar disease, and synchronous, metachronous, or recurrent diagnosis. Treatment characteristics included surgical approach (i.e., open or minimally invasive), use of preoperative chemotherapy, type of hospital

where treatment took place (regional hospital or tertiary referral centre), and major liver resection, defined as three or more adjacent Couinaud segments [24].

2.5. Statistical analysis

Descriptive statistics were used to compare patients with and without TO per indication for liver resection. Categorical variables were compared using χ^2 test and presented as numbers with percentages. Continuous variables were analysed using Student's *t*-test. Normally distributed variables were presented as mean with standard deviation, and skewed variables were presented as median with inter-quartile range (IQR).

Due to sample size, analysis for the association of case-mix factors and TO, and assessment of hospital and oncological network variation were exclusively performed for patients undergoing liver resection for CRLM. Univariate and multivariable logistic regression models were used to investigate possible associations between case-mix factors and TO. Univariate logistic regression was applied to study the associations between TO and selected patient, tumour, and treatment characteristics. For case-mix adjustment all available patient and tumour characteristics were used and entered in a multivariable logistic regression model. Missing items below 5% were excluded from analysis and when exceeding 5% analysed as separate groups. Based on the case-mix of all patients, the expected TO was calculated per patient using a multivariable logistic regression model. The expected (E) TO is the sum of the patients' estimated predicted probabilities for achieving TO. O/E ratios were calculated by dividing the observed (O) TO rates by the expected TO rates of the same hospital or oncological network. O/E ratios indicates the performance of a hospital or oncological network. A ratio higher than 1 indicates that a hospital or network performed above expectation. Ratios lower than 1 indicate that a hospital or network performed below expectation. O/E ratios were displayed using funnel plots with a sequence of 95% confidence intervals (CI). The 95% CI indicate statistical significance of the O/E ratio of one hospital or oncological network compared to the mean O/E ratio of all hospitals or oncological networks together.

Multicollinearity was tested through the Variance Inflation Factor (VIF) to test collinearity between the covariates. A VIF of 3 or more was the cut-off value indicating collinearity. All analyses were performed in R version 4.0.5. (R Core Team (2020). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria).

3. Results

In 2019 and 2020, a total of 2521 patients registered in the DHBA were eligible. Of these, 145 were excluded because of missing essential data. The final cohort consisted of 1711 (72%) patients with CRLM, 250 (11%) patients with other metastases, 247 (10%) patients with HCC, and 169 (7%) patients with biliary cancer. Of patients who underwent liver resection for biliary cancer, 68 (40%) patients underwent resection for perihilar cholangiocarcinoma, 71 (42%) patients for intrahepatic cholangiocarcinoma, and 25 (15%) patients for gallbladder carcinoma.

3.1. Textbook outcome rates

The overall proportion of patients achieving TO was 77%. TO was accomplished in 1380 (80.7%) patients with CRLM, in 192 (76.8%) patients with other liver metastases, in 183 (74.1%) patients with HCC, and 86 (51.2%) patients with biliary cancer. Most substantial decrease in TO was due to severe complications (Figure A1, Table SB1). Patient, tumour, and treatment characteristics of patients with and without TO are shown in table A1 and Table SA1. LOS at P_{90} corresponds with 12 days for CLRM and other metastases, 16 days for HCC, and 24 days for biliary cancer (Table SC1).

3.2. Factors associated with TO in patients with colorectal liver metastases

Factors independently associated with lower TO rates in patients with CRLM included ASA-score $\geq$3 (aOR 0.70, CI 0.51–0.95, $p = 0.02$), extrahepatic disease (aOR 0.64, CI 0.44–0.95, $p = 0.02$), tumour size >55 mm (aOR 0.56, CI 0.34–0.94, $p = 0.02$), CCI $\geq$2 (aOR 0.73, CI 0.54–0.98, $p = 0.04$), and major liver resection (aOR 0.50, CI 0.36–0.69, $p < 0.001$) (Table B1). Multicollinearity was not observed. Due to the number of events (n = 331) no restriction was needed.

The following case-mix factors were significantly different between hospitals: age, CCI $\geq$2, ASA score $\leq$3, histopathological parenchymal liver disease, history of liver resection, preoperative chemotherapy, resection $\geq$3 CRLM, bilobar disease, synchronous metastases, rectal primary tumour, extra hepatic disease and major liver resection. Table SD1 shows an overview in the range of mean percentages between hospitals.

3.3. Hospital variation in TO in patients with colorectal liver metastases

In 2019 and 2020, 23 hospitals performed liver resections in the Netherlands. Unadjusted TO rates for CRLM varied between hospitals, ranging from 65.7% to 92.9% (Figure B1). Expected percentage of TO per hospital varied between 76.6% and 85.7% (Figure SA1). When adjusted for all possible case-mix factors, O/E ratios ranged from 0.77 to 1.11. None of the hospitals performing liver surgery for CRLM had significant lower TO rates than expected. No significant variation was found among hospitals for achieving TO after resection for CRLM (Figure B2).

3.4. Oncological network variation in TO in patients with colorectal liver metastases

Between oncological networks, unadjusted TO rates for CRLM varied with a range of 78.3%–84.7% (Figure C1). Expected percentage of TO per oncological network varied between 80.8% and 85.6% (Figure SB1). After correction for case-mix factors, O/E ratios ranged from 0.96 to 1.02. After case-mix correction, no variation between oncological networks was observed for achieving TO in patients with CRLM (Figure C2).

4. Discussion

This nationwide population-based study showed that TO rates differed per indication for liver resection and allowed comparison per specific indication. Several patient and tumour characteristics were associated with worse TO rates. This study confirmed that adjustment for case-mix factors is necessary when comparing TO for liver surgery between hospitals or oncological networks, since variation in TO rates were not observed after case-mix correction.

Oncological liver resections are heterogeneous due to tumour localization, extent of liver resection, and divergent patient and tumour characteristics for distinct tumour types. For example,

patients with HCC more often have an impaired liver function due to cirrhosis, and a known risk factor for postoperative death is persistent jaundice in patients with hilar malignancy [25,26]. Consequently, this results in differences in TO rates for anatomical variations of liver resection and for different liver tumour types. Previous studies showed TO rates in liver or hepatopancreatic surgery, without further distinction in tumour type [14,23,27,28]. This hampers the translatability of TO in daily practice and makes hospital or oncological network comparison difficult. Differences in TO rates between current study and other studies were observed. This study found TO rates of 80% in CRLM compared with 68% earlier described [23]. For HCC, TO was reached in 74%, an international study found 62% [29]. For cholangiocarcinoma, previously described TO rates were 25%, while this study found 51% [13]. Differences in TO definitions cause discordant results. Possibly, differences in study populations (e.g., international multicentre databases vs. Dutch clinical audit data) or differences in case-mix factors also contributed to these discordant results.

TO should represent an ideal postoperative course [10]. Several definitions of TO for liver surgery have been proposed in prior studies. Overlapping parameters in proposed definitions included adequate tumour resection margins and absence of postoperative complications, readmission, mortality, and prolonged LOS [13,22,23]. However, there is no agreed definition on what these parameters constitute (e.g., prior studies defined prolonged LOS as > P_{50}, >P_{75}, or >4–9 days) [13,23,29]. Thereby, previous studies proposed to include absence of intraoperative incidents of grade ≥2 and blood transfusion. Both not registered in the DHBA and thus could not contribute to our TO definition [13,23]. Other proposed parameters included reinterventions and bile leakage grade B, which commonly requires radiologic or endoscopic interventions [23,30]. In our definition, reinterventions are captured by Clavien-Dindo grade 3 [18]. Altogether, proposed parameters for the definition of TO in this study are mostly accordant with previous studies, yet definitions for LOS and adequate resection margins differ.

Embedding LOS in the definition of TO is under discussion due to described variation in LOS across nations, explained by variability in cultural norms, paying schemes, and availability of home care nursing [5,10,13,31]. Nevertheless, LOS is frequently used to assess quality of liver surgery and is strongly associated with postoperative complications [32,33]. Of note, ageing of patients who underwent liver resection increases the chance of a complicated course, mainly due to non-liver specific complications, which eventually increases LOS [34]. Furthermore, one could hypothesize that if patients experience a prolonged LOS regardless of the cause this is not their ideal postoperative outcome. In prior studies TO rates were relatively low compared with other single outcomes indicators used to define quality of liver surgery, and TO was most frequently not accomplished due to prolonged LOS [5,14,22,23]. Although LOS is important, it should not exceed importance over mortality or severe complications. Since LOS is dynamic, a relative cut-off for prolonged LOS is required to construct a sustainable definition for TO. For these reasons, we proposed the definition of prolonged LOS as LOS > P_{90}.

Compared to other TO definitions, our definition incorporates R1 resections margins. When feasible, tumour-free resection margins should be the goal. However, R1 resection is considered adequate because this could be intentional (e.g., metastasis adjacent to major vascular or biliary structure) or may be caused by the chosen resection technique (e.g., Cavitron Ultrasonic Surgical Aspirator) and is no longer a technical error [35,36]. Furthermore, a previous study showed that R1 resection was no predictive value for overall and disease-free survival in patients with CRLM treated with neoadjuvant chemotherapy [37]. For cholangiocarcinoma and HCC, previous studies showed that resection margin did not influence overall survival as long as complete clearance is achieved [38–40]. Therefore authors include R1 resection margins in the definition of TO.

This study explored patient, tumour, and treatment-related factors associated with not achieving TO after liver resection for CRLM. In line with our result, a previous study designated ASA-score and major hepatectomy as the most important case-mix variables for mortality and morbidity after liver resection for CRLM and also showed that extrahepatic disease was associated with 30-day mortality [7]. Görgec et al. found that tumour size was associated with not achieving TO for all liver resections. They found that ASA-score, extend of resection, tumour type, and previous abdominal surgery were associated with worse TO rates after laparoscopic liver resection. Their results mainly correspond with the current study despite the different TO definition and without stratification for tumour type [23]. In previous studies, higher CCI scores were found to be a risk factor for developing complications after liver resection and in elderly higher CCI scores were predictive for mortality after surgery [34,41]. Outcomes of this study could help surgical teams provide insight into potential risk factors and can assist healthcare providers in identifying high-risk patients and taking measurements to improve treatment of these patients, which consequently improves TO.

Observed hospital and oncological network variation in uncorrected TO rates diminished after adjustment for case-mix factors. No hospital or oncological network performed better or worse than expected. Nonetheless, individual hospital differences in TO rates are considerable. The discriminative effect of TO among oncological networks in the Netherlands is limited. Low between-network variability could possibly be explained by improved referral patterns within networks, improving collaboration between hospitals, and decreased variability in case-mix outcomes, which is described in a recent study investigating the Dutch oncological networks for liver surgery [16]. We showed that case-mix adjustment leads to reduction in bias and is obligated to make a reliable comparison for TO between hospitals or oncological networks [42].

The ultimate goal of clinical auditing is to improve healthcare [1]. Typically, results of single outcome parameters would be compared against benchmarked criteria. Results of this study provide more insight into the use of a composite outcome measure to compare quality of surgical care after liver resections. However, in TO the unique influence of different parameters is not taken into account. TO as a composite quality indicator can be embedded in the DHBA and other clinical audits in addition to single outcome measures without replacing them, whereby hospitals receive information on their case-mix adjusted TO rates in order to improve the quality of care.

Limitations of this study include the design. As a clinical audit database was used for analysis, not all detailed parameters were available, possibly limiting profound causal analysis for not reaching TO and hampers an adjustment for all potential confounders. Furthermore, 90—day, extent of R1 resection, oncological outcomes and patient-related outcomes are not registered in the DHBA and therefore this study could not account for these factors in the definition of TO. Due to sample size in this study, only in-depth analyses for TO of patients with CRLM could be performed.

5. Conclusion

In conclusion, TO captures different aspects of the surgical care process in a single outcome measure and gives a more reliable representation of quality of care for liver surgery. TO rates are different between indications for liver resection. This study showed TO is a quality measure which could assess between hospital or oncological network variation in liver surgery, although this requires case-mix adjustment. .

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Michelle R. de Graaff: Conceptualization, Data curation, Formal analysis, Writing – original draft. **Arthur K.E. Elfrink:** Conceptualization, Data curation, Formal analysis, Writing – review & editing. **Carlijn I. Buis:** Conceptualization, Data curation, Formal analysis, Writing – review & editing. **Rutger-Jan Swijnenburg:** Conceptualization, Data curation, Writing – review & editing. **Joris I. Erdmann:** W, Conceptualization, Data curation, Writing – review & editing. **Geert Kazemier:** Conceptualization, Data curation, Writing – review & editing. **Cornelis Verhoef:** Conceptualization, Data curation, Writing – review & editing. **J. Sven D. Mieog:** Conceptualization, Data curation, Writing – review & editing. **Wouter J.M. Derksen:** Conceptualization, Data curation, Writing – review & editing. **Peter B. van den Boezem:** Conceptualization, Data curation, Writing – review & editing. **Ninos Ayez:** Conceptualization, Data curation, Writing – review & editing. **Mike S.L. Liem:** Conceptualization, Data curation, Writing – review & editing. **Wouter K.G Leclercq:** Conceptualization, Data curation, Writing – review & editing. **Koert F.D. Kuhlmann:** Conceptualization, Data curation, Writing – review & editing. **Hendrik A. Marsman:** Conceptualization, Data curation, Writing – review & editing. **Peter van Duijvendijk:** Conceptualization, Data curation, Writing – review & editing. **Niels F.M. Kok:** Conceptualization, Data curation, Writing – review & editing, Formal analysis, Supervision. **Joost M. Klaase:** Conceptualization, Data curation, Writing – review & editing, Formal analysis, Supervision. **Cornelis H.C. Dejong:** Conceptualization, Data curation, Writing – review & editing, Formal analysis, Supervision. **Dirk J. Grünhagen:** Conceptualization, Data curation, Writing – review & editing, Formal analysis, Supervision. **Marcel den Dulk:** Conceptualization, Data curation, Writing – review & editing, Formal analysis, Supervision. **Marc G.H. Besselink:** Conceptualization, Data curation, Writing – review & editing. **Eric. R Manusama:** Conceptualization, Data curation, Writing – review & editing. **Eric J.T. van Belt:** Conceptualization, Data curation, Writing – review & editing. **Koop Bosscha:** Conceptualization, Data curation, Writing – review & editing. **Maarten Vermaas:** Conceptualization, Data curation, Writing – review & editing. **Steven J. Oosterling:** Conceptualization, Data curation, Writing – review & editing. **Marieke T. de Boer:** Conceptualization, Data curation, Writing – review & editing. **Andries E. Braat:** Conceptualization, Data curation, Writing – review & editing. **Jeroen Hagendoorn:** Conceptualization, Data curation, Writing – review & editing. **Gijs A. Patijn:** Conceptualization, Data curation, Writing – review & editing. **Frederik J.H. Hoogwater:** Conceptualization, Data curation, Writing – review & editing. **N. Tjarda van Heek:** Conceptualization, Data curation, Writing – review & editing. **Esther C.J. Consten:** Conceptualization, Data curation, Writing – review & editing. **Quintus Molenaar:** Conceptualization, Data curation, Writing – review & editing. **Otto M. van Delden:** Conceptualization, Data curation, Writing – review & editing. **Christiaan van der Leij:** Conceptualization, Data curation, Writing – review & editing. **Adriaan Moelker:** Conceptualization, Data curation, Writing – review & editing. **Warner Prevoo:** Conceptualization, Data curation, Writing – review & editing. **Thomas M. van Gulik:** Conceptualization, Data curation, Writing – review & editing. **Mark C. Burgmans:** Conceptualization, Data curation, Writing – review & editing. **Wouter W. te Riele:** Conceptualization, Data curation, Writing – review & editing.

Declaration of competing interest

All authors declare no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejso.2022.06.012.

Table A.1
Baseline characteristics and achievement of Textbook Outcome per type of tumour of patients who underwent a liver resection between 2019 and 2020 in the Netherlands.

TABLE A1	**CRLM**			**Other Metastases**			**HCC**			**Biliary cancer**			**Total**		
FACTOR	TO N = 1380	No TO N = 331	p-value	TO N = 192	No TO N = 58	p-value	TO N = 183	No TO N = 64	p-value	TO N = 86	No TO N = 82	p-value	TO N = 1841	No TO N = 535	p-value
Sex			0.65			0.69			**0.04**			0.88			0.75
Male(%)	910 (66)	211 (63)		85 (44)	28 (48)		107 (59)	47 (73)		45 (52)	41 (50)		1147 (62)	327 (61)	
Missing	1 (0.1)	0		0	0		0	0		0	0		1 (0.1)	0	
Age (years)			0.23			0.69			0.71			0.85			0.23
<50	112 (8)	26 (8)		37 (19)	9 (16)		23 (13)	10 (16)		9 (11)	9 (11)		181 (10)	54 (10)	
50–64	557 (40)	115 (35)		73 (38)	24 (41)		43 (23)	13 (20)		27 (31)	28 (34)		700 (38)	180 (34)	
65–80	614 (45)	161 (48)		77 (40)	22 (38)		99 (54)	37 (58)		42 (49)	35 (43)		832 (45)	255 (48)	
>80	97 (7)	29 (9)		5 (3)	3 (5)		18 (10)	4 (6)		8 (9)	10 (12)		128 (7)	46 (8)	
Charlson Comorbidity Index (CCI)			0.08			0.51			0.20			1			0.16
CCI 0/1	881 (64)	194 (59)		97 (51)	28 (48)		73 (40)	15 (23)		49 (57)	47 (57)		1100 (60)	284 (53)	
CCI 2+	499 (36)	137 (41)		95 (49)	30 (52)		110 (60)	49 (77)		37 (43)	35 (43)		741 (40)	251 (47)	
BMI *			0.51			0.74			0.52			0.70			0.21
Mean(SD)	26.5 (4.4)	26.3 (4.6)			25.6 (3.9)			26.5 (5.5)			25.2 (4.2)		26.4 (4.4)	26.1 (4.6)	

Table A.1 (*continued*)

TABLE A1	**CRLM**			**Other Metastases**			**HCC**			**Biliary cancer**			**Total**		
FACTOR	TO N = 1380	No TO N = 331	p-value	TO N = 192	No TO N = 58	p-value	TO N = 183	No TO N = 64	p-value	TO N = 86	No TO N = 82	p-value	TO N = 1841	No TO N = 535	p-value
				25.4 (4.55)			27.0 (4.6)			25.5 (4.64)					
Missing	14 (1)	1 (0.3)		0 (0)	1 (2)		2 (1)	1 (2)		0 (0)	1 (1)		16 (2)	4 (1)	
ASA Score*			**0.01**			**0.005**			0.31			0.38			**<0.001**
ASA 1/2	992 (72)	214 (65)		145 (76)	32 (55)		101 (55)	30 (47)		60 (70)	51 (62)		1298 (71)	327 (61)	
ASA 3+	388 (28)	117 (35)		47 (24)	26 (45)		82 (45)	34 (53)		26 (30)	31 (38)		543 (29i)	208 (39)	
History of liver resection			0.84			0.87			0.53			0.49			0.15
Yes	297 (22)	69 (21)		10 (5)	4 (7)		15 (8)	3 (5)		2 (2)	0 (0)		324 (18)	76 (14)	
Histopathology liver parenchyma **			**0.002**			0.11			0.69			0.17			**0.04**
Normal liver	1018 (74)	230 (69)		137 (71)	38 (65)		67 (37)	24 (38)		60 (70)	57 (70)		1282 (70)	349 (65)	
Steatosis	266 (19)	59 (18)		23 (12)	14 (24)		50 (27)	20 (31)		11 (13)	8 (10)		350 (19)	101 (19)	
Other	42 (3)	13 (4)		8 (4)	1 (2)		63 (34)	20 (31)		5 (6)	12 (14)		118 (6)	46 (9)	
Missing	54 (4)	29 (9)		24 (13)	5 (9)		3 (2)	0 (0)		10 (12)	5 (6)		91 (5)	39 (7)	
Preoperative Chemotherapy			**<0.001**			**0.02**			1			0.97			0.43
Yes	391 (28)	129 (39)		51 (27)	7 (12)		2 (1)	1 (2)		3 (4)	2 (2)		447 (24)	139 (26)	
Missing	42 (3)	12 (4)		7 (4)	0 (0)		4 (2)	0 (0)		15 (17)	9 (11)		68 (4)	21 (4)	
Number of lesions			**<0.001**			0.28			0.73						**<0.001**
1	619 (45)	118 (36)		109 (57)	26 (45)		143 (78)	53 (83)		–	–		871 (47)	197 (37)	
2	264 (19)	58 (18)		36 (19)	9 (15)		26 (14)	8 (12)		–	–		326 (18)	75 (14)	
3	148 (10)	41 (12)		16 (8)	7 (12)		3 (2)	2 (3)		–	–		167 (9)	50 (9)	
4	107 (8)	18 (5)		6 (3)	3 (5)		3 (2)	0 (0)		–	–		116 (6)	21 (4)	
5	93 (7)	38 (11)		6 (3)	1 (2)		3 (2)	1 (2)		–	–		102 (5)	40 (8)	
>5	110 (8)	41 (12)		8 (4)	4 (7)		2 (1)	0 (0)		–	–		120 (7)	45 (8)	
Missing	39 (3)	17 (5)		11 (6)	8 (14)		3 (2)	0 (0)		–	–		139 (8)	107 (20)	
Maximum diameter largest tumour (mm)			**<0.001**			**0.01**			0.22			0.65			**<0.001**
<20	415 (30)	66 (20)		57 (30)	7 (12)		21 (11)	4 (6)		12 (14)	9 (10)		505 (27)	78 (16)	
20–34	446 (32)	97 (29)		52 (27)	14 (24)		43 (24)	10 (16)		19 (22)	23 (28)		560 (30)	129 (27)	
35–54	284 (21)	81 (24)		27 (14)	12 (21)		40 (22)	12 (19)		6 (7)	9 (11)		357 (19)	95 (21)	
55–998	130 (9)	58 (18)		21 (11)	14 (24)		76 (41)	36 (56)		6 (7)	7 (9)		233 (13)	103 (21)	
Missing	105 (8)	29 (9)		35 (18)	11 (19)		3 (2)	2 (3)		43 (50)	34 (42)		186 (10)	70 (15)	
Bilobar disease			0.06			**<0.001**			0.39			0.24			**0.02**
Yes	462 (34)	133 (40)		28 (15)	23 (40)		32 (18)	15 (23)		11 (13)	17 (21)		533 (29)	188 (35)	
Missing	11 (1)	3 (1)		5 (3)	2 (3)		0 (0)	0 (0)		0 (0)	0 (0)		16 (1)	5 (1)	
Major liver resection			**<0.001**			0.42			**0.04**			**0.003**			**<0.001**
Yes	247 (18)	113 (34)		29 (15)	12 (21)		58 (32)	30 (47)		54 (63)	69 (84)		388 (21)	224 (42)	
Type of hospital**			0.95			0.26			**0.04**			0.12			**<0.001**
Other hospitals	739 (54)	176 (53)		67 (35)	15 (26)		28 (15)	3 (5)		11 (13)	4 (5)		845 (46)	198 (37)	
Tertiary centres	641 (46)	155 (47)		125 (65)	43 (74)		155 (85)	61 (95)		75 (87)	78 (95)		996 (54)	337 (63)	
Annual hospital volume			0.67			0.24			0.11			0.11			**0.02**
0–39	209 (15)	45 (13)		17 (9)	4 (7)		13 (7)	0 (0)		2 (2)	1 (1)		241 (13)	50 (9)	
40–59	110 (8)	32 (10)		10 (5)	0 (0)		2 (1)	2 (3)		3 (4)	0 (0)		125 (7)	34 (7)	
60–79	234 (17)	53 (16)		22 (11)	5 (9)		16 (9)	5 (8)		14 (16)	7 (9)		286 (15)	70 (13)	
>80	827 (60)	201 (61)		143 (75)	49 (84)		152 (83)	57 (89)		67 (78)	74 (90)		1189 (65)	381 (71)	
Minimal invasive			**<0.001**			0.40			0.24			**0.001**			**<0.001**
Yes	604 (44)	96 (29)		80 (42)	20 (35)		77 (42)	21 (33)		17 (20)	2 (2)		778 (42)	139 (26)	

* Abbreviations: BMI indicates body mass index; ASA score indicates American Association of Anesthsiologist.
** Histopathology of the liver on the basis of pathological examination in millimetre, other including: fibrosis, cirrhosis or sinusoidal dilatation; type of hospital tertiary centre indicates hospitals with the highest expertise on oncological surgery.

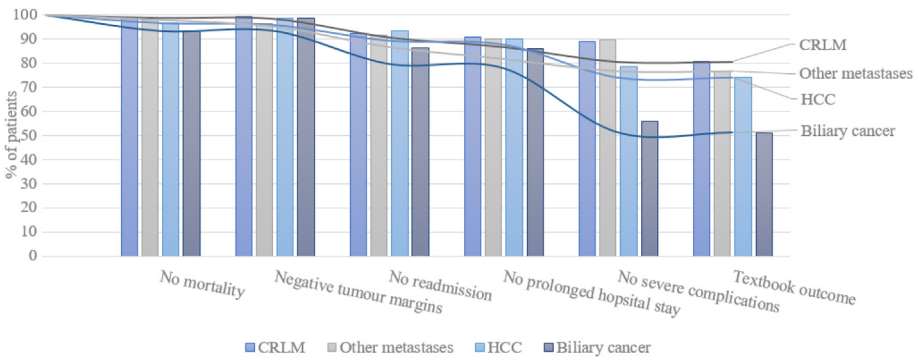

Fig. A.1. Textbook Outcome: a composite measure of outcome parameters in patients undergoing liver resection for CRLM, Other metastases, HCC, and biliary cancers between 2019 and 2020 in the Netherlands. Per parameter and cumulative percentages. *30 day or in-hospital mortality. * No prolonged hospital stay > P_{90}. * No complications Clavien-Dindo grade 3a or higher.

Table B1
Univariable and multivariable logistic regression model of patient and tumour characteristics associated with Textbook Outcome in patients who underwent liver resection for CRLM between 2019 and 2020 in the Netherlands.

TABLE B1		**Univariable**			**Multivariable**		
FACTOR	N	OR	95% CI	p-value	aOR	95% CI	p-value
Sex				0.44			0.69
Male	1121	1.00			1.00		
Female	589	0.90	0.70–1.16		0.94	0.69–1.27	
Missing*	1						
Age(Years)				0.23			0.08
<50	138	1.00			1.00		
50–64	672	1.12	0.69–1.77	0.62	1.20	0.68–2.06	0.49
65–80	775	0.88	0.54–1.38	0.60	0.92	0.52–1.56	0.76
>80	126	0.77	0.42–1.40	0.40	0.60	0.29–1.21	0.15
Charlson Comorbidity Index(CCI)				0.07			**0.04**
CCI 0/1	1075	1.00			1.00		
CCI 2+	636	0.80	0.62–1.02		0.73	0.54–0.98	
BMI **				0.51			0.93
Mean(SD)	1696	1.01	0.98–1.03		1.01	0.96–1.03	
Missing*	15						
ASA Score **				0.009			**0.02**
ASA 1/2	1206	1.00			1.00		
ASA 3+	505	0.71	0.55–0.92		0.70	0.51–0.95	
History of liver resection				0.78			0.87
No	1345	1.00			1.00		
Yes	366	1.04	0.77–1.40		1.03	0.66–1.66	
Histopathology liver parenchyma £				0.62			0.91
Normal liver	1248	1.00			1.00		
Steatosis	325	1.01	0.74–1.40	0.90	0.97	0.68–1.41	0.90
Other	55	0.72	0.39–1.43	0.33	0.84	0.39–1.97	0.67
Missing*	83						
Preoperative chemotherapy				<0.001			0.11
No	1137	1.00			1.00		
Yes	520	0.60	0.47–0.78		0.74	0.51–1.07	
Missing*	54						
Number of lesions				<0.001			0.06
1	737	1.00			1.00		
2	322	0.86	0.61–1.23	0.42	1.10	0.72–1.69	0.65
3	189	0.68	0.46–1.03	0.06	0.92	0.55–1.57	0.77
4	125	1.13	0.67–1.99	0.64	1.82	0.92–3.86	0.09
5	131	0.46	0.30–0.71	<0.001	0.70	0.38–1.31	0.26
>5	151	0.51	0.34–0.77	0.001	0.63	0.33–1.18	0.14
Missing*	56						
Maximum diameter of largest tumour (mm)				<0.001			0.19
<20	481	1.00			1.00		
20–34	543	0.73	0.51–1.02	0.07	0.78	0.52–1.14	0.20
35–54	365	0.55	0.38–0.79	0.001	0.77	0.50–1.17	0.22
55–998	188	0.35	0.23–0.53	<0.001	0.56	0.34–0.94	**0.02**
Missing	134	0.57	0.35–0.94	0.02	1.06	0.57–2.03	0.85
Bilobar disease				0.02			0.88
No	1102	1.00			1.00		
Yes	595	0.74	0.58–0.95		1.03	0.68–1.54	
Missing*	14						
Extra hepatic disease				0.006			**0.02**
No	1432	1.00			1.00		
Yes	250	0.64	0.47–0.89		0.64	0.44–0.95	
Missing*	29						
Location of primary tumour				0.10			0.21
Colon	1156	1.00			1.00		
Rectal	555	1.24	0.95–1.61		1.21	0.89–1.66	
Timing of metastases				0.02			
Metachronous	854	1.00			1.00		0.25
Synchronous	670	0.69	0.54–0.89	0.005	0.77	0.55–1.08	0.13
Recurrence	142	0.90	0.57–1.46	0.67	0.77	0.41–1.46	0.43
Missing*	45						
Major liver resection				<0.001			**<0.001**
No	1351	1.00			1.00		
Yes	360	0.42	0.32–0.54		0.50	0.36–0.69	
Type of hospital				0.90			0.28
Other hospitals	915	1.00			1.00		
University medical centres	796	0.98	0.77–1.25		1.24	0.83–1.83	
Annual hospital volume				0.68			0.54
0–39	254	1.00			1.00		
40–59	142	0.74	0.44–1.23	0.24	0.69	0.38–1.24	0.21
60–79	287	0.95	0.61–1.47	0.82	0.99	0.58–1.68	0.99
>80	1028	0.88	0.61–1.25	0.50	0.84	0.50–1.40	0.51

* Missing's where excluded from analyses when less than 5%.
** Abbreviations: BMI indicates body mass index; ASA score indicates American Association of Anesthesiologist; £ Histopathology of the liver on the basis of pathological examination in millimetre, other including: fibrosis, cirrhosis or sinusoidal dilatation; type of hospital tertiary centre indicates hospitals with the highest expertise on oncological surgery.

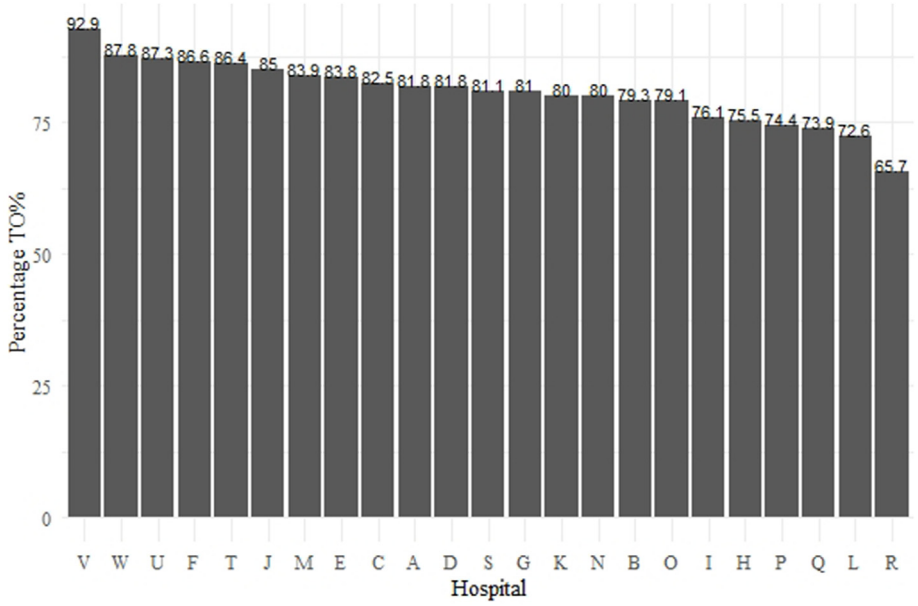

Figure B.1. Unadjusted hospital variation in Textbook outcome after liver surgery for CRLM in the Netherlands between 2019 – 2020.

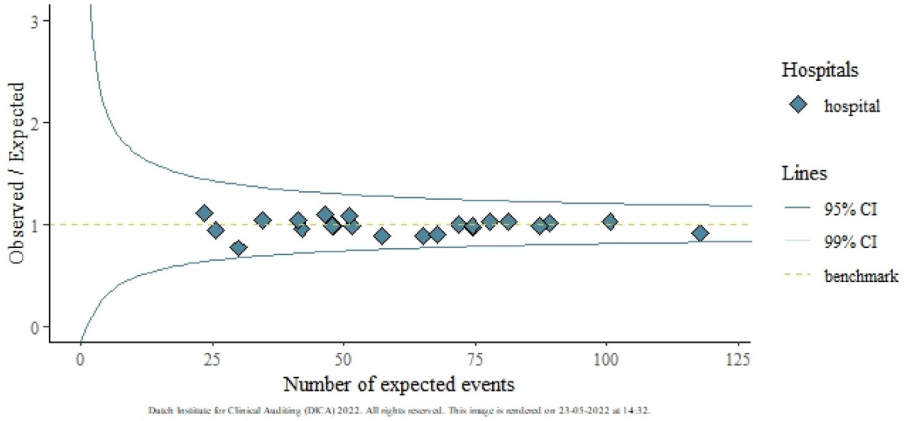

Figure B.2. Funnel plot of case-mix corrected hospital variation in Textbook outcome after liver resection for CRLM in the Netherlands between 2019-2020. Observed/Expected: O/E ratio. Number of expected events: expected number of patients achieving TO based on population characteristics. Case-mix adjusted for: Sex, Age, Charlson Comorbidity Score, American Association of Anesthesiologist score, BMI, history of liver resection, preoperative chemotherapy, major liver resection, type of hospital, diameter of largest tumour, bilobar disease, number of tumours.

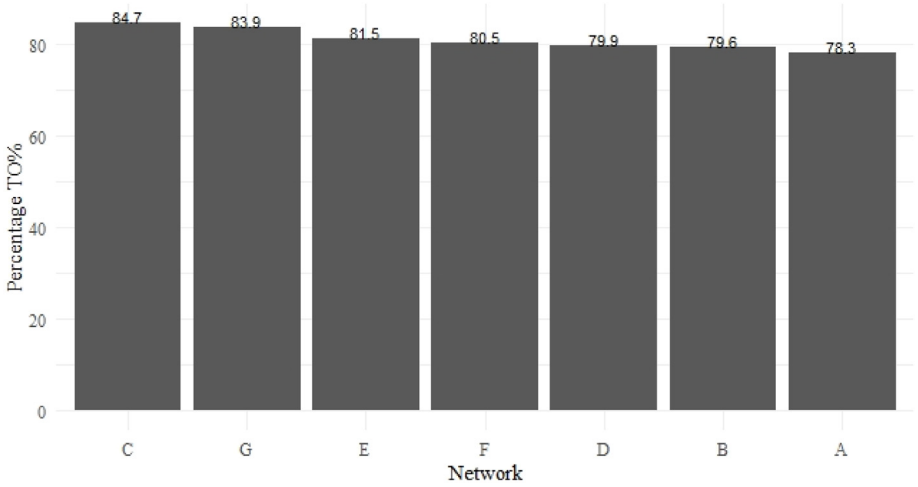

Figure C.1. Unadjusted oncological network variation in Textbook outcome after liver surgery for CRLM in the Netherlands between 2019 – 2020.

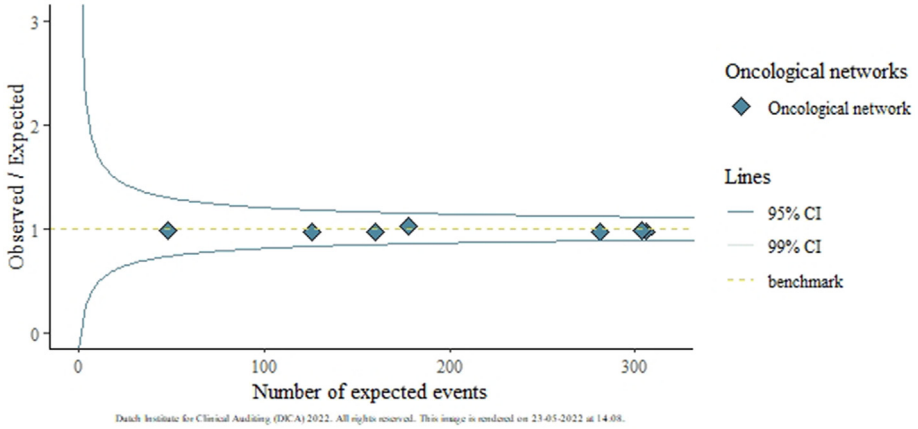

Figure C.2. Funnel plot of case-mix corrected oncological network variation in Textbook outcome after liver resection for CRLM in the Netherlands between 2019-2020. Observed/Expected: O/E ratio. Number of expected events: expected number of patients achieving TO based on population characteristics. Case-mix adjusted for: Sex, Age, Charlson Comorbidity score, American Association of Anesthesiologist score, BMI, history of liver resection, preoperative chemotherapy, major liver resection, type of hospital, diameter of largest tumour, bilobar disease, number of tumours.

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