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Association between textbook outcome and long-term survival after surgery for colorectal liver metastases

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Introduction

Textbook outcome is a multidimensional quality measurement, which comprises the desirable short-term outcomes after surgery. This composite measure is reached when a patient meets all predefined requirements, resulting in a broader reflection of quality of care than single outcome measures. This aids clinicians in daily practice, giving insight into the quality of the entire surgical pathway from surgery to postoperative outcomes. Textbook outcome also provides an opportunity to evaluate variation between hospitals in a more objective manner, as it provides higher event rates and more power to detect differences than single outcomes.

Textbook outcome has been evaluated in different surgical fields, and confirmed to be a feasible parameter for assessment of short-term outcomes^{1–8}. A recent study provided a consensus-based definition specifically for colorectal liver metastases used for nationwide auditing in the Netherlands. Textbook outcome for colorectal liver metastases, as described by de Graaff *et al.*⁹, consists of five short-term postoperative outcome measures from surgery to 1 month after discharge. The aim of this study was to assess the association between textbook outcome and overall and disease-free survival in patients with colorectal liver metastases.

Methods

The study was approved by the local ethics authorities of Erasmus Medical Centre (MEC-2020-0294). All patients who underwent surgery for colorectal liver metastases at Erasmus MC Cancer Institute between 2009 and 2020 were identified from a retrospective database. Patients were excluded when resection margins or data on postoperative outcomes such as death or readmission were missing, when they underwent thermal ablation only, or when they underwent adjuvant hepatic arterial infusion chemotherapy in the context of the PUMP trial¹⁰.

The primary outcome of this study was the association between textbook outcome after colorectal liver metastasis surgery and long-term overall and disease-free survival. Secondary outcomes

were the association between recurrence-free interval and textbook outcome, and predictors of textbook outcome. Full methods, including the statistical analysis plan, are available in the [supplementary material](#).

Results

During the study interval, a total of 591 patients were eligible for inclusion. Of these, 495 (83.8 per cent) achieved a textbook outcome after resection of colorectal liver metastases. Patient characteristics are summarized in [Table S1](#).

Median overall survival was 51 (i.q.r. 29–103) months for patients who achieved textbook outcome compared with 39 (19–80) months for those who did not, resulting in a survival benefit of 12 months. Median follow-up for survivors was 91 (i.q.r. 67–111) months. Patients who achieved a textbook outcome had a superior 5-year overall survival rate of 43 (95 per cent c.i. 38 to 48) per cent, compared with 35 (26 to 48) per cent for those who did not ($P=0.013$) ([Fig. 1a](#)). A textbook outcome was associated with improved overall survival in multivariable regression analysis (adjusted HR for death 0.71, 95 per cent c.i. 0.52 to 0.95; $P=0.021$). Neither Charlson Co-morbidity Index score (adjusted HR 1.06, 0.77 to 1.47; $P=0.708$) nor ASA grade above II (adjusted HR 1.40, 0.99 to 1.99; $P=0.059$) was associated with impaired overall survival. The full results are shown in [Table 1](#).

No differences were found in disease-free survival at 5 years between patients who achieved a textbook outcome and those who did not (21 (18 to 25) versus 15 (9 to 25) per cent; $P=0.280$) ([Fig. 1b](#)). Full results, including exploratory analyses, are available in the [supplementary material](#).

Discussion

Textbook outcome is a composite quality measure that has the potential to aid clinicians in daily practice by giving insight into the perioperative pathway. Textbook outcome was independent of preoperative status of the patient, demonstrated by indices

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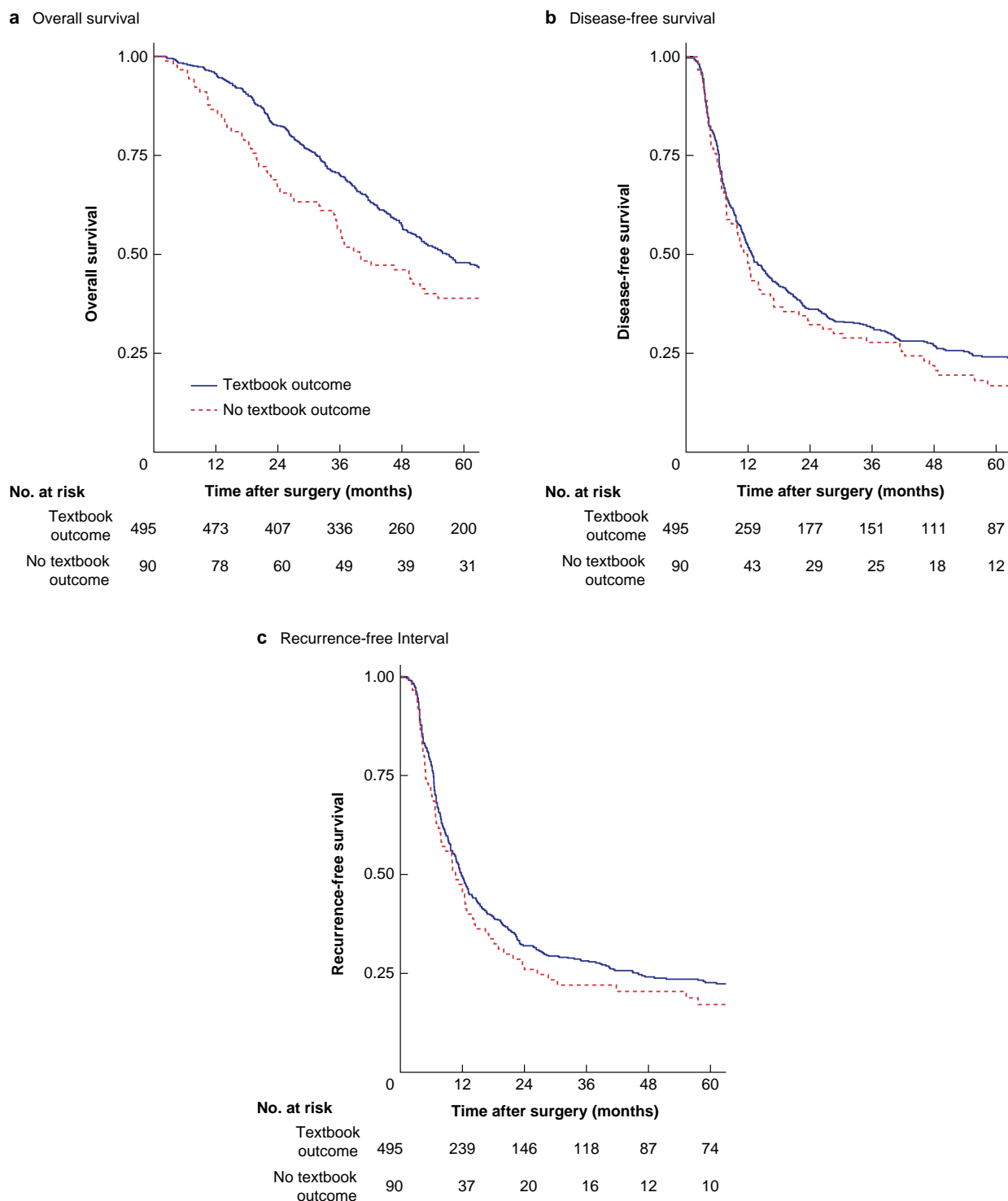


Fig. 1 Survival and recurrence outcomes for patients with and without a textbook outcome
 Kaplan-Meier survival curves showing **a** overall survival, **b** disease-free survival, and **c** recurrence-free interval for patients with and without a textbook outcome. **a** $P = 0.013$, **b** $P = 0.280$, and **c** $P = 0.290$ (log rank test).

such as ASA grade and Charlson Co-morbidity Index scores. Achieving a textbook outcome was associated with better overall survival. This illustrates the association between improved short-term outcomes and long-term survival and the importance of reducing postoperative complications.

Recently, Neary et al.¹¹ investigated the association between textbook outcome after surgery for colorectal liver metastases

and long-term overall survival, using an alternative definition of textbook outcome. In the present study, achieving a textbook outcome was associated with improved long-term overall survival after resection of colorectal liver metastases. The survival benefit at 12 months highlights the importance of the perioperative phase. Pursuing a textbook outcome during this interval has the potential to ultimately lead to improved

Table 1 Univariable and multivariable Cox regression analyses for overall survival

	Univariable analysis		Multivariable analysis	
	HR	P	HR	P
Textbook outcome	0.71 (0.55, 0.93)	0.014	0.71 (0.52, 0.95)	0.021
Female sex	0.87 (0.70, 1.08)	0.207	0.90 (0.70, 1.15)	0.403
Age at CRLM resection (years)	1.02 (1.01, 1.03)	0.002	1.02 (1.01, 1.04)	< 0.001
Charlson Co-morbidity Index score ≥ 2	1.05 (0.78, 1.40)	0.764	1.06 (0.77, 1.47)	0.708
ASA fitness grade > II	1.48 (1.08, 2.01)	0.013	1.40 (0.99, 1.99)	0.059
Primary tumour location				
Right side	1.00 (reference)			
Left side	0.69 (0.52, 0.90)	0.007	0.74 (0.55, 0.99)	0.044
Rectum	0.72 (0.54, 0.95)	0.021	0.72 (0.53, 0.98)	0.034
Nodal involvement (N+)	1.62 (1.30, 2.01)	< 0.001	1.56 (1.23, 1.98)	< 0.001
DFI < 1 year	1.41 (1.10, 1.80)	0.006	1.36 (1.01, 1.82)	0.042
CEA ($\mu\text{g/L}$)	1.00 (1.00, 1.00)	0.554	1.00 (1.00, 1.00)	0.511
> 1 CRLM treated	1.33 (1.07, 1.66)	0.010	1.31 (1.00, 1.71)	0.050
CRLM size > 5 cm	1.26 (0.97, 1.65)	0.086	1.26 (0.91, 1.74)	0.157
Neoadjuvant chemotherapy	1.20 (0.98, 1.47)	0.081	1.08 (0.82, 1.41)	0.585
Extrahepatic disease	1.31 (0.97, 1.77)	0.081	1.45 (1.04, 2.03)	0.029

Values in parentheses are 95% confidence intervals. CRLM, colorectal liver metastasis; DFI, disease-free interval; CEA, carcinoembryonic antigen.

survival rates. Improvement of individual parameters and, therefore, textbook outcome will further enhance the quality of care in surgery for colorectal liver metastases.

In the present study, the textbook outcome rate was 84 per cent (495 of 591) in colorectal liver metastasis surgery, similar to that in the nationwide Dutch Hepato Biliary Audit study, which also used data from this centre. The textbook outcome definition used here was established in the DHBA through expert opinion and previously published definitions⁹. As textbook outcome is primarily meant for clinical auditing of short-term results, the parameters used in its definition should be readily available, preferably from standard reporting in electronic patient files. An international expert Delphi consensus on defining textbook outcome has been published recently¹². In addition to the five parameters, Görgec *et al.*¹³ included intraoperative incidents of grade 2 or higher (Oslo classification), postoperative reinterventions, and postoperative bile leakage to their definition of textbook outcome, resulting in a lower rate of textbook outcome achievement of 67.4 per cent. The additional variables in this version of the definition are not registered consistently in routine practice, and the present authors were unable to retrieve these from electronic patient files. The measurements of Delphi consensus of textbook outcome in most patients led to a higher Clavien–Dindo grade and a prolonged hospital stay, both of which are included in the DHBA definition of textbook outcome. The Delphi consensus is an expert-driven consensus, in contrast to the data-driven definition of the DHBA⁹.

Achieving a textbook outcome in surgery for colorectal liver metastases was shown not to improve disease-free survival or recurrence-free interval. Including tumour-specific parameters in textbook outcome could potentially lead to a more significant difference in disease-free survival and, therefore, in finding associations between textbook outcome and disease recurrence. Adequate resection margins are the obvious tumour-specific parameters in liver surgery for colorectal liver metastases, and indeed the authors' exploratory analyses using R0 *versus* R1/2 instead of R0/1 *versus* R2 as cut-off revealed an association between textbook outcome and disease-free survival. There is ongoing debate on intentional R1 resections (vascular R1 *versus* parenchymal R1, R1 after induction chemotherapy)^{14–16}. Tumour-free resection margins are, if attainable, always the

most favourable outcome of every resection. However, R1 resections may be performed intentionally when important anatomical structures are at risk, or could result from a chosen resection technique. Inability to achieve an R0 resection when R1 is deemed possible should not be a contraindication to resection but, in fact, is part of a modern, multidisciplinary approach to colorectal liver metastases.

The multivariable logistic regression analysis in this study revealed no predictors for achieving textbook outcome. In particular, there was no association between poor preoperative status (ASA grade and Charlson Co-morbidity Index score) and not achieving textbook outcome. This highlights the importance of the perioperative care pathway as achievement of textbook outcome in this study was not related to patient factors but depended on the perioperative factors associated with the care delivered.

Limitations of this study are related to its retrospective nature and setting in a tertiary referral centre. It may be possible that readmissions within 30 days after discharge were not registered adequately and/or communicated when patients were readmitted to the referring centres. The retrospective database did not distinguish between R1 and R2 resections, thereby reducing the potential for identifying differences in disease recurrence. Another limitation of this study was the lack of data on somatic mutations such as those in RAS, TP53, and BRAF.

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Author contributions

Kelly Voigt (Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Visualization, Writing—original draft), Lissa Wullaert (Conceptualization, Formal analysis, Investigation, Methodology, Visualization, Writing—original draft), Michelle de Graaff (Conceptualization, Formal analysis, Methodology, Validation, Visualization, Writing—review & editing), Kees Verhoef (Conceptualization, Formal analysis, Investigation, Supervision, Validation, Visualization, Writing—review & editing), and Dirk Grünhagen (Conceptualization, Formal analysis, Investigation,

Methodology, Project administration, Resources, Supervision, Validation, Visualization, Writing—review & editing).

Disclosure

The authors declare no conflict of interest.

Supplementary material

Supplementary material is available at *BJS* online.

Data availability

Data will be made available upon reasonable request.

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