

ORIGINAL ARTICLE

The association between preoperative physical functioning and short-term postoperative outcomes: a cohort study of patients undergoing elective hepatic resection

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Abstract

Background: This study evaluated the association between practical performance-based indices of preoperative physical functioning and short-term postoperative outcomes in patients undergoing hepatic resection.

Method: Preoperative characteristics and results of practical performance-based tests of physical functioning were analyzed concerning the effect on postoperative outcomes (recovery of physical functioning, non-surgical complications, and length of hospital stay) using univariable and multivariable logistic regression.

Results: Perioperative data of 96 patients showed that besides the conventional risk-factors (American Society of Anesthesiologists grade III and BMI), lower absolute steep ramp test performance (in watts; OR 0.992), and lower perceived level of functional capacity to perform activities of daily living (ADL) on Duke activity status index (in metabolic equivalent of task (MET); OR 0.806) and lower score on the veterans-specific activity questionnaire (in MET, OR 0.875) were associated with delayed recovery of physical functioning. Furthermore, more comorbidities, worse functional mobility, and lower levels of perceived functional capacity to perform ADL were associated with non-surgical complications and length of hospital stay.

Conclusion: Adequate preoperative performance and perceived level of functional capacity to perform ADL appear to be of importance to identify individual patients that are at risk of a complicated post-operative course.

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Introduction

Hepatic resection is the primary modality of treatment in patients diagnosed with benign and malign hepatic tumors.¹ Despite advances in diagnostic, surgical, and anesthetic

techniques, as well as improvements in perioperative care management due to enhanced recovery after surgery (ERAS)² and fast-track programs,³ hepatic resection remains an operation with a high risk of morbidity and mortality. In the Netherlands, morbidity rate ranges from 8.9% to 22%, whereas

mortality ranges from 1.0% to 5.0%, which is dependent on the type of the surgery and the extent of the hepatic resection.⁴ Besides advances in perioperative care management, it remains to be seen what type of patient-related factors can be improved in order to lower the risk of inappropriate postoperative outcomes. For instance, the patient's physical functioning level prior to elective major abdominal surgery is known to be associated with postoperative morbidity and mortality in patients undergoing colorectal resection.^{5,6}

Preoperative aerobic capacity measured by cardiopulmonary exercise testing (CPET) has been reported to be a valuable non-invasive performance test to predict part of the risk for postoperative morbidity, mortality, and length of stay in patients undergoing hepatic resection.^{7–12} However, its use requires sophisticated equipment and trained staff. Hence, to use practical performance tests to evaluate a patient's preoperative physical functioning level prior to surgery should be considered. Practical performance-based tests such as the timed up-and-go (TUG) test, stair-climb test, incremental shuttle walk test, and six-minute walk test (6MWT) have been identified as feasible and relatively accurate in predicting postoperative complications in patients undergoing all sorts of surgery,^{13–15} including elective abdominal surgery.^{16–18}

Consequently, the added value of the use of practical performance-based tests in the preoperative risk assessment should become clear as a prerequisite for clinical reasoning and shared decision-making concerning the choice and use of prophylactic, surgical and anesthetic interventions. By doing so, their risk for perioperative morbidity and mortality might be decrease.^{19–21} In this study we describe pre- and postoperative functioning in patients undergoing elective hepatic resection by evaluating the role of preoperative practical performance-based tests and its association with short-term (30-day) postoperative outcomes (time to recovery of physical functioning, non-surgical complications, and length of hospital stay).

Methods

This was a single-center prospective cohort study in patients undergoing hepatic resection for benign or malignant tumors at the Maastricht University Medical Center (Maastricht UMC+), Maastricht, the Netherlands. Patients with benign or malignant pathology with an American Society of Anesthesiologists (ASA) score of I-IV undergoing hepatic resection for benign and malignant tumors were monitored pre- and postoperatively on their physical functioning as part of usual care. All consecutive patients with no objection for using their usual care data for research purposes were included. When essential data about pre- and postoperative outcomes was missing, the data from that patient was excluded from analysis. The data collection was performed between March 2016 and December 2017. Baseline patient characteristics included age, sex, body mass index (BMI,

in kg/m²), ASA score, Charlson comorbidity index (CCI), surgical approach (laparoscopic or open), and type of liver resection (e.g., (extended) hemihepatectomy, segmental resection, wedge resection). The medical ethical committee of the Maastricht UMC + decided (15-4-234) that this study met the ethical policies of the Maastricht UMC+ and the regulations of the Dutch government.

Usual care pathway

As part of the preoperative multidisciplinary risk screening, patients scheduled for hepatic resection for benign and malignant tumors were referred by the hepatobiliary surgeon or nurse practitioner to a physical therapist at the outpatient physical therapy department, approximately three weeks prior to surgery. The physical therapist screened the patient for their level of physical functioning. Additionally, patients received an information leaflet about the content and expectations of the postoperative physical therapy treatment during hospitalization and were educated regarding the importance of physical activity pre- and postoperatively. All patients were routinely admitted one day prior to surgery to the HPB ward. Intraoperatively, patients received a thoracic epidural for analgesia. Approximately 72 h post-surgery, the thoracic epidural was removed. Postoperatively, patients were transferred to the HPB ward as soon as possible. After surgery, all patients received postoperative physical therapy once a day, starting the first day after surgery (postoperative day 1). Physical therapy consisted of airway clearing exercises, practicing transfers, walking, and other functional abilities based on the individual patient needs and progress. The recovery of physical functioning was monitored by the physical therapist using the modified Iowa levels of assistance scale (mILAS).²²

Preoperative performance and perception of physical functioning

All patients were screened by an experienced physical therapist with help of a protocolled test battery on aerobic capacity, muscle strength, functional mobility, and perceived level of functional capacity to perform activities of daily living (ADL). Prior to the preoperative assessment, the physical activity readiness questionnaire²³ was filled out by the patient under supervision of the physical therapist as a simple screening tool to evaluate whether there were contra-indications for exercise testing.

Aerobic capacity

The steep ramp test (SRT), a short-time maximal exercise test performed on a cycle ergometer,²⁴ was used to estimate the patient's aerobic capacity. A previous study in adult cancer survivors demonstrated a strong correlation between the primary outcome measure of the SRT, the attained peak work rate (WR_{peak}), and the peak oxygen uptake (VO_{2peak}) achieved during CPET (*r* of 0.82).²⁵ This suggests that the SRT is a valid test to estimate aerobic capacity at the group level. De Backer *et al.* also

showed that the SRT is a reliable test (intra-class correlation coefficient [ICC] for the achieved WR_{peak} of 0.996).²⁵ For each patient, seat height was adjusted to a comfortable leg length. During the test, heart rate was monitored by using an elastic belt with a heart rate sensor (Polar T31i transmitter, Polar, Kempele, Finland). To make the SRT suitable for our surgical population, the original protocol (work rate increments of 25 W each 10 s²⁶) was modified. After a two-minute warm-up of unloaded cycling, the test started by applying resistance on a calibrated cycle ergometer (Lode Corival Rehab, Lode BV, Groningen, the Netherlands) with increments of 10 W every 10 s in a ramp like manner (1 W/s). The patient was instructed to maintain a pedaling frequency around 80 rotations/min. The protocol continued until there was a sustained drop in the patient's pedaling frequency below 60 rotations/min despite strong verbal encouragement. The main outcome measure of the SRT was the attained WR_{peak} , the point at which the patient's pedaling frequency definitely dropped <60 rotations/min. Efforts were considered to be maximal when the patient showed subjective signs of intense effort (e.g., unsteady biking, sweating, facial flushing, and clear unwillingness to continue despite encouragement).

Muscle strength

Muscle strength was evaluated using the five times sit-to-stand (FTSTS) test and by measuring the patient's handgrip strength (HGS). The FTSTS test is commonly used to measure lower extremity muscle strength and functional mobility.^{27,28} The patient was instructed to start the test from a sitting position on a chair (43–47 cm in height) with the arms folded across the chest and the feet placed comfortably on the floor (knees flexed 90°). From this position, the physical therapist encouraged the patient to stand up from the chair to a fully erected position and to sit down again, five times, as quickly as possible. The time, ending with timing after the fifth stand, required for the five repetitions of rising from a chair and sitting was timed with a stopwatch (two decimals). The test was performed three times, with 30 s rest in between, and the best performance in seconds was used. The FTSTS test is easy to perform in clinical practice and has been reported to be a reliable method to assess test-re-test reliability (ICC of 0.89) in community-dwelling elderly.²⁹

HGS of the dominant hand was measured to estimate the patient's general muscle strength by using a hand-held dynamometer (JAMAR® Hydraulic Hand Dynamometer, JAMAR, Patterson Medical Holdings, Inc., Illinois, USA). The patient was seated in a chair (43–47 cm in height) with the shoulders adducted, the elbow flexed at 90°, and the forearm in neutral position without any support from the chair. The handle of the dynamometer was placed in such a position that the middle phalanges had to rest on the handle. The patient was asked to squeeze the dynamometer to maximum ability with encouragement of the physical therapist. The maximal grip score (kg)

of the three attempts (with 30 s of rest in between) was recorded. Handgrip strength measured with the Jamar dynamometer has been shown to have an adequate intra- and interrater reliability (ICC values from 0.85 to 0.98) in healthy adults.³⁰

Functional mobility

The two-minute walk test (2MWT) and the TUG test were used to measure functional mobility.³¹ The 2MWT measures the functional walking capacity and was performed in a corridor of the physical therapy department over a length of 15 m. Patients were instructed to walk as far as they could in two minutes using their customary walking aid, if applicable. During the test, the physical therapist encouraged the patient after one-minute elapse by saying “you are doing well, you have one-minute left”. The distance walked (in m) was recorded. The test has an adequate test-retest reliability (ICC of 0.82) in community-dwelling healthy adults (18–85 years).³²

The TUG test measures basic functional mobility and reflects the ability to rise from an arm chair (43–47 cm in height), walk a short distance (3 m), return to the chair, and sit down again, all as quick as possible.³³ The patient has three attempts, with 30 s of rest between attempts. The physical therapist recorded the time of each attempt and the best attempt was used for analysis. The inter-rater (ICC of 0.99) and intra-rater (ICC of 0.99) reliability of the TUG test has been reported to be excellent in geriatric patients.³³

Perceived level of functional capacity to perform ADL

To gain insight in the patient's perceived level of functional capacity to perform ADL, each patient filled out two questionnaires with help of the physical therapist: the veterans-specific activity questionnaire (VSAQ) and the Duke activity status index (DASI). The VSAQ consists of a list of activities presented in a progressive order and linked to a particular metabolic equivalent of task (MET) score, with a maximum of 13 METs. Patients were asked to determine which kind of daily activities they were able to perform routinely without experiencing symptoms or with only minimal symptoms. A line is drawn below those activities and the corresponding MET score is noted. The VSAQ has a good intra- (ICC of 0.882) and inter-rater reliability (ICC of 0.904), measured in healthy older adults, to assess the patient's performance of daily activities.³⁴

The DASI is a self-administered twelve-item questionnaire measuring the ability to perform a common set of activities of daily living and recreational activities to assess functional capacity.³⁵ Each item of the questionnaire has a corresponding weight. The total score of the DASI consist of the weights for each ‘yes’ response. The DASI score correlated well with aerobic capacity (VO_{2peak} , Spearman correlation coefficient of 0.81) and a rough estimation of a patients VO_{2peak} can be made by the formula: $VO_{2peak} = (DASI \text{ Score} \times 4.6) + 9.2$.³⁵ Dividing the estimated VO_{2peak} by 3.5 (1 MET equals an oxygen uptake of

3.5 mL/kg/min), an estimation of the patient's peak MET score (intensity of physical activities) can be made.

Postoperative outcomes

The primary postoperative outcome measure was time to recovery of physical functioning (measured by mLAS).²² Time to recovery of physical functioning was defined as the time between the day of surgery and day at which the patient reached a mLAS score of 0 (in days). Secondary postoperative outcome measures were 30-day morbidity (non-surgical complications), and length of hospital stay (in days). Complications were categorized recorded by Clavien-Dindo classification and were divided in surgical (defined as wound infection, bile leak, hemorrhage, liver failure, abdominal abscess, and pleura effusion) and non-surgical complications (defined as pneumonia, cardiac, and thromboembolic complications).

Statistical analysis

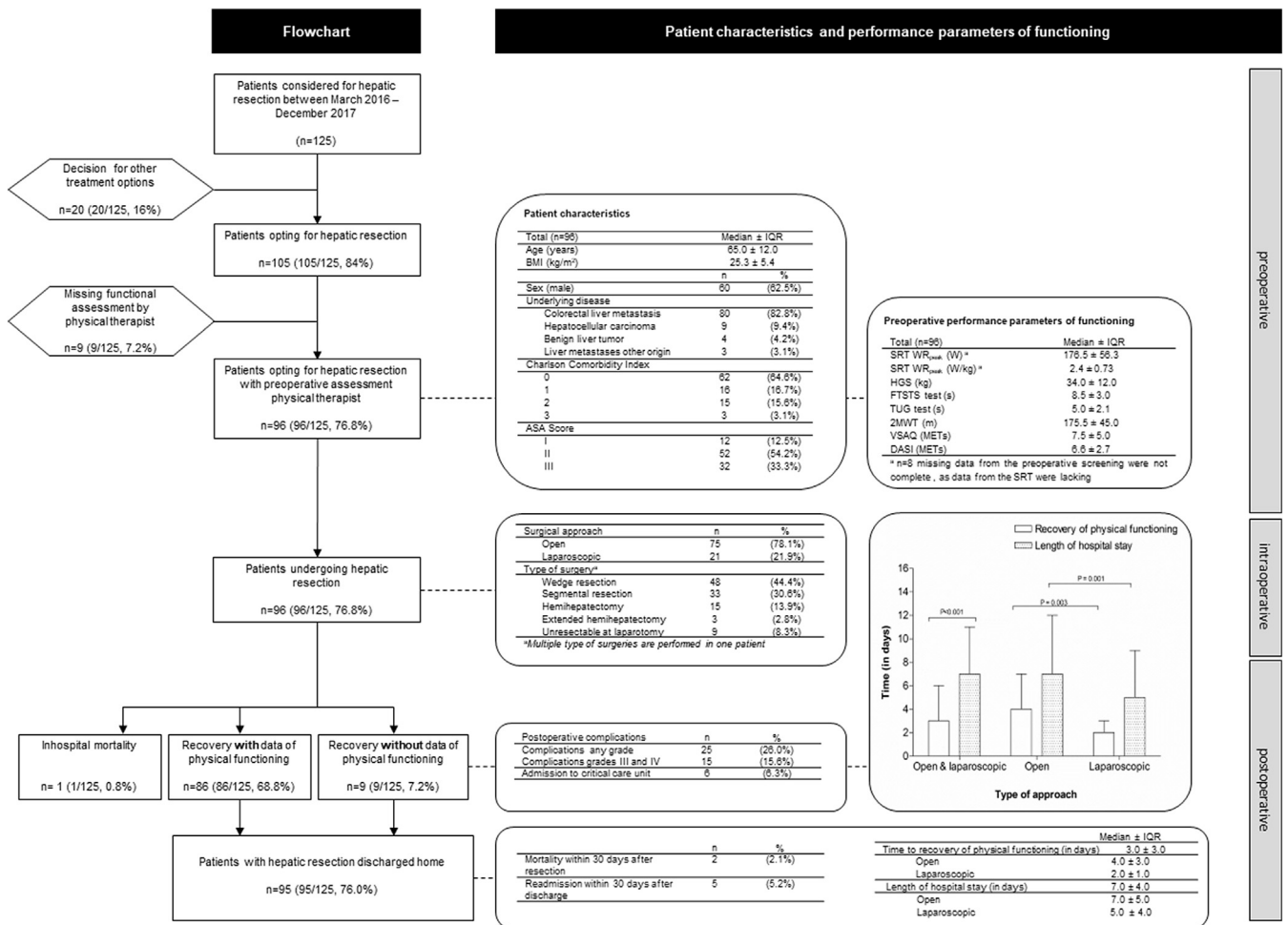
The Statistical Package for the Social Sciences for Windows (version 23.0; IBM, SPSS Inc., Chicago, IL, USA) was used for statistical analysis. For all continuous variables, normality was tested with the Kolmogorov-Smirnov test. The association between the independent variables and dependent variables was assessed using univariable logistic regression. We chose a less stringent alpha for pre-selection of variables of 0.20 instead of 0.05 to prevent too early deletion of variables from the model, as suggested by prediction modeling guidelines.³⁶ As a result, 95% confidence intervals of the estimated odds ratios (ORs) may contain 1.0. However, this is a proven strategy to explore univariate associations between potential predictor variables and outcome variables. Dependent variables were dichotomized according to median time to recovery of physical functioning (0 = recovery of physical functioning ≤ 3 days, 1 = recovery of physical functioning ≥ 4 days), development of non-surgical complications (0 = absent, 1 = present), and median prolonged length of hospital stay (0 = hospital length of stay ≤ 7 days, 1 = hospital length of stay ≥ 8 days). Multivariable logistic regression with backward stepwise elimination was used to determine the strongest independent predictors for the dependent variables with ten events per independent variable. The selection of the predictors was based on the literature, expert opinion, and results from univariable logistic regression (P -value of < 0.200). A combination of conventional predictors and physical functioning predictors was chosen. Correlations between each two variable were checked and if they were < 0.70 we chose to include only the variable we considered is easiest to measure. The Akaike Information Criterion was used as stopping rule for the backward stepwise elimination, which is equivalent to using an alpha of 0.157 for variables of 1 degree-of-freedom, as per prediction modeling guidelines.³⁷ Receiver operating characteristic (ROC) curve analysis was performed to evaluate the diagnostic ability of the tests to discriminate between the two patient states.

Results

In total 125 patients were identified as potential candidate for the study. Twenty-nine patients (23.2%) were excluded for analysis because they received other treatments for their hepatic malignancies instead of hepatic resection or did not receive a preoperative screening. Hence, we eventually analyzed data from 96 patients (76.8%) undergoing hepatic resection for benign or malign tumors that received pre- and postoperative physical therapy. In eight patients (8.3%), data from the preoperative screening were not complete, as data from the SRT were lacking (not available because of logistic problems ($n = 1$, 12.5%), contra-indications (cardiac ($n = 2$) and neurological ($n = 1$) based on the PAR-Q ($n = 3$, 37.5%)), personal reasons of the patient ($n = 3$, 37.5%), and software problems during the test ($n = 1$, 12.5%)). No adverse events occurred during the preoperative screening and no adverse events were reported by patients later on. Postoperative recovery of physical functioning (mILAS scores) data of ten patients (10.4%) were missing because of logistic problems. In Fig. 1, the preoperative characteristics and performance parameters of physical functioning and postoperative outcomes are presented. Two patients (2.1%) died after surgery. One patient died nine days after surgery because of systemic inflammatory response syndrome leading to multi-organ failure. The other patient was discharged after nine days in a good physical status but was readmitted after three days because of an abscess with abdominal wound dehiscence. He died during his second surgery because of cardiac arrest.

Time to recovery of physical functioning ($n = 86$)

The median \pm IQR time to recovery of physical functioning (mILAS score of 0) was 3.0 ± 3.0 days. When data were clustered according to surgical approach (open approach ($n = 68$, 79.1%) versus laparoscopic approach ($n = 18$, 20.9%)), a statistically significant difference in time to recovery of physical functioning (4.0 ± 3.0 versus 2.0 ± 1.0 days; $P = 0.003$) was observed (Fig. 1, Box 3). Early recovery of physical functioning (recovery of physical functioning ≤ 3 days) was present in 49 patients (57.0%) and delayed recovery of physical functioning (recovery of physical functioning ≥ 4 days) was present in 37 patients (42.0%). A BMI between 25 and 30 kg/m², ASA score III, aerobic capacity (absolute SRT performance), and preoperative perceived level of functional capacity to perform ADL (VSAQ and DASI) all showed an univariate association ($p < 0.200$) with time to recovery of physical functioning. Results of the univariable regression analysis are shown in Table 1. For aerobic capacity measured with the SRT, the odds ratio (OR) was 0.992 per watt (OR 0.818 per 45 W). The area under the curve (AUC) was 0.616 (95% CI 0.491 to 0.740, $P = 0.076$). With a one-MET difference at the VSAQ, the OR of a delayed recovery of physical functioning was 0.875. For a patient with an ASA score III, the



OR of a delayed recovery of physical functioning was 2.349 compared with patients with an ASA score I-II. Multivariable logistic regression with stepwise elimination starting with four variables, two conventional (ASA and BMI) and two physical functioning parameters (absolute SRT performance and HGS) yielded a model including two variables ($p < 0.157$), ASA score III vs I-II (OR of 2.405; 95% CI of 0.901–6.420; $P = 0.080$) and absolute SRT performance (OR of 0.993; 95% CI 0.984 to 1.002; $P = 0.144$). Patients with an ASA score III and a lower absolute WR_{peak} (in W) at the SRT were more likely to have a prolonged recovery of physical functioning.

Non-surgical complications

Forty-three postoperative complications were registered in a total of 25 patients (26.0%). Of these 25 patients, ten (40.0%)

experienced surgical complications, thirteen (52.0%) had non-surgical complications and two (8.0%) experienced both surgical and non-surgical complications. Univariable logistic regression revealed that BMI ≥ 30 kg/m², ASA score III, CCI, aerobic capacity (both absolute and relative SRT performance), muscle strength (FTSTS test), functional mobility (TUG test and 2MWT) and the preoperative perceived level of functional capacity to perform ADL (VSAQ and DASI) were associated with non-surgical complications ($P < 0.200$). The ORs are listed in Table 1. A higher estimated aerobic capacity and a higher level of functional capacity to perform ADL were associated with smaller ORs. Patients with higher scores on the FTSTS test and TUG test were more likely to experience non-surgical complications. If walking distance on the 2MWT increased by 1 m, the OR of experiencing non-surgical complication

Table 1 Results of univariable regression analysis ($P < 0.200$) for the association between preoperative predictor variables and delayed recovery of physical functioning, non-surgical complications, and prolonged hospital length of stay

Postoperative outcome variable	Preoperative predictor variable	B	P-value	OR	AUC	
Time to recovery of physical functioning, mLAS = 0 (0 = recovery of physical functioning ≤ 3 days, 1 = recovery of physical functioning ≥ 4 days)	BMI				0.466	
	<25 kg/m ²			1.00		
	25–30 kg/m ²	-0.811	0.129	0.444	(0.157–1.267)	
	>30 kg/m ²	-0.223	0.680	0.800	(0.277–2.311)	
	ASA score				0.641	
	I – II			1.00		
	III	0.854	0.069	2.349	(0.936–5.897)	
	SRT WR _{peak} (W)	-0.008	0.100	0.992	(0.983–1.001)	0.616
	VSAQ score (METs) ^a	-0.134	0.098	0.875	(0.747–1.025)	0.606
	DASI score (METs) ^a	-0.215	0.135	0.806	(0.608–1.069)	0.590
Non- surgical complications (0 = absent, 1 = present)	BMI				0.472	
	<25 kg/m ²			1.00		
	25–30 kg/m ²	0.551	0.373	1.736	(0.515–5.846)	
	>30 kg/m ²	-1.572	0.164	0.208	(0.023–1.900)	
	ASA				0.658	
	I – II			1.00		
	III	1.330	0.022	3.783	(1.209–11.831)	
	CCI	0.719	0.011	2.052	(1.175–3.582)	0.704
	SRT WR _{peak} (W)	-0.010	0.096	0.990	(0.978–1.002)	0.653
	SRT WR _{peak} (W/kg)	-0.841	0.067	0.431	(0.176–1.059)	0.679
	TUG test (s) ^b	0.197	0.189	1.217	(0.908–1.633)	0.624
	FTSTS test (s) ^c	0.215	0.026	1.239	(1.026–1.497)	0.643
	2MWT (m) ^d	-0.028	0.007	0.972	(0.952–0.992)	0.735
	VSAQ score (METs)	-0.359	0.004	0.698	(0.546–0.893)	0.750
	DASI score (METs)	-0.073	0.006	0.930	(0.883–0.979)	0.749
Length of hospital stay (0 = length of stay ≤ 7 days, 1 = length of stay ≥ 8 days)	CCI	0.407	0.080	1.503	(0.952–2.731)	0.560
	FTSTS test (s)	0.130	0.142	1.139	(0.957–1.356)	0.522
	2MWT (m)	-0.010	0.159	0.990	(0.975–1.004)	0.602
	VSAQ score (METs)	-0.135	0.078	0.874	(0.752–1.015)	0.605
	DASI score (METs)	-0.037	0.029	0.964	(0.932–0.996)	0.636

Abbreviations: ASA = American Society of Anesthesiologists; AUC = area under the curve; BMI = body mass index; CCI = Charlson Comorbidity Index; DASI = Duke activity status index; FTSTS = five times sit-to-stand; mLAS = modified Iowa level of assistance scale; OR = odds ratio; SRT = steep ramp test; TUG = timed up-and-go; VSAQ = veterans-specific activity questionnaire; WR_{peak} = peak work rate; 2MWT = two-minute walk test.

^a A higher score means a higher level of self-reported physical activity.

^b A higher score means a worse functional mobility.

^c A higher score means a lower level of muscle strength and functional mobility.

^d A higher score means a better functional mobility.

decreased by 0.028 and with an increase of 25 m the OR of experiencing non-surgical complications decreased by 0.497. The area under the curve for the 2MWT was 0.735 (95% CI 0.607 to 0.862; $P = 0.004$). Further analysis in a multivariable logistic regression model for non-surgical complications was not performed since the insufficient number of events (fifteen events).

Length of hospital stay

A prolonged length of hospital stay (≥ 8 days) was present in 36 patients (37.5%). Univariable logistic regression analysis identified that CCI, functional mobility (FTSTS test and 2MWT), and preoperative perceived level of functional capacity to perform ADL (VSAQ and DASI) were associated with a longer length of hospital stay (≥ 8 days) ($P < 0.200$, see

Table 1). The OR for the FTSTS test was 1.139, with an increase of 5 s on the FTSTS test the OR of a prolonged hospital length of stay is 1.916. With a one-MET difference at the VSAQ, the OR of a prolonged length of hospital stay was 0.874. Further analysis in a multivariable logistic regression model provided no additional value in predicting a prolonged hospital length of stay.

Discussion

Our study, focusing on preoperative physical functioning and its association with short-term (30-day) postoperative outcomes in patients undergoing hepatic resection, revealed potential areas for mitigation of modifiable risk factors. Our data suggest that the performance of a patient on practical performance-based tests of physical functioning, in combination with conventional patient-related characteristics, is associated with postoperative outcomes. A lower estimated aerobic capacity, a lower level of perceived functional capacity to perform ADL, BMI, and ASA score III were independently associated with a delayed time to recovery of physical functioning. Additionally, a lower estimated aerobic capacity, a lower functional mobility, a lower perceived level of functional capacity to perform ADL, a higher CCI, BMI and ASA score III were independently associated with non-surgical complications. Finally, a lower functional mobility, a lower preoperative perceived level of functional capacity to perform ADL, and a higher CCI were associated with a prolonged length of hospital stay. Regarding surgery-related risk factors, patients who underwent laparoscopic surgery in our study showed a shorter time to recovery of physical functioning (2.0 ± 1.0 days) and length of hospital stay (5.0 ± 4.0 days) compared to those who had open surgery. With reference to postoperative care management-related risk factors, we found a notable difference between time to recovery of physical functioning and length of hospital stay in both open and laparoscopic surgery (median difference of 3.0 ± 4.0 days).

The relation between preoperative performance of patients on the practical performance-based tests of physical functioning and postoperative time to recovery of physical functioning and incidence of postoperative complications is consistent with previously published research in identical patient populations.^{5,6,13–15} Our data show that a lower aerobic capacity as estimated with the SRT is associated with delayed recovery of physical functioning (≥ 4 days) and non-surgical complications. Measuring a patient's aerobic capacity by CPET (gold standard) is a valuable non-invasive performance test to estimate the risk for postoperative morbidity, mortality, and length of stay in patients undergoing hepatic resection.^{9–12} Since preoperative CPET is not yet usual care in our hospital, we use a modified SRT to estimate preoperative aerobic capacity. A previous study in cancer survivors indicated that the prediction of aerobic capacity based on SRT performance is adequate at the group level.²⁵

Hence, the SRT might be a practical short-time maximal exercise test to identify high- and low risk patients preoperatively. However, further research should investigate whether our modified SRT protocol is a valid test to estimate preoperative aerobic capacity in individual patients undergoing major elective abdominal surgery. Recently, Stuver *et al.*³⁸ concluded that prediction equations do not provide sufficiently accurate estimations of aerobic capacity in individual cancer survivors. Moreover, our findings are congruent with other reports confirming the important role of practical performance-based tests in predicting postoperative complications, besides conventional risk factors (ASA score and CCI). However, different practical performance-based tests were used.^{16–18} For instance, Hayashi *et al.*¹⁷ showed that a lower 6MWT distance was associated with an increased risk for the event of a major postoperative complication (Clavien-Dindo grade ≥ 3 , with OR of 1.537) in patients undergoing elective abdominal surgery for hepatic-biliary-disease. Hereto, practical performance-based tests seem useful for preoperative decision-support of patients and their (informal) caregivers, as these are related with postoperative outcomes.

Besides patient-related risk factors, perioperative surgical risk factors should also be taken into account. The ability of the individual patient to respond adequately to the increased metabolic demand due to surgical stress will vary greatly, depending on surgery-related risk factors next to patient-related risk factors. The current study results demonstrate that laparoscopic surgery is accompanied by a shorter time to recovery of physical functioning and a shorter length of hospital stay. However, it should be noted that laparoscopic procedures in our study cohort mainly consisted of less invasive laparoscopic resections (86% wedge or segment resections). When comparing laparoscopic surgery and open surgery on their short-term outcomes in a recent meta-analysis (ten papers, 2259 patients) shows that laparoscopic surgery is more favorable in terms of morbidity (OR of 0.57), length of hospital stay (weighed mean difference (WMD) of -2.13 days), blood loss (WMD of -124.68 mL), and blood transfusion rate (OR of 0.46).³⁹ Therefore, surgeons should consider to perform minimally invasive surgery in individuals who are classified as high-risk for adverse postoperative outcomes. Of equal importance as patient- and surgical-related risk factors are postoperative care management related risk factors. We found that there is a great discrepancy between the time to recovery of physical functioning and length of hospital stay (in days). The predominant culture of physical inactivity during the clinical recovery phase challenges the psychophysiological system of the patient and contributes to the progressive loss of functional capacity to perform activities of daily life, called hospital-associated disability.^{40–42}

Identifying risk factors in time in the perioperative management for patients undergoing hepatic resection is important to develop targeted perioperative strategies to anticipate and reduce

adverse postoperative outcomes. For patient-related risk factors, our results, in addition to those of others, underline the importance of the preoperative level of physical functioning in patients undergoing major abdominal surgery. However, more personalized risk models have to be developed. These should incorporate higher volumes of patients, combining medical and functional data, and advanced statistics that can be used in daily clinical practice as clinical decision-support system.^{43,44} Although such an integral clinical decision support tool is not yet available, we should not refrain high-risk patients from prehabilitation interventions. For patients undergoing hepatic resection, prehabilitation is feasible and results in an improvement of preoperative aerobic capacity.⁴⁵ Additionally, knowledge about patients with a low risk of adverse postoperative outcomes should be identified. These low risk patients have to be provided with adequate technology, decision support systems, and minimal support of healthcare professionals to monitor their physical functioning pre- and postoperatively. To improve surgical and postoperative care management risk factors, attitudes of healthcare professionals with regard to the inactivating culture and infrastructure should be identified and postoperative care management should focus on facilitating a swift return to adequate performance of ADL.^{19,20} Multimodal multidisciplinary ERAS programs describe how perioperative care management can be optimized and underline the importance of early mobilization in the patient's recovery to physical functioning.⁴⁶

In conclusion, preoperative physical functioning is associated with short-term (30-day) time to recovery of physical functioning, non-surgical complications, and length of hospital stay in patients undergoing hepatic resection. Consequently, preoperative evaluation of physical functioning seems valuable to establish whether patients have adequate functional reserve capacity to cope with stress during the patient-journey and should play an integral part in the conversation in clinical practice for the decision-making and preparation for surgery. Further exploration is needed on how already established patient related risk-factors can be integrated in a decision-support system which can be used in the preoperative evaluation in daily clinical practice. In the meantime, optimization of peri- and postoperative management in its context and processes is advocated to reduce surgical and postoperative related risk-factors to minimize the risks of adverse postoperative outcomes.

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Conflicts of interest

None declared.

References

1. Parks RW, Garden OJ. (2001) Liver resection for cancer. *World J Gastroenterol* 7:766–771. <https://doi.org/10.3748/wjg.v7.i6.766>.
2. Melloul E, Hubner M, Scott M, Snowden C, Prentis J, Dejong CH *et al.* (2016) Guidelines for perioperative care for liver surgery: enhanced recovery after surgery (ERAS) society recommendations. *World J Surg* 40: 2425–2440. <https://doi.org/10.1007/s00268-016-3700-1>.
3. Li M, Zhang W, Jiang L, Yang J, Yan L. (2016) Fast track for open hepatectomy: a systemic review and meta-analysis. *Int J Surg* 36: 81–89. <https://doi.org/10.1016/j.ijsu.2016.10.019>.
4. Dutch Institute for Clinical Auditing (DICA) Leiden. (2015) *DICA jaar-rapportage 2015*. DSCA [accessed January 2017] <http://www.clinicalaudit.nl/jaarrapportage/2015/dsca.html>.
5. Dronkers JJ, Chorus AMJ, van Meeteren NLU, Hopman-Rock M. (2013) The association of pre-operative physical fitness and physical activity with outcome after scheduled major abdominal surgery. *Anaesthesia* 68:67–73. <https://doi.org/10.1111/anae.12066>.
6. Heldens A, Bongers BC, Lenssen AF, Stassen LPS, Buhre WF, van Meeteren NLU. (2017) The association between performance parameters of physical fitness and postoperative outcomes in patients undergoing colorectal surgery: an evaluation of care data. *Eur J Surg* 43: 2084–2092. <https://doi.org/10.1016/j.ejso.2017.08.012>.
7. Older PO, Levett DZH. (2017) Cardiopulmonary exercise testing and surgery. *Ann Am Thorac Soc* 14:S74–S83. <https://doi.org/10.1513/AnnalsATS.201610-780FR>.
8. Moran J, Wilson F, Guinan E, McCormick P, Hussey J, Moriarty J. (2016) Role of cardiopulmonary exercise testing as a risk-assessment method in patients undergoing intra-abdominal surgery: a systematic review. *Br J Anaesth* 116:177–191. <https://doi.org/10.1093/bja/aev454>.
9. Snowden CP, Prentis J, Jacques B, Anderson H, Manas D, Jones D *et al.* (2013) Cardiorespiratory fitness predicts mortality and hospital length of stay after major elective surgery in older people. *Ann Surg* 257: 999–1004. <https://doi.org/10.1097/SLA.0b013e31828dbac2>.
10. Junejo MA, Mason JM, Sheen AJ, Moore J, Foster P, Atkinson D *et al.* (2012) Cardiopulmonary exercise testing for preoperative risk assessment before hepatic resection. *Br J Surg* 99:1097–1104. <https://doi.org/10.1245/s10434-014-3493-0>.
11. Kasivisvanathan R, Abbassi-Ghadi N, McLeod AD, Oliver A, Rao Baikady R, Jhanji S *et al.* (2015) Cardiopulmonary exercise testing for predicting postoperative morbidity in patients undergoing hepatic resection surgery. *HPB* 17:637–643. <https://doi.org/10.1111/hpb.12420>.
12. Ulyett S, Wiggans MG, Bowles MJ, Aroori S, Briggs CD, Erasmus P *et al.* (2015) Clinical assessment before hepatectomy identifies high-risk patients. *J Surg Res* 198:87–92. <https://doi.org/10.1016/j.jss.2015.05.044>.
13. Elings J, van der Sluis G, Goldbohm S, Galindo-Garre F, Gast A, Hoogeboom T *et al.* (2016) Development of a risk stratification model for delayed inpatient recovery of physical activities in patients undergoing total hip replacement. *J Orthop Sport Phys Ther* 46:135–143. <https://doi.org/10.2519/jospt.2016.6124>.
14. Oosting E, Hoogeboom T, Appelman S, Swets A, Dronkers J, Meeteren N. (2015) Preoperative prediction of inpatient recovery of function after total hip arthroplasty using performance-based tests: a prospective cohort study. *Disabil Rehabil* 38:1243–1249. <https://doi.org/10.3109/09638288.2015.1076074>.
15. van der Sluis GA, Goldbohm RE, Elings J, Nijhuis-van der Sanden MP, Akkermans R, Bimmel R *et al.* (2017) Pre-operative functional mobility as an independent determinant of inpatient functional recovery after total knee arthroplasty during three periods that coincided with changes in clinical pathways. *Bone Joint J* 99-B:211–217. <https://doi.org/10.1302/0301-620X.99B2.BJJ-2016-0508.R1>.

16. Huisman MG, van Leeuwen BL, Ugolini G, Montroni I, Spiliotis J, Stabilini C *et al.* (2014) "Timed Up & Go": a screening tool for predicting 30-day morbidity in onco-geriatric surgical patients? A multicenter cohort study. *PLoS One* 9, e86863. <https://doi.org/10.1371/journal.pone.0086863>.
17. Hayashi K, Yokoyama Y, Nakajima H, Nagino M, Inoue T, Nagaya M *et al.* (2017) Preoperative 6-minute walk distance accurately predicts postoperative complications after operations for hepato-pancreato-biliary cancer. *Surgery* 161:525–532. <https://doi.org/10.1016/j.surg.2016.08.002>.
18. Reddy S, Contreras CM, Singletary B, Bradford TM, Waldrop MG, Mims AH *et al.* (2016) Timed stair climbing is the single strongest predictor of perioperative complications in patients undergoing abdominal surgery. *J Am Coll Surg* 222:559–566. <https://doi.org/10.1016/j.jamcollsurg.2016.01.010>.
19. Hulzebos EH, van Meeteren NL. (2016) Making the elderly fit for surgery. *Br J Surg* 103:463. <https://doi.org/10.1002/bjs.10134>.
20. Hulzebos EH, van Meeteren NL. (2016) Making the elderly fit for surgery. *Br J Surg* 103:e12–e15. <https://doi.org/10.1002/bjs.10033>.
21. Carli F, Ferreira V. (2018) Prehabilitation: a new area of integration between geriatricians, anesthesiologists, and exercise therapists. *Aging Clin Exp Res* 30:241–244. <https://doi.org/10.1007/s40520-017-0875-8>.
22. Shields RK, Enloe LJ, Evans RE, Smith KB, Steckel SD. (1995) Reliability, validity, and responsiveness of functional tests in patients with total joint replacement. *Phys Ther* 75:169–176.
23. Thomas S, Reading J, Shephard RJ. (1992) Revision of the physical activity readiness questionnaire (PAR-Q). *Can J Sport Sci* 17:338–345.
24. Bongers BC, Takken T. (2014) The paediatric version of the steep ramp test. *J Physiother* 60:113. <https://doi.org/10.1016/j.jphys.2014.03.002>.
25. De Backer IC, Schep G, Hoogeveen A, Vreugdenhil G, Kester AD, van Breda E. (2007) Exercise testing and training in a cancer rehabilitation program: the advantage of the steep ramp test. *Arch Phys Med Rehabil* 88:610–616. <https://doi.org/10.1016/j.apmr.2007.02.013>.
26. Meyer K, Samek L, Schwaibold M, Westbrook S, Hajric R, Lehmann M *et al.* (1996) Physical responses to different modes of interval exercise in patients with chronic heart failure—application to exercise training. *Eur Heart J* 17:1040–1047.
27. Bohannon RW. (2006) Reference values for the five-repetition sit-to-stand test: a descriptive meta-analysis of data from elders. *Percept Mot Skills* 103:215–222. <https://doi.org/10.2466/pms.103.1.215-222>.
28. Lord SR, Murray SM, Chapman K, Munro B, Tiedemann A. (2002) Sit-to-stand performance depends on sensation, speed, balance, and psychological status in addition to strength in older people. *J Gerontol A Biol Sci Med Sci* 57:M539–M543. <https://doi.org/10.1093/gerona/57.8.M539>.
29. Tiedemann A, Shimada H, Sherrington C, Murray S, Lord S. (2008) The comparative ability of eight functional mobility tests for predicting falls in community-dwelling older people. *Age Ageing* 37:430–435. <https://doi.org/10.1093/ageing/afn100>.
30. Peolsson A, Hedlund R, Oberg B. (2001) Intra- and inter-tester reliability and reference values for hand strength. *J Rehabil Med* 33:36–41.
31. Brooks D, Davis AM, Naglie G. (2006) Validity of 3 physical performance measures in inpatient geriatric rehabilitation. *Arch Phys Med Rehabil* 87:105–110. <https://doi.org/10.1016/j.apmr.2005.08.109>.
32. Bohannon RW, Wang YC, Gershon RC. (2015) Two-minute walk test performance by adults 18 to 85 years: normative values, reliability, and responsiveness. *Arch Phys Med Rehabil* 96:472–477. <https://doi.org/10.1016/j.apmr.2014.10.006>.
33. Podsiadlo D, Richardson S. (1991) The timed "up & go": a test of basic functional mobility for frail elderly persons. *J Am Geriatr Soc* 39:142–148.
34. de Carvalho Bastone A, de Souza Moreira B, Teixeira CP, Dias JM, Dias RC. (2016) Is the veterans specific activity questionnaire valid to assess older adults aerobic fitness? *J Geriatr Phys Ther* 39:117–124. <https://doi.org/10.1519/jpt.0000000000000062>.
35. Hlatky MA, Boineau RE, Higginbotham MB, Lee KL, Mark DB, Califf RM *et al.* (1989) A brief self-administered questionnaire to determine functional capacity (the Duke Activity Status Index). *Am J Cardiol* 64:651–654.
36. Steyerberg EW. (2009) Statistical models for prediction. In: Steyerberg EW, ed. *Clinical prediction models: A practical approach to development, validation, and updating*, 1st ed.. New York: Springer-Verlag, pp. 53–83.
37. Steyerberg EW, Eijkemans MJ, Harrell FE, Jr., Habbema JD. (2000) Prognostic modelling with logistic regression analysis: a comparison of selection and estimation methods in small data sets. *Stat Med* 19:1059–1079.
38. Stuiver MM, Kampshoff CS, Persoon S, Groen W, van Mechelen W, Chinapaw MJM *et al.* (2017) Validation and refinement of prediction models to estimate exercise capacity in cancer survivors using the steep ramp test. *Arch Phys Med Rehabil* 98:2167–2173. <https://doi.org/10.1016/j.apmr.2017.02.013>.
39. Zhang X-L, Liu R-F, Zhang D, Zhang Y-S, Wang T. (2017) Laparoscopic versus open liver resection for colorectal liver metastases: a systematic review and meta-analysis of studies with propensity score-based analysis. *Int J Surg* 44:191–203. <https://doi.org/10.1016/j.ijsu.2017.05.073>.
40. Dronkers J, Witteman B, van Meeteren N. (2016) Surgery and functional mobility: doing the right thing at the right time. *Tech Coloproctol* 20:339–341. <https://doi.org/10.1007/s10151-016-1487-6>.
41. Covinsky KE, Pierluissi E, Johnston C. (2011) Hospitalization-associated disability: "she was probably able to ambulate, but i'm not sure". *JAMA* 306:1782–1793. <https://doi.org/10.1001/jama.2011.1556>.
42. Sourdset S, Lafont C, Rolland Y, Nourhashemi F, Andrieu S, Vellas B. (2015) Preventable iatrogenic disability in elderly patients during hospitalization. *J Am Med Di Assoc* 16:674–681. <https://doi.org/10.1016/j.jamda.2015.03.011>.
43. Lambin P, Zindler J, Vanneste BGL, De Voorde LV, Eekers D, Compter I *et al.* (2017) Decision support systems for personalized and participative radiation oncology. *Adv Drug Deliv Rev* 109:131–153. <https://doi.org/10.1016/j.addr.2016.01.006>.
44. Jones BD, Jones R, Dunne DF, Astles T, Fenwick SW, Poston GJ *et al.* (2018) Patient selection and perioperative optimisation in surgery for colorectal liver metastases. *Eur Surg* 50:87–92. <https://doi.org/10.1007/s10353-018-0539-8>.
45. Dunne DF, Jack S, Jones RP, Jones L, Lythgoe DT, Malik HZ *et al.* (2016) Randomized clinical trial of prehabilitation before planned liver resection. *Br J Surg* 103:504–512. <https://doi.org/10.1002/bjs.10096>.
46. Ljungqvist O, Scott M, Fearon KC. (2017) Enhanced recovery after surgery: a review. *JAMA Surg* 152:292–298. <https://doi.org/10.1001/jamasurg.2016.4952>.