

ORIGINAL ARTICLE

Preoperative risk analysis index for frailty predicts short-term outcomes after hepatopancreatobiliary surgery

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Abstract

Background: The Risk Analysis Index (RAI) for frailty is a rapid survey for comorbidities and performance status, which predicts mortality after general surgery. We aimed to validate the RAI in predicting outcomes after hepatopancreatobiliary surgery.

Methods: Associations of RAI, determined in 162 patients prior to undergoing hepatopancreatobiliary surgery, with prospectively collected 30-day post-operative outcomes were analyzed with multivariate logistic and linear regression.

Results: Patients (age 62 ± 14 , 51% female) had a median RAI of 7, range 0–25. With every unit increase in RAI, length of stay increased by 5% (95% CI: 2–7%), odds of ICU admission increased by 10% (0–20%), ICU length of stay increased by 21% (9–34%), and odds of discharge to a nursing facility increased by 8% (0–17%) (all $P < 0.05$). Particularly in patients who suffered a first post-operative complication, RAI was associated with additional complications (1.6 unit increase in Comprehensive Complication Index per unit increase in RAI, $P = 0.002$). In a direct comparison in a subset of 74 patients, RAI and the ACS-NSQIP Risk Calculator performed comparably in predicting outcomes.

Conclusion: While RAI and ACS-NSQIP Risk Calculator comparatively predicted short-term outcomes after HPB surgery, RAI has been specifically designed to identify frail patients who can potentially benefit from preoperative prehabilitation interventions.

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Introduction

The life expectancy at birth has increased significantly over the past 50 years,¹ contributing to aging of the US population. This has resulted in increasing numbers of elderly patients being evaluated for surgery.^{2,3} Insight into perioperative risks is important to select the appropriate procedure for a patient at the right time. Although postoperative morbidity and mortality increase with age, our group previously found that age alone is not necessarily of help to patient and surgeon in assessing benefits

and risks of elective hepatopancreatobiliary (HPB) surgery at the individual level.⁴ Recently, the assessment of frailty, which is a clinically recognizable phenotype of decreased physiologic reserve and resistance to stressors,⁵ has increasingly been used as a preoperative tool to determine a patient's chances to withstand the insult of the operation and make a successful recovery. However, no consensus on the definition of frailty and no ideal tool to measure frailty exist. A recent meta-analysis of more than one million patients undergoing major abdominal surgery clearly showed the association of frailty with increased post-operative morbidity and mortality.⁶ In several studies, frailty has been shown to more accurately predict perioperative morbidity, mortality, and cost than age or comorbidity alone,^{7–10} a correlation that has also been observed in patients undergoing

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HPB surgery.^{11–14} In addition, frail patients are less likely to be discharged to home postoperatively,¹⁵ and more likely to be readmitted to a hospital within 30 days of discharge.¹⁶ In the most recent guidelines by the American College of Surgery, the preoperative assessment of frailty in elderly patients is therefore recommended.¹⁷

The comprehensive Risk Analysis Index (RAI) for frailty has been shown to predict mortality in a large cohort of surgical patients.⁷ The RAI consists of a 14-item survey to assess activities of daily living and comorbidities. It was initially developed using variables from the Minimum Data Set (MDS) Mortality Risk Index–Revised (MMRI-R) that most accurately predicted 6-month mortality in nursing home residents.^{18,19} RAI is based exclusively on the report of the patient (or surrogate) and can be rapidly obtained without the need for functional assessment or patient record review. An analysis of RAI scores in patients presenting to various clinics at our institution revealed that patients with hepatopancreatobiliary disease are among the most frail patients, only second to patients presenting for cardiovascular surgery. Therefore, the aim of this study was to validate the performance of RAI in predicting short-term postoperative outcomes in patients undergoing hepatopancreatobiliary surgery, a significantly frail patient population.

Methods

Following approval by the Institutional Review Board of the University of Pittsburgh, we prospectively collected outcome data for a cohort of 162 patients for whom RAI score was determined prior to elective surgery at the HPB surgery department. The 14 variables that are evaluated by the RAI include information on demographics, signs and symptoms, comorbid diagnoses, and level of independence in daily activities, as listed in Table 1. Full details on the weight of each variable in the RAI scoring system have been provided by Melin *et al.*²⁰ Since a majority of our patients undergo surgery for a malignant condition and a diagnosis of cancer adds a significant number of points to the RAI without affecting frailty per se, non-cancer RAI

scores were used for the analyses, as previously described.⁷ The performed operations were divided into minor surgery (such as laparoscopic radiofrequency ablation, laparoscopic cholecystectomy in patients with underlying liver disease), intermediate surgery (such as liver resection up to 3 segments, distal pancreatectomy), and major surgery (such as hemihepatectomy, hepatic trisegmentectomy, pancreaticoduodenectomy, combined colon/liver resections). Data on comorbidities not included in RAI, such as hypertension, diabetes mellitus, coronary artery disease, and liver disease (by model for end-stage liver disease [MELD] score calculation according to the Organ Procurement and Transplantation Network) were also collected.

Data on 30-day postoperative outcomes were prospectively collected. Complications were scored according to the Clavien-Dindo classification and the Comprehensive Complication Index (CCI) was calculated for each patient resulting in a score on a scale from 0–100.²¹ Other assessed postoperative outcomes included overall length of stay (LOS), ICU admission, ICU LOS, disposition (discharge to home vs. nursing facility), and readmission to a hospital within 30 days. The correlation between RAI and LOS in days was analyzed with negative binomial regression. Correlations between RAI and ICU admission, disposition, and 30 days readmission were analyzed with logistic regression. For the ICU length of stay, the distribution was overdispersed with an excess of zero values (most patients did not require ICU admission), so we employed a standard negative binomial model, as well as a zero-inflated negative binomial model. With Vuong's test the two models were compared and found to be non-significantly different, so we applied negative binomial modeling for the analysis. The correlation between RAI and CCI was analyzed by linear regression.

Other variables that can affect outcomes after HPB surgery, but are not covered by the RAI, are diabetes, coronary artery disease, magnitude of the operation, and underlying liver disease. As such, we performed multivariate analyses to identify covariates associated with the outcome that are not accounted for by the RAI. The multivariate analysis was done including 2 quantitative variables (MELD and intraoperative estimated blood loss) and 4 qualitative variables (type of surgery being either minor, intermediate, or major, presence or absence of diabetes, presence or absence of coronary artery disease, and cancer stage). The influence of these covariates on the various outcome measures was analyzed. Backward stepwise selection was applied with elimination of covariates with $P > 0.2$ from the full model. The hospital and ICU LOS were analyzed via a negative binomial regression. The disposition, ICU admission, 30-day readmissions were analyzed via logistic regression. The CCI was analyzed via linear regression.

The RAI was compared to the ACS NSQIP Surgical Risk Calculator for its performance to predict outcomes after HPB surgery. Our institution participates in the American College of Surgery National Surgical Quality Improvement Program (ACS NSQIP) and we matched our HPB surgery cohort to our

Table 1 The 14 variables assessed by the Risk Analysis Index

Demographics	Clinical signs/symptoms	Disease history	(In)dependence in ADL
Age	Shortness of breath	Congestive heart failure	Mobility
Sex	Poor appetite	Renal failure	Toilet Use
Independent living	Recent weight loss	History of cancer in last 5yrs	Eating
	Recent cognitive decline		Personal Hygiene

ADL – Activities of daily living.

institution's ACS NSQIP data. ACS NSQIP data were available for patients undergoing major hepatectomy, distal pancreatectomy, and pancreatoduodenectomy, and we identified 74 patients (46% of the total cohort) for whom data existed in both databases. For these 74 patients, a comparison between RAI and the ACS Surgical Risk Calculator was performed for 3 important outcomes being occurrence of complications, disposition, and readmission. As these variables have a binary outcome (0 and 1), ROC curves for both prediction models could be constructed and compared for metrics of discrimination (area under the curve - AUC) and overall accuracy (Brier scores). All data analysis was conducted using Stata v14SE (StataCorp; College Station, TX).

Results

Characteristics of patients undergoing HPB surgery

Age of the 162 patients who underwent HPB surgery was 62 ± 14 (mean \pm SD), and 83 (51%) were female. Baseline characteristics are listed in Table 2. The cohort was nearly equally distributed for those undergoing minor, intermediate, or major operations. Sixty-one patients (38%) were operated on for benign disease, whereas 101 (62%) patients underwent surgery for primary malignant or metastatic disease. The median RAI was 7, with most patients having an RAI of 6–10 (Fig. 1).

Outcomes after HPB surgery

Data for outcome variables are summarized in Table 3. The median length of stay was 3.8 days, interquartile range (IQR) 1–5.6 days. Twenty-six (16%) patients were admitted to ICU post-operatively for a median of 2.5 (IQR 1–4) days. Two patients (1.2%) died within 30 days; one patient (RAI of 13) died 4 days after isolated hepatic perfusion complicated by intraoperative blood loss and subsequent development of multiorgan failure; one patient (RAI of 11) died 27 days after pancreaticoduodenectomy after being readmitted with failure to thrive, malnutrition and congestive heart failure. CCI based on classification of complications according to the Clavien-Dindo system was 0 (no complications) for 104 patients (64%). Fifty-eight patients (36%) developed at least 1 complication with a median CCI of 23 with IQR 21–37. Disposition to home, with or without home health care, was deemed appropriate for 152 patients (94%), whereas 9 patients (6%) were discharged to a facility for post-hospital care.

Frailty predicts postoperative outcomes

Investigations of the correlation between RAI and outcome variables revealed that with every unit increase in RAI score, length of stay increased by 4.9% (IRR 1.049; 95% CI 1.022–1.077, $P < 0.001$), the odds of admission to the ICU increased by 10.6% (OR 1.106; 95% CI 1.021–1.199, $P = 0.014$), the expected ICU length of stay increased by 17.4% (IRR = 1.174; 95% CI 1.058–1.301, $P = 0.002$), and the odds of discharging the patient to a special care facility increased by

Table 2 Baseline characteristics of patients undergoing HPB surgery

Demographic	Total N = 162
Age, mean \pm SD	61.50 \pm 14
Age, number of patients (%)	
≤ 40	13 (8%)
41–60	49 (30%)
61–80	89 (55%)
≥ 81	11 (7%)
Gender (%)	
Female	83 (51%)
Male	79 (49%)
Type of Surgery, number of patients (%)	
Minor	55 (34%)
Intermediate	56 (35%)
Major	51 (31%)
BMI, mean \pm SD	28.7 \pm 6.4 ^a
Hypertension, number of patients (%)	72 (44%)
Diabetes, number of patients (%)	31 (19%)
Coronary artery disease, number of patients (%)	31 (19%)
MELD, median (IQR)	7 (6–8) ^b
ASA class, number of patients (%)	
1	3 (2%)
2	39 (24%)
3	105 (65%)
4	15 (9%)
Intraoperative EBL, median (IQR)	100 (20–300)
Cancer Stage, number of patients (%)	
0	61 (38%)
1	17 (10%)
2	19 (12%)
3	7 (4%)
4	58 (36%)

BMI – body mass index, ASA – American Society of Anesthesiology, EBL – estimated blood loss, IQR – interquartile range.

^a Data missing for 3 patients.

^b Data missing for 6 patients.

9.8% (OR 1.098; 95% CI 1.025–1.176, $P = 0.008$). The odds of readmission increased by 8.2%, but statistical significance for this outcome was not reached (OR = 1.082; 95% CI 0.999–1.173, $P = 0.054$). RAI did not accurately predict if post-operative complications would occur or not (comparing CCI = 0 vs. CCI ≥ 1 , $P = 0.37$). However, among patients who developed at least 1 complication, RAI was significantly predictive for the number and severity of complications (per unit increase in RAI the CCI increased by 1.6 point (coefficient 1.60; 95% CI 0.61–2.58, $p < 0.002$) (Fig. 2).

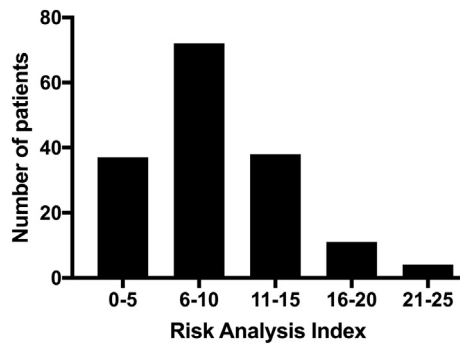


Figure 1 Distribution of RAI scores of patients undergoing HPB surgery

Table 3 Outcomes after HPB surgery

Outcome	N = 162
LOS, days, median (IQR)	3.8 (1–5.6)
ICU admission (%)	26 (16%)
ICU LOS, days (SD)	13 (17)
CCI	
0	104 (64%)
≥1	58 (34%)
median CCI (IQR) if CCI ≥1	23 (21–37)
30-day mortality (%)	2 (1.23%)
Discharge disposition (%)	
Home with or without home health care	152 (94%)
Nursing facility/Rehabilitation facility	9 (6%)
Readmission within 30 days (%)	25 (15%)

LOS – length of stay, IQR – interquartile range, CCI – Comprehensive Complication Index

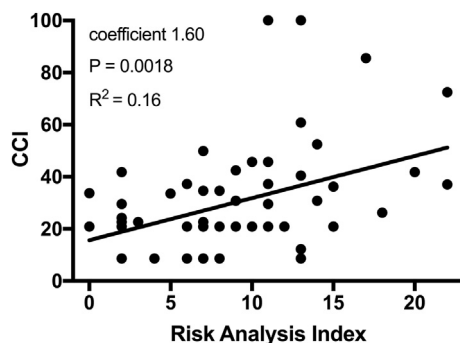


Figure 2 Correlation between RAI score and CCI among patients with at least 1 post-operative complication

RAI is an independent predictor of outcomes on multivariate analysis

Covariates that are not included in RAI but likely to have an effect on outcomes were analyzed using multivariate analysis in

which variables associated with the outcome with a $P < 0.2$ were included in the final model, as shown for hospital LOS in Table 4. When adjusted for covariates, RAI remained an independent predictor for hospital LOS with a 4.7% increase in LOS per unit increase in RAI (IRR 1.047; 95% CI 1.024–1.069, $P < 0.001$). Using a similar strategy, multivariate models were created for the correlations of RAI with the other outcome measures of interest. The final results of these multivariate analyses are listed in Table 5. In addition to being predictive of hospital LOS, every 1 unit increase in RAI independently predicted a 9.8% increase in the need for intensive care (OR 1.098; 95% CI 1.003–1.201, $P = 0.042$), a 20.5% increase in ICU LOS (IRR 1.205; 95% CI 1.085–1.338, $P = 0.001$), a 1.2 unit increase in CCI (coefficient 1.202; 95% CI 0.290–2.113, $P = 0.011$), and an 8.0% increase in discharge to a facility for post-hospital care (OR 1.080; 95% CI 1.002–1.165, $P = 0.44$).

Comparison of RAI with ACS NSQIP Surgical Risk Calculator

For 3 important binary outcomes (being complications, disposition, and readmissions), ROC curves for RAI and ACS Surgical Risk Calculator were compared for a subgroup of 74 patients. We found that both RAI and ACS NSQIP were moderate predictors of the outcomes (AUC 0.6–0.8) (Fig. 3). ACS performed better in predicting the occurrence of any complication than RAI (concordant with our results for the entire cohort that RAI only associates well with additional complications once a first complication occurs), although correcting the RAI for confounding variables improved its AUC from 0.56 to 0.70 (vs. 0.75 for ACS). Regarding disposition (home vs. specialty care facility), RAI and ACS performed comparably (AUC 0.62 vs 0.65, respectively), while RAI was superior in predicting readmissions for this subcohort (AUC 0.76 vs. 0.69 in ACS).

Discussion

The pre-operative assessment of frailty is increasingly used as an important tool to predict peri-operative risks and the prospect of an uncomplicated recovery. The Risk Analysis Index for frailty has been shown to be an independent prognosticator for outcomes after surgery,⁷ but patients undergoing HPB surgery were not included in this cohort. We opted to prospectively validate the performance of RAI in predicting post-operative outcomes in our specific patient population by including all consecutive patients scheduled for HPB surgery during a 6 months period in our high-volume HPB surgery center. Here we present novel evidence that RAI can be a fast, easy and accurate tool to identify frail patients at risk for unfavorable outcomes after HPB surgery. Our analysis demonstrates that RAI is an independent predictor for post-operative complications, need for intensive care, LOS, and need for post-discharge nursing home care. RAI may therefore be an aid in pre-operative decision making for treatment allocation for HPB diseases, e.g. to determine patient

Table 4 Univariate and multivariate analysis of RAI as predictor for hospital LOS

	Univariate		Multivariate Full Model		Multivariate Reduced Model	
	IRR (95% CI)	P value	IRR	P value	IRR	P value
RAI	1.049 (1.022,1.077)	<0.001	1.044 (1.021,1.068)	<0.001	1.047 (1.024–1.069)	<0.001
CAD			1.340 (0.982–1.827)	0.065	1.383 (1.038–1.842)	0.027
Diabetes			0.926 (0.689–1.243)	0.608		
MELD score			1.021 (0.967–1.078)	0.463		
Surgery						
Minor			1.0 (1.0–1.0)	1.0		
Intermediate			2.439 (1.719–3.461)	<0.001	2.497 (1.820–3.426)	<0.001
Major			3.783 (2.586–5.532)	<0.001	3.954 (2.872–5.444)	<0.001
EBL			1.0 (1.0–1.0)	0.791		
Cancer stage						
0			1.0 (1.0–1.0)	1.0		
1			1.068 (0.687–1.660)	0.770		
2			1.154 (0.755–1.763)	0.509		
3			1.0 (0.531–1.882)	0.999		
4			1.387 (0.994–1.936)	0.054	1.329 (1.040–1.698)	0.023

IRR – Incident Rate Ratio, RAI – Risk Analysis Index, CAD – coronary artery disease, MELD – model for end-stage liver disease, EBL – estimated blood loss.

Table 5 Multivariate analyses of the effect of 1 point increase in RAI on outcomes after HPB surgery, adjusted for confounding variables

Outcome	Adjusted measure of correlation (95% CI)	p-value
LOS	IRR 1.047 (1.024–1.069)	<0.001
ICU admission	OR 1.098 (1.003–1.201)	0.042
ICU LOS	IRR 1.205 (1.085–1.338)	0.001
CCI ≥ 1	Coefficient 1.202 (0.290–2.113)	0.011
Disposition other than home	OR 1.080 (1.002–1.165)	0.044
Readmission	OR 1.081 (0.993–1.177)	0.072

LOS – length of stay, CCI – Comprehensive Complication Index, IRR – Incident Rate Ratio, OR – Odds ratio.

suitability for surgical intervention, or potentially better tolerable locoregional therapy such as transarterial chemoembolization for liver tumors in case of frailty.

The effect of frailty on surgical outcomes has been demonstrated in multiple studies.^{7–10} Sandini *et al.*⁶ recently performed a systematic review and aggregated the results of original studies in a meta-analysis of more than one million patients. The analysis revealed that the risk of short-term post-operative mortality in frail patients is more than five-fold elevated. Since frailty is the result of many domains, defined by an international expert panel to include physical performance, gait speed, mobility, nutritional status, mental health, and cognition,²² a diversity of measures exists to evaluate some or all of these domains. In the meta-analysis, in which the inclusion criteria were

kept broad, this resulted in the inclusion of studies with 12 different definitions of frailty, which incorporated from one to 70 variables in different combinations.⁶ Although the American College of Surgery recommends the assessment of frailty in the pre-operative setting, there is no consensus on the definition of frailty and no ideal tool to measure it. Certain frailty assessments have been validated in patients undergoing surgery, such as the Charlson comorbidity index, time for a patient to get up and walk, and the MiniCog score to evaluate cognition.^{15,23} In addition, a reduction in muscle mass (sarcopenia) measured on CT images has been shown to correlate with mortality after HPB surgery.^{12,13} Ideally, the assessment of frailty would be sensitive, specific, rapid, cost-effective, and well-suited for research protocols. The RAI was designed to effectively distinguish between frail and robust, and was developed and validated in large cohorts of patients undergoing surgery.^{7,24} The RAI relies exclusively on the report of the patient (or surrogate) and can be easily administered by personnel at all levels of training.²⁴ It requires neither functional assessment of patient performance nor medical record review, and is therefore easy to integrate in the already existing workflow. Frailty has been shown to most accurately predict mortality within the 30-day post-operative period.²⁵ Here we show that the RAI, used to measure frailty, is predictive of most of the relevant short-term post-operative outcomes after hepatopancreatobiliary surgery.

To provide reference for the performance of RAI in predicting outcomes, we compared the RAI to the ACS Surgical Risk Calculator, an externally validated scoring system that predicts the risk percentage of 11 postoperative (adverse) outcomes. RAI

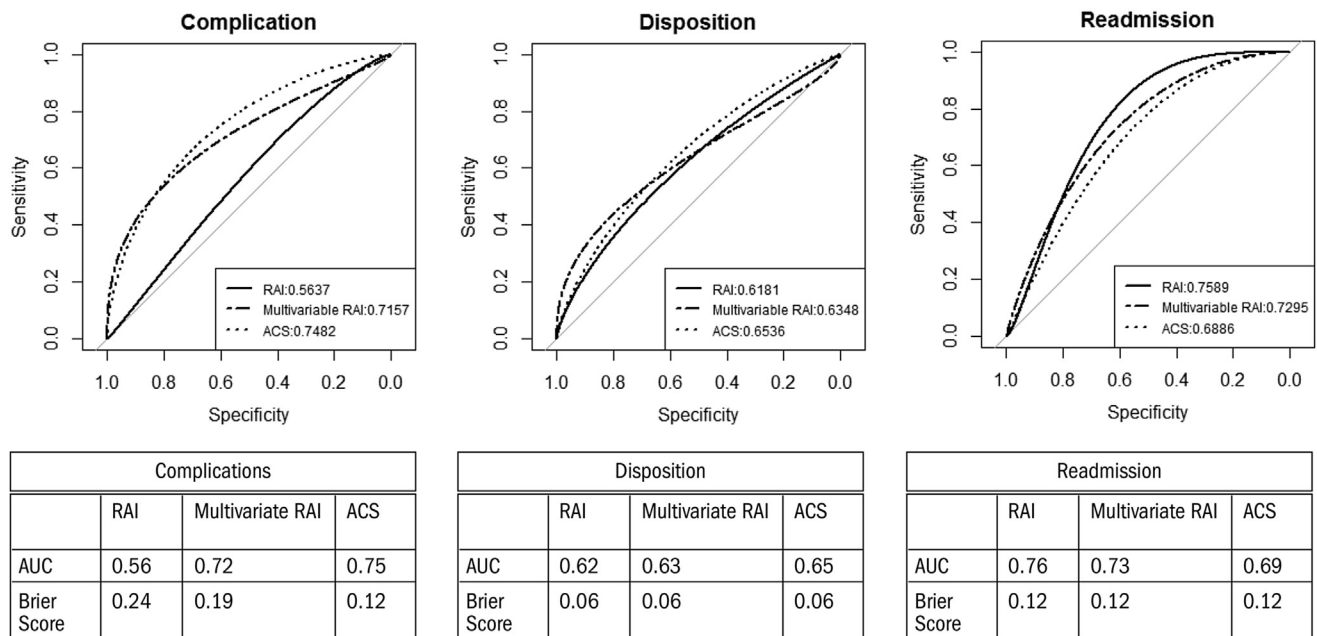


Figure 3 Comparison between RAI and ACS NSQIP risk calculator

and ACS were comparable in predicting postoperative outcomes, albeit with some variation depending on the specific outcome that was looked at. Although ACS is a model that was intentionally developed to identify predictors of poor outcomes, it was not developed to identify frail patients. RAI is a model initially developed to identify frailty, for which we now present evidence that in HPB surgical patients it predicts outcomes comparably to the ACS Surgical Risk Calculator. Therefore, while comparable in predicting outcomes, we will prefer RAI for its specific ability to identify frail patients that would hypothetically benefit from preoperative prehabilitation interventions to improve outcomes through an improvement in their frailty.

In our study, the RAI score correlated with the length of stay, the need for intensive care, ICU length of stay, complication rate, the odds of being discharged to a specialized nursing facility, and the odds of being readmitted. We observed higher ICU admission rates and an increase in ICU length of stay with every unit increase of RAI. Our data are concordant with prior studies in which frailty has been repeatedly associated with admission to ICU, summarized in a meta-analysis that demonstrated an odds ratio of 2.14 (95% CI 2.01–2.21) for frail patients to be admitted to the ICU.²⁶ The Comprehensive Complication Index (CCI) expresses the number and severity of post-operative complications on a continuous scale. In our analysis, the CCI score was significantly correlated with RAI. Interestingly, this correlation was present only if patients without post-operative complications were not included in the analysis. This indicates that RAI did not directly predict whether a complication would occur or not. However, once a complication occurred, the RAI accurately predicted the incidence of additional and more severe

complications. These data are supportive of the idea that frail people can tolerate an operation, but can poorly tolerate the first complication after an operation, placing them at risk for entering a downward spiral resulting in a prolonged recovery with poor outcomes. The need for post-discharge transitional care, such as provided in skilled nursing and rehabilitation facilities, increased with every unit increase in RAI score. Likewise, it has been previously demonstrated that patients with poor functional status and poor pre-operative exercise tolerance had a correlation with discharge to a skilled nursing facility.²⁷ Frailty was also shown to be a significant predictor of non-home discharge following radical cystectomy.²⁸

Although in other studies MELD score was significantly associated with mortality after HPB surgery,²⁹ MELD scores had a non-significant effect on outcomes in most of our multivariate analyses. This discordance can likely be explained by the fact that high MELD scores in particular predict unfavorable outcomes, whereas in our cohort MELD scores were relatively low (median 7). This indicates that a clinical selection in our cohort had taken place to assess fitness for elective surgical operation, and that highest risk patients may have been precluded from undergoing an operation. Along those lines it is noteworthy that 9.7% of patients seen in our HPB surgery clinics were defined as frail according to a previously defined cutoff of a non-cancer RAI score ≥ 21 ,⁷ whereas only 2.5% of the cohort undergoing surgery met this criteria. This indicates that our group of patients undergoing surgery is already a selection of the relatively fittest patients, and that surgery was not considered to be beneficial in the most severely frail patients. Nevertheless, in the cohort that was deemed sufficiently fit for surgery, RAI was still a strong

independent predictor of most short-term outcomes, with risks increasing by 5–20% per point increase in RAI.

With aging of the population, frailty in elderly seeking surgical consultation is increasingly prevalent. Elevated frailty scores can also be expected to occur more frequently in younger patients with severe comorbidities related to obesity,³⁰ which is thought to be a reason for a recently measured decline in life expectancy at birth in the US for certain ethnicities.¹ Insight in perioperative risks related to frailty is imperative for planning of elective HPB surgery for multiple reasons. First, HPB operations including major hepatectomy and pancreaticoduodenectomy are complex procedures with repeatedly documented risks of postoperative complications;^{31–34} hence the importance of an accurate assessment of who is at greatest risk for harm. In our multivariate analyses, we stratified for the complexity of the operation and found a clear stepwise increase in the risk of unfavorable outcomes when comparing minor to intermediate to major procedures. Although defining an operation as major remains arbitrary to some degree, the incremental increases in risk confirm that surgical magnitude was adequately stratified. Second, an evaluation of frailty that has predictive value for surgical outcomes may aid the surgeon in counseling of the patient to come to an individual optimum treatment plan in case less morbid treatment alternatives exist, such as minimally invasive approaches. One could hypothesize that especially in frail patients undergoing major surgery, a minimally invasive approach will be favorable. We are continuing to prospectively collect data on frailty and outcomes in our HPB surgical clinics to test this hypothesis in future analyses, by comparing outcomes of minimally invasive vs. open surgery in patients with equal frailty levels. For hepatobiliary diseases, radiofrequency ablation or trans-arterial chemoembolization could serve either as alternative or bridging therapy to open surgery. Finally, knowledge of frailty level may alert treating physicians and patient to have realistic expectations about certain foreseen complications, and help to point out opportunities for risk factor reduction through prehabilitation programs.

Various prehabilitation programs (including preoperative exercise and nutritional interventions) have been explored in surgical patient populations. To our knowledge, there has been one RCT on the effect of prehabilitation in HPB surgery patients, which showed improved cardiopulmonary fitness but no different post-operative outcomes.³⁵ Recently, systematic reviews and meta-analyses on prehabilitation in patients undergoing abdominal surgery have shown an overall beneficial effect of prehabilitation on post-operative complications, but warn that the included studies were heterogeneous and of very low methodologic quality.^{36–38} They conclude that there is a need for larger studies and standardization of methodology and assessment of outcomes.^{36,37} Patient selection is key for a successful completion of future prehabilitation trials, to avoid dilution of the effect of the intervention by non-frail patients that have favorable outcomes anyway. Patient selection is also important

for the efficient allocation of resources, as costs would likely prohibit applying the intervention to all patients. Here we demonstrated that RAI can have value in identifying patients in whom a prehabilitation intervention may be most beneficial. We are currently designing prehabilitation trials for frail patients scheduled for HPB surgery, using the RAI as inclusion criterion for patient selection.

In conclusion, frailty level measured by preoperative RAI score was significantly associated with short-term postoperative outcomes after HPB surgery, and can aid patient and surgeon in optimizing patients' risk profile prior to surgery, setting realistic goals and expectations, and select treatment options with the most favorable benefit/risk ratio.

Conflict of interest

None declared.

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