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Novel Prediction Score Including Pre- and Intraoperative Parameters Best Predicts Acute Kidney Injury after Liver Surgery

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Abstract

Background A recently published score predicts the occurrence of acute kidney injury (AKI) after liver resection based on preoperative parameters (chronic renal failure, cardiovascular disease, diabetes, and alanine-aminotransferase levels). By inclusion of additional intraoperative parameters we aimed to develop a new prediction model.

Methods A series of 549 consecutive patients were enrolled. The preoperative score and intraoperative parameters (blood transfusion, hepaticojejunostomy, oliguria, cirrhosis, diuretics, colloids, and catecholamine) were included in a multivariate logistic regression model. We added the strongest predictors that improved prediction of AKI compared to the existing score. An internal validation by fivefold cross validation was performed, followed by a decision curve analysis to evaluate unnecessary special care unit admissions.

Results Blood transfusions, hepaticojejunostomy, and oliguria were the strongest intraoperative predictors of AKI after liver resection. The new score ranges from 0 to 64 points predicting postoperative AKI with a probability of 3.5–95 %. Calibration was good in both models (15 % predicted risk vs. 15 % observed risk). The fivefold cross-validation indicated good accuracy of the new model (AUC 0.79 (95 % CI 0.73–0.84)). Discrimination was substantially higher in the new model (AUC_{new} 0.81 (95 % CI 0.76–0.86) versus $AUC_{preoperative}$ 0.60 (95 % CI 0.52–0.69), $p < 0.001$). The new score could reduce up to 84 unnecessary special care unit admissions per 100 patients depending on the decision threshold.

Conclusions By combining three intraoperative parameters with the existing preoperative risk score, a new prediction model was developed that more accurately predicts postoperative AKI. It may reduce unnecessary admissions to the special care unit and support management of patients at higher risk.

Milo A. Puhan and Pierre-Alain Clavien contributed as senior authors.

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Abbreviations

AKI	Acute kidney injury
ALT	Alanine aminotransferase
AUC	Area under the curve
RIFLE	Risk injury failure loss
p_t	Threshold probability
IQR	Interquartile range
CRF	Chronic renal failure
OR	Odds ratio
MAP	Mean arterial pressure

CVP	Central venous pressure
COPD	Chronic obstructive pulmonary disease
ASA	The American Society of Anesthesiologists
AST	Aspartate aminotransferase
TP	True positive
FP	False positive
FN	False negative
TN	True negative

Introduction

The development and validation of a prediction score to anticipate acute kidney injury (AKI) after liver resection was recently reported [1]. The initial score was derived exclusively from parameters available preoperatively such as pre-existing chronic renal dysfunction, cardiovascular disease, diabetes, and increased alanine-aminotransferase levels. The rationale for this strategy was to identify preoperatively patients at risk for AKI in order to intraoperatively adjust blood pressure and fluid management accordingly. It may, however, be equally important to individualize therapy in the postoperative period according to the risk for AKI, which may require close monitoring and pre-emptive treatment against AKI in a special care unit setting, such as an intermediate care or intensive care unit.

Postoperative AKI occurs not only because of pre-existing conditions but also as a result of intraoperative events, particularly unexpected events such as, e.g., bleeding and/or prolonged need for colloids[2–6]. It remains unclear from the previous study [1] and others [7] whether adding intraoperative parameters may improve the prediction of postoperative AKI. Additionally, common metrics for the accuracy of risk scores (predicted vs. observed risk or area under the curve [AOC]) do not allow for a straightforward clinical interpretation of the usefulness of a risk score [8, 9]. Therefore, our aim was primarily to assess whether adding intraoperative predictors to our preoperative risk score improves the prediction of AKI and secondarily to compare the clinical usefulness of the existing score with the new prediction score with regard to postoperative management.

Materials and methods

Study population and design

Consecutive patients undergoing any type of liver surgery were included between 1 July 2002 and 31 October 2007 from a single tertiary care center (Swiss Hepato-Pancreato-Biliary (HPB) Centre, University Hospital of Zurich, Switzerland) identically to the previously published database [1]. All patients with liver trauma and incomplete intraoperative data sets were excluded. All data were collected and entered into the database of the Swiss HPB Centre. The study was approved by the institutional review board for human studies (StV 33-2009) and internationally registered at clinicaltrials.gov (NCT01318798).

Definition of postoperative AKI

As in the previous study [1], postoperative AKI was defined according to the "R" of the RIFLE criteria as an absolute increase in serum creatinine of more than 0.3 mg/dl above baseline, or an increase >1.5 times the preoperative baseline value within 48 h after surgery [10–14].

Selection criteria of predictors for AKI

Intraoperative strategies may have an impact on the development of postoperative AKI. Therefore an improvement of the preoperative prediction score by intraoperative parameters will already offer the possibility for intraoperative treatment strategies in patients with increased risk for AKI. To improve the preoperatively predicted risk of AKI, intraoperative parameters were considered that are readily available but that do not have a strong association among themselves. A priori, the number of potential intraoperative predictors was restricted to fewer than ten to minimize the risk of developing overfitted models that would limit the applicability of the score in clinical practice.

Seven intraoperative predictive parameters—namely, the need for blood transfusion (no/yes), the presence of liver cirrhosis (no/yes), the presences of oliguria (no/yes), the need for hepaticojejunostomy (no/yes), the use of colloids (no/yes), the use of diuretics (no/yes), and the use of a bolus of catecholamines (no/yes)—were investigated. Liver cirrhosis was defined as a surgical diagnosis reported in the operation reports and assured by the histology of an intraoperative biopsy. Other liver-specific factors, such as inflow occlusion and operative time, among others, were not considered as additional parameters in order to prevent overlapping with other parameters. Oliguria was defined as an intraoperative urinary output of less than 400 ml/24 h [8]. The predictive parameter "diuretics" included the intraoperative use of osmotic or loop diuretics. The predictor "bolus of catecholamines" was defined as the intraoperative use of epinephrine, norepinephrine, and/or dopamine. Predictive parameters like hypotension, hypovolemia, use of vasopressor infusion, or the total vasopressor dose were not considered because of a possible interaction between one of the seven chosen intraoperative [9, 15–19]. Additionally, predictive parameters such as mean arterial pressure, total urinary output, total balance, or operative time were also not considered as additional parameters in order to prevent overlapping with other parameters, or because those parameters were not identified as predictors in the literature of non-cardiac surgery [3].

Statistical analysis

Because the selected predictors are easily available and we excluded 20 patients with incomplete data sets, no values for the predictors were missed. The distribution of data was expressed by using means and standard deviation for normally distributed data and medians and interquartile ranges for nonparametric data.

A multivariate logistic regression model was fitted to predict AKI with the preoperative score (from 0 to 7 points), blood transfusion, cirrhosis, oliguria, hepaticojejunostomy, colloids, diuretics, and bolus of catecholamines as candidate predictors. A stepwise backward logistic regression model was used to select the strongest predictors ($p < 0.157$) [20]. Bootstrapping was used to repeat the selection process 549 times (size of the study population) and retained predictors which were left in the model in more than 75 % of the bootstrap samples. The shrinkage was used to reduce the risk of overestimation of the association of the predictors with AKI with the multivariable logistic regression model [21]. A constant factor (the so-called Copas factor) was calculated to indicate the degree of potential overfitting, and all regression coefficients were multiplied with that factor [21].

For the validation, the AUC was calculated to estimate how well the new model discriminated between patients with and without AKI. A model with an AUC of more than 0.7 is generally considered to be a good model [22]. Calibration was investigated by plotting the observed risk of AKI against five predicted risk groups of equal size for AKI and to test the Hosmer–Lemeshow test to see whether predicted and observed risks differed significantly from each other, which would indicate poor calibration [23, 24]. Fivefold cross-validation for internal validation was also performed [23, 25].

Table 1 Patient characteristics

	Postoperative normal kidney function $n = 467$ (85.1 %)	Postoperative acute kidney injury $n = 82$ (14.9 %)
Age, years; median (IQR)	58 (47–65)	67 (58–73)
Gender, male/female (%)	257/210 (55/45)	45/37 54.9 %/45.1 %
Body mass index, kg/m^2; median (IQR)	24.6 (22–28)	25 (22–30)
Cardiovascular disease (%)[a]	43 (9.2)	24 (29.3 %)
Chronic renal failure (%)	43 (9.2	28 (34.1 %)
COPD (%)	23 (4.9)	9 (11 %)
Diabetes (%)	40 (8.6)	19 (23.2 %)
Viral hepatitis (%)	27 (5.8)	12 (14.6 %)
Charlson index[b], mean ± SD	5.0 ± 3.7	5.8 ± 3.1
ASA score; median (IQR)	2 (2–3)	3 (2–3)
≤2 (%)	349 (74.7)	39 (47.6 %)
>2 (%)	118 (25.3)	43 (52.4 %)
Benign/malignant disease (%)	128/339 (27.4/72.6)	13/69 (15.9/84.1)
Primary/secondary liver tumor (%)	226/225 (48.4/48.2)	46/31 (56.1/37.8)
Preoperative chemotherapy (%)	183 (39.2)	22 (26.8 %)
Creatinine clearance, ml/h; median (IQR)	85.5 (71.3–106.7)	64.4 (55.2–80.2)
Creatinine, µmol/l; median (IQR)	79 (69–87)	90.5 (77–107)
Bilirubin, µmol/l; median (IQR)	10 (7–14)	13 (10–21)
AST, U/l; median (IQR)	28 (23–45)	37.5 (28–61)
ALT, U/l; median (IQR)	31 (21–53)	43 (24–72.5)

COPD chronic obstructive pulmonary disease; *ASA* American Society of Anesthesiologists score; *IQR* interquartile range; *ALT* alanine-aminotransferase; *AST* aspartate-aminotransferase; *SD* standard deviation

[a] Cardiovascular disease is defined as the presence of coronary artery disease, previous coronary revascularization, or cerebral arterial occlusive disease and/or peripheral vascular occlusive disease

[b] Charslon comorbidity index [34]

Numbers that are given, are numbers of patients unless otherwise stated

Table 2 Intraoperative parameters of patients

	Postoperative normal kidney function $n = 467$ (85.1 %)	Postoperative acute kidney injury $n = 82$ (14.9 %)
General		
Operative time, min; median (IQR)	275 (205–360)	327.5 (260–450)
Liver resection (%)		
Minor	230 (49.3)	29 (35.4 %)
Major	143 (30.6)	31 (37.8 %)
Extended	94 (20.1)	22 (26.8 %)
Pringle maneuver (%)	350 (74.9)	69 (84.1 %)
Pringle time, min; median (IQR)	30 (15–35)	30 (19.5–37.5)
Blood loss, ml; median (IQR)	400 (250–700)	700 (400–1500)
Blood transfusion		
Erythrocytes (%)	50 (10.7)	26 (31.7 %)
Fresh frozen plasma (%)	14 (3)	12 (14.6 %)
Thrombocytes (%)	1 (0.2)	2 (2.4 %)
Hepaticojejunostomy (%)	48 (10.3)	24 (29.3 %)
Portal vein ligation (%)	15 (3.2)	0 %
Vessels resected (%)		
Portal vein resection (%)	14 (3)	7 (8.5 %)
Hepatic artery resection (%)	3 (0.6)	2 (2.4 %)
Cava vein resection (%)	3 (0.6)	2 (2.4 %)
Hepatic vein resection (%)	1 (0.2)	0 %
Radiofrequency ablation (%)	19 (4.1)	5 (6.1 %)
Cirrhosis (%)	27 (5.8)	10 (12.2 %)
Cryotherapy (%)	6 (1.3)	1 (1.2 %)
Intraoperative blood perfusion outcome		
Central venous pressure (mmHg) during Pringle maneuver; median (IQR)	3 (1–4)	3 (2–6)
Mean MAP (mmHg); median (IQR)	70 (65–75)	70 (65–70)
Lower MAP < 70 mmHg (%)	447 (95.7 %)	80 (97.6 %)
Number of MAP periods lower than 70 mmHg; median (IQR)	4 (3–6)	5 (4–8)
Minimal MAP, mmHg; median (IQR)	55 (50–60)	55 (50–60)
Catecholamines (%)	429 (91.9)	80 (97.6 %)
Catecholamines bolus dose (%)	281 (60.2)	59 (72 %)
Dosage, µg; median (IQR)	10 (0–40)	30 (0–70)
Catecholamines continuously intravenous; median (IQR)	416 (89.1 %)	78 (95.1 %)
Dosage, µg/h	3.3 (2–5)	4.85 (3.2–6.5)
Minimal dosage, µg/h	0.5 (0–1)	1 (0–1)
Maximal dosage, µg/h	6 (4–10)	10 (7–15)
Length of time, min	270 (175–365)	370 (270–495)

IQR interquartile range, *MAP* mean arterial pressure

Numbers that are given, are numbers of patients unless otherwise stated

To facilitate the clinical applicability of the new prediction score, we also developed a new point system following an established approach [26]. The regression coefficients of the predictors were transformed into points so that they reflected the strengths of association with the outcome (AKI). The points for each predictor were summed, and we calculated the predicted risk of AKI according to a standard approach [26].

Finally, we used a theoretical model of decision curve analysis [27, 28] to compare how in many patients an unwarranted decision (e.g., unnecessary special care unit referral because the risk for AKI is very low) can be avoided by the use of different decision strategies. This is a theoretical model that may overestimate or even underestimate the usefulness of the model because there are other causes for the need for admission to a special care unit than

Table 3 Intraoperative kidney outcome

	Postoperative normal kidney function $n = 467$ (85.1 %)	Postoperative acute kidney injury $n = 82$ (14.9 %)
Diuresis per hour (ml/h), median (IQR)	111.2 (74.1–172)	93.8 (59.2–156)
Oliguria (%)[a]	95 (20.3 %)	29 (35.4 %)
Anuria (%)[b]	21 (4.5 %)	10 (12.2 %)
Diuretics (%)	87 (18.6 %)	26 (31.7 %)
Furosemide (%)	69 (14.8 %)	22 (26.8 %)
Osmotic diuretic (%)	15 (3.2 %)	3 (3.7 %)
Both furosemide and osmotic diuretics (%)	3 (0.6 %)	1 (1.2 %)
Total balance of infusion (ml), median (IQR)	2,020 (1,230–2,960)	2,730 (1,640–4,650)
Balance of infusion per hour (ml/h), median (IQR)	446 (294–665.1)	514.6 (360–773.8)
Colloids (%)	380 (81.4)	75 (91.5 %)
Dosage (ml), median (IQR)	1,000 (500–1,500)	1,000 (750–1,500)

Total balance of infusion (ml) means the total amount of infusions during the whole surgery. Balance of infusion per hour (ml/h) means the median amount of infusion in mL during one hour of surgery

IQR interquartile range

[a] Oliguria is a reduction in urinary output to less than 400 ml/24 h

[b] Anuria is a reduction in urinary output to less than 100 ml/24 h

only AKI. Therefore the threshold at which special care unit treatment is needed depends much on the judgment of the physicians and immediate circumstances. For example, while some physicians in a setting with constrained resources may only refer patients to a special care unit after liver resection if the risk is >10 %, other physicians may be more conservative and refer each patient at risk for AKI of >5 %. Decision curve analyses compare different decision strategies and take these potential treatment thresholds into consideration. In the present study the use of the preoperative score was compared with the improved score in order to refer patients to a special care unit, with additional comparisons to the referral of all or no patients. Decision curve analysis ultimately tells how in many patients a wrong decision (e.g., unnecessary special care unit referral because the risk for AKI is very low) can be avoided by the use of different decision strategies. In our study the use of the preoperative score was compared with the new score in order to refer patients for special care, with additional comparisons to the referral of all or no patients.

We used STATA 10 (Stata Corp., College Station, TX) for the statistical analyses and SPSS (version 19, SPSS inc., Chicago, IL) for the graphical presentations.

Results

Study population

A series of 576 consecutive patients were assessed for eligibility. After exclusion of seven trauma patients and 20

Table 4 Development of the new prediction score based on a multivariate logistic regression model

Predictor	Category	Odds ratio β (95 % CI)	Regression coefficient β	Shrunken regression coefficient β_s	p value	Reference value W_i (midpoint)	$\beta_s \times (W_{ij} - W_{ireference})$	Risk score ($\beta_s \times [W_i - W_{ireference}]/B$)[a]
Preoperative score	0	1.84 (1.55–2.18)	0.609	0.584	<0.001	0 ($W_{1reference}$)	0	0
	1					0.5	0.283	3
	2					1.5	0.849	9
	3					2.5	1.415	15
	4					3.5	1.981	20
	5					4.5	2.547	26
	6					5.5	3.113	32
	7					6.5	3.679	36
Preoperative score	No	2.68	0.986	0.946	0.005	0 ($W_{2reference}$)	0	0
	Yes	(1.36–5.30)				1	0.946	10
Hepaticojejunostomy	No	2.52	0.925	0.887	0.005	0 ($W_{3reference}$)	0	0
	Yes	(1.32–4.82)				1	0.887	9
Oliguria	No	2.52	0.924	0.886	0.001	0 ($W_{4reference}$)	0	0
	Yes	(2.52–4.40)				1	0.886	9

[a] Constant B is a coefficient = 0.1; shrinkage coefficient: 0.959

Table 5 Prediction of risk of acute kidney injury

Risk score based on 4 predictors	Risk of acute kidney injury, %
1	3.5
2	3.8
3	4.2
4	4.6
5	5.1
6	5.6
7	6.1
8	6.7
9	7.4
10	8.1
11	8.9
12	9.7
13	10.6
14	11.6
15	12.7
16	13.8
17	15.1
18	16.4
19	17.8
20	19.3
21	20.9
22	22.6
23	24.4
24	26.3
25	28.3
26	30.4
27	32.5
28	34.8
29	37.1
30	39.4
31	41.8
32	44.3
33	46.8
34	49.3
35	51.8
36	54.2
37	56.7
38	59.1
39	61.5
40	63.9
41	66.2
42	68.4
43	70.5
44	72.5
45	74.5
46	76.3
47	78.1
48	79.7
49	81.3
50	82.8
51	84.2
52	85.4
53	86.6
54	87.8
55	88.8
56	89.8
57	90.6
58	91.5
59	92.2
60	92.9
61	93.5
62	94.1
63	94.6
64	95.1

patients with incomplete data sets, 549 patients were finally included in the analysis. The frequency of postoperative AKI was 14.9 % (82 of 549 patients). The overall morbidity was 54.3 % (298 of 549 patients), and 4.2 % of the patients died within 30 days (23 of 549 patients). Table 1 shows the characteristics of the two groups of patients, with and without postoperative AKI.

Table 2 demonstrates the intraoperative parameters. Length of operation was prolonged (median: 328 min [interquartile range (IQR) 260–450 min] vs. 275 min [IQR 205–360 min]), the extent of resection was larger (38 vs. 31 % major resections), the application of the Pringle maneuver (inflow occlusion) was more frequent (84 vs. 75 %), and the use of transfusions of blood products was higher in patients with postoperative AKI compared to patients without postoperative AKI. In addition, the rates of hepaticojejunostomy (29 vs. 10 %), vessel resection (13 vs. 4 %), as well as the occurrence of liver cirrhosis identified intraoperatively by surgeons (12 vs. 6 %) were higher in patients with AKI. Evaluating intraoperative perfusion parameters showed that patients with postoperative AKI received more frequent and higher dosages of catecholamines than patients with normal postoperative kidney function.

Regarding intraoperative kidney parameters (Table 3), in patients with postoperative AKI intraoperative diuresis per hour was lower (median 93.8 ml/h [IQR 59.2–156 ml/h] vs. 111.2 ml/h [IQR 74.1–172 ml/h]), the occurrence of intraoperative oliguria (36 vs. 20 %) and anuria (12 vs. 4.5 %) was higher, and the use of diuretics (32 vs. 19 %) was more frequent than in patients without postoperative AKI.

Development of the new prediction model

Table 4 presents the multivariate logistic regression model with the four strongest predictors (preoperative score, intraoperative blood transfusion [no/yes], hepaticojejunostomy [no/yes], and oliguria [no/yes]) of AKI, and the corresponding risk score. All three intraoperative predictors had the greatest association with postoperative AKI (odds ratio [OR] for blood transfusion 2.7, for hepaticojejunostomy [OR = 2.5] and for oliguria [OR = 2.5]) than the preoperative score (OR 1.8). The predictive risk for postoperative AKI based on the new risk score is summarized in Table 5. The score ranged from 0 to 64 points, corresponding to a predictive risk of AKI from 3.5 to 95 %.

Validation of the new prediction model

Discrimination represented by the AUC was higher for the new prediction model than for the preoperative model (0.81 (95 % confidence interval [CI] 0.76–0.86) vs. 0.60 [95 % CI 0.52–0.69]; $p < 0.001$) (Fig. 1). Calibration was good in both the preoperative model and in the new model, with predicted risks (15 %) matching with the observed risk (15 %). The Hosmer–Lemeshow test for the new model ($p = 0.93$), as well as for the preoperative score ($p = 0.84$), showed a nonsignificant difference between predicted and observed risks across five risk classes (Fig. 1). The fivefold cross-validation indicated good internal validity as discrimination (AUC = 0.79 [95 % CI 0.73–0.84]) was only slightly lower than for the derived model (0.81).

Clinical usefulness of the preoperative and new risk scores

Table 6 presents the decision curve analysis for referring patients to a special care unit with regard to the new prediction model compared to the preoperative score, but it provides a proposition for referring patients to a special care unit after liver resection. First, the diagram shows that both prediction scores were clearly better than the strategy that all patients would be referred to a special care unit following liver resection. Tables 6 and Appendix in Supplementary Material. Figure 1 translates the decision curve analysis into the number of patients, where unnecessary special care unit treatment could be avoided without missing patients who need a special care unit admission according to a specific threshold. The diagram shows that the improved prediction score, compared with the preoperative score, better

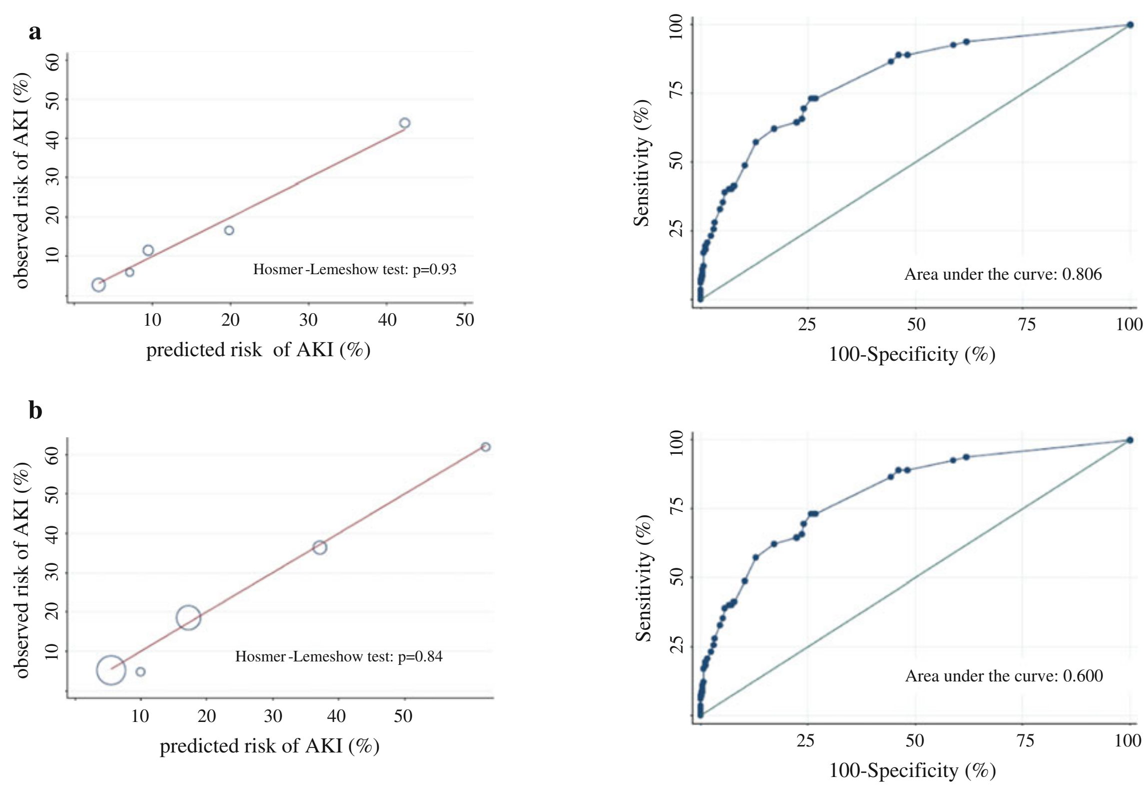

Fig. 1 **a** Calibration and discrimination plots of the *new* prediction score. **b**. Calibration and discrimination plots of the *preoperative* prediction score. The area under the curve (AUC) represents the discrimination which indicates a better discrimination of patients with and without AKI by the new prediction model than for the preoperative model (AUC 0.81 (95 % confidence interval [CI] 0.76–0.86) vs. 0.60 [95 % CI 0.52–0.69]; $p < 0.001$)

Table 6 Decision curve analysis: calculation of the net benefit for special care unit referrals comparing the preoperative and new prediction model using threshold probability p_t

Threshold probability, %	Net benefit new prediction model	Net benefit preoperative prediction model	Net benefit treat all	Net benefit treat none	Net benefit new	Net benefit preoperative	Reducing the number of unnecessary special care unit referrals per 100 patients with the new score	Reducing the number of unnecessary special care unit referrals per 100 patients with the preoperative score
1	0.141	0.141	0.140	0	0.000	0.000	4	4
2	0.132	0.132	0.132	0	0.000	0.000	2	2
3	0.123	0.123	0.123	0	0.000	0.000	1	1
4	0.118	0.114	0.114	0	0.005	0.000	11	1
5	0.113	0.105	0.104	0	0.008	0.000	16	1
6	0.106	0.099	0.095	0	0.012	0.005	18	7
7	0.101	0.095	0.085	0	0.016	0.010	21	13
8	0.097	0.090	0.075	0	0.022	0.015	25	18
9	0.092	0.086	0.065	0	0.027	0.021	28	21
10	0.084	0.083	0.054	0	0.030	0.029	27	26
15	0.071	0.060	−0.001	0	0.072	0.062	41	35
20	0.049	0.041	−0.064	0	0.113	0.104	45	42
25	0.044	0.034	−0.135	0	0.178	0.169	54	51
30	0.034	0.025	−0.216	0	0.250	0.240	58	56
35	0.027	0.019	−0.309	0	0.336	0.328	62	61
40	0.022	0.012	−0.418	0	0.441	0.430	66	65
45	0.020	0.012	−0.547	0	0.567	0.559	69	68
50	0.018	0.009	−0.702	0	0.720	0.711	72	71
55	0.015	0.006	−0.891	0	0.906	0.897	74	73
60	0.017	0.000	−1.128	0	1.145	1.128	76	75
65	0.010	−0.001	−1.431	0	1.441	1.430	78	77
70	0.004	−0.003	−1.837	0	1.841	1.834	79	79
75	0.011	0.002	−2.404	0	2.415	2.406	80	80
80	0.009	0.002	−3.255	0	3.264	3.257	82	81
85	0.004	0.000	−4.673	0	4.677	4.673	83	82
90	0.002	0.000	−7.510	0	7.512	7.510	83	83
95	0.000	0.000	−16.020	0	16.020	16.020	84	84

discriminates between those who may or need special care unit care, particularly for low threshold probabilities from 4 to 20 %. For example, with a decision threshold of 6 % for AKI following liver resection, the clinical use of the new prediction score would avoid the unnecessary special care unit admission of 18 % compared to a strategy where all patients would be referred to a special care unit after surgery. However, by using the preoperative prediction score, only 7 % of the patients would avoid an unnecessary special care unit admission. Figure 2 presents the decision curve with all four treatment strategies.

Discussion

Prediction scores aim to support the decision-making process of patients and physicians. They help to allocate patients to different treatment strategies with the goal of avoiding under treatment for those who may need more care and overtreatment for those who require less intensive care. Our study showed that a prediction score integrating intraoperative parameters is superior in identifying patients who would benefit from a special care unit stay in terms of care for AKI compared to the preoperative prediction score alone. The use of the new prediction model may likewise prevent many unnecessary special care unit admissions following liver resection, particularly for low threshold probabilities (4–20 %) for AKI. Those results suggest that the preoperative score should be used for intraoperative decision making and the full score for admission to a special care unit for specific protective strategies targeting the kidney.

Postoperative AKI is known to significantly impair the outcome after major surgery [29]. Postoperative AKI was

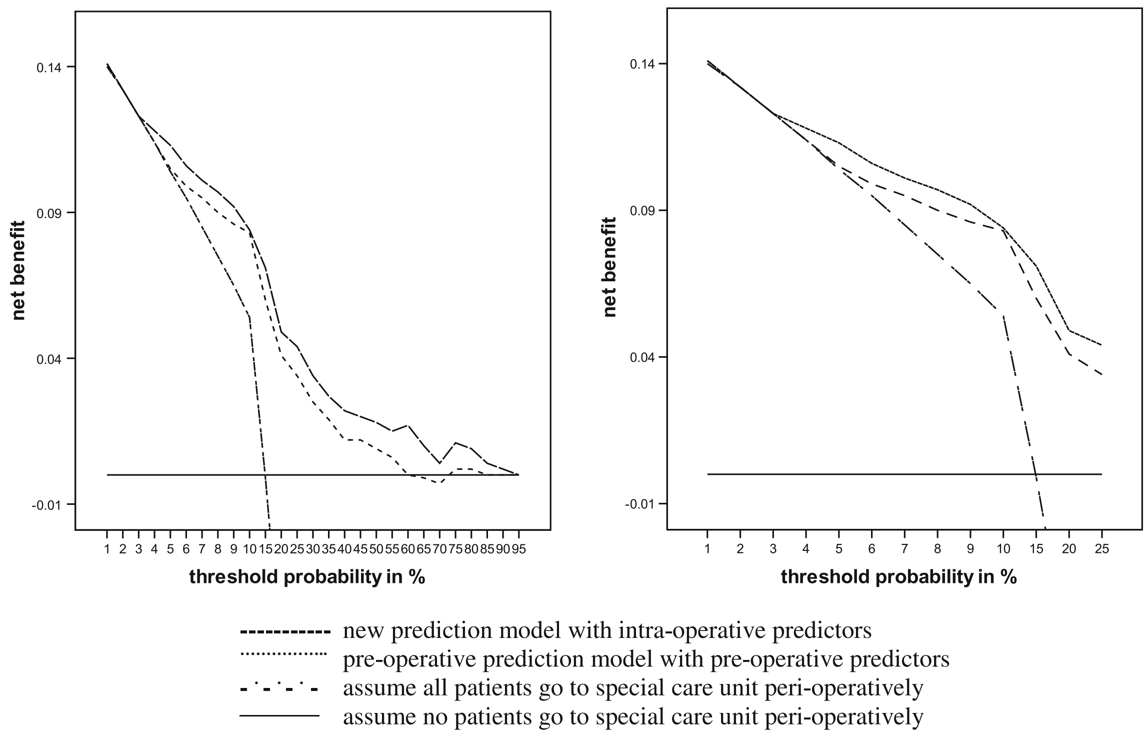

Fig. 2 Decision curve for special care unit referrals for acute kidney injury following liver resection. Comparison of four approaches for decision making in special care unit referrals. The graph presents the expected net benefit per patient relative to no special care unit admission of any patients

documented in 15 % of the patients following liver resection, and it significantly correlated not only with increased mortality compared to patients without postoperative AKI (23 vs. 0.8 %; $p < 0.001$), but also with a prolonged length of hospital stay (adjusted difference 9.5 days [95 % CI 6.7–12.4]; $p < 0.001$) and special care unit stay (adjusted difference 7.9 days [95 % CI 6.4–9.3]; $p < 0.001$) stay. In the present study, AKI was the main reason for death in more than half of the patients who died, whereas the second most frequent cause of death was infection. Of those patients who developed an AKI within 48 h after surgery, 72 % fully recovered, whereas 28 % needed postoperative hemofiltration, and 6 % of that group needed persistent hemodialysis. Kidney function may have recovered in most of the patients because of fast and adequate therapy in the special care unit. Otherwise, we might have observed more patients requiring postoperative hemofiltrations and persistent hemodialysis.

After a liver resection, the surgeon and anesthesiologist have to decide whether the patient might benefit from treatment in a special care unit for the prevention or treatment of AKI. In case of serious comorbidities or intraoperative problems, a special care unit referral decision is easy, but the difficulty persists with patients who may develop AKI or other complications. Special care unit referrals are more expensive than postoperative referral to the ward. Therefore a reduction of unnecessary special care unit admissions is economically beneficial and ensures a quieter and more comfortable recovery for patients. Our improved score also offers a theoretical tool for special care unit triage, presenting a possible decision-making model for postoperative AKI. It does not inform, however, about the needed length of the special care unit stay. Further studies have to externally validate the score and also evaluate the optimal length of special care unit stay in order to protect the patient with impaired kidney function from such postoperative risk factors as low arterial pressure and hypotension by optimizing fluid management and pain-controlled epidural anesthesia application. Therefore, a precise triage to a special care unit after surgery is highly relevant to the patient's recovery, and also takes into account the availability of a special care unit bed and the added health care cost.

We analyzed the clinical consequences of our preoperative score, as well as the new prediction score, by means of a theoretical model of a decision curve analysis that evaluates the scores' clinical usefulness [27, 28, 30]. This goes beyond the traditional validation of diagnostic and prognostic models, where typically the accuracy of a model is analyzed. The interpretation of measures of discrimination and calibration is sometimes not straightforward, and it is difficult to recognize whether one model offers advantages over another. Decision analysis goes beyond these measures and evaluates the expected clinical consequences of different prediction models [27]. The decision curve analysis presented here suggests that the new prediction score would theoretically reduce up to 84 unnecessary special care unit admissions per 100 patients, depending on the decision threshold, compared to the preoperative prediction score. Given the substantial potential reduction of unnecessary special care unit admissions, the additional effort to use the new prediction score seems to be justified and may reduce overall costs in the future.

Strengths of the present study are the large sample size allowing us to update a pre-existing prediction score with easy and widely available intraoperative predictors. We internally validated the new prediction score by performing a k-fold cross-validation [23, 25, 31–33]. Furthermore, the application of advanced statistical methods, such as shrinkage, increases the validity and applicability of the prediction score in other study populations. Another strength is the decision curve analysis that provides insights into the potential clinical usefulness of the new risk score.

In contrast, the patient cohort from only a single center may have to be considered a limitation for generalizability of this study. Therefore an external validation on geographically different patient populations is needed for both scores. A second limitation of this study is that we only tested one possible clinical strategy (postoperative special care unit referrals due to increased risk for AKI) and its consequences and importance by the decision curve analysis, and that the model may therefore overestimate or even underestimate the clinical usefulness because there are many other reasons for an admission to a special care unit. A third limitation is that we used AKI as the only indication for postoperative ICU referral rather than multiple indication outcomes. However, it would require much larger sample sizes to develop scores that consider multiple indications as well as their combinations.

In conclusion, we developed a new score to predict the risk for AKI after liver resection that has the potential to better support decision making for special care unit referrals, than using only the preoperative score. Given the substantial potential reduction of unnecessary special care unit admissions and easy applicability of the new score, the additional effort to use a risk score postoperatively also seems justified.

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