



Comparison of the Extent Classification and the New Complexity Classification of Hepatectomy for Prediction of Surgical Outcomes: a Retrospective Cohort Study

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Abstract

Background In predicting the risk for posthepatectomy complications, hepatectomy is traditionally classified into minor or major resection based on the number of resected segments. Recently, a new hepatectomy complexity classification was proposed. This study aimed to compare the value of the traditional and that of the new classification in perioperative outcomes prediction.

Methods Demographics, perioperative laboratory tests, intraoperative and postoperative outcomes, and follow-up data of patients with hepatocellular carcinoma who underwent liver resection were retrospectively analyzed.

Results A total of 302 patients were included in our study. Multivariable analysis of intraoperative variables showed that the complexity classification could independently predict the occurrence of blood loss > 800 mL, operation time > 4 h, intraoperative transfusion, and the use of Pringle's maneuver (all $p < 0.05$). For postoperative outcomes, the high-complexity group was independently associated with severe complications, and hepatic-related complications (all $p < 0.05$); the traditional classification was independently associated only with posthepatectomy liver failure (PHLF) ($p = 0.004$).

Conclusions Complexity classification could be used to assess the difficulty of surgery and was independently associated with postoperative complications. The traditional classification did not reflect operation complexity and was associated only with PHLF.

Keywords Hepatocellular carcinoma · Hepatectomy · Surgical complexity · Postoperative complications · Classification

Xiao-long Wu and Zhi-yu Li contributed equally to this work.

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Introduction

Hepatocellular carcinoma (HCC) is the third leading cause of cancer-related mortality worldwide.¹ Liver resection is currently regarded as the mainstream treatment for patients with resectable lesions. The first report of true right hepatectomy was in 1952, and the operation was considered challenging with high mortality.² Over the past decades, deeper understanding of liver anatomy and physiology, advances in perioperative management, and better surgical techniques have contributed to the safety of liver resection.

Currently, the operation risk is regularly assessed based on multiple preoperative factors. The most frequent postoperative complications are liver failure, bile leak, peritoneal abscess, and hemorrhage.^{3–9} The extent of liver resection, which could be decided pre- or intraoperatively, is a crucial factor that could directly influence complications and postoperative

mortality.^{3,10,11} Traditionally, based on the number of resected liver segments, hepatectomy is grouped into “minor” or “major”.¹² This concept, in which minor hepatectomy includes resection of ≤ 2 liver segments, has been used to predict mortality and morbidity for > 30 years.^{7,13–17}

Recently, the traditional classification is questioned in terms of the number of resected segments involved and its predictive value. Some research suggested that resection of three or even four segments be classified under minor liver resection.^{18–20} Additionally, some indicated that the traditional classification could only indirectly reflect the volume of the remnant liver and not represent the difficulty and complexity of operation or predict the risk.^{21–23}

To improve the classification, Lee et al. designed a four-question survey and sent it by e-mail to some expert liver surgeons. The experts were asked to score the difficulty of various hepatectomy from 1 to 10. Based on the scores, liver resection procedures were grouped into low, medium, or high complexity.²² A study subsequently validated that such classification is correlated with the risk of operation and major postoperative complications and mortality.²⁴

Recently, Lee et al. sent the second survey including more factors and completed their new classification (Table 1).²⁵ This study aims to compare the value of the traditional classification and that of the new complexity classification in the prediction of intraoperative and postoperative outcomes.

Materials and Methods

Patients

In this study, we retrospectively analyzed patients with HCC who underwent curative intent hepatic resection in our hospital from January 2011 to December 2014. Pathological examination of the resected specimen confirmed the diagnosis of HCC. Liver resection was guided by preoperative computed tomography (CT), magnetic resonance imaging (MRI), and intraoperative ultrasonography. For patients with multiple tumors, if the tumors were resected separately rather than obtaining a whole specimen, these patients were excluded from the study. Patients with intraoperative suspicious R1 or R2 liver resection were excluded, because routine intraoperative radiotherapy performed for them in our hospital may affect the perioperative outcomes. In addition to these patients, no patient obtained positive postoperative pathological margins during this time. A total of 302 patients with R0 liver resection were included in this study. All patients had complete demographics, perioperative laboratory tests, operation-related variables, pathological reports, postoperative complications, and follow-up data. All patients provided written informed consent. This study was approved by the Institutional Review Board of our hospital.

Definitions and Classification

HCC was diagnosed according to clinical guidelines and confirmed by postoperative pathological examination by two pathologists. Seropositive HBsAg patients were diagnosed as having HBV infection; those with antibody against HCV detected by laboratory test, hepatitis C virus (HCV) infection. Preoperative liver function was evaluated by Child-Pugh classification and liver enzyme tests. Tumor number and size were measured by CT or MRI. Cirrhosis was diagnosed based on postoperative pathological examination. Postoperative complications were classified according to the Clavien-Dindo classification (grade 1 to 5); grade 3 to 5 complications were regarded as severe. Posthepatectomy liver failure (PHLF), bile leak, hemorrhage, and peritoneal abscess were regarded as hepatic-related complications. The 2011 International Liver Surgery Group criteria were used to diagnose PHLF. Postoperative complications within 90 days after surgery were recorded. The number of resected segments was recorded using the Couinaud's division, which was rounded to a whole number when a non-anatomic resection was performed. Based on the traditional classification, resection of ≥ 3 segments was classified under major hepatectomy. The types of liver resection were defined according to the Brisbane 2000 terminology, which were divided into three levels in terms of the new complexity classification.

Statistics

Patient data were expressed using frequencies and percentages for categorical variables and means and standard deviations for continuous variables. Comparisons were performed using chi-squared analyses or Fisher exact test for categorical variables and analysis of variance test or Kruskal-Wallis test for continuous variables. Predictors of intraoperative-related variables and postoperative complications were evaluated by logistic regression. These predictors were selected based on the univariable analysis of each variable. A two-tailed p value < 0.05 was considered statistically significant. Receiver operating characteristic (ROC) curves were evaluated and sketched using MedCalc bvba version 18.2.1 (Seoul, Korea), and the areas under the ROC curves (AUCs) were also compared. Other statistical analysis was performed using SPSS 19.0 for Windows (SPSS, Inc., Chicago, IL).

Results

The Baseline Characteristics of the Patients

Baseline demographics and clinical characteristics of the patients are shown in Supplementary Table 1 (male 255 (84.4%) and female 47 (15.6%); mean age 54.3 ± 10.2 years). Hepatitis

Table 1 The new liver resection complexity classification and the details of the operation in 302 patients

Group	Procedure	Complexity score	Number (%)
Low complexity	Peripheral wedge resection, <3 cm	1.361	90 (29.8)
	Left lateral sectionectomy	1.994	42 (13.9)
Medium complexity	Left hepatectomy without caudate resection	4.392	9 (3.0)
	Right hepatectomy without caudate resection	4.866	32 (10.6)
	Right posterior sectionectomy	5.479	78 (25.8)
	Left hepatectomy with caudate resection	5.505	1 (0.3)
	Isolated caudate resection	5.895	2 (0.7)
	Right trisectionectomy	6.206	1 (0.3)
High complexity	Right anterior sectionectomy	6.583	33 (10.9)
	Right hepatectomy with caudate resection	6.767	1 (0.3)
	Right hepatectomy with hepaticojejunostomy	6.850	0
	Anatomic middle hepatectomy	7.205	11 (3.6)
	Right trisectionectomy with caudate resection	7.239	0
	Left trisectionectomy without caudate resection	7.378	2 (0.7)
	Right trisectionectomy with hepaticojejunostomy	7.522	0
	Left trisectionectomy with caudate resection	8.257	0
	Right hepatectomy with portal vein reconstruction (main to left)	8.754	0
	Right trisectionectomy with portal vein reconstruction (main to left)	8.988	0
	Right hepatectomy with IVC reconstruction	9.351	302

IVC inferior vena cava

B virus (HBV) infection was found to be the only cause of the underlying chronic disease in 226 (74.8%) patients, and liver cirrhosis was present in 198 (65.6%) patients. Mean tumor diameter was 4.3 ± 2.4 cm. Two hundred seventy-five (91.1%) patients had a solitary tumor, and 27 (8.9%) patients had multiple tumors. The types of hepatectomy are summarized in Table 1. According to the complexity classification, 132 (43.7%), 123 (40.7%), and 47 (15.6%) patients were assigned to the low-, medium-, and high-complexity groups, respectively. Fifty-seven (18.9%) patients had major hepatectomy, and minor hepatectomy was performed in 245 (81.1%) patients. Postoperative complications were found in 60 (19.9%) patients, which were graded according to the Clavien-Dindo classification. Three patients died within 90 days (2 died of PHLF and 1 died of respiratory failure), resulting in a postoperative mortality of 1.0%. The median day of hospital stay was 8.5 (range 4 to 56).

Comparisons of Baseline Characteristics in Different Classifications

With the complexity classification, no significant differences in the baseline variables, including age, gender, viral infection, total bilirubin, prothrombin time, alpha-fetoprotein (AFP), Child-Pugh class, and tumor number, were found among the three levels of complexity (Table 2). The low- and high-

complexity groups had higher presence rates of cirrhosis than the medium-complexity group (low vs. medium vs. high, 74.2 vs. 52.0 vs. 76.6%, respectively; $p < 0.001$). Additionally, the mean tumor size of the low-complexity group was smaller than that of the medium- and high-complexity groups (low vs. medium vs. high, 3.1 vs. 5.4 vs. 4.6; $p < 0.001$).

When classified according to hepatectomy extent, the baseline variables of the patients, including age, gender, viral infection, total bilirubin, prothrombin time, Child-Pugh class, tumor number, and liver cirrhosis, had no significant differences. However, patients in the major hepatectomy group had higher AFP values and larger tumor size than those in the minor hepatectomy group (AFP 6613.9 vs. 1799.6, $p = 0.006$; tumor size 7.0 vs. 3.7, $p < 0.001$).

Comparisons of Intraoperative Outcomes in Different Classifications

For patients in the three levels of complexity, the intraoperative variables (operation time, blood loss, transfusion, and use of Pringle's maneuver) were all significantly different (Table 3). The intraoperative variables, except the use of Pringle's maneuver, were also significantly different between the two groups in the traditional classification.

Univariable analysis for the prediction of intraoperative outcomes was shown in Supplementary Table 2. On

Table 2 Baseline characteristics of the patients grouped according to complexity classification and traditional classification

	Complexity classification			<i>p</i> value	Traditional classification		<i>p</i> value
	Low (<i>n</i> = 132)	Medium (<i>n</i> = 123)	High (<i>n</i> = 47)		Minor (<i>n</i> = 245)	Major (<i>n</i> = 57)	
Age, years	53.8 ± 9.0	54.4 ± 10.7	55.4 ± 10.2	0.647	54.2 ± 9.9	54.7 ± 11.5	0.734
Gender				0.291			0.094
Male	108(81.8)	104(84.6)	43(91.5)		211(86.1)	44(77.2)	
Female	24(18.2)	19(15.4)	4(8.5)		34(13.9)	13(22.8)	
Viral infection	112(84.8)	98(79.7)	37(78.7)	0.474	202(82.4)	45(78.9)	0.537
Albumin, g/L	41.0 ± 4.1	41.2 ± 4.7	41.4 ± 4.3	0.885	41.3 ± 4.4	40.8 ± 3.9	0.284
Total bilirubin, μmol/L	11.4 ± 5.0	12.1 ± 6.9	12.5 ± 6.1	0.494	12.0 ± 6.2	11.3 ± 4.9	0.430
Prothrombin time, s	11.9 ± 0.9	11.9 ± 1.7	11.8 ± 0.8	0.844	11.9 ± 1.2	12.1 ± 1.5	0.208
AFP (ng/mL)	1522.3 ± 7708.8	3983.1 ± 15,720.2	2702.2 ± 9735.1	0.257	1799.6 ± 9562.9	6613.9 ± 18,561.7	<i>0.006</i>
Child-Pugh score				0.913			0.106
A	125(94.7)	115(93.5)	44(93.6)		233(95.1)	51(89.5)	
B	7(5.3)	8(6.5)	3(6.4)		12(4.9)	6(10.5)	
Cirrhosis				<i>< 0.001</i>			0.297
Absent	34(25.8)	59(48.0)	11(23.4)		81(33.1)	23(40.4)	
Present	98(74.2)	64(52.0)	36(76.6)		164(66.9)	34(59.6)	
Tumor number				0.295			0.326
1	122(92.4)	113(91.9)	40(85.1)		225(91.8)	50(87.7)	
≥ 2	10(7.6)	10(8.1)	7(14.9)		20(8.2)	7(12.3)	
Tumor size, cm	3.1 ± 1.9	5.4 ± 2.5	4.6 ± 2.1	<i>< 0.001</i>	3.7 ± 1.9	7.0 ± 2.7	<i>< 0.001</i>

Data are expressed as number (percentage), mean ± standard deviation (SD), or median (range). Significant results were expressed in italics
 AFP alpha-fetoprotein

Table 3 Details of intraoperative and postoperative outcomes according to complexity classification and traditional classification

	Complexity classification			<i>p</i> value	Traditional classification		<i>p</i> value
	Low (<i>n</i> = 132)	Medium (<i>n</i> = 123)	High (<i>n</i> = 47)		Minor (<i>n</i> = 245)	Major (<i>n</i> = 57)	
Operation time > 4 h	8 (6.1)	41 (33.3)	33 (70.2)	<i>< 0.001</i>	25 (10.2)	19 (33.3)	<i>< 0.001</i>
Intraoperative blood loss > 800 ml	3 (2.3)	21 (17.1)	20 (42.6)	<i>< 0.001</i>	25 (10.2)	19 (33.3)	<i>< 0.001</i>
Intraoperative transfusion	16 (12.1)	28 (22.8)	18 (38.3)	<i>0.001</i>	43 (17.6)	19 (33.3)	<i>0.008</i>
Pringle's maneuver	17 (12.9)	29 (23.6)	16 (34.0)	<i>0.005</i>	46 (18.8)	16 (28.1)	0.118
Overall postoperative complications	15 (11.4)	28 (22.8)	23 (48.9)	<i>< 0.001</i>	49 (20.0)	17 (29.8)	0.106
Clavien-Dindo classification				0.245			0.136
1	6 (40.0)	5 (17.9)	5 (21.7)		12 (24.5)	4 (23.5)	
2	4 (26.7)	8 (28.6)	6 (26.1)		15 (30.6)	3 (17.6)	
3	3 (20.0)	7 (25.0)	8 (34.8)		15 (30.6)	3 (17.6)	
4	2 (13.3)	7 (25.0)	2 (8.7)		7 (14.3)	4 (23.5)	
5	0	1 (3.6)	2 (8.7)		0	3 (17.6)	
Severe postoperative complications	5 (3.8)	15 (12.2)	12 (25.5)	<i>< 0.001</i>	22 (9.0)	10 (17.5)	0.090
Hepatic complications	4 (3.0)	13 (10.6)	14 (29.8)	<i>< 0.001</i>	22 (9.0)	9 (15.8)	0.127
Bile leak	0	6 (4.9)	5 (10.6)	<i>0.002</i>	10 (4.1)	1 (1.8)	0.651
PHLF	2 (1.5)	7 (5.7)	3 (6.4)	0.154	6 (2.4)	6 (10.5)	<i>0.015</i>
Peritoneal abscess	2 (1.5)	6 (4.9)	3 (6.4)	0.199	6 (2.4)	5 (8.8)	0.057
Length of stay, days	9.0 ± 2.6	10.5 ± 6.8	11.7 ± 6.9	<i>0.008</i>	10.0 ± 5.6	10.5 ± 4.8	0.517

Data are expressed as number (percentage), mean ± standard deviation (SD), or median (range). Significant results were expressed in italics
 PHLF posthepatectomy liver failure, DFS disease-free survival, OS overall survival

Table 4 Multivariable analysis for intraoperative outcomes

	<i>B</i>	Odds ratio	95% CI	<i>p</i> value
Blood loss > 800 mL				
Child-Pugh score	1.385	3.993	1.110–14.370	<i>0.034</i>
Tumor size, cm	0.204	1.226	1.029–1.462	<i>0.023</i>
Extent of hepatectomy	0.313	1.368	0.543–3.445	0.569
Complexity classification(ref: low)				
Medium	1.565	4.784	1.268–18.052	<i>0.021</i>
High	3.188	24.228	6.415–91.503	<i>< 0.001</i>
Cirrhosis	−0.170	0.843	6.433–91.388	0.667
AFP (ng/mL)	0.000	1.000	1.000–1.000	0.464
Operation time > 4 h				
Tumor size, cm	0.132	1.141	0.974–1.337	0.101
BMI, kg/m ²	0.004	1.004	0.916–1.101	0.927
Previous TACE	1.022	2.778	1.099–7.024	<i>0.031</i>
Extent of hepatectomy	−0.127	0.881	0.390–1.986	0.759
Complexity classification(ref: low)				
Medium	1.619	5.046	1.998–12.745	<i>0.001</i>
High	3.013	20.355	7.437–55.717	<i>< 0.001</i>
Cirrhosis	−0.066	0.936	0.483–1.815	0.846
AFP (ng/mL)	0.000	1.000	1.000–1.000	0.978
Transfusion				
Age, years	0.025	1.025	0.994–1.056	0.110
Child-Pugh score	1.313	3.717	1.272–10.865	<i>0.016</i>
Tumor size, cm	0.153	1.166	0.990–1.356	0.062
Previous TACE	0.457	1.580	0.620–4.023	0.338
Extent of hepatectomy	0.006	1.006	0.429–2.357	0.989
Complexity classification (ref: low)				
Medium	0.447	1.564	0.714–3.427	0.264
High	1.239	3.452	1.480–8.052	<i>0.004</i>
Cirrhosis	0.438	1.549	0.790–3.036	0.203
AFP (ng/mL)	0.000	1.000	1.000–1.000	0.717

Significant results were expressed in italics

BMI body mass index, *TACE* transcatheter arterial chemoembolization, *CI* confidence interval

multivariable analysis (Table 4), Child-Pugh class, tumor size, and complexity classification were independently associated with intraoperative blood loss > 800 mL; tumor size and complexity classification were independently associated with operation time > 4 h; and Child-Pugh class and high-complexity group were independently associated with intraoperative transfusion.

Comparisons and Predictors of Postoperative Outcomes in Different Classifications

Differences in postoperative complications, including overall, severe, and hepatic-related complications, were all compared among different groups in each classification (Table 3). The rates of overall, severe, and hepatic-related complications

were significantly different in the complexity classification; only the rate of PHLF was significantly different in the traditional classification (minor vs. major, 2.4 vs. 10.5%; $p = 0.015$).

Univariable analysis for the prediction of postoperative outcomes was shown in Supplementary Table 3. Multivariable analysis (Table 5) revealed that high-complexity classification and transfusion were independently associated with severe complications. Moreover, high-complexity classification and blood loss > 800 mL were independently associated with hepatic-related complications, and only traditional classification was independently associated with PHLF.

Comparisons of the AUCs of the ROC Curves for Perioperative Outcomes in Different Classifications

The ROC curves for perioperative outcomes are shown in Fig. 1. For blood loss > 800 ml, the AUC was significantly greater in the complexity classification than in the extent of hepatectomy group (0.781 vs. 0.642; $p = 0.0035$). Moreover, the AUCs for operation time > 4 h (0.770 vs. 0.594; $p < 0.001$), transfusion (0.669 vs. 0.563; $p = 0.0089$), severe complications (0.760 vs. 0.612; $p = 0.0152$), hepatic-related complications (0.731 vs. 0.586; $p = 0.0211$), and PHLF (0.696 vs. 0.827; $p = 0.0357$) were all significantly different between the complexity classification and the extent of hepatectomy group.

Discussion

The opinion of equivalence between hepatectomy complexity and hepatectomy extent is inaccurate. For example, according to the new classification, right anterior sectionectomy is more complex than right hepatectomy; the former needs to deal with not only the midplane of the liver but also the right intersectional plane. The extra procedure may lead to longer operation time and higher bleeding risk but may retain more remnant volume. Hence, whether a complex hepatectomy could affect postoperative liver function and some other complications remains unknown. Currently, no standard guidelines to identify patients at high risk for posthepatectomy mortality and morbidity exist. The new complexity classification was first proposed about 2 years ago, and the completed edition was reported recently.^{22,25} The first edition has been validated and could be used for risk classification of hepatectomy.²⁴ However, it did not assess some variables, such as caudate resection, hepaticojejunostomy, or vascular resection. Subsequently, a detailed study was performed and the second edition was completed, which integrated more factors. The new classification may be superior to the traditional

Table 5 Multivariable analysis for overall complications, severe complications, hepatic-related complications, and PHLF

	<i>B</i>	Odds ratio	95% CI	<i>p</i> value
Severe complications				
Complexity classification (ref: low)				
Medium	1.076	2.932	0.681–12.627	0.149
High	2.169	8.750	1.894–40.422	<i>0.005</i>
Operation time > 4 h	–0.073	0.930	0.343–2.518	0.886
Blood loss > 800 mL	0.261	1.298	0.308–5.471	0.722
Transfusion	1.497	4.470	1.162–17.195	<i>0.029</i>
Cirrhosis	–0.363	0.695	0.255–1.894	0.477
AFP (ng/mL)	0.000	1.000	1.000–1.000	0.581
Tumor size, cm	–0.034	0.966	0.786–1.188	0.745
Hepatic-related complications				
Tumor size, cm	0.073	1.076	0.876–1.322	0.893
Complexity classification (ref: low)				
Medium	0.580	1.785	0.461–6.911	0.255
High	1.860	6.423	1.564–26.378	<i>0.035</i>
Operation time > 4 h	–0.950	0.387	0.130–1.148	0.863
Blood loss > 800 mL	2.462	11.734	2.026–67.945	<i>0.007</i>
Transfusion	–0.010	0.990	0.180–5.437	0.868
Cirrhosis	–0.178	0.837	0.308–2.274	0.727
AFP (ng/mL)	0.000	1.000	1.000–1.000	0.136
PHLF				
Extent of hepatectomy	2.175	8.801	2.040–37.964	<i>0.004</i>
Transfusion	1.103	3.012	0.902–10.059	0.073
Cirrhosis	0.629	1.877	0.462–7.620	0.379
AFP (ng/mL)	0.000	1.000	1.000–1.000	0.396
Tumor size, cm	–0.129	0.879	0.652–1.186	0.399

Significant results were expressed in italics

PHLF posthepatectomy liver failure, CI confidence interval

classification. Jang et al. has reported comparative performance of the complexity classification and the traditional classification for predicting the difficulty of liver resection for hepatocellular carcinoma, but the study-recruited patients underwent both open and laparoscopic hepatectomy.²⁶ The complexity of open and laparoscopic hepatectomy may be completely different, and we suggest these two operation methods should be analyzed separately. Thus, we performed this research to compare the two classifications' values in assessing relevant perioperative outcomes for patients who underwent open hepatectomy.

Evaluating operation complexity could help surgeons understand the associated risk and difficulty and improve perioperative management. A surgeon's skills could directly determine surgical outcomes; thus, in this study, we selected patients who were all treated by the same team of experienced surgeons and who had no differences in their baseline clinicopathological characteristics, including age, gender, viral infection, total bilirubin, prothrombin time, Child-Pugh class, and tumor number (both in the new and traditional classifications).

Additionally, 131 patients (43.3%) had tumor < 3 cm, and most of them (73.3%) were treated with peripheral wedge resection or left lateral sectionectomy, which are the types of hepatectomy in the low-complexity group. Thus, the tumor size in the low-complexity group was significantly smaller than the other two groups. Larger tumors tended to be associated with higher AFP value and more frequently required major hepatectomy. In patients with severe liver cirrhosis, surgeons always attempted to perform wedge resection or improve operation complexity to retain more remnant liver volume; consequently, a higher proportion of liver cirrhosis was found in the low- and high-complexity groups.

Hepatectomy complexity is normally subjective, and classifying the complexity of any liver resection could be difficult. Because of the difficulty of quantifying the operation complexity directly, we analyzed the operation time, the use of Pringle's maneuver, estimated blood loss, and blood transfusion to reflect the complexity indirectly. These intraoperative outcomes were significantly associated with the two classifications on univariable analysis but only the complexity

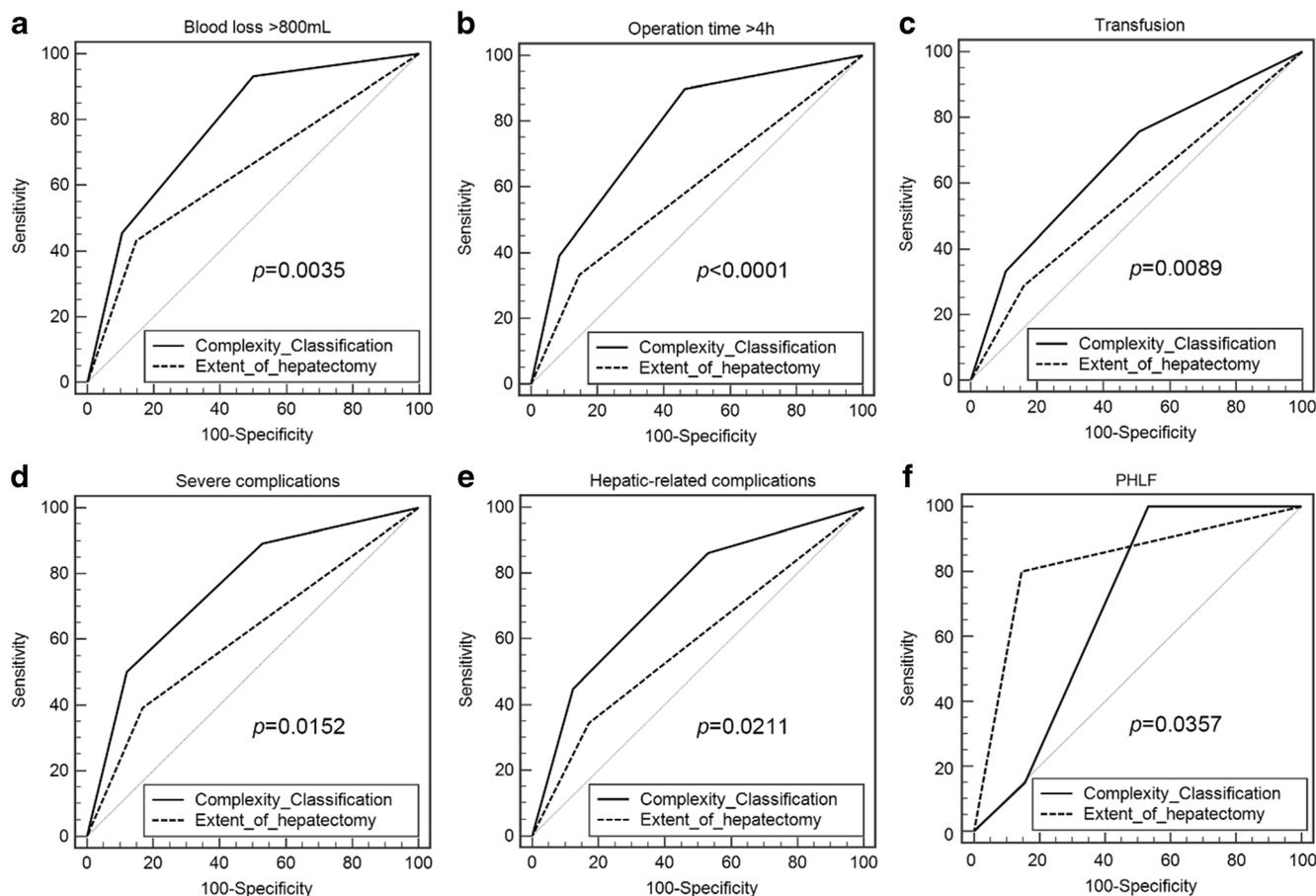


Fig. 1 ROC curves for predicting perioperative outcomes in different classifications. **a** Blood loss > 800 mL (complexity classification vs. extent of hepatectomy): AUC, 0.781 vs. 0.642; $p = 0.0035$. **b** Operation time > 4 h (complexity classification vs. extent of hepatectomy): AUC, 0.770 vs. 0.594; $p < 0.0001$. **c** Transfusion (complexity classification vs. extent of hepatectomy): AUC, 0.669 vs. 0.563; $p = 0.0089$. **d** Severe

complications (complexity classification vs. extent of hepatectomy): AUC, 0.760 vs. 0.612; $p = 0.0152$. **e** Hepatic-related complications (complexity classification vs. extent of hepatectomy): AUC, 0.731 vs. 0.586; $p = 0.0211$. **f** PHLF (complexity classification vs. extent of hepatectomy): AUC, 0.696 vs. 0.827; $p = 0.0357$

classification was the independent predictor of these outcomes on multivariable analysis. Furthermore, according to the comparisons of the AUCs of the ROC curves, the complexity classification is better predictive of blood loss > 800 mL, operation time > 4 h, transfusion. This result is consistent with the development of liver anatomy and surgical skills.^{3,18,27–29}

Remnant liver volume is closely associated with complications after hepatectomy, and the extent of resection is an alternative way to measure it. In this study, according to the comparisons of the AUCs of the ROC curves, the complexity classification is better predictive of severe complications, hepatic-related complications, while the extent of hepatectomy only has better predictive power for PHLF. Furthermore, the highly complex operation affects the intraoperative outcomes and is thus closely associated with postoperative complications, which in turn could prolong postoperative recovery. Because of the effects on the aforementioned variables, the complexity classification is more precise in predicting morbidity than the traditional classification.

This study has several limitations. First, although the three levels of complexity in the new classification had a significant predictive value for intraoperative outcomes and postoperative morbidity, we failed to validate whether each type of resection in a single level had a similar outcome prediction ability because some types of hepatectomy had a few cases where validation may lead to potential bias. Thus, future studies should include a larger database. Second, the most useful way to validate a complexity classification is to ask the surgeons about the difficulty of the procedure. However, our study was retrospective; thus, to recall the process and details of the operations they performed several years ago was challenging. In other words, although we collected the accurate objective data of intraoperative details from operation record written within 24 h after operation, we lacked the evaluation of the subjective feelings of the surgeon. Further study to include the surgeons' subjective complexity evaluation into the analysis may be more accurate. Third, because of the high proportion of cirrhosis in Chinese patients with liver cancer, we used the traditional classification's

definition of major hepatectomy (≥ 3 segments), despite the reports of inaccuracy of this definition by some studies. More research need is warranted, and a new, compelling standard needs to be established. Lastly, patients visiting our hospital came from all over the country, so our research may reflect the characteristics of Chinese patients to some extent. However, whether similar results could be obtained in patients elsewhere in the world remains unknown. Further research is needed to prove that the complexity classification is equally applicable to patients with different genetic backgrounds, different liver underlying diseases, and different lifestyles from the Chinese population.

Conclusion

In conclusion, the complexity classification could be used to assess the difficulty of surgery and was associated with post-operative complications. The traditional classification could not reflect operation complexity and was associated only with PHLF. Both classifications were not independent predictive factors of recurrence and survival.

Author Contributions XLW and ZYL contributed to design, perform the research study, and write the paper. XYB, HZ, and JJZ contributed to perform the research study and collected clinical data. ZH, and YFZ contributed to collect and analyze clinical data. YJ contributed to analyze clinical data. JQC and XYB contributed to design and perform the research study, and also took responsibility for the integrity of the work as a whole. All the authors approved the final version of the article, including the authorship list.

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Compliance with Ethical Standards

This study was approved by the Institutional Review Board of our hospital.

Conflict of Interest The authors declare that they have no conflict of interest.

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