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Original Article

Assessment of the postoperative prognosis in patients with hepatocellular carcinoma using vibration-controlled transient elastography: A systemic review and meta-analysis

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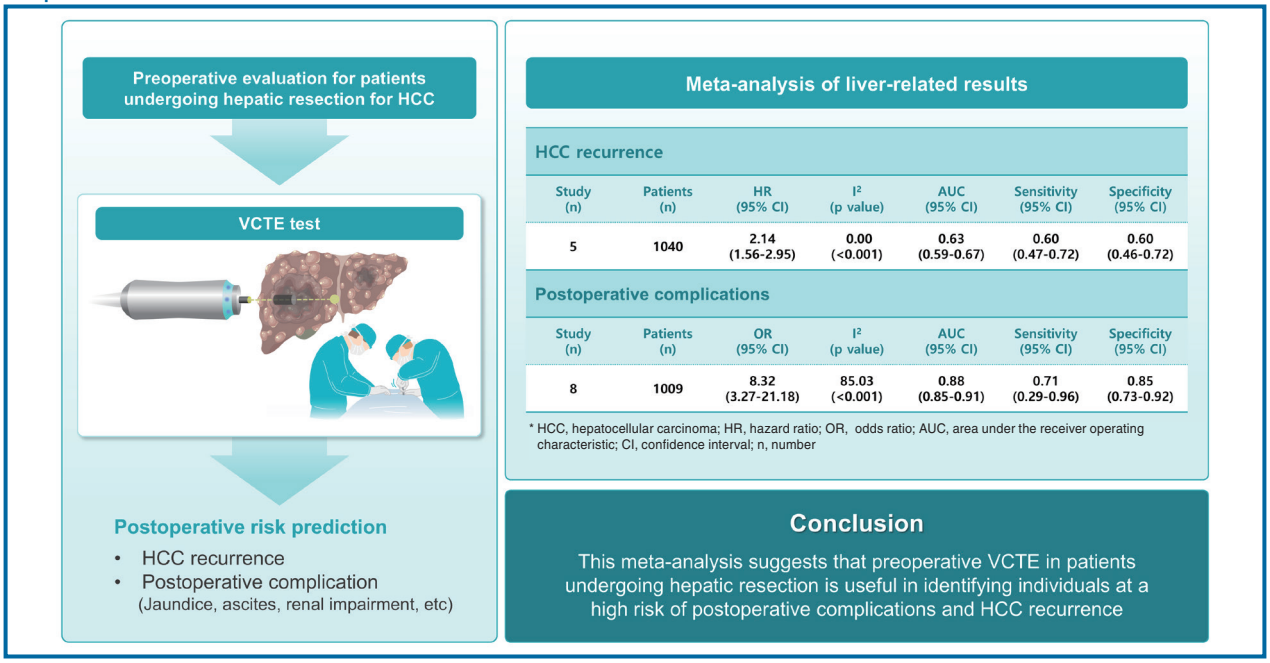
Graphical Abstract



Study Highlights

- HCC patients with high VCTE results had a significantly increased HCC recurrence rate after hepatic resection.
- HCC patients with high VCTE results also had significantly increased postoperative complications compared to patients with low VCTE results.
- This meta-analysis suggests that preoperative VCTE in patients undergoing hepatic resection is useful in identifying individuals at a high risk of postoperative complications and HCC recurrence.

Backgrounds/Aims: This meta-analysis examined whether preoperative vibration-controlled transient elastography (VCTE) can predict postoperative complications and recurrence in patients undergoing hepatic resection for hepatocellular carcinoma (HCC).

Methods: A systematic literature search was conducted using Ovid-Medline, EMBASE, Cochrane, and KoreaMed databases. Out of 431 individual studies, thirteen published between 2008 and 2022 were included. Five studies focused on HCC recurrence, while eight examined postoperative complications.

Results: The meta-analysis of five studies on HCC recurrence showed that the high-risk group with a high VCTE score had a significantly increased recurrence rate after hepatic resection (hazard ratio 2.14). The cutoff value of VCTE in the high-risk group of HCC recurrence was 7.4–13.4 kPa, the sensitivity was 0.60 (95% confidence interval [CI] 0.47–0.72), and the specificity was 0.60 (95% CI 0.46–0.72). The area under the receiver operating characteristic curve (AUC) of the liver stiffness measured by VCTE to predict the HCC recurrence was 0.63 (95% CI 0.59–0.67). The meta-analysis on the postoperative complications revealed a significantly increased risk of postoperative complications in the high-risk group (12–25.6 kPa) with a high VCTE value (odds ratio [OR], 8.32). The AUC of the liver stiffness measured by VCTE to predict the postoperative complications was 0.87 (95% CI 0.84–0.90), the sensitivity was 0.76 (95% CI 0.55–0.89) and the specificity was 0.85 (95% CI 0.73–0.92).

Conclusions: This meta-analysis suggests that preoperative VCTE in patients undergoing hepatic resection for HCC is useful in identifying individuals at a high risk of postoperative complications and HCC recurrence. **(Clin Mol Hepatol 2024;30(Suppl):S186-S198)**

Keywords: Noninvasive test; Transient elastography; Hepatocellular carcinoma

INTRODUCTION

The postoperative complications and hepatocellular carcinoma (HCC) recurrence are critical factors for determining the prognosis of patients with HCC who undergo hepatic resection. Cirrhosis or advanced liver fibrosis has a significant impact on liver complications and mortality after hepatic resection. Therefore, evaluating liver stiffness in patients undergoing hepatic resection is believed to be very meaningful in predicting the prognosis of HCC patients.[1] Recently, various noninvasive tests, such as vibration-controlled transient elastography (VCTE), magnetic resonance elastography (MRE), and shear wave elastography (SWE), have been developed, enabling more diverse

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Abbreviations:

HCC, hepatocellular carcinoma; VCTE, vibration-controlled transient elastography; MRE, magnetic resonance elastography; SWE, shear wave elastography; HR, hazard ratio; CI, confidence interval; LSM, liver stiffness measurement; QUADAS, The Quality Assessment of Diagnostic Accuracy Studies; AUC, area under the receiver operating characteristic curve; CP, Child-Pugh score; MELD, model for end-stage liver disease

methods to identify liver fibrosis that was previously confirmed using a liver biopsy. Accordingly, various studies have reported the application of these noninvasive tests in patients undergoing hepatic resection for HCC.

VCTE is a noninvasive device that assesses the hardness of the liver via the technique of transient elastography and is widely used in patients with liver disease because of its simplicity and accuracy in measuring liver stiffness.[2] Considering that no suitable test has been established to predict recurrence and prognosis in patients with HCC undergoing hepatic resection, VCTE is emerging as the most powerful option among various noninvasive tests. Recently, several studies have predicted HCC recurrence and postoperative complications using preoperative VCTE in patients undergoing hepatic resection for HCC and in selected high-risk groups.[3-8] Although studies have shown significant differences in the cause of HCC and the cutoff value for selecting high-risk groups, the VCTE test has shown the potential to become a standard test in the future, through its ability to provide noteworthy prognostic findings in most studies.

Thus, through this meta-analysis, we aimed to predict the occurrence of postoperative complications and recurrence in patients with HCC undergoing hepatic resection and to evaluate the usefulness of VCTE for screening high-risk patients.

MATERIALS AND METHODS

This systematic review and meta-analyses were conducted according to the guidance provided by the Cochrane Handbook (Higgins JPT, Green S, eds. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available at: www.cochrane-handbook.org). And this systemic review was based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.9 This meta-analysis is registered with PROSPERO (www.crd.york.ac.uk/prospero) and has a registration ID of CRD 42024557467.

Study selection

To identify all relevant articles on the role of TE in assessing postoperative prognosis in HCC patients undergoing hepatic resection, a systematic literature search of Ovid-Medline, EMBASE, Cochrane, and KoreaMed (January 1, 2000 to June 30, 2023) was conducted with the help of an expert librarian. Medical subject terms used in the literature search included a combination of “hepatectomy”, “resection”, “operation” “VCTE”, “fibro scan”, “transient elastography” combined with “prognos*”, “recurrence”, “complication”, “predict*”. The Ovid-Medline, EMBASE, Cochrane, and KoreaMed electronic databases were searched on June 9, 2023, and details of the search strategy are included in Supplementary Table 1. The title and abstract of studies identified in the search were reviewed by 2 authors independently (JW Yu and JW Han) to exclude studies that did not include the research-related question, based on pre-defined inclusion and exclusion criteria. The full text of the remaining studies was reviewed in detail to identify whether it contained information directly related to the present study.

Inclusion and exclusion criteria

Given the predictive goal of this systematic review, we included prospective and historical cohort studies. The inclusion criteria were as follows: (1) VCTE was performed at the time of pre-operation in patients with HCC; (2) systematically assessed the development of HCC recurrence or postoperative complications in patients undergoing hepatic resection; (3) had a follow-up period of at least 6 months for enrolled study subjects; and (4) reported on relevance measures; sensitivity, specificity, and hazard ratio (HR) of VCTE for assessing the postoperative prognosis in HCC patients undergoing hepatic resection or provided enough data for their calculation. The exclusion criteria were as follows: (1) conference, case series, case-control studies, cross-sectional studies, and review articles; (2) studies conducted on other noninvasive tests other than VCTE; or (3) provided insufficient data on the relevance measures mentioned above. In case of duplicate publication or using duplicate results in different subject papers, only data from the most recent comprehensive paper were included and the others were excluded from the study. The flowsheet of the subjects enrolled in this study is shown in Figure 1.

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Data abstraction

The following data were abstracted: (1) study characteristics: name of primary author; time research period/year of publication; country where the study was conducted; study design; follow-up period (mean or median); (2) patient characteristics: age, sex, number of enrolled patients; etiology of HCC (viral hepatitis, other causes); VCTE values indicating liver fibrosis or cirrhosis stage; (3) outcomes assessment: HCC recurrence; development of complication; (4) statistical analysis: HR and 95% confidence intervals (CIs) with and without adjustment for confounding factors, or sensitivity/specificity of liver stiffness measurement (LSM) for HCC recurrence or post-operative complications. Supplementary Table 2 lists the definitions used in each study for postoperative complications. The authors of the included studies were contacted for missing data, and in case of missing data that were important to the study results, the original authors were contacted directly to obtain additional relevant data where possible.

Quality assessment

The Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool was employed to evaluate the quality of the included studies. The authors worked in pairs to independently assess the quality of selected studies, disagreements were addressed by consensus with the participation of a third reviewer (MC). The results of the QUADAS evaluation were visualized using Review Manager 5.3 (The Cochrane Collaboration). The details of the quality assessment are included in Supplementary Figure 1.

Statistical analysis

The meta-analysis was performed using the restricted Maximum Likelihood random effect model.[10] To assess the integration of diagnostic test accuracies obtained from each study, pooled sensitivity, pooled specificity, overall area under the receiver operating characteristic curve (AUC) value, confidence, and prediction contours in summary receiver operating characteristic curve space were calculated using the bivariate mixed effect model.[11]

To determine whether a dispersion existed among HRs, odd risk (OR), sensitivities, or specificities across studies, we used the I^2 statistic and Cochran's Q statistic, which are indexes of heterogeneity. A higher value of I^2 indicates that heterogeneity across studies is more likely to exist. In order to explore potential sources of heterogeneity, subgroup analysis was conducted. The presence of publication bias was assessed by an Egger's asymmetry test.[12]

Statistical significance was determined at α=0.05. Statis-

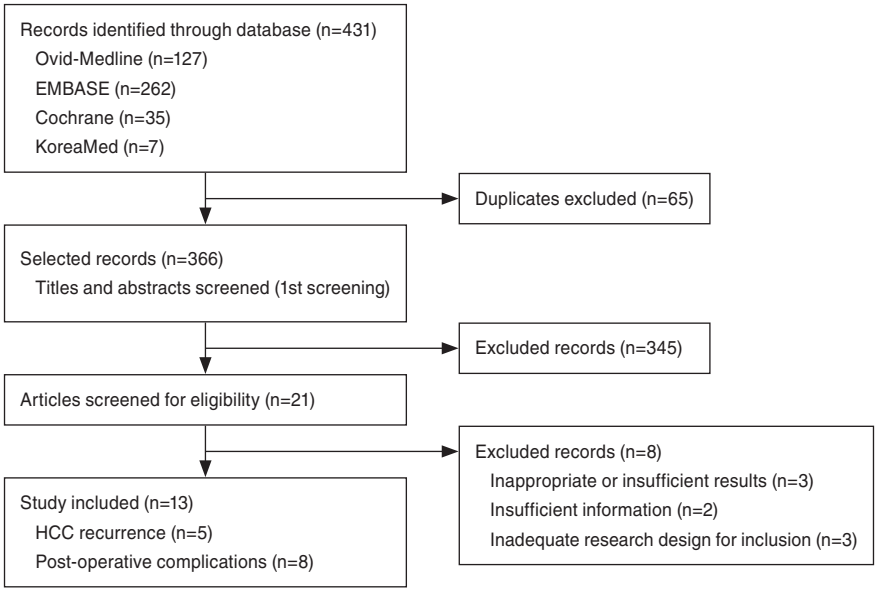

Figure 1. Flowchart showing the study identification, screening, and inclusion process. Of the 1,969 individual studies identified, 13 studies were finally registered. HCC, hepatocellular carcinoma.

tical analysis was performed using STATA software Version 18 (meta, midas, metandi, and metabias function; Stata Corporation, College Station, TX, USA).

RESULTS

Study characteristics

A total of 431 related records were screened using literature search strategies to determine whether VCTE measurements before hepatic resection are helpful in predicting postoperative complications and recurrence rates in patients with HCC. In total, 366 records, excluding duplications in the literature screening process, were screened using titles and abstracts, and 21 original texts were reviewed. Thirteen studies were selected by applying the predetermined selection/exclusion criteria (Fig. 1). Eight of these were selected through literature screening for complications after hepatic resection in patients with HCC, and five were cohort studies on HCC recurrence after hepatic resection.

Studies on recurrence rates after liver resection for HCC were mainly conducted in Asian countries such as Korea and China, and the majority (47–100%) of the patients studied had chronic hepatitis B. The mean follow-up duration for HCC recurrence was 25.0–38.3 months (Table 1). Among the studies on complications after hepatic resection in patients with HCC, six studies were conducted in Asian countries, including China, and two studies were conducted in Europe.[13-20] In the studies conducted in Asia, patients with chronic hepatitis B (64.8–100%) were mainly studied, but in Italy, patients with chronic hepatitis C comprised 68% of the patient's cohort, and in France, patients with HCC due to fatty liver disease comprised 71.3% of the cohort, which is significantly different from Asia. Most studies that investigated complications after hepatic resection confirmed the occurrence of postoperative liver failure, and two studies identified multiple occurrences as a major factor in complications (Table 2). Although there was a difference in the cause of HCC according to the region studied, all studies showed that the risk of postoperative complications and the risk of recurrence increased in the high-risk group with high VCTE results before hepatic resection.

Table 1. The fundamental features of the included studies (HCC recurrence)

Study	Country	Patients number(n)	Age (years)	Gender (male, %)	Study period	Etiology	F/U duration	LSM cut-off value (kPa)	Sensitivity	Specificity	AUC
Jung et al.[3] (2012)	Korea	133	57	117 (88)	2006–2009	HBV 86.5% HCV 6% Others 7.5%	25	13.4	64.7%	76.1%	0.676
Qi et al.[4] (2017)	China	263	58	168 (63.9)	2010–2015	HBV 100%	56	13.2	66.3%	84.7%	0.672
Wang et al.[5] (2021)	Taiwan	94	62.2	74 (78.7)	2012–2016	HBV 46.8% HCV 41.5% Others11.7%	38	8.5	70%	57.4%	0.641
Siu-Ting Lau et al.[6] (2022)	China	401	59.7	338 (84.3)	2010–2017	HBV 80.5% HCV 7.2% Others12.2%	27.2	12			
Hong et al.[7] (2022)	Korea	149	59.6	123 (82.6)	2015–2018	HBV 77.2% HCV 4.7% Others 18.1%	38.3	7.4	61.9%	61.7%	0.638

HCC, hepatocellular carcinoma; LSM, liver stiffness measurement; HBV, hepatitis B-virus; HCV, hepatitis C-virus; F/U, follow up; AUC, area under Receiver Operating Characteristic curve.

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Table 2. The fundamental features of the included studies (postoperative complication)

Study	Country	Patients number (n)	Age (years)	Gender (male, %)	Study period	Etiology	Outcomes	LSM cut-off value (kPa)	Sensitivity	Specificity	AUC
Kim et al.[13] (2008)	Korea	72	54.9	56 (72.2)	2006–2007	HBV 83.3% HCV 12.5% Others 4.2%	Hepatic insufficiency	25.6	71.4%	88.6%	0.824
Cescon et al.[14] (2012)	Italy	90	64	74 (82.2)	2008–2011	HBV 17.8% HCV 68% Others 16.6%	Post-hepatectomy liver failure	15.7	96.1%	97.8%	0.865
Wong et al.[15] (2013)	China	105	59	82 (78.1)	2010–2011	HBV 66.7% HCV 4.8% Others 28.6%	Complications	12	85.7%	71.8%	0.79
Li et al.[16] (2015)	China	75	52.2	59 (78.7)	2012–2014	HBV 100%	Post-hepatectomy liver failure Ascites	15.6	77%	98%	0.902
Lei et al.[17] (2017)	China	247	53.3	218 (86)	2015	HBV 100%	Post-hepatectomy liver failure	14	95%	68%	0.86
Rajakannu et al.[18] (2017)	France	106	67.5	84 (79.2)	2014–2016	Viral 38.7% NAFLD 24.5% Others 46.8%	Post-hepatectomy liver failure	22	42.9%	92.6%	0.81
Chong et al.[19] (2017)	China	255	69	218 (85.5)	2010–2014	HBV 81.6% HCV 6.7% Others 11.7%	Post-hepatectomy liver failure	12	43%	93%	0.65
Wu et al.[20] (2017)	China	54	48	49 (90.7)	2013–2014	HBV 64.8% HCV 7.4% Others 27.8%	Post-hepatectomy liver failure	16.2	71.4%	85.1%	0.76

LSM, liver stiffness measurement; HBV, hepatitis B-virus; HCV, hepatitis C-virus; AUC, area under Receiver Operating Characteristic curve.

Meta-analysis of HCC recurrence after hepatic resection

A meta-analysis was conducted on a total of five studies to determine whether VCTE is useful in predicting HCC recurrence after hepatic resection in patients with HCC. The high-risk group with high VCTE results had a significantly increased HCC recurrence rate after hepatic resection (HR, 2.14, Fig. 2). The cutoff value of VCTE for selecting high-risk groups for HCC recurrence was variously investigated at 7.4–13.4 kPa, with sensitivity around 0.60 (0.47–0.72) and specificity around 0.60 (0.46–0.72) (Fig. 3A). The AUC of the live stiffness measured by VCTE to predict the HCC recurrence was 0.63 (95% CI 0.59–0.67) (Fig. 3B). The AUC values are found to be somewhat lower, apparently due to the small sample size and lack of diversity in the studies included in the meta-analysis. The HCC recurrence rates for patients in the high-risk group ranged from 1.93 to 3.12 times, with no statistically significant differences between the studies.

Meta-analysis of complications after hepatic resection

In a meta-analysis of eight studies that examined the relationship between preoperative VCTE results and postoperative complications in patients who underwent hepatic resection for HCC, the high-risk group with high VCTE results had a higher risk of postoperative complications than the low-risk group with low VCTE results (OR, 8.32, Fig. 4). However, there was a limit that the VCTE cut value (12–25.6 kPa), which is the standard for selecting high-risk groups, varied from study to study, and the risk of complications after hepatic resection (3.27–21.18) also varied slightly from study to study. The sensitivity and specificity of the included study were 0.76 (0.55–0.89) and 0.85 (0.73–0.92), respectively (Fig. 5A). The AUC of the live stiffness measured by VCTE to predict the postoperative complications was 0.87 (95% CI 0.84–0.90) (Fig. 5B).

Subgroup analysis for HCC recurrence and postoperative complications

In a meta-analysis on the HCC recurrence after hepatic resection, subgroup analysis was performed to determine the differences according to the etiology of HCC. However, there was no significant difference in HCC recurrence rate between studies including viral hepatitis and various etiologies, possibly due to the factor that most studies included a large number of patients with hepatitis B. In the meta-analysis results on postoperative complications, subgroup analysis was also performed to determine the effects of the etiology of HCC and differences according to the studied region. The results revealed a significant difference in the occurrence of complications depending on the studies published in Europe and Asia, and some differences in the research results depending on the etiology of HCC were also observed. The results of this subgroup analysis may result in clinical heterogeneity depending on the etiology of HCC and the study area, which can be considered a factor affecting the heterogeneity of the overall study results (I^2=85.03%, P<0.001; Table 3).

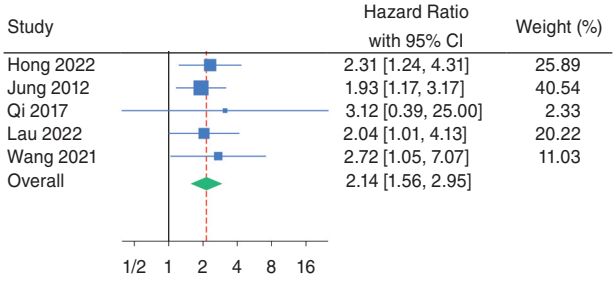

Figure 2. Forest plot on the association between VCTE value and HCC recurrence. HCC, hepatocellular carcinoma; VCTE, vibration-controlled transient elastography; CI, confidence interval.

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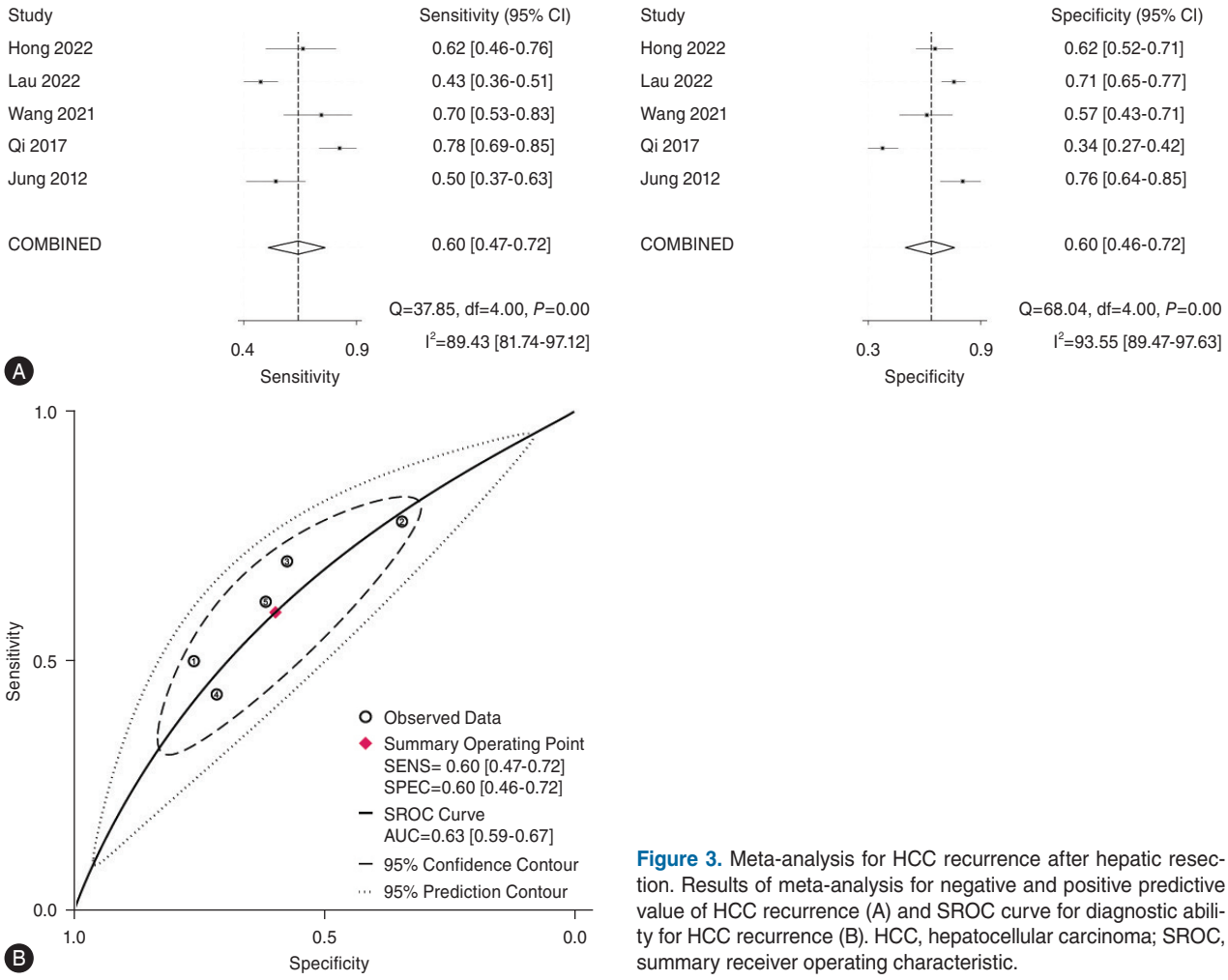
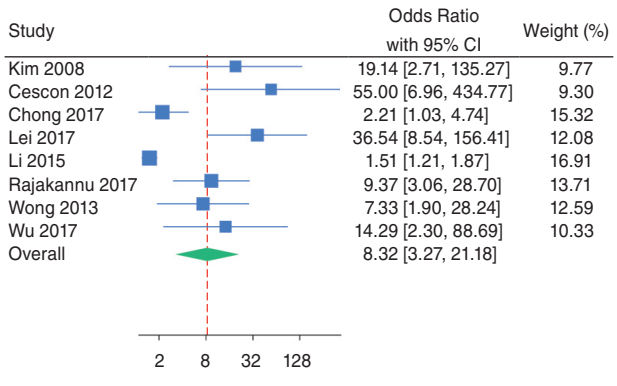


Figure 3. Meta-analysis for HCC recurrence after hepatic resection. Results of meta-analysis for negative and positive predictive value of HCC recurrence (A) and SROC curve for diagnostic ability for HCC recurrence (B). HCC, hepatocellular carcinoma; SROC, summary receiver operating characteristic.



Heterogeneity: τ^2=1.33, I^2=85.03%, H^2=6.68
Homogeneity test of $\theta_i=\theta_j$: Q(7)=52.22, *P*=0.00
Homogeneity test of θ=0: z=4.44, *P*=0.00

Random-effects REML model

Figure 4. Forest plot on the association between VCTE value and postoperative complications. VCTE, vibration-controlled transient elastography; CI, confidence interval.

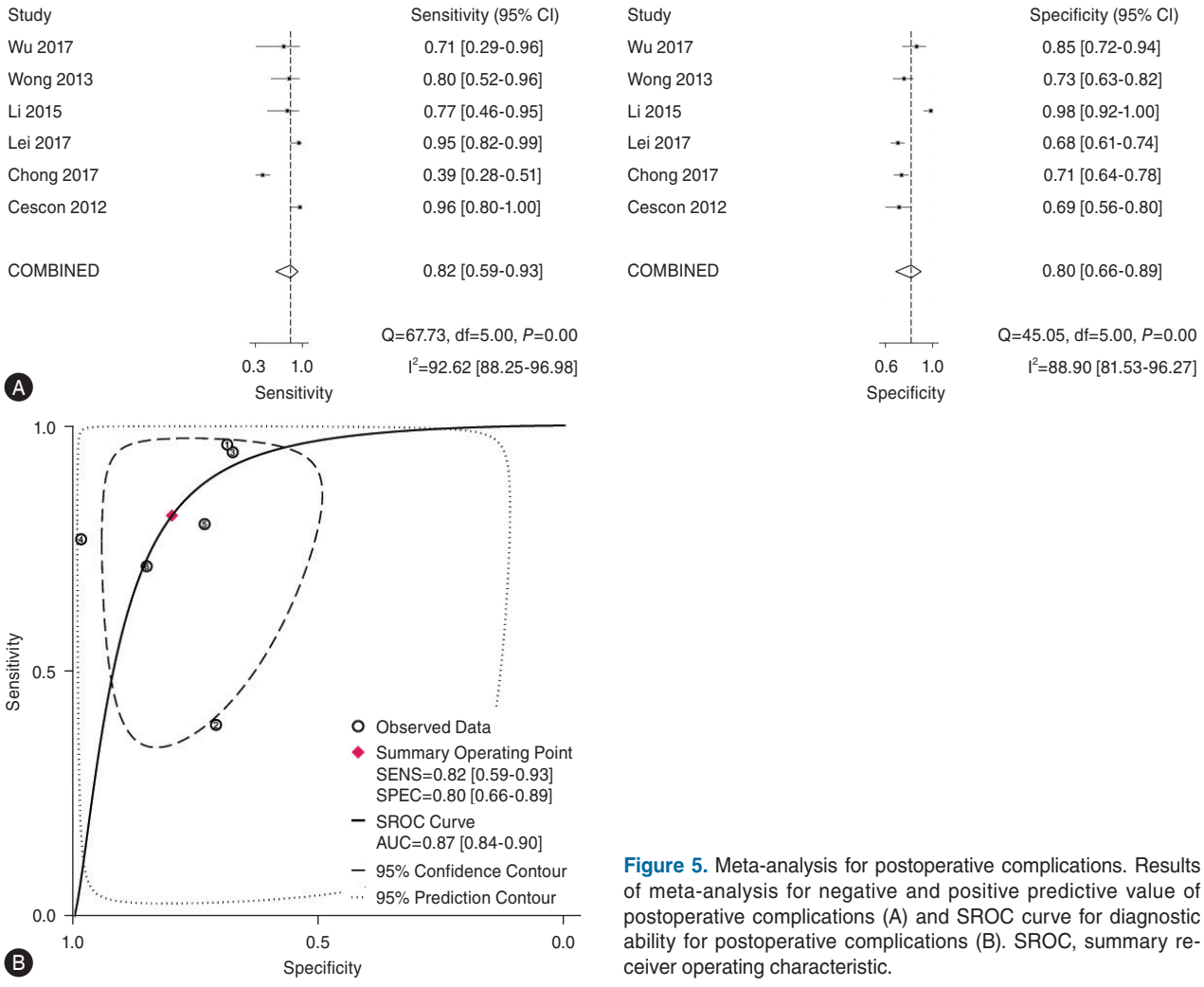


Figure 5. Meta-analysis for postoperative complications. Results of meta-analysis for negative and positive predictive value of postoperative complications (A) and SROC curve for diagnostic ability for postoperative complications (B). SROC, summary receiver operating characteristic.

Table 3. Subgroup analysis for HCC recurrence and postoperative complications

HCC recurrence						
Group factors	**Subgroup**	**Study number**	**Combined HR**	**95% CI**	**Heterogeneity (I^2)**	***P*-value**
Etiology of HCC	Viral Hepatitis	1	3.13	0.39–25.00	NA	NA
	Mixed	4	2.13	1.54–2.93	0.0%	0.920
Postoperative complications						
Group factors	**Subgroup**	**Study number**	**Combined OR**	**95% CI**	**Heterogeneity (I^2)**	***P*-value**
Regions	Asia	6	6.52	2.21–19.24	86.5%	<0.001
	Europe	2	18.18	3.39–97.37	54.1%	0.140
Etiology of HCC	Viral Hepatitis	2	6.82	0.3–154.55	94.5%	<0.001
	Mixed	6	8.96	3.62–22.16	60.9%	0.020

HCC, hepatocellular carcinoma; HR, hazard ration; CI, confidence interval; OR, odds ratios.

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DISCUSSION

This meta-analysis confirmed that preoperative VCTE tests are useful for predicting the recurrence of HCC and postoperative complications including hepatic failure, and ascites in patients with HCC undergoing hepatic resection. Although there were some differences in the risk of HCC recurrence or postoperative complications between studies, all studies showed that the relative risk was high in the high-risk group with a high VCTE value. In particular, in the studies that evaluated HCC recurrence after hepatic resection, the risk of recurrence did not differ much among the five studies (HR 2.14, 95% CI 1.56–2.95), and the heterogeneity of the studies was not significant (T^2=0.00, I^2=0.00%, *P*=0.96); thus, the results are expected to provide important evidence for the necessity of preoperative VCTE testing in patients with HCC undergoing hepatic resection.

Thus far, the Child-Pugh (CP) score, the model for end-stage liver disease (MELD) score, and indocyanine green retention rate at 15 minutes (ICG R15) have been mainly used as conventional methods to predict the postoperative liver function and the development of postoperative complications in patients undergoing hepatic resection.[15,19,21-23] Other methods that are sometimes used to evaluate hepatic fibrosis involve performing a liver biopsy or evaluating portal pressure by measuring the hepatic venous pressure gradient; however, these are not universally used owing to the limitations of invasive tests. Recently, with the increasing use of noninvasive tests such as MRE, VCTE, and SWE to evaluate liver fibrosis, many studies have assessed the postoperative prognosis of patients undergoing hepatic resection using these tests. This review focused on VCTE among various noninvasive tests to determine its usefulness in patients with HCC undergoing hepatic resection. This is because VCTE is a relatively convenient test validated through many studies and is a representative noninvasive test that is widely used in various medical centers.

The VCTE, also known as Fibroscan®, is a device for measuring liver stiffness and degree of fibrosis by evaluating the shear wave velocity. Compared with liver biopsy, VCTE provides a similar efficacy in assessing the degree of fibrosis, but can also provide a continuous value that may be more useful for risk stratification. Additionally, the results are highly reproducible and reflect 100 times more liver parenchyma than a liver biopsy. Therefore, many studies have recently reported the use of VCTE to predict the development of HCC and liver-related complications in patients with various liver diseases, such as hepatitis B, hepatitis C, and cirrhosis. Studies that have evaluated prognosis using VCTE in patients with HCC who underwent hepatic resection have also been reported and can be broadly divided into studies that investigated either the recurrence of HCC or postoperative complications.

The studies on HCC recurrence after hepatic resection using VCTE reported thus far have been conducted mainly in Asian countries, including Korea and China. Therefore, the proportion of hepatitis B (46.8–100%) as a cause of HCC was significantly higher than that of other causes of HCC, with follow-up for an average of 25 to 56 months. Depending on the study, there were differences in the interval between follow-up imaging tests, such as CT and MRI, after hepatic resection (3–6 months). Furthermore, some studies conducted analyses by separating early (within 1 or 2 years) and late recurrences according to their timeframe. Early recurrence may be associated with local or vascular invasion, whereas late recurrence may be considered de novo HCC, which may result in differences between study results. However, most of the studies included in this meta-analysis did not show any significant differences in early or late recurrence. In a study conducted in Korea, the VCTE value did not show significant results in predicting early HCC recurrence within one year after hepatic resection but was found to be useful in predicting late HCC recurrence after one year.[7] However, as this study included a small number of participants (n=149) and the follow-up period was relatively short (38 months), multicenter prospective follow-up studies are needed to confirm these results.

In patients with HCC undergoing hepatic resection for curative intent, the occurrence of postoperative complications is an important factor in determining the patient's prognosis, which is closely related to the presence of liver fibrosis and cirrhosis. As noninvasive tests for liver fibrosis have been developed, studies that predict complications after hepatic resection using VCTE, SWE, MRE, and acoustic radiation force impulse elastography have been reported.[8,24-28] However, each reported study had significant heterogeneity in that the definitions and criteria for postoperative complications differed, and the etiology of HCC also differed depending on the study region. There

has been a wide range of liver stiffness values derived to select high-risk groups, and the relative risk of postoperative complications also differed significantly between studies. Therefore, this study faced significant difficulties in deriving meaningful liver stiffness values through a meta-analysis; however, it proceeded with the analysis by focusing on VCTE and excluding as many heterogeneous studies as possible. Nevertheless, the heterogeneity of the studies included in this meta-analysis was significant and should be taken into consideration when interpreting our results. In addition, this meta-analysis showed that the overall VCTE cutoff value was higher overall in the high-risk group for postoperative complications compared to the high-risk group for HCC recurrence. These results suggest that in the case of postoperative complications, advanced fibrosis, such as portal hypertension due to increased fibrosis, is more closely related to the occurrence of complications.

This study has several limitations. First, most of the analyzed studies were conducted in Asian populations. Therefore, there are limitations to generalizing the results of this study worldwide, and it will be necessary to conduct a multinational study that includes patients with HCC of various races moving forward. Second, because the designs of the studies analyzed were not randomized controlled trials, heterogeneity among the studies was an unavoidable limitation. In particular, the different definitions of postoperative complications in each study are considered to be the biggest factors hindering the unity of this meta-analysis. We performed various subgroup analyses to overcome heterogeneity between studies, but there were limitations in explaining the heterogeneity observed in studies. Considering the heterogeneity among the included studies, an individual patient data meta-analysis could provide more detailed insights. However, access to individual patient data was not available for our study. Third, antiviral treatment for HBV or HCV generally not only lowers the LSM of VCTE but can also lower the rate of HCC recurrence or postoperative complications after hepatic resection. However, this study has limitations in that it is not possible to determine the efficacy of antiviral drugs in patients with HCC due to viral hepatitis because it could not be confirmed whether they were taking antiviral drugs. Fourth, although we have tried to determine a specific cut-off value for liver stiffness in predicting postoperative prognosis in patients with HCC, substantial heterogeneity among the included studies precluded this analysis. Finally, the superiority of the VCTE test was not confirmed through comparative analysis with other noninvasive tests, as well as previously used CP and MELD scores. Therefore, further studies are needed to confirm the superiority of VCTE over other noninvasive tests, including hematologic biomarkers. Moreover, research on a new and improved multiparametric risk prediction model that adds other clinical or imaging indicators in addition to VCTE is needed.

In conclusion, this meta-analysis confirmed that evaluating hepatic fibrosis using a VCTE test before hepatic resection is useful for predicting the prognosis of patients with HCC. Although there were differences in the absolute value of VCTE for patients at high risk of HCC recurrence and postoperative complications, and limitations, such as the absence of a global multicenter study, future follow-up studies are expected to support its wide use for patients with HCC undergoing hepatic resection.

Authors' contributions

JH Yu, JW Han, HA Lee, and MN Kim were responsible for the concept and design of the study, the data acquisition, analysis and interpretation of the data, and manuscript drafting. M Choi helped with the statistical analysis and data interpretation. DW Jun, YE Chon, HY Kim, JH An, YJ Jin, SU Kim, and HA Lee helped with the data interpretation.

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Conflicts of Interest

The authors have no conflict of interest to declare.

SUPPLEMENTARY MATERIAL

Supplementary material is available at Clinical and Molecular Hepatology website (http://www.e-cmh.org).

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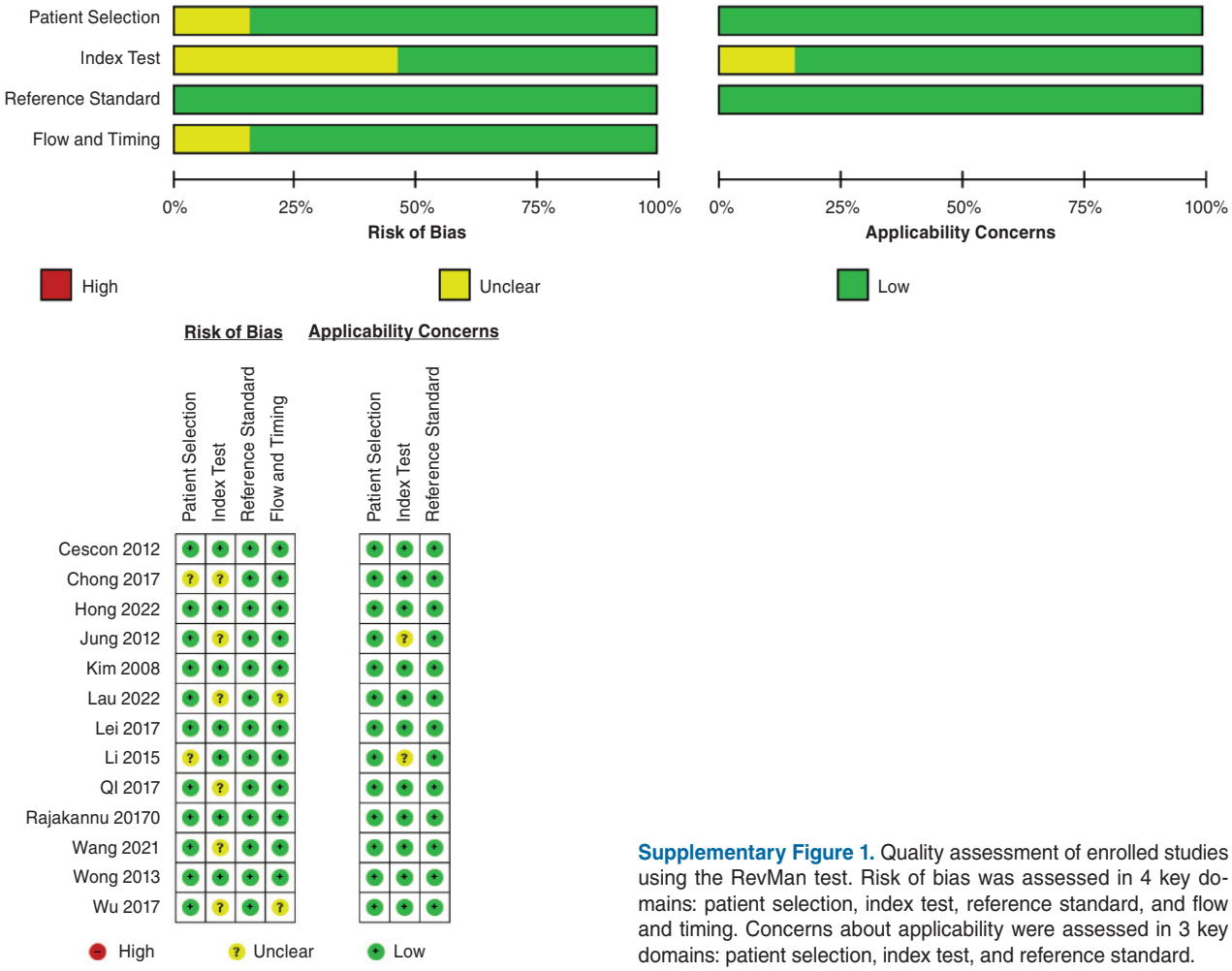

Supplementary Figure 1. Quality assessment of enrolled studies using the RevMan test. Risk of bias was assessed in 4 key domains: patient selection, index test, reference standard, and flow and timing. Concerns about applicability were assessed in 3 key domains: patient selection, index test, and reference standard.

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Supplementary Table 1. The search strategies used for each database

Ovid MEDLINE(R) 1946 to Present with Daily Update

Date: 2023. 06. 09			
	N	**Search word**	**Result**
P	1	Carcinoma, Hepatocellular/ OR Liver Neoplasms/ OR (Hepatocellular carcinoma or HCC or liver cancer or Liver Cell Carcinoma).tw,kw.	228,593
	2	Hepatectomy/ OR (hepatectomy or resection or surgery or operation or operative or post-op* or postop*).tw,kw.	2,254,051
	3	1 AND 2	44,248
I	4	(Fibroscan or (fibrosis adj2 staging) or transient elastograp* or liver stiffness measurement or TE or vibration controlled transient elastograp* or VCTE).tw,kw.	45,218
P&I	5	3 AND 4	127

Embase

Date: 2023. 06. 09			
	N	**Search word**	**Result**
P	1	'liver cell carcinoma'/exp OR 'liver tumor'/exp OR ('liver cell carcinoma' or HCC or 'liver tumor'):ab,ti,kw	376,771
	2	'hepatectomy'/exp OR ('hepatectomy' or 'resection' or 'surgery' or 'operation' or 'operative' or 'post-op*' or 'postop*'):ab,ti,kw	3,188,197
	3	#1 AND #2	82,154
I	4	('Fibroscan' or (fibrosis NEAR/2 staging) or 'transient elastography' or 'liver stiffness measurement' OR TE or 'vibration controlled transient elastography' or VCTE):ab,ti,kw	57,323
P&I	5	#3 AND #4	262

Cochrane library

Date: 2023. 06. 09			
	N	**Search word**	**Result**
P	1	[mh "Carcinoma, Hepatocellular"] OR [mh "Liver Neoplasms"] OR ("Carcinoma, Hepatocellular" or HCC or "Liver Neoplasms"):ab,ti,kw	6,492
	2	[mh "Hepatectomy"] OR ("hepatectomy" or "resection" or "surgery" or "operation" or "operative" or "post-op*" or "postop*"):ab,ti,kw	298,500
	3	#1 AND #2	2,369
I	4	("Fibroscan" or (fibrosis NEAR/2 staging) or "transient elastography" or "liver stiffness measurement" OR TE or "vibration controlled transient elastography" or VCTE):ab,ti,kw	5,948
P&I	5	#3 AND #4	35

KoreaMed

Date: 2023. 06. 09			
	N	**Search word**	**Result**
P	1	("Carcinoma, Hepatocellular"[MH]) OR ("Liver Neoplasms"[MH]) OR ("Carcinoma, Hepatocellular"[ALL] or "HCC"[ALL] or "Liver Neoplasms"[ALL])	3,457
	2	("Hepatectomy"[MH]) OR ("hepatectomy"[ALL] or "resection"[ALL] or "surgery"[ALL] or "operation"[ALL] or "operative"[ALL] or "post-op"[ALL] or "postoperative"[ALL])	97,950
	3	1 AND 2	1,239
I	4	("Fibroscan"[ALL] or "fibrosis staging"[ALL] or " staging fibrosis"[ALL] or "transient elastography"[ALL] or "liver stiffness measurement"[ALL] OR "TE"[ALL] or "vibration controlled transient elastography"[ALL] or "VCTE"[ALL])	748
P&I	5	3 AND 4	7

Supplementary Table 2. Definitions of postoperative complications used in each study

Study	Definitions of postoperative complications
Kim et al.[13] (2008)	Persistent hyperbilirubinemia (total bilirubin level 5 mg/dL) for more than 5 days after surgery or postoperative death without other causes.
Cescon et al.[14] (2012)	The Dindo-Clavien classification 1. occurrence of refractory ascites causing a delay in the removal of surgical drainages and/or requiring paracentesis (grade II or grade IIIa complication). 2. an increase of bilirubin levels to more than 3 mg/dL. 3. alteration of coagulation factors requiring fresh frozen plasma infusion with an INR of more than 1.50. 4. renal impairment, defined as BUN of more than 2.00 g/L and/or increase of serum creatinine to more than 2.00 mg/dL requiring only loop diuretics, dopamine/terlipressin, or dialysis.
Wong et al.[15] (2013)	The modified Clavien classification. Major complication was defined as grade 3 or above.
Li et al.[16] (2015)	1. Postoperative ascites; abdominal output greater than 500 mL/d, or ascites that require medical treatment) 2. Postoperative liver failure; both a prothrombin time less than 50% (INR >1.7) and a serum bilirubin concentration greater than 50 μmol/L on postoperative day 5)
Lei et al.[17] (2017)	1. occurrence of refractory ascites causing a delay in the removal of surgical drainages and/or postoperative drainage exceeding 500 ml/day 2. a continuous elevation of total serum bilirubin concentration (≥60 μmol/L) beyond postoperative day 7 3. alteration of coagulation factors requiring fresh frozen plasma infusion with an INR of more than 1.50
Rajakannu et al.[18] (2017)	The presence of at least one of the following: unresolved ascites, jaundice, and/or encephalopathy <3 months after hepatectomy
Chong et al.[19] (2017)	The modified Clavien classification. Major complication was defined as grade 3 or above.
Wu et al.[20] (2017)	PT <50% and serum bilirubin level 50 μmol/L on postoperative day 5.

INR, International normalized ratio; BUN, blood urea nitrogen; PT, Prothrombin time.

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