



Computed tomography for the diagnosis of gastroesophageal varices and risk assessment in patients with cirrhosis: a systematic review and meta-analysis

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PURPOSE

This meta-analysis aimed to evaluate the diagnostic accuracy of computed tomography (CT) for detecting gastroesophageal varices (GEVs) and identify high-risk GEVs in patients with cirrhosis.

METHODS

A comprehensive search of databases identified 28 studies reporting on CT-based diagnosis for GEVs confirmed via endoscopy. Meta-analyses were conducted to calculate pooled sensitivity (SEN) and pooled specificity (SPE), positive likelihood ratio (PLR) and negative likelihood ratio (NLR), diagnostic odds ratio (DOR), and the area under the curve (AUC).

RESULTS

Based on the number of patients (or varices), the pooled SEN, SPE, PLR, NLR, DOR, and AUC of CT-based diagnosis were estimated at 0.91 (0.92), 0.81 (0.45), 4.82 (1.67), 0.11 (0.17), 42.47 (10.26), and 0.93 (0.94), respectively, for any GEV and at 0.89 (0.89), 0.90 (0.79), 8.86 (4.28), 0.12 (0.14), 75.71 (30.19), and 0.95 (0.85), respectively, for high-risk GEVs. Subgroup analyses indicated that CT had a higher diagnostic accuracy for esophageal varices compared with gastric varices (AUC: 0.93 vs. 0.89, $P < 0.05$), and the 64-slice CT yielded superior SEN compared with 16-slice and <16-slice CT (AUC: 0.97 vs. 0.92 and 0.82, respectively, $P < 0.05$). Prospective studies demonstrated higher diagnostic accuracy than retrospective studies (AUC: 0.95 vs. 0.90, $P < 0.05$). Regarding variceal size, a cut-off of 3 mm and 5 mm discriminated between low- and high-risk individuals, respectively, with high diagnostic accuracy (AUC: 0.992 vs. 0.997, $P > 0.05$).

CONCLUSION

CT demonstrates promising diagnostic accuracy for identifying gastroesophageal varices and distinguishing high-risk GEVs in patients with cirrhosis. Further research to validate optimal variceal size cut-offs is warranted to enhance clinical utility.

CLINICAL SIGNIFICANCE

Such a high diagnostic accuracy of CT scans for predicting varices is clinically meaningful for patients with cirrhosis accompanied by portal hypertension. If high-risk varices are identified at CT scans, early intervention would be helpful to reduce the risk of variceal bleeding.

KEYWORDS

Computed tomography, gastroesophageal varices, gastric varices, esophageal varices, cirrhosis, meta-analysis

Bleeding of gastroesophageal varices (GEVs) is a serious complication of portal hypertension (PH) in cirrhosis.¹ Gastric varices (GVs) and esophageal varices (EVs) can occur concurrently or separately. EVs are more important for the collateral circulation of PH than GVVs and occur in 20%–40% and approximately 70% of compensated and decompensated patients with cirrhosis, respectively.² Esophagogastroduodenoscopy (EGD) is current-

ly the standard approach for assessment of GEVs when diagnosing cirrhosis.³ Presence of advanced liver disease (Child Pugh's score B or C), large varices (>5 mm), or varices with the red color (RC) sign specify patients with a high hemorrhage risk.^{4,5} The progression from small to large varices is detected in approximately 10% of patients with cirrhosis per year.⁶ In this context, it is of great significance to detect GEVs and predict variceal bleeding in time. EGD screening is recommended for patients with cirrhosis with small varices and patients without any varices every 1–2 and 2–3 years, respectively.^{7,8} However, as a screening method, EGD is limited due to its invasive nature and poor acceptance by patients.⁹ Additionally, it is obvious that a significant part of patients undergoing EGD screening, particularly those with compensated cirrhosis, have no varices or only small EVs. Furthermore, EGD fails to evaluate the entire spectrum of extraparietal GEVs and may miss some GVs.^{10,11}

These drawbacks have driven the ongoing studies to identify alternative, non-invasive techniques for repeat variceal detection.

The Baveno VI guidelines recommend that patients with alcoholic or viral cirrhosis, liver stiffness <20 kPa and a platelet count >150 G/L should avoid EGD screening, which is a highly sensitive approach with limited specificity for the detection of GEVs.¹² Computed tomography (CT) or magnetic resonance imaging of portosystemic collateral vessels has been shown to have a sensitivity of 95% and specificity of 36% in predicting high-risk EVs in patients who do not meet the Baveno VI criteria.¹³ Unlike EGD, contrast-enhanced CT can clearly show the portal vein system and collateral circulation,¹⁴ including in patients with periesophageal and perigastric fundal varices. Furthermore, CT is useful in assessing the risk of GEV bleeding.¹⁵

Main points

- Computed tomography (CT) demonstrates promising diagnostic accuracy for identifying gastroesophageal varices (GEVs) and distinguishing high-risk GEVs in patients with cirrhosis.
- CT with a >16-slice scanner showed a significantly better performance than the <16-slice CT.
- Varices of <3 mm and >5 mm may discriminate against low-risk and high-risk patients, respectively.
- Approximately 84.29% of patients prefer CT instead of endoscopy in screening for varices.

Herein, the study authors conduct a systematic review and meta-analysis to evaluate the diagnostic efficacy of CT for GEVs and analyze its predictive value for high-risk varices in patients with cirrhosis.

Methods

The present study is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement and the published recommendations. The detailed protocol is accessible in PROSPERO (CRD42020220384). Ethics information and informed consent forms were not required, as systematic reviews typically involve synthesizing and summarizing existing literature rather than directly engaging in human or animal experiments.

Literature search

To retrieve eligible studies on CT-based diagnosis of EV and/or GV, a systematic literature search in the PubMed, Embase, Cochrane Library, and Web of Science databases was performed from inception to November 30, 2023. The search was conducted based on the following search terms: "gastroesophageal varices," "gastric varices," "esophageal varices," "varices," "CT," and "computed tomography." The search strategy was determined after multiple pre-searches and combined free words with Medical Subject Headings terms for each database. No language or article-type restriction was applied. The references of the included studies and other systematic reviews and meta-analyses were also reviewed to obtain a comprehensive list of relevant studies.

Eligibility criteria

The inclusion criteria were as follows: (1) the patients were diagnosed with cirrhosis; (2) the diagnostic examination was contrast-enhanced CT; (3) EGD was performed to confirm the presence and/or grade of esophageal and/or GVs; (4) the data provided was sufficient to conduct a 2 × 2 table to assess the diagnostic sensitivity and specificity of CT for the varices; and (5) >20 patients were evaluated for reliable assessment.

The exclusion criteria were as follows: (1) patients without cirrhosis; (2) patients who were not evaluated via endoscopy or CT; (3) duplicates; (4) review articles; (5) case reports; and (6) conference papers, letters, and abstracts.

Study selection, data extraction, and quality assessment

The titles and abstracts of the search results were screened for eligibility by two independent readers (Y. Zhu and L. Wang with 3 years and 12 years of experience in abdominal imaging, respectively) according to the pre-enacted inclusion and exclusion criteria, and full texts meeting the inclusion criteria were retrieved. The following data were extracted according to the predefined data form: the first author's name, the study design (prospective or retrospective), publication year, country, sample size, age, gender, etiology of cirrhosis, Child–Pugh class, time interval between the CT and EGD, number of patients who underwent EGD, location of varices (EVs and/or GVs), prevalence of any-sized and/or high-risk varices, definitions of high-risk varices on CT and EGD, cut-off values (the maximal short-axis diameter of the largest varix), and CT imaging parameters (slice). The true-positive (TP), false-positive (FP), true-negative (TN), and false-negative (FN) values were also extracted directly or calculated. It should be recognized that all the data per study were extracted if the study involved several CT techniques or observers, and serial numbers to this study were given. Finally, two readers independently performed QUADAS-2 criteria¹⁶ assessments. Results were cross-checked at every step, and a consensus was reached in the case of discrepancy.

Statistical analysis

Analyses were performed using the STATA 15.0 (StataCorp, College Station, TX) and Revman 5.4 (The Cochrane Collaboration, 2020) software. However, in the case of <4 articles, MetaDiSc 1.4 was used for analysis, and I^2 statistics were used to analyze heterogeneity of the included studies.¹⁷ Significant heterogeneity was indicated by $I^2 > 50\%$ or $P < 0.10$.

If there is no heterogeneity or if the heterogeneity is low, a fixed effects model should be chosen. A random effects model allows for high heterogeneity, and a sensitivity analysis or subgroup analysis should then be carried out. The pooled sensitivity (SEN), pooled specificity (SPE), positive predictive values and negative predictive values, positive likelihood ratio (PLR) and negative likelihood ratio (NLR), and diagnostic odds ratio (DOR) with a 95% confidence interval (CI) were calculated based on the number of TPs, FPs, FNs, and TNs, respectively. Following

this, the summary receiver operating characteristic and its corresponding area under the curve (AUC) were calculated. If there was significant heterogeneity, subgroup analysis was carried out to identify the sources of heterogeneity. In addition, in the case of >9 studies, the authors assessed for any publication bias by applying Deeks et al.¹⁸ plot test. Statistical significance was indicated by $P < 0.05$.

Results

Literature search and study selection

This systematic review included 28 publications, involving 2,879 participants.^{10,19-45} The PRISMA flow chart of the literature screening is shown in Figure 1.

Study design and properties

The extractive data of the included studies are summarized in Table 1. The 28 selected articles were published between 2007 and 2023. In 27 of these papers, data were presented based on the number of patients,^{10,19-44} and the data in the remaining article (a retrospective report evaluating EVs in 104 participants) were presented based on the number of varices.⁴⁵ Among the patient-based studies, which assessed for varices of any size, 11 (40.7%) were retrospective,^{20,22-24,27,29,30,32,33,37,42} 12 (44.4%) were prospective,^{10,19,26,28,31,34,35,38-41,44} and 4 (14.9%) were undefined;^{21,25,36,43} 24 (88.9%) assessed for EVs^{10,19-35,38-41,43,44}, and 6 (22.2%)^{10,32,35,36,37,42} assessed for both EVs and GVs, including 3 for GVs only.^{10,32,35} The prevalence of EVs and GVs were 33.6%–98% and 10.5%–28.3%, respectively. Two studies included only patients with hepatocellular carcinoma.^{33,34} The remaining studies enrolled patients with various etiological factors, such as viral hepatitis, alcohol abuse, and cryptogenic cirrhosis.

Among the eligible studies, 18 assessed for high-risk varices.^{20-24,27,29-35,36,39,41,43,45} The detailed characteristics of these studies are shown in Supplementary Table 1. A total of 16 articles (88.9%) assessed for high-risk EVs,^{20-24,27,29-35,36,39,41,43,45} 1 assessed for high-risk GVs,³² and 1 assessed for high-risk GEVs.³⁵ The prevalence of high-risk EVs and GVs was 15.4%–75% and 16.5%, respectively. The varix size cut-off of high-risk varices on CT was 2 mm,^{21,22,33,34,45} 3 mm,^{30,41} 3.9 mm,²⁴ 4 mm,^{20,23} and 5 mm,^{31,32,35,36} respectively. Finally, 3 studies did not specify the cut-off on CT.^{27,29,39}

Additionally, 3 studies^{31,40,42} reported that the varix size on CT was significantly correlated with the presence and severity of the RC

sign. A cut-off of 4 or 5 mm was used to predict the RC sign.

A total of 5 studies^{10,38-41} concerned preferences of the patients for CT versus EGD. Most (84.3%) patients preferred undergoing a CT scan instead of EGD for varix screening.

Quality assessment

The results of the quality evaluation of the eligible articles are shown in Supplementary Figure 1. Most studies were identified as low-risk in terms of risk of bias and applicability

concerns, and all of the studies met >4 terms of the 7 total domains. The most common domain of unclear risk was the reference standard regarding the blinding of EGD interpretation to the CT imaging.

Diagnostic accuracy of computed tomography for gastroesophageal varices

The results of the meta-analyses are summarized in Table 2. Significant heterogeneity was observed in all the analyses ($P < 0.05$ and $I^2 > 50\%$).

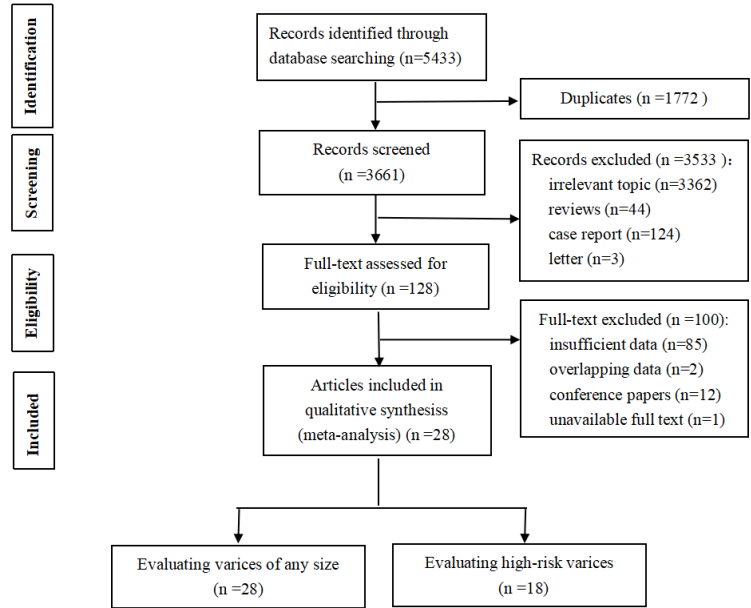


Figure 1. The study screening process.

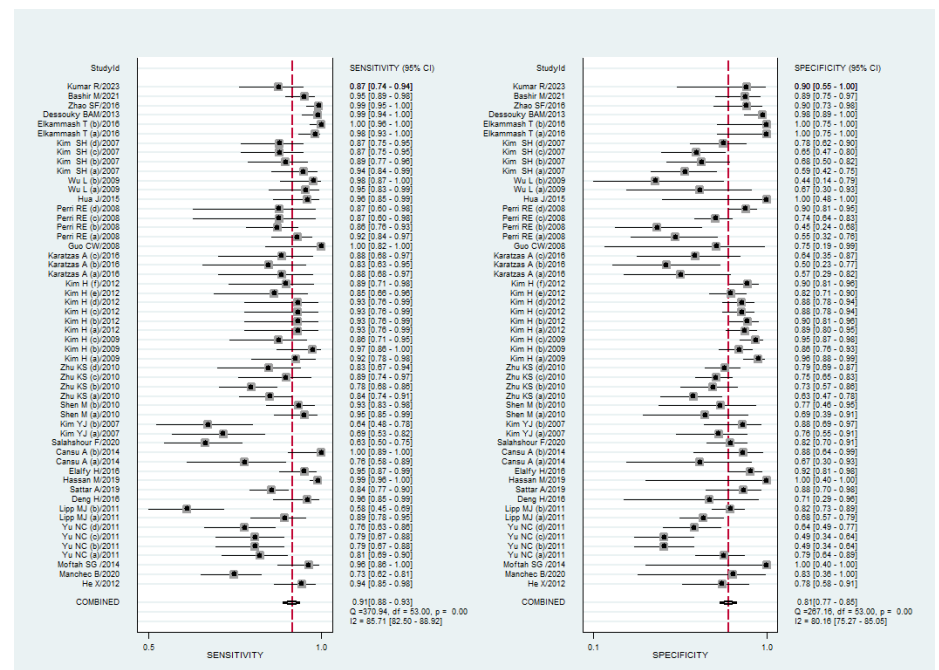


Figure 2. Coupled Forest plots of sensitivity and specificity for diagnosing gastroesophageal varices with CT. CT, computed tomography.

Table 1. Characteristics of computed tomography for diagnosing gastroesophageal varices

Study/journal/year	Study design	Country	Sample	M/ F	Mean age (y)	Etiology	Child-Pugh score
He et al. ¹⁹ , Chin J Radiol (China), 2012	P	China	92	73/19	51 (34–80)	Viral 78, alcohol 12, pancreatic 1, cholestatic 1	A 33, B 44, C 15
Manchec et al. ²⁰ , AJR Am J Roentgenol, 2020	R	US	97	64/33	54.4	HBV 2, HCV 35, alcohol 46, NASH 18	A 36, B 50, C 11
Moftah et al. ²¹ , Egypt J Radiol Nucl Med, 2014	/	Egypt	54	40/14	56.8 (38–75)	/	/
Yu et al. ²² , AJR Am J Roentgenol, 2011	R	US	109	60/49	55.9 (19–82)	HBV 7, HCV 51, alcohol 19, cryptogenic or others 32	/
Lipp et al. ²³ , Dig Dis Sci, 2011	R	US	195	/	55.2	/	/
Deng et al. ²⁴ , J Evid Based Med, 2017	R	China	52	33/19	55.4	HBV 13, HCV 2, HBV and HCV 1, alcohol 16, alcohol and HBV 5, others 15	A 25, B 21, C 6
Sattar et al. ²⁵ , Med Forum, 2019	/	Pakistan	172	96/76	45.01 (35–60)	/	/
Hassan et al. ²⁶ , Cureus, 2019	P	Pakistan	196	106/90	55.8 (11–82)	HBV 13, HCV 79, others 104	/
Elalfy et al. ²⁷ , World J Hepatol, 2016	R	Egypt	124	26/98	56.5	HCV 124	A 78, B 46, C 0
Cansu et al. ²⁸ , Eur J Radiol, 2014	P	Turkey	42 50	29/13 27/23	56.2 56.8	HBV 19, HCV 10, HBV and HCV 1, alcohol 2, others 10 HBV 20, HCV 15, HBV and HCV 2, alcohol 2, others 11	A 16, B 13, C 13 A 26, B 18, C 6
Salahshour et al. ²⁹ , Abdom Radiol (NY), 2020	R	Iran	124	76/48	50.38 (21–73)	HBV 30, HCV 7, alcohol 5, AIH 12, cryptogenic or others 70	/
Kim et al. ³⁰ , AJR Am J Roentgenol, 2007	R	US	67	39/28	56.2 (33–77)	HBV 15, HCV 24, HBV and HCV 6, alcohol 15, cryptogenic or others 7	A 16, B 25, C 26
Shen et al. ³¹ , Zhonghua Yi Xue Za Zhi, 2010	P	China	69	56/13	53 (23–76)	HBV 60, HCV 4, alcohol and HBV 3, alcohol 2	A 44, B 22, C 3
Zhu et al. ³² , J Clin Gastroenterol, 2010	R	China	127	96/31	45.2 (30–75)	HBV 95, HCV 6, alcohol 13, cryptogenic or others 13	A 48, B 47, C 32
Kim et al. ³³ , Dig Dis Sci, 2009	R	South Korea	110	81/29	61 (27–80)	HBV 67, HCV 32, HBV and HCV 2, alcohol 7, unknown 2	A 70, B 29, C 11
Kim et al. ³⁴ , World J Gastroenterol, 2012	P	South Korea	100	79/21	58.4 (35–82)	HBV 76, HCV 14, alcohol 5, unknown 5	A 89, B 10, C 1
Karatzas et al. ³⁵ , Ann Gastroenterol, 2016	P	Greece	38	30/8	63 (48–81)	Viral 13, alcohol 18, others 7	A 21, B 11, C 6
Perri et al. ¹⁰ , Hepatology, 2008	P	US	101	64/37	57.5	Viral 22, alcohol 19, cholestatic 18, NASH 15, others 27	A 45, B 40, C 16
Guo et al. ³⁶ , Chin J Med Imaging Technol, 2008	/	China	27	14/13	48.6 (28–71)	HBV 23, HCV 2, alcohol 2	A 10, B 12, C 5

Table 1. Continued

CT scanner	CT technique	Patients underwent EGD	Time interval	Patient acceptance	Varice location	Prevalence of varices (%)	TP	FP	FN	TN
64-slice	MSCT portography	92	Within 4 w	/	GEVs	70.65%	61	6	4	21
/	/	97	Within 3 m	/	EVs	94.80%	66	1	25	5
4 or 8-slice	MDCT	54	/	/	EVs	92.59%	48	0	2	4
							50	10	12	37
16 or 64-slice	MDCT with standard 5 mm and thin-section MPR	109	Within 10 w	/	EVs	56.88%	49	24	13	23
							49	24	13	23
							47	17	15	30
4 or 16 or 64-slice	MDCT	137	Within 3 m	/	EVs	44.52%	54	24	7	52
		165				43.03%	41	17	30	77
/	/	52	Within 4 w	/	EVs	86.54%	43	2	2	5
16-slice	MDCT	172	/	/	EVs	84.88%	123	3	23	23
64-slice	MDCT	196	Within 20 d	/	EVs	97.95%	190	0	2	4
16-slice	MDCT	124	/	/	EVs	59.68%	70	4	4	46
16-slice	MDCT with effervescent powder	42	Within 4 w	/	EVs	78.57%	25	3	8	6
16-slice	MDCT without effervescent powder	50	Within 4 w	/	EVs	66%	33	2	0	15
16 or 64-slice	MDCT	124	Within 6 m	/	EVs	50.81%	40	11	23	50
single or 4 slice	Single-detector helical CT or MDCT	67	Within 4 w	/	EVs	62.69%	29	6	13	19
							27	3	15	22
							53	4	3	9
320-slice	MDCT	69	Within 1 w	/	EVs	81.16%				
							52	3	4	10
							72	15	14	26
4-slice	MDCT	127	Within 4 w	/	EVs	67.72%	67	11	19	30
					GVs	28.34%	32	23	4	68
							30	19	6	72
							34	3	3	70
16-slice	MDCT	110	Within 4 w	/	EVs	33.64%	36	10	1	63
							32	4	5	69
							25	8	2	65
							25	7	2	66
64-slice	MDCT with and without MPR	100	Within 4 h	/	EVs	50.00%	25	9	2	64
							25	9	2	64
							23	13	4	60
							24	7	3	66
							21	6	3	8
					GEVs	63.16%	20	7	4	7
							21	5	3	9
							20	7	3	8
16-slice	MDCT	38	Within 1 m	/	EVs	60.53%	19	8	4	7
							20	6	3	9
							3	4	1	30
					GVs	10.53%	3	4	1	30
							3	4	1	30
							73	10	6	12
4 slice or higher	MDCT	101	Within 5 d	88% CT, 6% EGD, 6% no preference	EVs	78.22%	68	12	11	10
					GVs	14.85%	13	22	2	64
							13	9	2	77
64-slice	MSCT portography	23	/	/	GEVs	82.61%	19	1	0	3

Table 1. Continued

Study/journal/year	Study design	Country	Sample	M/ F	Mean age (y)	Etiology	Child– Pugh score
Hua et al. ³⁷ , J Dig Dis, 2015	R	China	90	57/33	54.4 (31–75)	HBV 49, HCV 3, alcohol 8, AIH 5, others 25	A 36, B 34, C 20
Wu et al. ³⁸ , Chin J Gastroenterol, 2009	P	China	50	30/20	57.7 (31–78)	HBV 38, HBV, and HCV 1, AIH 1, others 10	A 13, B 31, C 6
Kim et al. ³⁹ , Radiology, 2007	P	China	90	65/25	54.8 (21–77)	HBV 66, HCV 19, Alcohol 2, cryptogenic 3	A 73, B 17, C 0
Elkammash et al. ⁴⁰ , Egypt J Radiol Nucl Med, 2016	P	Egypt	112	77/45	51.4 (38–72)	HBV 52, HCV 49, bilharziasis 11	/
Dessouky and Abdel Aal ⁴¹ , Arab J Gastroenterol, 2013	P	Egypt	137	73/64	58.7 (45–77)	HBV 27, HCV 93, HBV and HCV 14, steatohepatitis 3	A 75, B 42, C 20
Zhao et al. ⁴² , Chin J Gastroenterol, 2016	R	China	143	96/47	52.39 (23–78)	HBV 101, HCV 5, alcohol 16, cryptogenic or others 21	A 54, B 48, C 41
Bashir et al. ⁴³ , P J M H S, 2021	/	Rawalpindi	145	/	35–80	/	/
Kumar et al. ⁴⁴ , Pol J Radiol, 2023	P	India	621	/	62	/	/
Kim et al. ⁴⁵ , J Gastroenterol Hepatol, 2009*	R	South Korea	104	77/27	59 (27–80)	HBV 75, HCV 13, alcohol 7, cryptogenic 9	A 43, B 32, C 29

*Data presented based on number of varices. R, retrospective; P, prospective; HBV, hepatitis B virus; HCV, hepatitis C virus; AIH, autoimmune hepatitis; PSC, primary sclerosing cholangitis; NASH, non-alcoholic steatohepatitis; MDCT, multi-detector computed tomography; MPR, multiplanar reconstruction; MSCT, multi-slice spiral computed tomography; EVs, esophageal varices; GVs, gastric varices; GEVs, gastroesophageal varices; TP, true-positive; FP, false-positive; TN, true-negative; FN, false-negative.

Based on the number of patients: In 27 studies,^{10,19–44} which contained 54 sets of data regarding GEVs of any size, the pooled SEN and SPE were 0.91 and 0.81, respectively (Figure 2), with an AUC of 0.93 (Supplementary Figure 2). There were 35 sets of data from 17 studies^{20–24,27,29–35,36,39,41,43} that assessed for high-risk GEVs. The pooled SEN and SPE were 0.90 and 0.90, respectively (Figure 3), with an AUC of 0.96 (Supplementary Figure 3). The pooled SPE and PLR for high-risk varices were significantly higher than those for varices of any size ($P = 0.001$ and 0.020 , respectively).

Based on the number of varices: There was only 1 study⁴⁵ with 3 sets of data. The pooled SEN, SPE and AUC for varices of any size (and high-risk EVs) were 0.92 (0.89), 0.45 (0.85), and 0.94 (0.95), respectively.

Patient-based subgroup analysis of gastro-esophageal varices of any size

To identify the sources of heterogeneity, the authors performed subgroup analysis according to the location of varices, study design, and CT scanners used.

Location of the varices

EVs: There were 47 sets of data from 24 studies^{10,20–35,38–41,43,44} that assessed for EVs of any size, and 32 sets of data from 15 studies^{20–24,27,29–31,33,34,36,37,41,43} that assessed for high-risk EVs (Table 2). The pooled SPE and PLR for high-risk EVs were significantly higher than those for EVs of any size ($P = 0.010$ and 0.034 , respectively). However, no statistically significant difference in SEN, NLR, DOR or AUC was found between high-risk EVs and EVs of any size (all $P > 0.05$). According to

the corresponding I^2 (82.5%–100%), there was substantial heterogeneity in the EV subgroup among the studies. Then, a subgroup analysis was carried out for EVs (Supplementary Table 2).

GVs: There were 7 data sets from 3 studies^{10,32,35} concerning the presence of GVs of any size (Table 2). There was no statistically significant heterogeneity in the GV subgroup among these studies. Since only 1 study³² reported on high-risk GVs, a pooled analysis could not be performed.

Study design

Prospective vs. retrospective: There were 29 and 21 sets of data from 12 prospective^{10,19,26,28,31,34,35,38–41,44} and 11 retrospective^{20,22–24,27,29,30,32,33,37,42} studies, respectively (Table 3). Between the prospective studies

Table 1. Continued

CT scanner	CT technique	Patients underwent EGD	Time interval	Patient acceptance	Varice location	Prevalence of varices (%)	TP	FP	FN	TN
/	MSCT	50	/	/	GEVs	90%	43	0	2	5
16-slice	MSCT	50	Within 4 w	74% CT, 1% EGD, 24% no preference	EVs	82%	39	3	2	6
							40	5	1	4
16-slice	CT esophagograms	90	Within 4 h	66.67% CT, 14.44% EGD, 18.89% no preference	EVs	58.89%	50	15	3	22
							47	12	6	25
							46	13	7	24
							46	8	7	29
64-slice	MDCT	112	Within 2 w	83% CT, 7.1% EGD, 9.9% no preference	EVs	88.39%	97	0	2	13
							99	0	0	13
16-slice	MDCT	137	Within 24 h	98% CT, 2% EGD	EVs	65.69%	89	1	1	46
64-slice	MDCT	143	Within 1 w	/	GEVs	80.42%	112	3	1	27
/	MDCT	145	/	/	EVs	74.5%	102	4	6	33
128-slice	MDCT	62	Within 2 d	/	EVs	37.30%	45	1	7	9
							180	9	8	11
16 or 64-slice	MDCT	104	Within 4 w	/	EVs	90.38%	169	9	19	11
							172	15	16	5

*Data presented based on number of varices. R, retrospective; P, prospective; HBV, hepatitis B virus; HCV, hepatitis C virus; AIH, autoimmune hepatitis; PSC, primary sclerosing cholangitis; NASH, non-alcoholic steatohepatitis; MDCT, multi-detector computed tomography; MPR, multiplanar reconstruction; MSCT, multi-slice spiral computed tomography; EVs, esophageal varices; GV, gastric varices; GEVs, gastroesophageal varices; TP, true-positive; FP, false-positive; TN, true-negative; FN, false-negative.

Table 2. Overall diagnostic accuracy of studies researching gastroesophageal varices

Study characteristic	No. of article/set/patient	SEN (95% CI)	SPE (95% CI)	PLR (95% CI)	NLR (95% CI)	DOR (95% CI)	AUC (95% CI)
Patient-based							
Any sized GEVs	27/54/5217	0.91 (0.88–0.93)	0.81 (0.77–0.85)	4.82 (3.84–6.03)	0.11 (0.08–0.15)	42.47 (26.61–67.77)	0.93 (0.90–0.95)
High-risk GEVs	17/35/3526	0.90 (0.85–0.93)	0.90 (0.86–0.93)	8.85 (6.25–12.70)	0.12 (0.08–0.17)	75.10 (41.44–136.11)	0.96 (0.93–0.97)
P value	/	0.682	0.001	0.020	0.728	0.215	0.069
Any sized EVs	24/47/4596	0.91 (0.87–0.93)	0.81 (0.76–0.85)	4.75 (3.67–6.15)	0.12 (0.08–0.16)	41.00 (24.17–69.55)	0.93 (0.90–0.95)
High-risk EVs	15/32/3234	0.90 (0.85–0.93)	0.89 (0.85–0.93)	8.36 (5.82–12.01)	0.11 (0.08–0.17)	73.75 (39.62–137.30)	0.95 (0.93–0.97)
P value	/	0.682	0.010	0.034	0.739	0.233	0.224
Any sized GVs	3/7/570	0.85 (0.76–0.91)	0.83 (0.77–0.87)	4.88 (3.59–6.62)	0.19 (0.12–0.30)	26.03 (14.02–48.33)	0.89 (0.86–0.92)
High-risk GVs*	1/2/252	0.83 (0.69–0.93)	0.97 (0.93–0.99)	25.06 (11.95–52.54)	0.17 (0.09–0.34)	149.43 (48.87–456.86)	/
P value	/	0.789	<0.001	<0.001	0.787	0.007	/
Varix-based							
Any sized (EVs)*	1/3/104	0.92 (0.90–0.94)	0.45 (0.32–0.58)	1.67 (1.07–2.61)	0.17 (0.08–0.36)	10.26 (3.38–31.17)	0.9373 (0.1522)
High-risk (EVs)*	1/3/104	0.89 (0.85–0.92)	0.79 (0.74–0.84)	4.28 (3.31–5.53)	0.14 (0.09–0.22)	30.19 (17.42–52.33)	0.8483 (0.0532)
P value	/	0.145	<0.001	<0.001	0.664	0.088	0.581

*Data calculated using Meta-Disc 1.4. GEVs, gastroesophageal varices; EVs, esophageal varices; GVs, gastric varices; SEN, sensitivity; SPE, specificity; PPV, positive predictive value; NPV, negative predictive value; DOR, diagnostic odds ratio; AUC, area under the curve; 95% CIs, corresponding 95% confidence interval.

and the retrospective studies, statistically significant differences were found in the pooled SEN, NLR, and AUC (0.93 vs. 0.85; 0.08 vs. 0.18; and 0.95 vs. 0.90, respectively; $P = 0.007$, 0.015, and 0.002, respectively), but no statistically significant difference in SPE or PLR was found ($P = 0.883$ and 0.598, respectively).

Computed tomography scanner

<16-slice vs. 16-slice vs. 64-slice: There were 7, 17, and 12 sets of data from 3,^{21,30,32} 8,^{25,27,28,33,35,38,39,41} and 6^{19,26,34,36,40,42} studies that assessed for varices by using the <16-slice, 16-slice, and 64-slice CT scans, respectively (Table 3). Among the three subgroups, the 64-slice CT yielded the highest SEN, whereas the 16-slice CT and 64-slice CT yielded a sim-

ilarly high SPE and AUC, which were higher than those of the <16-slice CT (all $P < 0.05$).

Patient-based subgroup analysis of the high-risk esophageal varices

The results of the subgroup analyses for high-risk EVs are summarized in Table 4. A study that used a cut-off of 3.9 mm²⁴ was classified into the 4 mm subgroup. The SEN from a cut-off of 2 mm was close to that from a cut-off of 3 mm (0.92 vs. 0.97, $P = 0.107$) and higher than that from a cut-off of 4 or 5 mm ($P < 0.001$). Likewise, the SPE from a cut-off of 3 mm was close to that from a cut-off of 5 mm (0.91 vs. 0.93, $P = 0.491$) and higher than that from a cut-off of 2 mm ($P = 0.001$ and <0.001 , respectively). Cut-offs of 3 and 5 mm shared the approximate AUC (0.992 vs. 0.997, $P = 0.657$), which was higher than for cut-offs of 2 and 4 mm ($P = 0.004$ and 0.006, respectively).

Publication bias

Deek's funnel plot (Supplementary Figure 4) revealed no evidence of significant publication bias ($P = 0.410$).

Discussion

In this study, the authors confirmed the feasibility of CT in diagnosing GEVs, including high-risk varices, in patients with cirrhosis. The data were analyzed according to each patient and lesion, the relationship between the GEV size and RC sign was assessed, and the patient's acceptance of CT and EGD was

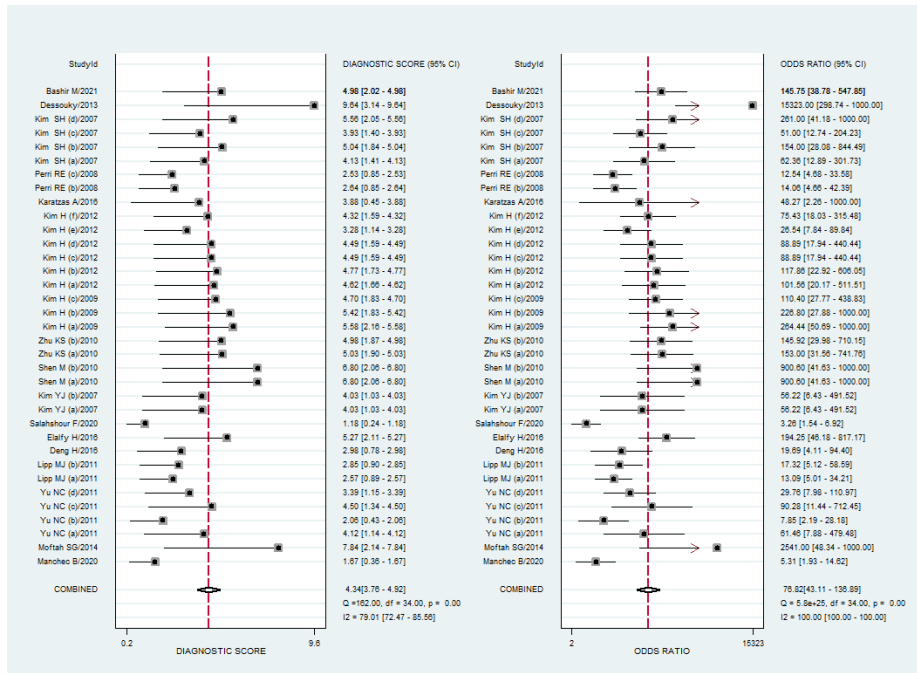


Figure 3. Coupled Forest plots of sensitivity and specificity for predicting high-risk varices with CT. CT, computed tomography.

Table 3. Subgroup results of meta-analyses regarding any sized gastroesophageal varices based on number of patients

Study subgroups	No. of article/ set/patient	SEN (95% CI)	SPE (95% CI)	PLR (95% CI)	NLR (95% CI)	DOR (95% CI)	AUC (95% CI)
Location of varices							
Any sized EVs	24/47/4596	0.91 (0.87–0.93)	0.81 (0.75–0.85)	4.75 (3.67–6.15)	0.12 (0.08–0.16)	41.00 (24.17–69.55)	0.93 (0.90–0.95)
Any sized GVVs	3/7/570	0.85 (0.76–0.91)	0.83 (0.77–0.87)	4.88 (3.59–6.62)	0.19 (0.12–0.30)	26.03 (14.02–48.33)	0.89 (0.86–0.92)
<i>P</i> value	/	0.164	0.585	0.896	0.117	0.302	0.046
Study design							
Retrospective	11/21/2300	0.85 (0.79–0.90)	0.80 (0.73–0.86)	4.32 (3.08–6.06)	0.18 (0.12–0.27)	23.56 (12.00–46.23)	0.90 (0.87–0.92)
Prospective	12/29/2519	0.93 (0.91–0.95)	0.81 (0.74–0.87)	4.93 (3.51–6.93)	0.08 (0.06–0.12)	60.52 (31.18–117.44)	0.95 (0.93–0.97)
<i>P</i> value	/	0.007	0.883	0.598	0.015	0.118	0.002
Computed tomography scanner							
<16 detector	3/7/696	0.82 (0.73–0.88)	0.76 (0.71–0.81)	3.39 (2.77–4.17)	0.24 (0.16–0.36)	14.10 (8.41–23.64)	0.81 (0.77–0.84)
16 detector	8/17/129	0.92 (0.88–0.94)	0.80 (0.70–0.88)	4.64 (2.97–7.25)	0.10 (0.07–0.16)	44.64 (20.44–97.50)	0.94 (0.92–0.96)
64 detector	6/12/1278	0.97 (0.93–0.98)	0.89 (0.85–0.93)	9.09 (6.45–12.82)	0.04 (0.02–0.08)	239.76 (99.27–579.06)	0.95 (0.93–0.97)
<i>P</i> _{<16 vs.16}	/	0.023	0.446	0.21	0.003	0.016	<0.001
<i>P</i> _{<16 vs.64}	/	0.001	<0.001	<0.001	<0.001	<0.001	<0.001
<i>P</i> _{16 vs.64}	/	0.014	0.089	0.019	0.026	0.005	0.488

GEVs, gastroesophageal varices; SEN, sensitivity; SPE, specificity; PPV, positive predictive value; NPV, negative predictive value; DOR, diagnostic odds ratio; AUC, area under the curve; 95% CIs, corresponding 95% confidence interval.

Table 4. Subgroup results of meta-analyses regarding high-risk esophageal varices based on number of patients

Study subgroups	No. of article/ set/patient	SEN (95% CI)	SPE (95% CI)	PLR (95% CI)	NLR (95% CI)	DOR (95% CI)	AUC (95% CI)
Study design							
Retrospective	9/17/1732	0.89 (0.81–0.93)	0.87 (0.78–0.92)	6.67 (3.96–4.76)	0.13 (0.08–0.22)	50.68 (22.08–116.31)	0.94 (0.92–0.96)
Prospective	4/13/1299	0.90 (0.82–0.95)	0.90 (0.87–0.93)	4.95 (3.48–7.05)	0.11 (0.06–0.20)	82.17 (35.20–191.81)	0.95 (0.93–0.97)
<i>P</i> value	/	0.828	0.455	0.109	0.677	0.425	0.488
Cut-off of high-risk in computed tomography							
≥2 mm	4/14/1420	0.92 (0.89–0.94)	0.83 (0.81–0.86)	6.63 (4.26–10.31)	0.11 (0.08–0.16)	70.24 (39.22–125.81)	0.9599 (0.0089)*
≥3 mm	2/3/271	0.97 (0.89–1.00)	0.91 (0.87–0.95)	11.11 (2.17–56.78)	0.07 (0.02–0.23)	227.33 (13.44–3846.11)	0.9919 (0.0066)*
≥4 mm	3/4/451	0.72 (0.64–0.78)	0.87 (0.82–0.91)	3.93 (1.57–9.82)	0.39 (0.22–0.68)	11.13 (6.21–19.96)	0.8270 (0.0301)*
≥5 mm	2/4/340	0.78 (0.71–0.84)	0.93 (0.88–0.96)	9.98 (3.23–30.83)	0.20 (0.08–0.48)	59.06 (9.67–360.73)	0.9974 (0.0105)*
<i>P</i> _{≥2 mm vs. ≥3 mm}	/	0.107	0.001	0.550	0.485	0.425	0.004
<i>P</i> _{≥2 mm vs. ≥4 mm}	/	<0.001	0.125	0.314	<0.001	<0.001	<0.001
<i>P</i> _{≥2 mm vs. ≥5 mm}	/	<0.001	<0.001	0.508	0.223	0.858	0.006
<i>P</i> _{≥3 mm vs. ≥4 mm}	/	<0.001	0.196	0.277	0.012	0.041	<0.001
<i>P</i> _{≥3 mm vs. ≥5 mm}	/	<0.001	0.491	0.916	0.174	0.431	0.657
<i>P</i> _{≥4 mm vs. ≥5 mm}	/	0.227	0.054	0.209	0.216	0.085	<0.001

*Data calculated using Meta-Disc 1.4. EVs, esophageal varices; SEN, sensitivity; SPE, specificity; PPV, positive predictive value; NPV, negative predictive value; DOR, diagnostic odds ratio; AUC, area under the curve; 95% CIs, corresponding 95% confidence interval.

evaluated. The diagnosis of high-risk GEVs showed higher specificity than that of any-sized GEVs, without compromising the sensitivity. The sensitivity of CT is currently not sufficient to replace EGD as the first screening approach for GEVs in these patients. Additionally, given the high accuracy and better patient acceptance, CT may be used in cases where patients refuse to or are unable to undergo EGD. Furthermore, several subgroup analyses of GEVs were also conducted according to the location of varices, study design, and CT scanner.

The authors observed a better diagnostic performance of CT in detecting GEVs than that observed by a previous meta-analysis.⁴⁶ Based on the location of varices, the AUC of CT for EVs was found to be significantly higher than that for GV, which was inconsistent with the previous study.⁴⁶ This discrepancy might be due to the different sample sizes or inclusion/exclusion criteria of the studies. Additionally, more recent studies, which used CT with >16 slices to detect varices and mostly evaluated EVs, were included. The present subgroup-analysis results also confirmed that the >16-slice CT showed a significantly better performance for diagnosing varices of any size than the <16-slice CT, and the 64-slice CT yielded the highest sensitivity. With recent advancements in multi-detector CT, CT with >16 detectors provide isotropic or near isotropic data sets that enable multi-planner details, and consequently, GEVs can be easily evaluated. In addition,

prospective studies demonstrated higher diagnostic accuracy compared with retrospective studies, which is likely attributable to their stringent inclusion criteria, standardized data collection protocols, fostering of homogeneity in study populations, and enhanced control over confounding variables.

In the subgroup analyses, CT yielded a higher specificity in identifying high-risk EVs than EVs of any size, which was similar to the previous report.⁴⁷ At present, there is no consensus regarding the diagnostic criteria for high-risk EVs on CT, and no systematic review or meta-analysis has used multiple thresholds to risk-stratify patients. Therefore, the authors of the present study attempted to perform subgroup analyses based on the cut-off values for high-risk EVs on CT. They identified an interesting result: a threshold of 3 mm provided the highest sensitivity and a high specificity, with a PLR of 11.11 and an NLR of 0.07 as substantial evidence to rule in or rule out a large varix, respectively. These results suggested that EGD is not necessary in individuals with small (<3 mm) or undetectable EVs via CT scan since they are unlikely to experience variceal bleeding, which is in line with a previous case-control study.⁴⁸ In contrast, a cut-off of 5 mm provided similar specificity and AUC, but lower sensitivity for large varices than that of a cut-off of 3 mm. Preventive medication with beta-blockers might be considered against possible bleeding in this setting. Only patients who have contraindications to beta-blockers and need

endoscopic variceal ligation would require EGD. Consequently, EGD may be efficiently allocated to those who need it the most. However, given the small number of included studies in the subgroup, it would be best evaluated using prospective cohort studies to demonstrate the diagnostic and prognostic value of these different variceal sizes.

Bleeding events caused by GVs tend to be more severe than EV bleeds.⁴⁹ It is clinically meaningful to accurately identify patients at a high risk of GV bleeding. The authors identified that CT has a relatively high sensitivity and specificity in detecting GVs of any size, and a relatively high sensitivity and extremely high specificity in detecting large GVs. The size of GVs has been reported to be the most important risk factor for GV bleeding.⁵⁰ However, only 1 included study³² was concerned with high-risk GVs with a diameter >5 mm. GVs are always located in deep submucosa or subserosa and the overlying mucosa is normal, meaning the endoscopic diagnosis of GVs is limited. Studies have found that CT is more sensitive than EGD in identifying GVs, detecting GVs missed by EGD.^{10,11,42,51} The clinical implications of these results need to be verified using additional prospective cohorts in the future.

Although variceal size is a valuable predictor of bleeding, other important risk factors, such as the RC sign, cannot be observed in CT images.⁵² Studies have revealed that the presence and severity of the RC sign are significantly correlated with CT variceal grade

or size.^{15,31,40,41,53} Such a significant correlation may serve as a basis for a CT-based screening method. A diameter of 4 mm^{15,41} or 5 mm³¹ was used as the cut-off value to predict the RC sign, with a sensitivity of 97%–100%.

Although the present findings are significant, several limitations should be acknowledged. First, there was a variable time interval (from 4 hours to 6 months) between the EGD and CT assessments. Therefore, the interval progression or regression of GEVs cannot be entirely ruled out. Second, the definitions or cut-off values of high-risk varices were different among the analyzed studies. Thus, we could not determine a standard diagnostic cut-off size for CT assessment of GEVs. Third, contrast-enhanced CT has a risk of radiation and allergy. Nevertheless, CT is routinely used to evaluate the complications of cirrhosis and hepatocellular carcinoma, as well as concurrently assess for GEVs without adding extra cost and radiation exposure. Such a dual-screening strategy would further improve the cost-effectiveness of CT.

In conclusion, contrast-enhanced CT, especially with >16 slices, has a high diagnostic accuracy for GEVs and high-risk varices in patients with cirrhosis. Although EGD remains the gold standard for the diagnosis and risk stratification of GEVs, CT is a relatively more tolerable modality and may be an effective alternative in patients unwilling or contraindicated to undergo EGD.

Conflict of interest disclosure

The authors declared no conflicts of interest.

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Supplementary Table 1. Characteristics of CT to predict high-risk varices

Study/journal/year	Study design	CT canner	Patients underwent EGD	Varices location	Prevalence of high-risk varices (%)	Cut-off of high-risk varices on EGD	Cut-off of high-risk varices on CT	TP	FP	FN	TN
Manchec et al. ²⁰ , AJR Am J Roentgenol, 2020	R	/	97	EVs	60.82%	Grade 3 or higher	≥4 mm	51	18	8	15
Moftah et al. ²¹ , Egypt J Radiol Nucl Med, 2014	/	4 or 8-slice	54	EVs	29.63%	Grade 3 or 4, mucosal red signs, recommendation of endoscopic or medical prophylactic therapy	≥2 mm	16	0	0	38
Yu et al. ²² , AJR Am J Roentgenol, 2011	R	16 or 64-slice	109	EVs	23.85%	Grade 3 or 4, variceal mucosal red signs or platelet plug	≥2 mm	25	24	1	59
Lipp et al. ²³ , Dig Dis Sci, 2011	R	4 or 16 or 64-slice	137	EVs	15.38%	≥5 mm, or ≥3/4 of the normal esophageal lumen being obstructed	≥4 mm	18	11	12	96
Deng et al. ²⁴ , J Evid Based Med, 2016	R	/	52	EVs	75%	Slight tortuous varices with RC signs; or snake-like varices with or without RC signs; or beady, nodular, or tumor-shaped varices with or without RC signs	≥3.9 mm	35	4	4	9
Elalfy et al. ²⁷ , World J Hepatol, 2016	R	16-slice	124	EVs	37.10%	medium/large varices	/	42	4	4	74
Salahshour et al. ²⁹ , Abdom Radiol (NY), 2020	R	16 or 64-slice	124	EVs	40.32%	grade 2, 3, or grade 1 with red signs or Child-Pugh class C	/	29	22	21	52
Kim et al. ³⁰ , AJR Am J Roentgenol, 2007	R	single or 4 slice	67	EVs	17.91%	Protrude into the esophageal lumen and touch each other	≥3 mm	11	9	1	46
Shen et al. ³¹ , Zhonghua Yi Xue Za Zhi, 2010	P	320 slice	69	EVs	59.42%	Grade 2 and 3	≥5 mm	39	0	2	28
Zhu et al. ³² , J Clin Gastroenterol, 2010	R	4 slice	127	GVs	16.54%	≥5mm	≥5 mm	39	0	2	28
								18	4	3	102
								17	3	4	103

Supplementary Table 1. Continued

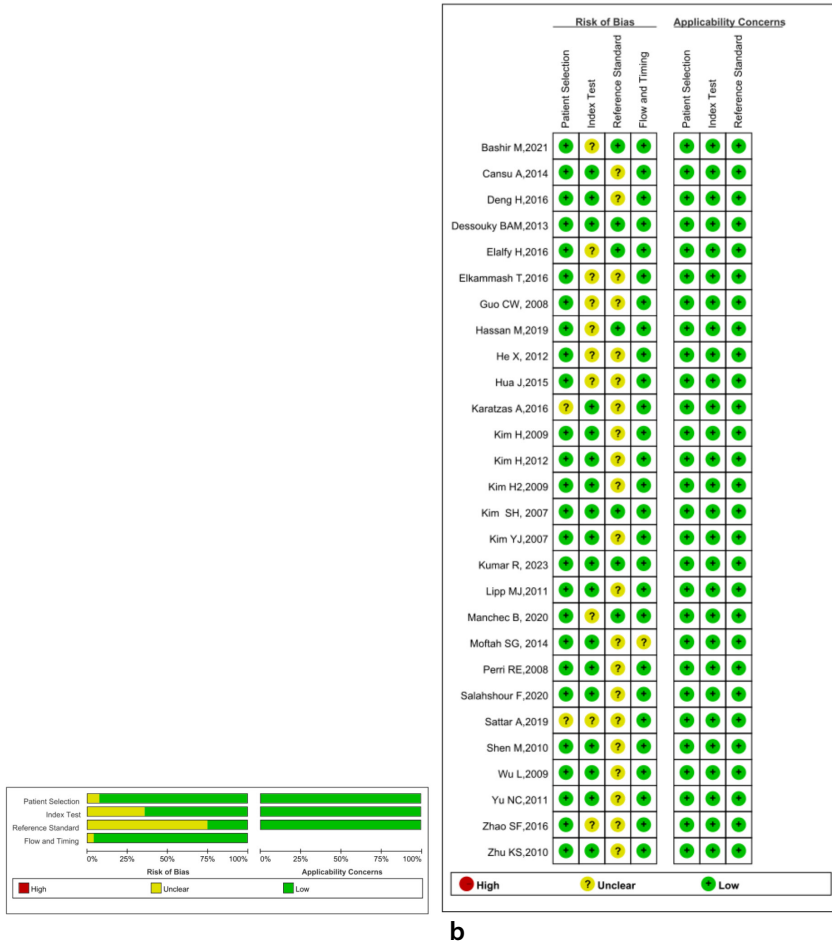
Study/journal/year	Study design	CT scanner	Patients underwent EGD	Varices location	Prevalence of high-risk varices (%)	Cut-off of high-risk varices on EGD	Cut-off of high-risk varices on CT	TP	FP	FN	TN
Kim et al. ³³ , Dig Dis Sci, 2009	R	16-slice	110	EVs	33.63%	Grade 2 and 3	≥2 mm	34	3	3	70
Kim et al. ³⁴ , World J Gastroenterol, 2012	P	64-slice	100	EVs	27.00%	Grade 2 and 3	≥2 mm	36	10	1	63
								32	4	5	69
								25	8	2	65
								25	7	2	66
								25	9	2	64
								25	9	2	64
								23	13	4	60
								24	7	3	66
Karatzas et al. ³⁵ , Ann Gastroenterol, 2016	P	16-slice	38	EVs + GVs	10.52%	≥5 mm	≥5 mm	4	5	0	29
Perri et al. ¹⁰ , Hepatology, 2008	P	4 slice or higher	101	EVs	40.59%	≥5 mm	≥5 mm	23	5	18	55
								27	8	14	52
Kim et al. ³⁹ , Radiology, 2007	P	16-slice	90	EVs	33.33%	Grade 2 and 3	/	28	11	2	49
								28	5	2	55
								27	9	3	51
								27	2	3	58
Dessouky and Abdel Aal ⁴¹ , Arab J Gastroenterol, 2013	P	16-slice	137	EVs	27.74%	≥ Grade 2	≥3 mm	38	0	0	99
Bashir et al. ⁴³ , P J M H S, 2021	/	/	145	EVs	74.5%	/	/	102	4	6	33
Kim et al. ⁴⁵ , J Gastroenterol Hepatol, 2009 *	R	16 or 64-slice	104	EVs	64.42%	Grade 2 and 3	≥2 mm	123	15	9	61
								113	17	19	59
								115	15	17	61

*Data presented base on number of varices. R, retrospective; P, prospective; EGD, Esophagogastroduodenoscopy; EVs, esophageal varices; GVs, gastric varices; TP, true positive; FP, false-positive; FN, true-negative; TN, false-negative; Grade 2: Varices show beaded appearance; Grade 3: Varices run in oblique course and are tortuous with tumorlike appearance.

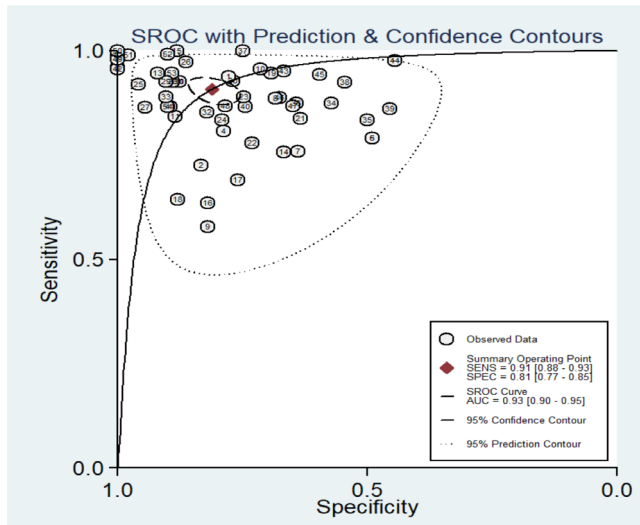
Supplementary Table 2. Subgroup results of meta-analyses regarding any sized EVs based on number of patients

Study subgroups	No.of article/set/patient	SEN (95% CI)	SPE (95% CI)	PLR (95% CI)	NLR (95% CI)	DOR (95% CI)	AUC (95% CI)
Study design							
Retrospective	9/17/1853	0.82 (0.75–0.87)	0.79 (0.71–0.87)	3.95 (2.72–5.73)	0.23 (0.16–0.33)	17.29 (8.96–33.33)	0.88 (0.84–0.90)
Prospective	11/26/2225	0.94 (0.91–0.96)	0.81 (0.73–0.87)	4.91 (3.34–7.23)	0.08 (0.05–0.12)	61.81 (29.22–130.76)	0.95 (0.93–0.97)
P value	/	<0.001	0.715	0.444	<0.001	0.095	<0.001
CT scanner							
<16 detector	3/7/696	0.82 (0.73–0.88)	0.76 (0.71–0.81)	3.39 (2.77–4.17)	0.24 (0.16–0.36)	14.10 (8.41–23.64)	0.81 (0.77–0.84)
16 detector	8/17/1429	0.92 (0.88–0.94)	0.80 (0.70–0.88)	4.64 (3.00–7.25)	0.10 (0.07–0.16)	44.64 (20.44–97.50)	0.94 (0.92–0.96)
64 detector	3/9/1020	0.96 (0.91–0.98)	0.91 (0.85–0.94)	10.19 (6.31–16.44)	0.05 (0.02–0.10)	228.85 (75.50–693.65)	0.96 (0.94–0.98)
P < _{16 vs. 16}	/	0.023	0.446	0.206	0.003	0.016	<0.001
P < _{16 vs. 64}	/	0.002	<0.001	<0.001	<0.001	<0.001	<0.001
P _{16 vs. 64}	/	0.093	0.043	0.018	0.133	0.018	0.166

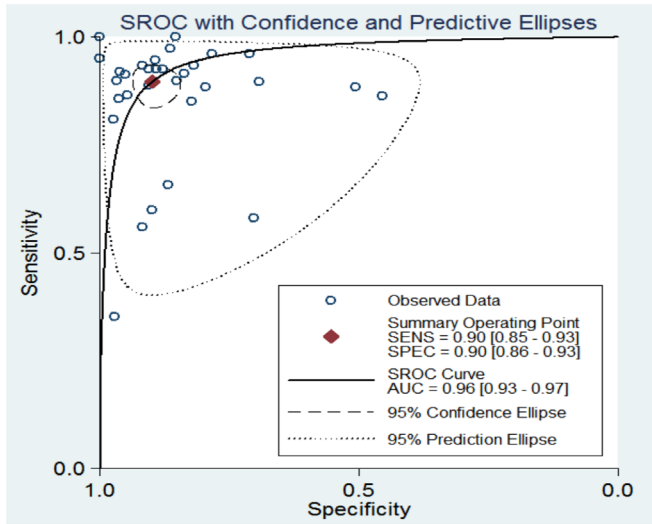
EVs, esophageal varices; SEN, sensitivity; SPE, specificity; PPV, positive predictive value; NPV, negative predictive value; DOR, diagnosis odds ratio; AUC, area under the curve; 95% CIs, corresponding 95% confidence interval.



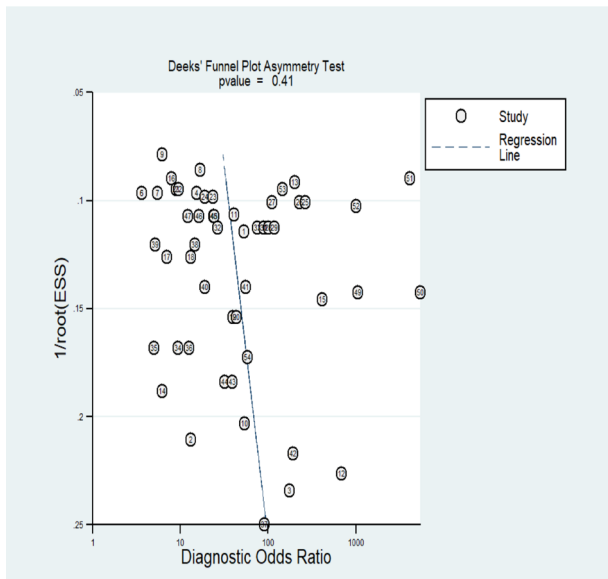
Supplementary Figure 1. Risk bias and applicability concerns of QUDADS 2 assessment in summary (a) and graph (b).



Supplementary Figure 2. Summary receiver operating characteristics (SROC) curves of computed tomography (CT) for diagnosing gastroesophageal varices with CT.



Supplementary Figure 3. Summary receiver operating characteristics (SROC) curves of computed tomography (CT) for predicting high-risk varices with CT.



Supplementary Figure 4. Deeks' funnel plot for evaluation of publication bias of studies.