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Acoustic Radiation Force Impulse (ARFI) Elastography for non-invasive evaluation of hepatic fibrosis in chronic hepatitis B and C patients: a systematic review and meta-analysis

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Abstract

Aim: The purpose of the study was to assess the effect of Acoustic Radiation Force Impulse (ARFI) elastography in the diagnosis of liver fibrosis in chronic hepatitis B and C patients through Meta-analysis. **Material and methods:** Four databases (PubMed, the Cochrane Library, WanFang data, and CNKI) were searched. The key words were: ("ARFI" or "acoustic radiation force impulse") combined with "liver fibrosis" and ("chronic hepatitis" or "HBV HCV"). Heterogeneity (I^2) was assessed, and its source was analyzed through meta-regression. **Results:** 21 articles with 2,691 patients were included. The composite Se=0.79 (95% CI: 0.76-0.83) and Sp=0.86 (95% CI: 0.85-0.88). ARFI elastography showed a better ability to evaluate higher-stage liver fibrosis and liver cirrhosis (F=3 and F=4, respectively). For F≥3, Se=0.84 (95% CI: 0.80-0.88, I^2=61.37), Sp=0.90 (95% CI: 0.86-0.92, I^2=65.10), and AUROC=0.94 (95% CI: 0.91-0.95). Se and Sp and AUROC of F=4 were 0.86 (95% CI: 0.80-0.91, I^2=70.67), 0.84 (95% CI: 0.80–0.88, I^2=78.94) and 0.91 (95% CI: 0.89-0.94), respectively. Besides, the combined ARFI values indicate that CHC patients had higher ARFI values especially in the F3 stage (1.87 [95% CI: 1.67-2.06] and 2.31 [95% CI: 2.09-2.52] for CHB and CHC, respectively). **Conclusion:** ARFI elastography is accurate and reliable in the diagnosis of CHB- and CHC-induced liver fibrosis and is especially suitable for the evaluation of stages F≥3 and F=4. CHC patients manifest higher ARFI values than CHB patients especially in the F3 stage.

Keywords: Acoustic Radiation Force Impulse (ARFI); hepatic fibrosis; chronic hepatitis C; chronic hepatitis B; meta-analysis.

Introduction

Chronic hepatitis B (CHB), caused by the hepatitis B virus (HBV), is one of the most serious and prevalent liver conditions. Globally, more than 350 million chronic hepatitis patients are HBV carriers [1-3]. Similarly to CHB, chronic hepatitis C (CHC) results from an infection with the hepatitis C virus (HCV). Worldwide, approximately 150 million people are infected with HCV, and each year 3 to 4 million new cases of infection have been reported [4,5]. People with CHB or CHC have a risk to develop hepatic fibrosis, cirrhosis, and liver failure, or even hepatocellular carcinoma [6-8]. Patients with absent or mild liver fibrosis at diagnosis are considered to have a relatively lower risk (25%–30%) of progression to cirrhosis over the next 20 years [9]. Thus, the prognosis and treatment decisions often depend on the fibrosis severity, and therefore, the evaluation of liver fibrosis is crucial to the successful therapeutic outcomes [10]. Liver biopsy (LB) is considered the golden standard for liver fibrosis assessment. However, it has some limitations. The primary limitation is the invasiveness of the procedure. Although the damage is "minimal", LB procedure still causes pain and minor or major bleeding (0.3%) and can lead to complications even under ideal clinical conditions [11]. In the second place, the accuracy of liver biopsy is limited by intra- and inter-observer variability and sampling error [12].

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In the recent years, some alternative methods, including acoustic radiation force impulse (ARFI) elastography, have received widespread attention. ARFI is a new and promising ultrasound-based diagnostic technique. By short-duration acoustic radiation forces (less than 1 ms), the selected region of interest localizes the displacements without any external compression, and thus the operator dependency is reduced. The generated wave scan provides qualitative or quantitative responses (wave velocity and ARFI values) [13].

The effect of ARFI elastography on liver fibrosis has been extensively evaluated, and several meta-analyses have been published, but the debates over the effect of ARFI elastography on liver fibrosis have never stopped. However, some new studies published over the recent years have not been included in the previous meta-analyses. Thus, in this meta-analysis, we have exerted the maximal effort to find and combine every single analysis to evaluate the efficacy of ARFI elastography on liver fibrosis caused by CHB and CHC.

The purpose of the present review was to broaden the sample size and narrow the error through meta-analysis to assess the overall effect of ARFI in the diagnosis of liver fibrosis in CHB and CHC patients.

Material and methods

Article Search Strategy

To obtain the maximum possible number of publications, we searched not only PubMed and the Cochrane Library but also the Chinese databases WanFang data and China National Knowledge Infrastructure (CNKI). The key words were: ("ARFI" or "acoustic radiation force impulse") combined with "liver fibrosis" and ("chronic hepatitis" or "HBV HCV"). Only human studies were included, with no time lower limit (up to April 25, 2016).

Inclusion criteria

The following inclusion criteria were applied: 1) The studies were diagnostic tests and evaluated the effect of ARFI elastography in disease diagnosis in different stages of hepatic fibrosis; 2) The studies focused on CHB and CHC or on other diseases but contained solo data of CHB or CHC; 3) The patients were adults; 4) The studies provided data of comparisons between ARFI and LB (the golden standard).

Exclusion criteria

Articles were excluded if they had the following characteristics: 1) No solo data for CHB or CHC; 2) The studies focused on the probe type of ARFI or used spleen ARFI to examine hepatic fibrosis; 3) Animal research was conducted; 4) The publications were case reports, supplements, abstracts, reviews, systematic reviews, and meta-analyses; 5) Data deficiency existed; 6) HIV co-infection was present.

Quality assessment

The Quality Assessment of Studies of Diagnostic Accuracy (QUADAS-2 tool) was used to assess the Quality of each study [14].

Data extraction

We extracted the following data from original articles: the author's name , year of publication, patient's country of origin, age, gender ratio, ARFI values and standard error (SE), fibrosis stage (diagnosed by LB), patients' number in each of the different fibrosis stages, as well as the values of the true positive (tp), false positive (fp), false negative (fn), and true negative (tn) detection rates, sensitivity (Se), specificity (Sp), and area under ROC curve (AUROC), and 95% confidence interval (95% CI). The extraction of all data was performed by Microsoft Excel 2007.

Statistical analysis

The values of tp, fp, fn, and tn of different fibrosis stages had to be calculated if the original data did not provide them. Then, we used the Midas command in Stata 12.1 Meta-analysis model to combine tp, fp, fn, and tn to estimate the combined sensitivities, specificities, and AUROC of the different fibrosis stages. ROC curves were also obtained. Meanwhile, we combined the ARFI values that had been divided by CHC and CHB by different fibrosis stages.

I^2 was used to assess heterogeneity. If I^2 >50%, the presence of heterogeneity was indicated. When I^2 <50%, we combined the data by the fixed-effect model; otherwise, we used the random-effect model. If heterogeneity existed, we analyzed its source through meta-regression. Report bias was determined by funnel plot. All statistical analyses were performed by Stata 12.1.

Results

Article selection

We collected a total of 445 articles: 369 articles of them were obtained after searching PubMed and the Cochrane Library, and 76 Chinese articles were found through a search on Wanfang data and CNKI s. Articles that were repeated or met the exclusion criteria, were excluded. To combine sensitivity, specificity, and AUROC, 21 [15-35] articles with 22 studies and 2,691 patients were included in the diagnosis analysis. Of the 21 articles, 11 [15,18,20,22,26-30,33,35] articles provided ARFI values that were combined in the analysis. Details are present in figure 1.

Quality assessment

Articles which were intended to be combined into meta-analysis needed to receive quality assessment by

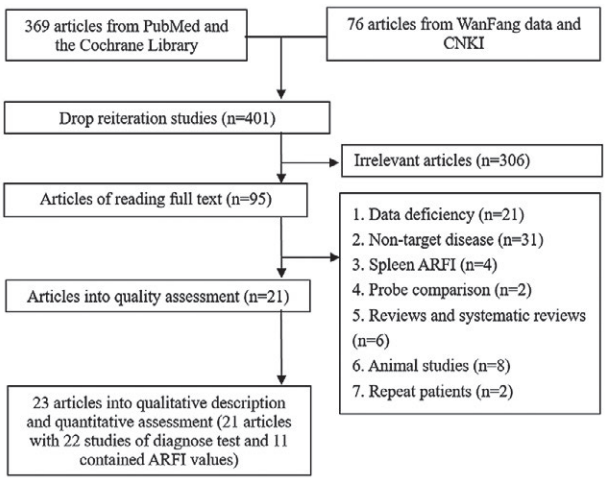

Fig 1. Details of article research.

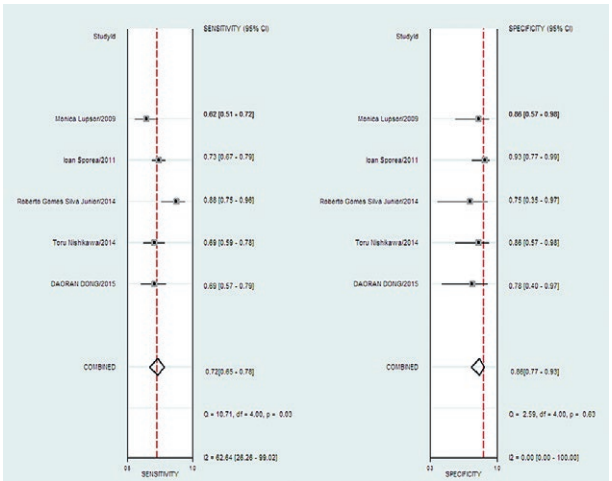

Fig 2. Pooled specificity and sensitivity of F ≥1.

Table I. Quality assessment details

Studies	Risk of bias				Applicability concerns		
	Patient selection	Index test	Reference standard	Flow and timing	Patient selection	Index test	Reference standard
Zhang 2015 [15]	Low	Low	Unclear	Unclear	Low	Unclear	Unclear
Dong 2015 [16]	Low	Low	Unclear	Unclear	Low	Unclear	Unclear
Friedrich-Rust 2013 [17]	Low	Low	Unclear	Low	Low	Low	Low
Zhang 2013 [18]	Low	Unclear	Unclear	Unclear	Low	Low	Unclear
Liu 2015 [19]	Low	Low	Unclear	Unclear	Low	Unclear	Low
Li 2014 [20]	Low	Low	Unclear	Low	Low	Low	Low
Nishikawa 2014 [21]	Low	Low	Low	Low	Low	Low	Low
Park 2016 [22]	Low	Unclear	Low	Low	Low	Low	Low
Silva Junior 2014 [23]	Low	Low	Low	Low	Low	Low	Low
Yamada2014 [24]	Low	Low	Low	Low	Low	Low	Low
Chen 2015 [25]	Low	Low	Unclear	Unclear	Unclear	Low	Low
Chen 2012 [26]	Low	Low	Unclear	Unclear	Unclear	Low	Low
Ye 2012[27]	Low	Unclear	Unclear	Unclear	Unclear	Low	Low
Takaki 2014 [28]	Low	Low	Low	Low	Low	Low	Low
Sporea 2011 [29]	Low	Low	Low	Low	Low	Low	Low
Lupsor 2009 [30]	Low	Low	Low	Low	Low	Low	Low
Cabassa 2015 [31]	Unclear	Low	Low	Low	Unclear	Low	Low
Tai 2015 [32]	Low	Low	Low	Low	Low	Low	Unclear
Sporea 2010 [33]	Low	Low	Low	Low	Low	Unclear	Unclear
Friedrich-Rust 2009 [34]	Low	Low	Low	Low	Low	Low	Unclear
Goertz 2010 [35]	Low	Low	Low	Low	Low	Low	Low

the QUADAS-2 tool (Table I). Articles' characteristics are presented in Table II, and the results of the diagnostic tests and ARFI values are listed in Table III.

Analysis of the Results

We combined the Se and Sp of different fibrosis stages as can be seen in Table IV. The summary sensitivity was 0.79 (95% CI: 0.76–0.83) and the summary specificity was 0.86 (95% CI: 0.85–0.88). The higher the Se, the better the positive predictive efficacy, and similarly, the higher the Sp, the better the negative predictive efficacy. Thus the results indicated that ARFI elastography has a moderate efficacy in the detection of liver fibrosis and non-liver fibrosis patients in CHB and CHC patients. The pooled Se and Sp of F≥1 were 0.72 (95% CI: 0.65–0.78, I^2=62.64) and 0.86 (95% CI: 0.77–0.93, I^2=0.00), respectively (fig 2). In addition, we found that the combined Se and Sp of F=2 were 0.75 (95% CI: 0.69–0.80, I^2=79.62) and 0.85 (95% CI: 0.81–0.89, I^2=48.53) (fig 3). Se and Sp of F≥3 were 0.84 (95% CI: 0.80–0.88, I^2=61.37) and 0.90 (95% CI: 0.86–0.92, I^2=65.1) (fig 4). On the oth-

Table II. Details of article characteristics concerning the diagnosis test

Author, year, country	Histological score	Disease	N, Age [year (SE)]	Gender (M/F)	R	Stage	Cut off (m/s)	tp + fn	fp + tn	Se	Sp	AUROC
Zhang 2015 China [15]	Scheuer	CHB	180 36.4 (10.96)	139/41	0.599	F≥2	1.46	129	51	0.59	0.88	0.764
						F≥3	1.59	69	111	0.71	0.86	0.852
						F=4	1.75	33	147	0.73	0.84	0.825
Dong 2015 China [16]	CPC*	CHB	83 41 (11.4)	71/10	0.577	F≥1	1.295	74	9	0.683	0.8	0.72
						F≥2	1.295	49	34	0.829	0.65	0.762
						F≥3	1.54	24	59	0.762	0.9	0.884
						F=4	1.835	8	75	0.667	0.855	0.723
Friedrich-Rust 2013 Germany, Holland [17]	Metavir	CHB	114 39 (12)	77/37	0.415	F≥1	-	81	33	-	-	0.66
						F≥2	-	36	83	-	-	0.73
						F≥3	-	13	101	-	-	0.94
						F=4	-	5	109			0.97
Zhang 2013 China [18]	CPC*	CHC	108 44.2 (13.3)	54/54	0.61	F≥2	1.529	72	36	0.569	0.889	0.779
						F≥3	1.78	41	67	0.732	0.925	0.863
						F=4	1.797	14	94	0.786	0.745	0.79
Liu 2015 [19 China]	Metavir	CHB	108 39.8 (9.7)	81/27	0.63	F≥2	1.27	66	42	0.84	0.831	-
						F=4	1.65	29	79	0.931	0.768	-
Li 2014 China [20]	Metavir	CHC	128 69.1 (4.7)	86/42	0.649	F≥2	1.53	87	41	0.576	0.895	0.775
						F≥3	1.79	47	81	0.764	0.965	0.901
						F=4	1.789	17	111	0.789	0.765	0.792
Nishikawa 2014 Japan [21]	Metavir	CHC	108 59.5 (12.6)	56/52	0.872	F≥1	1.28	94	14	0.691	0.857	0.81
						F≥2	1.28	77	31	0.818	0.871	0.909
						F≥3	1.44	45	63	0.889	0.825	0.869
						F=4	1.73	14	94	0.857	0.862	0.885
Park 2016 Korea [22]	Ludwig	CHB	105 47	73/32	-	F≥ 2	-	78	27	-	-	0.814
						F≥3	-	51	54	-	-	0.848
						F=4	-	30	75	-	-	0.752
Silva Junior 2014 Brazil [23]	Metavir	CHC	51 53.8 (1.53)	18/33	0.833	F≥1	1.19	43	8	0.884	0.75	0.88
						F≥2	1.31	28	23	0.893	0.87	0.9
						F≥3	1.68	18	33	0.944	0.909	0.97
						F=4	1.95	9	42	1	0.952	0.98
Yamada 2014 Japan [24]	Metavir	CHC	124 57.0 (12.1)	56/68	0.764	F≥2	1.26	40	84	0.925	0.762	0.89
						F≥3	1.46	26	98	0.846	0.878	0.943
Chen 2015 Taiwan [25]	Metavir	CHC	137 54	63/74	0.593	F≥2	1.59	103	34	0.728	0.794	0.9349
						F≥3	1.73	58	79	0.914	0.772	0.8997
						F=4	1.96	24	113	1	0.681	0.8647
Chen 2012 Taiwan [26]	Metavir	CHC	127	59/68	0.696	F≥2	1.55	81	46	0.741	0.87	0.847
						F≥3	1.18	41	86	0.902	0.895	0.902
						F=4	1.98	18	109	0.889	0.798	0.831
Ye 2011 China [27]	Metavir	CHB	264 39.3 (13.7)	158/106	0.87	F≥3	1.69	164	100	0.939	0.95	0.99
						F=4	1.88	141	123	0.957	0.918	0.97
Takaki 2014 Japan [28]	Metavir	CHC	176 61.2 (11.94)	84/92	0.725	F≥2	1.25	128	37	0.75	0.781	0.773
						F≥3	1.595	37	128	0.849	0.815	0.863
						F=4	1.775	12	153	0.856	0.889	0.915
Sporea 2011 Romania [29]	Metavir	CHC	274 50.1 (11.8)	113/161	0.727	F≥1	1.19	233	29	0.73	0.93	0.88
						F≥2	1.21	190	72	0.84	0.91	0.893
						F≥3	1.58	116	146	0.84	0.94	0.908
						F=4	1.82	65	197	0.91	0.9	0.937
Lupsor 2009 Romania [30]	Metavir	CHC	112 48.9 (12.28)	45/67	0.717	F≥1	1.19	92	14	0.621	0.857	0.725
						F≥2	1.34	63	43	0.678	0.929	0.869
						F≥3	1.61	45	61	0.791	0.948	0.9
						F=4	2	38	68	0.8	0.955	0.936
Cabassa 2015 Italy [31]	Knodell	B&C	84	40/44	-	F≥ 3	2.11	26	58	0.73	0.92	0.879
Tai 2015 Taiwan [32]	Metavir	CHB	121, 48 (11)	98/23	-	F=4	1.35	43	74	0.628	0.705	0.681
		CHC	83, 53 (11)	48/35	-	F=4	1.41	17	66	0.706	0.803	0.802
Sporea 2010 Romania [33]	Metavir	B&C	71 50.7 (12.9)	41/30	-	F≥2	1.33	65	6	0.71	0.66	0.649
						F=4	1.8	16	55	1	0.77	0.868
Friedrich-Rust 2009 Germany [34]	Metavir	B&C	81 48 (14)	46/35	0.71	F≥2	1.37	54	27	68.5	92.6	-
						F≥3	1.45	31	50	83.9	86	-
						F=4	1.75	22	59	81.8	91.5	
Goertz 2012 Germany [35]	Ludwig	B&C	57 45 (11)	30/27	0.64	F≥2	-	30	27	-	-	0.85
						F≥3	-	16	41	-	-	0.92
						F=4	-	12	45			0.87

*Chinese Program of Prevention and Cure for Viral Hepatitis, N: number of patients, SE: standard error, M/F: Male/Female, B&C: CHB and CHC. F: acronym of the fibrosis stages.

Table III. Details of article characteristics for ARFI values

Author	Disease	Stage	n	ARFI
Zhang [15]	CHB	F0-1	51	1.24
		F2	60	1.4
		F3	36	1.93
		F4	33	2.19
Zhang [18]	CHC	F0-1	36	1.26
		F2	31	1.45
		F3	27	2.01
		F4	14	2.28
Li [20]	CHC	F0-1	41	1.23
		F2	40	1.48
		F3	30	2.06
		F4	17	2.3
Park [22]	CHB	F0-1	27	1.38
		F2	27	1.61
		F3	21	2.17
		F4	30	2.4
Chen [26]	CHC	F0-1	46	1.283
		F2	40	1.63
		F3	23	2.433
		F4	18	2.619
Ye [27]	CHB	F0-1	60	1.13
		F0-1	17	1.27
		F2	23	1.5
		F3	23	1.85
		F4	141	2.5
Takaki [28]	CHC	F1	37	1.165
		F2	91	1.315
		F3	25	1.75
		F4	12	2.55
Sporea [29]	CHC	F0-1	29	0.97
		F0-1	43	1.07
		F2	74	1.33
		F3	51	1.71
		F4	65	2.6
Lupsor [30]	CHC	F0-1	14	1.103
		F0-1	29	1.067
		F2	18	1.504
		F3	7	1.52
		F4	38	2.552
Sporea [33]	CHB	F0-1	8	1.24
		F2	25	1.39
		F3	12	1.6
		F4	5	2.39
	CHC	F0-1	6	1.14
		F0-1	9	1.16
		F2	37	1.33
		F3	31	1.55
		F4	13	2.46
Goertz [35]	CHB	F0-1	14	1.24
		F2	2	1.42
		F3	2	1.87
		F4	3	2.67
	CHC	F0-1	13	1.53
		F2	12	1.5
		F3	2	3.79
		F4	9	2.38

N: number of patients, . F: acronym of the fibrosis stages.

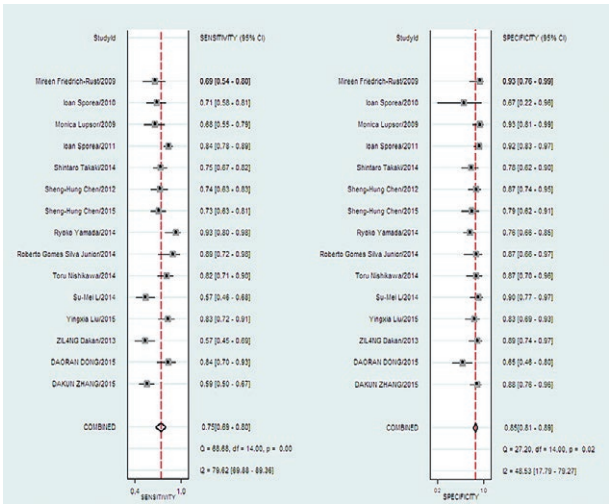

Fig 3. Pooled specificity and sensitivity of F ≥2.

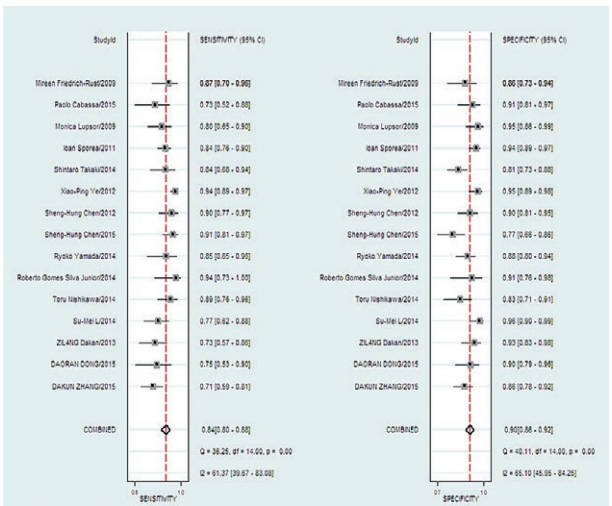

Fig 4. Pooled specificity and sensitivity of F ≥3.

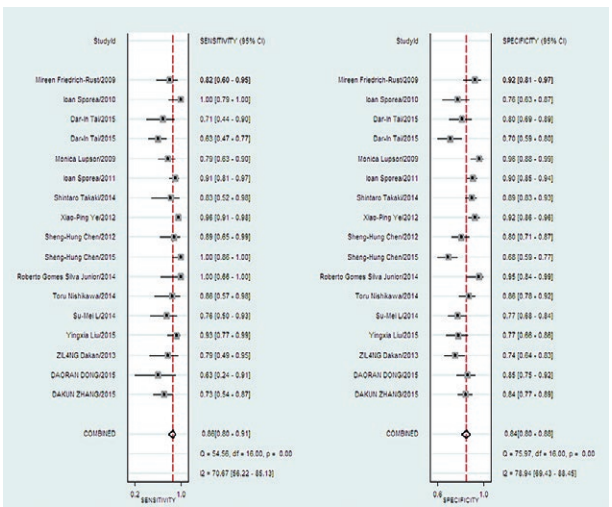

Fig 5. Pooled specificity and sensitivity of F = 4.

er hand, the pooled Se and Sp of F=4 were 0.86 (95% CI: 0.80–0.91, I^2 =70.67) and 0.84 (95% CI: 0.80–0.88, $I^{2=}$78.94), respectively (fig 5). The separate analysis results of different liver fibrosis stages also showed a good predictive value of ARFI elastography in liver fibrosis examinations especially in stage F≥3 and F=4 since the Se and Sp were relatively higher than other stages. To determine the source of heterogeneity, we used meta-regression and included in the model different parameters, including country of origin, age group, histological evaluation approach, patients' number, disease type, and the respective cut-off values. However, no statistical significance was established except for the cut-off value of F≥2 in sensitivity (coef=0.6, p=0.004) (fig 6).

We also obtained the ROC curves of the different fibrosis stages as the comprehensive indicator to reflect diagnosis efficacy of ARFI elastography. The larger the area under the ROC curves, the greater the diagnosis accuracy. As is shown in figure 7, the following values were obtained: for F≥1, AUROC=0.88, 95% CI: 0.85–0.91; for F≥2, AUROC=0.88, 95% CI: 0.85–0.91 r for F≥3, AUROC=0.94, 95% CI: 0.91–0.95; and for F=4, AUROC=0.91, 95% CI: 0.89–0.94. The results indicated that the area under ROC curves were high especially in stages F≥3 and F=4, which indicate that ARFI elastography has a good diagnosis accuracy in liver fibrosis examinations especially in stage F≥3 and F=4.

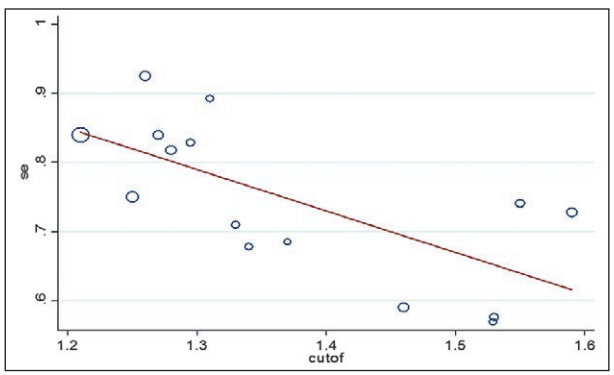

Fig 6. Meta-regression of F ≥2 for sensitivity.

Table IV. Pooled diagnostic test characteristics

Effect	Stage	Estimate result (%)	95% CI	I2
Sensitivity (0.79; 95% CI: 0.76–0.83)	F≥1	0.72	0.65–0.78	62.64
	F≥2	0.75	0.69–0.80	79.62
	F≥3	0.84	0.80–0.88	61.37
	F=4	0.86	0.80–0.91	70.67
Specificity (0.86; 95% CI: 0.85–0.88)	F≥1	0.86	0.77–0.93	0.0
	F≥2	0.85	0.81–0.89	48.53
	F≥3	0.90	0.86–0.92	65.10
	F=4	0.84	0.80–0.88	78.94

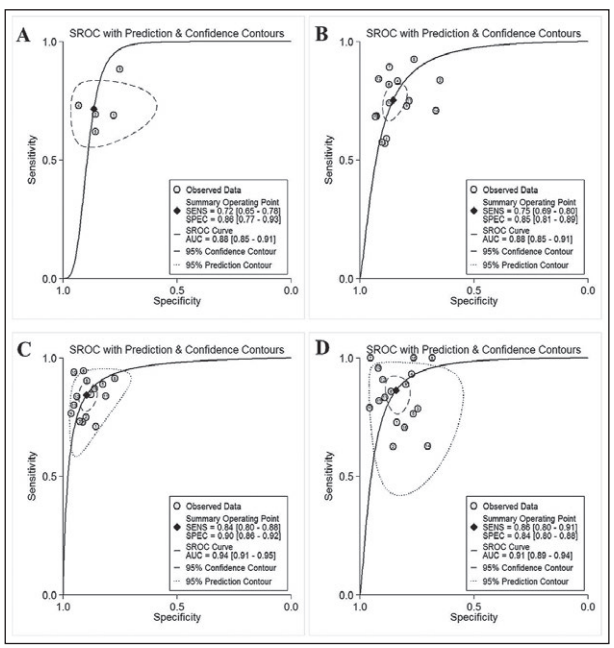

Fig 7. ROC curves of different fibrosis stage. A: ROC curve of F≥1; B: ROC curve of F ≥2: C: ROC curve of F ≥3; D: ROC curve of F=4.

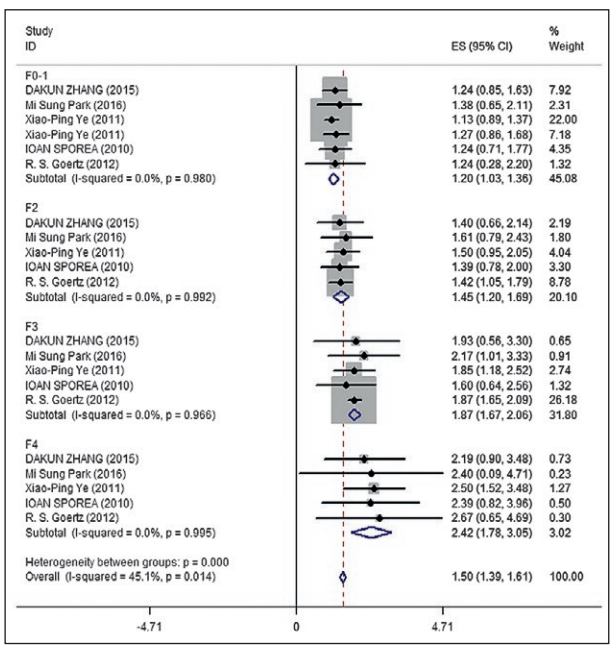

Fig 8. Forest plot for ARFI values of CHB in different stages.

We combined the ARFI values of CHB and CHC patients in different stages and found that CHC patients had higher ARFI values, especially in the F3 stage, 1.87 (95% CI: 1.67, 2.06, fig 8) for CHB and 2.31 (95% CI: 2.09, 2.52, fig 9) for CHC. There was no report bias as indicated by the funnel plot results which are illustrated in figure 10.

Discussions

LB is the "golden" standard to evaluate the stages of liver fibrosis, but its application poses a risk of complications and bias. Thus, ARFI elastography has been researched and used widely, as a promising alternative non-invasive method [36]. In the current systematic review and meta-analysis, we evaluated the accuracy of ARFI elastography in patients with CHB and CHC. The composite sensitivity=0.79 (95% CI: 0.76–0.83) and specificity=0.86 (95% CI: 0.85–0.88) were presented which indicates that ARFI elastography has a moderately good efficacy in positive and negative predictive values. The separated analysis results of stages indicate that ARFI elastography has a moderately good efficacy in positive and negative predictive values in different stages (reflected from Se and Sp) and has a moderate accuracy in diagnosis of stage F≥1 and F≥2 (F≥1: Se=0.72, 95% CI: 0.65–0.78; Sp=0.86, 95% CI: 0.77–0.93; AUROC=0.88, 95% CI: 0.85–0.91; and F≥2: Se=0.75. 95% CI: 0.69–0.80; Sp=0.85, 95% CI: 0.81–0.89; AUROC=0.88, 95% CI: 0.85–0.91) and good diagnosis accuracy for stage F≥3 and F=4 reflected through AUROC values (AUROC=0.94, 95% CI: 0.91-0.95 and AUROC=0.91, 95% CI: 0.89–0.94 of F≥3 and F=4, respectively).

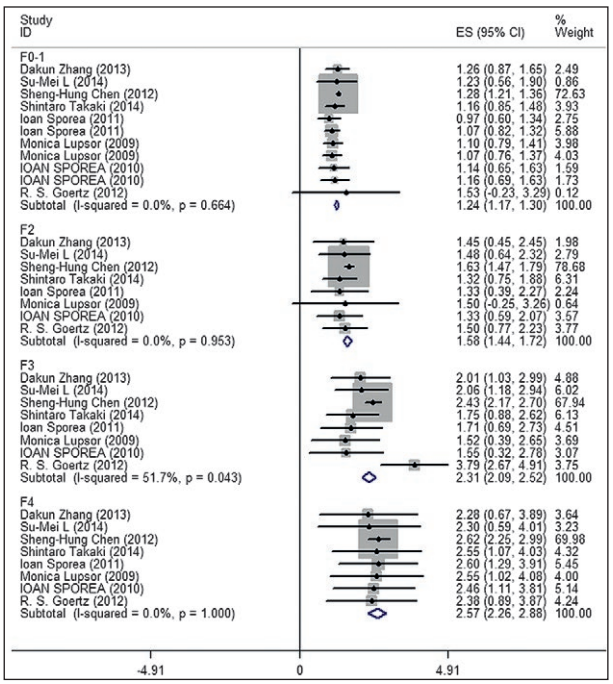

Fig 9. Forest plot for ARFI values of CHB in different stages.

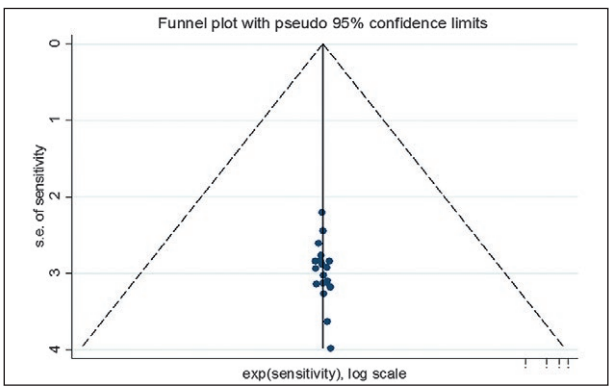

Fig 10. Funnel plot of the diagnosis test.

Our study results demonstrate that ARFI elastography is moderately accurate which is consistent with the findings of Bota et al [37] indicating that ARFI is a suitable method for assessing liver fibrosis. Moreover, our results also showed that ARFI elastography has a better ability to evaluate higher-stage liver fibrosis and liver cirrhosis (F=3 and F=4, respectively). When diagnosing a higher stage of these diseases, especially for liver fibrosis over stage 3 (F≥3), ARFI elastography has a higher sensitivity, specificity, and AUROC values than F≥2 and F≥1 liver fibrosis stage. In addition, ARFI elastography also shows a better efficacy in the diagnosis of liver cirrhosis (F=4), than in that of stages F≥2 and F≥1 of liver fibrosis, which is not consistent with the conclusions of Nierhoff et al [12]. Their meta-analysis revealed that ARFI had an excellent diagnostic accuracy for F=4 [12], whereas we found that ARFI showed excellent diagnostic accuracy for F≥3 but not for F=4. This discrepancy may have derived from our selection of the population of patients with liver fibrosis that were induced by CHC and CHB, but the population studied by Nierhoff et al included patients with all types of liver fibrosis.

Intriguingly, the combined ARFI values indicated that CHC patients had higher ARFI values in all stages, especially in the F3 stage (ARFI value=1.87, 95% CI: 1.67-2.06 and ARFI value=2.31, 95% CI: 2.09-2.52 for CHB and CHC, respectively). Perhaps future studies will elucidate the cause of such a difference.

In recent years, many studies have focused on scan probes to evaluate the accuracy of ARFI elastography in liver fibrosis. Cassinotto et al [38] conducted a study aimed at comparing the efficacy of FibroScan M, XL-Probes, and ARFI elastography in patients with chronic

liver disease. He found that ARFI elastography had a lower failure rate and was exceedingly reliable. Potthoff et al [39] discovered that ARFI elastography linear and curve probes exhibited a similar accuracy in the diagnosis of liver fibrosis, but the linear probe had higher ARFI values. It is worth mentioning that to investigate the influence factors, such as interquartile range, success rate, and ARFI performed location, on ARFI elastography efficacy, Bota et al [40] performed an analysis and found that the best correlation between ARFI and fibrosis was obtained at an interquartile range of <30% with a success rate of ≥60%.

ARFI elastography in the diagnosis of liver fibrosis in HIV-HCV co-infection patients is also an important issue. In an earlier investigation, Frulio et al [41] evaluated the application of ARFI elastography in HIV-HCV co-infection patients and established that ARFI showed promising results in the assessment of morphology and fibrosis during the same session. Natsuda et al [42] also verified that ARFI elastography was useful in staging liver fibrosis in patients with HIV-HCV co-infection.

Our meta-analysis has three strengths. Firstly, to the best of our knowledge, our work is the first meta-analysis to evaluate the accuracy of ARFI elastography in patients with CHB and CHC; there was no published meta-analysis on this subject until the time of manuscript preparation. Secondly, we found that ARFI elastography is better in the assessment of higher liver fibrosis stages and liver cirrhosis than in the lower liver fibrosis stages. Thirdly, in our analysis, we pooled the latest published studies including a total of 2,691 patients.

Nevertheless, our work has also some limitations. We were not able to completely solve the problem with heterogeneity. In addition, although we exerted maximum efforts to obtain all articles available, we still could not obtain grey articles or articles which were not in English or Chinese.

Conclusion

ARFI elastography is an accurate and reliable method for examination in patients with liver fibrosis induced by CHB and CHC. Importantly, this approach is especially valuable in the evaluation of higher-stage liver fibrosis and liver cirrhosis. CHC patients have higher ARFI values than CHB patients, especially in the F3 stage.

Conflict of interest: none

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