Echocardiography in Chronic Liver Disease: Systematic Review

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Abstract

Background: Doppler echocardiography (Echo) is a non-invasive method of excellent accuracy to screen portopulmonary hypertension (PPH) and to assess intrapulmonary shunts (IPS) in chronic liver disease (CLD). In the past decade, Echo proved to play a fundamental role in the diagnosis of cirrhotic cardiomyopathy (CCM).

Objective: To perform a systematic review of relevant articles on the subject 'Echo in CLD'.

Methods: In November 2011, a systematic review was performed in the PubMed, LILACS and SciELO databases, and the characteristics of the studies selected were reported.

Results: The search based on descriptors and free terms obtained 204 articles (179 in Pubmed, 21 in LILACS, and 1 in SciELO). Of those 204 articles, 22 were selected for systematic review. A meta-analysis could not be performed because of the heterogeneity of the articles.

Conclusion: Echo should be part of CLD stratification for screening PPH, IPS and CCM, because, most of the time, such complications are diagnosed only when patients are already waiting for a liver transplant. (Arq Bras Cardiol. 2013;100(4):376-385)

Keywords: Echocardiography, Doppler; Liver Diseases; Hepatopulmonary Syndrome; Schistosomiasis.

Introduction

Chronic liver disease (CLD) has high incidence and prevalence worldwide[1]. Among its major causes, chronic and excessive alcohol consumption and viral hepatites stand out[1]. Since 1977, echocardiographic findings in patients with CLD have been studied[2]. However, the association between liver disease and the cardiovascular system has been described for more than 50 years[3]. The relationship between CLD and the cardiovascular system has been defined as cirrhotic cardiomyopathy (CCM)[3,4]. The impairment of the respiratory system by CLD has been called hepatopulmonary syndrome[5].

Liver function deterioration is marked by the increase in nitric oxide and other inflammatory mediators, which have been implicated in splanchnic vasodilation and reduced arterial compliance, acting in the physiopathogeny of CCM and hepatopulmonary syndrome[3-5]. Zardi et al[3] and Moller et al[4] have defined CCM as a chronic cardiac dysfunction in patients with liver cirrhosis and/or portal hypertension, characterized by a sudden decrease in the cardiac contractile response to physical, pathological or pharmacological stress, but with normal cardiac output at rest. The hepatopulmonary syndrome, however, is characterized as a triad consisting of CLD, alveolar-arterial oxygen gradient (A-aO2 gradient) ≥ 15 mm Hg or arterial oxygen partial pressure (PaO2) ≤ 80 mm Hg, and presence of intrapulmonary shunt (IPS)[5-13].

Updating that subject might help health professionals with the early diagnosis and treatment of cardiopulmonary complications in patients with CLD. This systematic review was aimed at assessing articles on the echocardiographic changes in patients with CLD.

Methods

Research strategy

This systematic review of the literature was elaborated in November 2011 from the following databases: Medical Literature Analysis and Retrieval System Online (MedLine); *Literatura Latino-Americana e do Caribe em Ciências da Saúde* (LILACS); and Scientific Electronic Library Online (SciELO). The research strategy consisted in crossing descriptors (DeCS), which are keywords for retrieving a subject in the scientific literature, and free terms (FT), which are found among neither the DeCS nor the MeSH headings, but are important to search data on the subject.

In Pubmed, the syntax used in the search was as follows: "echocardiography" (*MeSH*) AND "cirrhotic cadiomyopathy"

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(free term); "echocardiography" (*MeSH*) AND "schistosomiasis" (*MeSH*); "echocardiography" (*MeSH*) AND "hepatopulmonary syndrome" (*MeSH*); "echocardiography" (*MeSH*) AND "portal hypertension" (*MeSH*). In LILACS and SciELO, the following keywords were used: *"ecocardiografia"*; *"cardiomiopatia cirrótica"*; *"esquistossomose"*; *"síndrome hepatopulmonar"*; and *"hipertensão portal"*.

Selecting criteria

The inclusion criteria for the studies obtained from the search in the databases were as follows: to be original articles (editorials and case study were excluded); the study subjects had to have CLD; the study should approach the cardiac function changes in that population by using Doppler echocardiography; the study should be published in Portuguese, English and Spanish. Studies not referring to the echocardiographic changes of CLD in their titles were excluded.

Data analysis

The articles obtained from the search in the different databases were selected in three steps. In the first step, the titles of the studies found were read. Those that did not meet the inclusion criteria of this study were excluded. In the second step, the abstracts of the articles selected in the first step were read. Again, those not meeting the inclusion criteria were excluded. In the third step, the full text of all studies selected in the two previous steps were read to be included in this systematic review.

In the MedLine database, via PubMed, the keywords and free terms were crossed, and 204 articles were obtained, 120 of which were excluded based on their titles, 84 abstracts were read, and 32 articles were selected to be fully read. Of those 32 articles, 22 were chosen for this systematic review (Figure 1).

In the SciELO and LILACS databases, 22 articles were found, and all of them were excluded from this review based on their titles.

One single article was excluded because it was written in German, and seven articles were repeated (Figure 1).

Results

General characteristics of the studies included (Table 1).

It became evident that the 'echocardiography in CLD' research line was divided into the three following study areas: portopulmonary hypertension; hepatopulmonary syndrome; and CCM (in which, diastolic dysfunction assessment stands out). It was also evidenced that the production of manuscripts was intensified in the 1990s and first decade of the 21st century.

The geographic distribution of the publications was predominantly European (40%), mainly Italian and Spanish studies. The American Continent appears as second (22%), with Brazil standing out as the number one producer of articles on the topic (18%). There was only one multicenter study[14].

Twenty-one articles were observational studies. There was only one cohort study[14]. The mean sample size was 50 patients. The article[15] with the smallest sample had 15 participants and that with the largest sample had 130 participants[16]. In all studies but one[7], the male sex predominated. The mean age of the individuals in the studies included was approximately 50 years. Only two studies[13,17] had children in their samples. Only one study[15] had no control group, and only two studies[13,18] had patients with schistosomiasis and no other CLD associated. The samples of the remaining studies comprised cirrhotic patients.

The prevalence of IPS ranged from 15% to 82%[16,19]. Contrast-enhanced transthoracic echocardiography (CE-TTE) showed sensitivity of 75% and specificity of 100% for detecting IPS as compared with contrast-enhanced transesophageal echocardiography (CE-TEE)[6].

It is worth noting that, in all studies[17,18,20-23] assessing concomitantly portopulmonary hypertension and right ventricular (RV) echocardiographic parameters, the catheterization of right cardiac chambers proved to have higher diagnostic accuracy than transthoracic echocardiography. In addition, there was enlargement of the right cardiac chambers and/or RV dysfunction as compared to the control group. The prevalence of portopulmonary hypertension ranged from 4% to 15%[21,23]. The transthoracic echocardiography showed sensitivity of 100% and specificity of 80% to detect portopulmonary hypertension as compared with the catheterization of right cardiac chambers[23].

Chronology of the studies

Studies from the 1980s

The first studies on the echocardiographic assessment of CLD were published in the 1980s, although one study of 1977[2], which did not share the strategy of this review, used echocardiography to assess cardiovascular abnormalities in cirrhotic patients. The first article meeting our research criteria was published in 1984[15], being followed by two other articles in the same decade. A ten-year period followed with no article on that topic being published.

The publications in the 1980s[15,19] focused on the occurrence of IPS in patients with CLD. Sanno et al[15], in 1984, assessed the presence of IPS by use of CE-TTE. In 1988, Mimidis et al[19], comparing the diagnostic accuracy of CE-TTE with that of lung perfusion scan with technetium^{99m} macro aggregated albumin (Tc^{99m}MAA), showed the diagnostic superiority of CE-TTE. At the end of that decade, Keller et al[24] collected left ventricular (LV) parameters, and findings suggestive of CCM began to be elucidated: the increase in the LV end-diastolic and end-systolic volumes after intrahepatic portosystemic shunt[24].

Studies from the 1990s

The studies from the 1990s[9,10] focused on comparing CE-TTE and CE-TEE in the diagnosis of IPS. In 1997, Vedrinne et al[9] had no significant sample to compare those methods. In 1999, Aller et al[10] showed the better diagnostic accuracy of CE-TEE, and also correlated lower degrees of IPS with lower hypercapnia and diffusion capacity of carbon monoxide.

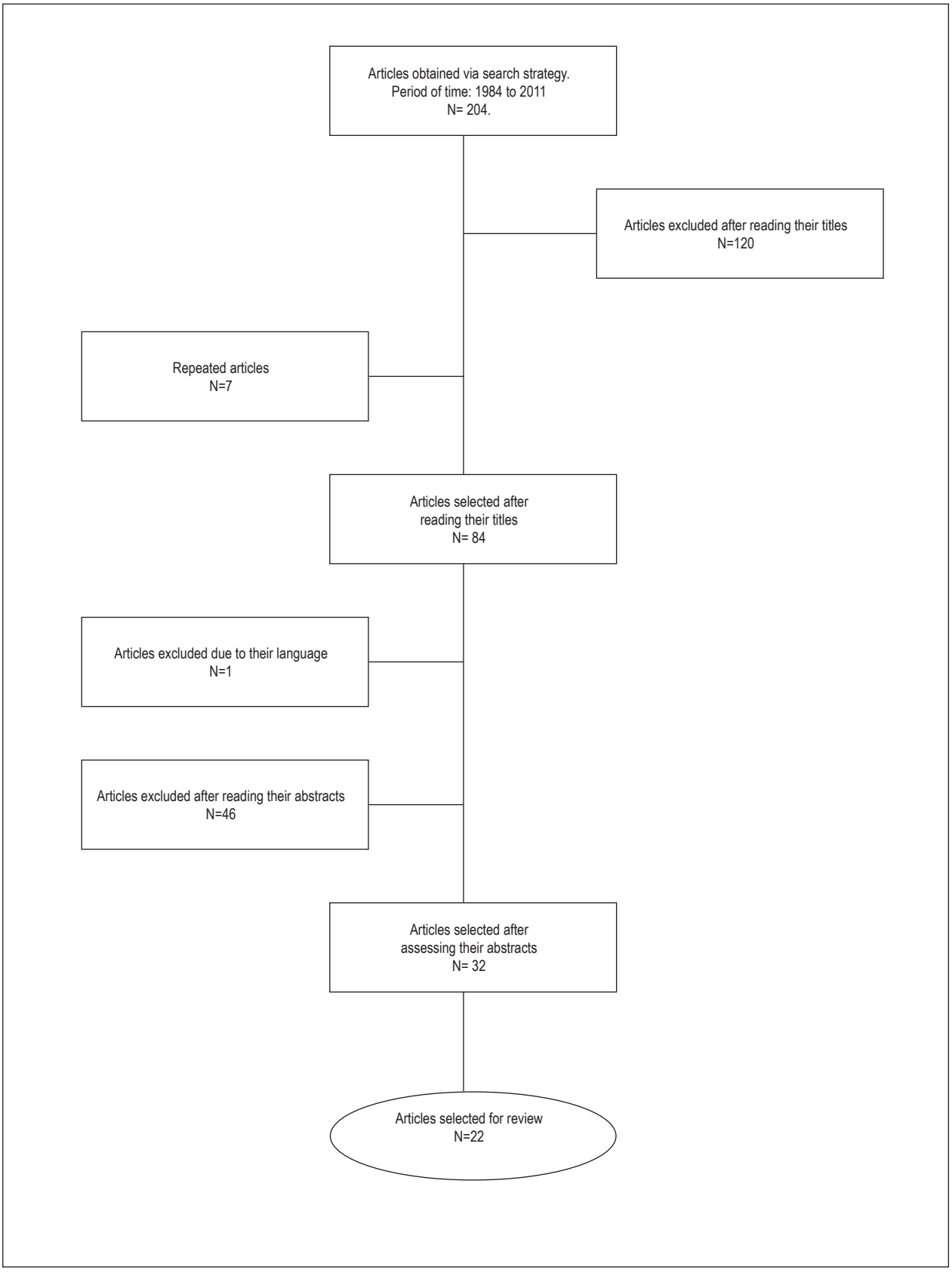

Figure 1 - *Flowchart of the number of articles found and selected after applying the inclusion and exclusion criteria according to descriptors and databases.*

Studies from the 21st century

In the beginning of the 21st century, the trend toward studying portopulmonary hypertension and RV parameters appears[22]. In 2000, Auletta et al[22], assessing 83 patients, showed the high prevalence of portopulmonary hypertension (20%) and LV diastolic dysfunction, in addition to larger diameters of the right atrium and right ventricle in patients with advanced CLD as compared with a group without portopulmonary hypertension and a control group. As a limitation, that was the only study investigating portopulmonary hypertension that has not compared transthoracic echocardiography with right cardiac chamber catheterization, considered the gold-standard test for diagnosing portopulmonary hypertension. From that study onward, the aim of the articles alternated as follows: assessment of portopulmonary hypertension[17,20,21,23,25] and the diagnostic comparison of transthoracic echocardiography with right cardiac chamber catheterization[20,21,23]; IPS screening[6,7,11-13,16,26]; comparison of the diagnostic accuracy of CE-TTE and CE-TEE for assessing IPS[6,12]; comparison of the diagnostic sensitivity between echocardiography and Tc^{99m}MAA for assessing IPS[13,19,26]; and diastolic function assessment of both the right and left ventricles[7,11,14,17,25,27,28]. Only one study[28] has reported the use of dobutamine stress echocardiography, while another[25] has assessed the mean variation of LV strain. It is worth noting that some studies[11,14,16,20,21,23,25-28] have assessed the correlation between diagnostic methods and the CLD severity criteria, specially the Child-Pugh-Turcotte score and the Model for End-Stage Liver Disease.

Studies assessing IPS were resumed in 2004, after five years with no article on the subject. Kim et al, in a cross-sectional study with 130 patients[16], have reported that 82% had IPS on CE-TTE. The severity of the IPS correlated with the Child-Pugh-Turcotte score. Similarly to the end of the 1990s, two other articles[6,12] published in Brazil confirmed the diagnostic superiority of CE-TEE over CE-TTE, although Pavarino et al, in 2004, reported similar efficacy of CE-TTE and CE-TEE.

In addition, in 2007, in a cross-sectional study with 41 patients with hepatopulmonary syndrome, Zamirian et al[7] described the increase in left atrial volume as a predictor of that syndrome[7]. In 2008, Lenci et al[11] also correlated the most severe shunts with hypoxemia, and associated IPS severity with a higher severity of liver decompensation by use of the Child-Pugh-Turcotte classification. Another important finding of that study was that the increase in IPS severity in the vertical position was not statistically greater than that in the supine position.

In 2010, El-Shabraw et al[13], investigating the IPS, compared CE-TTE and Tc^{99m}MAA[13]. Conducted in children and unlike the two previous studies[19,29], it showed a higher prevalence of IPS in patients undergoing Tc^{99m}MAA as compared with CE-TTE. In that same year, Fischer et al[12], using CE-TEE, reported a greater A-aO2 in patients with IPS.

In 2005, Pozzi et al[27] resumed the articles directed to CCM. Their study with 100 patients evidenced the presence of eccentric LV hypertrophy and of diastolic dysfunction more evident in patients with hepatitis C virus cirrhosis classified as Child-Pugh-Turcotte A than in patients with hepatitis B virus and those of the control group.

In 2010, Rabie et al[14], studying 101 patients, the only cohort of this review, reported that mild diastolic dysfunction predicted low ascites clearance and mortality after percutaneous intrahepatic portosystemic stent shunt insertion. In that same year, Kim et al[28] re-stated that cirrhotic patients abstaining from alcohol for six months, when undergoing stress echocardiography, showed more diastolic dysfunction, low prevalence of coronary artery disease, decrease in the ejection fraction, and increase in LV diastolic and systolic volumes than the control group. The last article on CCM, published in 2011 by Kazankov et al[25], innovated by assessing the reduction in mean strain rate of all cirrhotic patients.

Discussion

This is a systematic review about echocardiography in CLD. A meta-analysis could not be performed, because of the elevated heterogeneity and inconsistency of information of the studies here reviewed. There was neither analysis of the selection of the research subjects, nor report on the calculation of the sample size, nor whether it involved convenience sampling.

Other data not found in most studies reviewed were as follows: CLD severity; patients' clinical, social, and demographic characteristics; and time elapsed between the CLD diagnosis and the time the study was performed. Only age group and sex seemed to be homogeneous properties. The greater prevalence of CLD in the age group of 40 to 70 years might result from the long course of that disease.

Most articles reported liver cirrhosis as the etiology of CLD. In such patients, there was a greater trend towards assessing diastolic function and comparing the diagnostic methods for IPS screening. It is worth noting that the studies with patients with CLD whose etiology was hepatosplenic schistosomiasis (HSS) tended to assess portopulmonary hypertension and the right ventricle. Only Brazil and Egypt have published studies with patients with HSS, probably because that disease is endemic in some regions of those countries[13,18]. Some articles reviewed have reported that their patients had concomitant mixed liver disease[20-22,28] (Table 1).

It is worth noting that currently the diagnosis of CCM requires eliminating other causes of underlying heart disease (coronary artery disease, arterial hypertension, and heart valve disease) and of liver cirrhosis (some etiologies, such as iron overload and alcohol consumption), which have an impact on myocardial structure and function[3,4]. It was only in 2010 that Kim et al[28] clearly considered that in a study. Most articles assessing CCM in this review have not excluded alcoholic patients.

Through our research and also out of our search strategy, we observed that echocardiography is the gold-standard test to diagnose IPS[30] and CCM[3,4], and to screen portopulmonary hypertension[31]. Although it is a systematized, standardized, reliable, reproducible method of easy use to research those pathologies, there is still certain heterogeneity in the gradation and investigation methodology of IPS[6,7,9-13,15,16,19,29]. However, from the practical viewpoint, those discrepancies do not change the presence of IPS. Nevertheless, the universal standardization of the IPS screening technique

Table 1 - Studies assessing the echocardiographic findings in patients with chronic liver disease (CLD)

Author/ year	Country	Type of study	Sample	Mean age (years)	Control group	Etiology of CLD	CLD severity score	Type of echocardiography
Carvalho et al[18], 2011	Brazil	Cross-sectional	83 patients (sex not reported)	42.9 ± 13.7 years	Yes (39 patients)	Schistosomiasis	Not applicable	TTE
Kazankov et al[25], 2011	Denmark	Cross-sectional	44 patients (27 men and 17 women)	53 ± 9 years	Yes (23 patients)	73% alcohol, 27% non-alcoholic origin (HBV, autoimmune, HCV, primary and cryptogenic biliary cirrhosis)	CPT MELD	TTE
El-Shabrawi et al[13], 2010	Egypt	Cross-sectional	40 patients (22 men and 18 women)	5-12 years (mean, 9.5 years)	Yes (20)	HBV and HCV (50%); inborn errors of liver metabolism (35%) and HSS (15%)	Not classified	CE-TTE
Kim et al[28], 2010	Korea	Cross-sectional	71 patients (60 men and 11 women)	52 ± 8.1 years	Yes (8)	Cirrhotic patients: alcohol (45), HBV (12), HCV (1), HBV and alcohol (8), autoimmune (4) and cryptogenic (1)	CPT MELD	TTE
Fischer et al[12], 2010	Brazil	Cross-sectional	63 patients (51 men and 12 women)	50 ± 11 years	Yes (20)	Cirrhotic	Not classified	CE-TTE and CE-TEE
Rabie et al[14]., 2010	Canada and Italy	Cohort	101 patients (73 men and 28 women)	57.5 ± 0.9 years	Yes*	Cirrhotic *alcohol	CPT MELD	TTE
Ferreira et al[26], 2009	Brazil	Cross-sectional	28 patients (19 men and 9 women)	47.5 years	Yes*	Cirrhotic candidates to Tx	CPT	CE-TTE
Hua et al[23], 2009	China	Cross-sectional	105 patients (66 men and 39 women)	49.5 ± 11.8 years	Yes*	Cirrhotic candidates to Tx	CPT	CE-TTE
Lenci et al[11], 2008	United Kingdom	Cross-sectional	50 patients (30 men and 20 women)	53 years	Yes*	Cirrhotic candidates to Tx with IPS	CPT MELD	CE-TTE
Zamirian et al[7], 2007	Iran	Cross-sectional	41 patients diagnosed with HPS (46% men and 54% women)	47 ± 10.6 years	Yes (108)	Cirrhotic candidates to Tx	Not classified	CE-TTE
Polat et al[17], 2006	Turkey	Cross-sectional	63 patients (37 men and 26 women)	9.6 ± 3.4 years	Yes (35)	Chronic infection by HBV	Not classified	TTE
Pozzi et al[27], 2005	Italy	Cross-sectional	109 patients	Group 1: (49±11/ 53±7.4 years) Group 2: (56.3±6.1 years). Group 3: (59.4±6.6 years)	Yes (17)	Chronic infection by HCV (52); cirrhotic patients: HCV Child A (31) and Child C (26)	Not classified	TTE

Second harmonic	Doppler echocardiographic variables assessed	Contrast medium used	Grade of the shunt	Storage media	Statistically significant results
Not disclosed	RVEDA, S', RVMPI, RAA, TG	Not performed	Not performed	Digital media	Patients with HSS had greater RAA and RVEDA as compared with patients with HIS. Patients with HSS, showed a positive correlation between TG and RAA and between TRV and RVMPI
Not disclosed	E'/A', E, E', LVDD, IPS, PW, EF, EWDT, LV mass, S', SR	Not performed	Not performed	Digital media	The EF, S' and mean SR variation were reduced in all cirrhotic patients. They had a mild increase in VS, PW, LVSV and LVDV greater than that in the control group
Not disclosed	Not disclosed	Saline solution	+ or -	Not disclosed	17.5% of the patients had IPS on lung perfusion scan and 15% on CE-TTE. Hypoxemia greater in cirrhotic patients than in non-cirrhotic ones
Not disclosed	E, A, EF, E/A, LVDV, LVSV, VS, PW,	Not performed	Not performed	Not disclosed	Cirrhotic patients had more markers of diastolic dysfunction than controls. Although the result was within the normal range of DSE, 25.4% of cirrhotic patients had a drop in EF and increase in LVDV and LVSV
Not disclosed	Not disclosed	Saline solution	CE-TTE: + or - CE-TEE: trivial, mild, moderate, important (≥ moderate consideredas +)	Not disclosed	75% of the patients had IPS on CE-TEE, and 36% had IPS on CE-TTE. Patients with IPS had significantly higher A-aO2 gradient
Not disclosed	LVDD, LVSD, EF, LVSV, EF, E, A, E/A, EWDT, IVRT, LV mass	Not performed	Not performed	Optical disc and videotape	E/A ≤ 1 predicted low ascites clearance and mortality after TIPS insertion
Not disclosed	Not disclosed	Saline solution	1 to 4	Videotape	55% of the patients had IPS. The echocardiographic classification of IPS severity correlated with the values assessed on scintigraphy and the shunt value obtained on blood gas analysis. The DLCO and PO2 values were significantly higher in IPS grades 1 and 2 than in grades 3 and 4
Not disclosed	PASP, PFAT, TRV	Not performed	Not performed	Not disclosed	3.8% of the patients had PPH. PASP and PAMP correlated positively. Sensitivity and specificity of TTE for detecting PPH were 100% and 82%, respectively
Yes	S', E/A, E', E', LVDD, RVDD, IPS, EF, CFPV, LAV, RV and LV Tei index, TAPSE, TRV	Saline solution and patient's blood	Mild (< 5 bubbles); moderate (5-20 bubbles); important (> 20 bubbles)	Optical disc	26% of the patients had IPS. Patients with HPS had lower PaO2 and higher CPT score than those with no IPS. Echocardiographic parameters did not distinguish between patients with and without HPS. The increase in the number and degree of IPS in the vertical position was not statistically higher than that in the supine position
Not disclosed	LAV, E/A and pulmonary venous flow	Saline solution	+ or -	Not disclosed	LAV ≥ 50 mL is a possible predictor of HPS. LAV was higher in patients with HPS than in the control group
Not disclosed	S', E'/A', IVRT, E', A', RVSP, LADD, LVDD, LVSD, IPS, EF, EWDT	Not performed.	Not performed	Not disclosed	Correlation of the inflammation grade and fibrosis of CLD with RV diastolic dysfunction
Not disclosed	E/A, IPS, PW, EF, EWDT, LV mass, IVRT	Not performed	Not performed	Videotape	Increased LV thickness and presence of diastolic dysfunction more prevalent in patients with CLD due to HCV Child A than in those with Child C and control group

Continuation - Table 1 - Studies assessing the echocardiographic findings in patients with chronic liver disease (CLD)

Author/ year	Country	Type of study	Sample	Mean age (years)	Control group	Etiology of CLD	CLD severity score	Type of echocardiography
Pavarino et al[6], 2004	Brazil	Cross-sectional	76 patients (59 men and 18 women)	44 ± 14.6 years	Yes*	72 cirrhotic patients and 4 with liver fibrosis candidate to Tx	Not classified	CE-TTE and CE-TEE
Kim et al[16], 2004	South Korea	Cross-sectional	130 patients (89 men and 41 women)	47 ± 10 years	Yes*	All cirrhotic candidates to Tx	CPT	CE-TTE
Cotton et al[20], 2002	United States of America	Cross-sectional	78 patients (48 men and 30 women)	51 ± 9.6 years	Yes*	Cirrhotic patients due to HBV, HCV, cryptogenic, MLD and alcohol. Candidates to Tx	CPT	TTE
Torregrosa et al[21], 2001	Spain	Cross-sectional	107 patients (61% men and 39% women)	57 ± 8 years	Yes	Cirrhotic candidates to Tx: 40% viral hepatitis, 21% alcohol, 13% alcohol + hepatitis, and the others due to other etiologies	CPT	TTE
Auletta et al[22], 2000	Italy	Cross-sectional	83 patients (51 men and 32 women)	41-70 years	Yes (60), 39 men 21 women	Cirrhotic patients: 10 due to alcohol, 21 HBV, 38 HCV, 5 HCV + alcohol, 9 cryptogenic	Not classified	TTE
Aller et al[10], 1999	Spain	Cross-sectional	88 patients (58 men and 30 women)	56 ± 10.9 years	Yes	All cirrhotic patients	CPT	CE-TTE and CE-TEE
Vedrinne et al[9], 1997	France	Cross-sectional	37 patients (26 men and 11 women)	49 ± 8 years	Yes	All cirrhotic candidates to Tx	CPT	CE-TTE and CE-TEE
Keller et al[24], 1988	Germany	Cross-sectional	30 cirrhotic patients (20 men and 10 women)	50 ± 8 years/ 48 ± 11 in control	Yes 20 patients with IPS (13 men and 7 women)	Group: 24 alcohol and 6 with post-hepatic cirrhosis. Control: 14 post-hepatic cirrhosis and 6 due to alcohol	Not classified	TTE
Mimidis et al[19], 1988	Greece	Cross-sectional	56 patients (37 men and 19 women)	57.5 ± 10.9 years	Yes (50)	Normoxemic cirrhotic patients, CPT A and B secondary to alcohol, HBV and HCV	Not classified	TTE
Sanno et al[15], 1984	Japan	Case series	15 patients	27-59 years	No	8 cirrhotic patients, 2 with chronic hepatitis, 5 with PH	Not classified	CE-TTE

A': early diastolic velocity; RAA: right atrial area; A-aO2 gradient: alveolar-arterial oxygen gradient; RAD: right atrial diameter; RVEDA: RV end-diastolic area; RVDD: right ventricular diastolic diameter; LVDD: left ventricular diastolic diameter; MLD: mixed liver disease; LVSD: left ventricular systolic diameter; E': early diastolic velocity; CE-TTE: contrast-enhanced transthoracic echocardiography; CE-TEE: contrast-enhanced transesophageal echocardiography; EF: left ventricular ejection fraction; TG: tricuspid gradient; RVMPI: right ventricular myocardial performance index; MELD: Model for End-Stage Liver Disease; PaCO2: parcial pressure of carbon dioxide; PAMP: pulmonary artery mean pressure; HPS: hepatopulmonary syndrome; SR: strain rate; PFAT: pulmonary flow acceleration time; TAPSE: tricuspid annular plane systolic excursion; EWDT: E wave deceleration time; LV: left ventricle; CFPV: color flow propagation velocity; NPV: negative predictive value; PPV: positive predictive value; LVSV: left ventricular systolic volume; TRV: tricuspid regurgitation velocity;

Second harmonic	Doppler echocardiographic variables assessed	Contrast medium used	Grade of the shunt	Storage media	Statistically significant results
Yes	RVSP, LADD, LVDD, LVSD, IPS, EF (cube method)	Saline solution	CE-TTE: +or- CE-TEE: 1 to 6. Grades 1 and 2 considered physiological	Videotape	54% of the patients had IPS on CE-TEE and 49%, on CE-TTE. Similar efficacy of CE-TTE and CE-TEE
Yes	Not disclosed	Saline solution	1 to 4	Not disclosed	82% of the patients had IPS. Correlation of IPS grade and CPT classification
Not disclosed	PASP	Not performed	Not performed	Not disclosed	12% of the patients had PAH. The PPV and NPV of Echo to identify clinically significant pulmonary hypertension (PASP > 50 mm Hg) were 37.5% and 91.9%, respectively. Mean PASP on Echo was significantly higher than PASP assessed on RCCC. There was a weak correlation between PASP assessed on Echo and on RCCC.
Not disclosed	PASP, PFAT	Not performed	Not performed	Not disclosed	15% of the patients had PPH. TTE had sensitivity of 100% and specificity of 80% to detect PPH. The diagnostic accuracy of PFAT alone (96%) was higher than that of PASP alone (90%). Patients with PFAT < 100 ms had higher pulmonary vascular resistance
Not disclosed	PASP, RVDD, E/A, RAD	Not performed	Not performed	Not disclosed	Patients with advanced liver disease and PH had a high prevalence (20%) of PAH on TTE. Cirrhotic patients with PAH had higher RAD, RV diameter and diastolic dysfunction than those without PAH and control group
Yes	Not disclosed	Saline solution	CE-TTE: +or- CE-TEE: 1 to 6. Grades 1 and 2 considered physiological	Videotape	IPS prevalence of 42% on CE-TEE and of 28% on CE-TTE. Lower PaCO2 and DLCO than in patients without IPS
Yes	Not disclosed	Saline solution	CE-TTE: +or- CE-TEE: 1 to 4	Videotape	Non significantly higher IPS prevalence on CE-TEE (51%) than on CE-TTE (32%), due to small sampling
Not disclosed	LVDD, LVSD, LVSV, EF	Not performed	Not performed	Videotape	Patients treated with TIPS showed increased LVDV and LVSV as compared with those without TIPS or control group
Not disclosed	Not disclosed	Saline solution	+ or -	Videotape	14.3% of the patients had IPS on Echo, but none of them showed IPS on lung perfusion scan
No	Not disclosed	Dextrose solution	Sporadic, moderate, remarkable	Videotape	33% of the patients had IPS

RCCC: right cardiac chambers catheterization; CPT: Child-Pugh-Turcotte; LADD: left atrial diastolic diameter; CLD: chronic liver disease; DLCO: diffusion capacity of carbon monoxide; HSS: hepatosplenic schistosomiasis; HIS: hepatointestinal schistosomiasis; Echo: echocardiography; DSE= dobutamine stress echocardiography; TTE= transthoracic echocardiography; PAH: pulmonary arterial hypertension; HBV: hepatitis B virus; HCV: hepatitis C virus; PH: portal hypertension; PPH: portopulmonary hypertension; PW: posterior wall; PASP: pulmonary artery systolic pressure; RVSP: right ventricular systolic pressure; S'= peak systolic velocity; IPS: intrapulmonary shunt; VS: ventricular septum; TIPS: transjugular intrahepatic portosystemic shunt; IVRT: isovolumetric relaxation time; Tx: transplant; LAV: left atrial volume; RV: right ventricle; LVDV: left ventricular diastolic volume; (*) internal comparison between groups; Tx: transplantation.

is required so that future meta-analyses can be performed on the subject. Such results indicate the need for more detailed studies in that population, considering the heterogeneity found. Thus, further investments in systematic methods and standardized tests are required.

Conclusion

From this review, we concluded that CCM is underdiagnosed in patients with CLD, because, most of the time, the diagnosis of CCM is only established in the terminal phases of CLD. The following diagnostic criteria for CCM have been established: diastolic dysfunction, mainly when assessed on tissue and pulsed Doppler echocardiography; and left atrial volume. When assessing systolic function, stress echocardiography and cardiac strain imaging have been poorly studied.

In the context of diagnosing IPS, contrast-enhanced echocardiography is currently considered gold standard. It is worth noting that, when CE-TTE is dubious or the acoustic window is unsatisfactory, CE-TEE is recommended.

Echocardiography should be part of the screening of patients with CLD, because patients with systolic and/or diastolic dysfunction and portopulmonary hypertension have higher morbidity and mortality. A better understanding of the echocardiographic findings, mainly cardiac strain imaging and 3D echocardiography, in patients with CLD will improve their management.

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Author contributions

Conception and design of the research, Acquisition of data, Analysis and interpretation of the data, Statistical analysis, Obtaining funding, Writing of the manuscript, Critical revision of the manuscript for intellectual content: Mota VG, Markman Filho B.

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No potential conflict of interest relevant to this article was reported.

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