European Journal of Clinical Pharmacy
Print ISSN: 2385-409X **Online ISSN**: 3105-0409
Website: https://farmclin.com/

Original Research Article

The Role Bubbles Test in Detection of Porto-pulmonary Shunt in Liver Cirrhosis Patients by Echocardiography and Its Correlation with Right Ventricular Indices

Article History:

Received: 12-05-2026
Revised: 25-05-2026
Accepted: 01-06-2026
Published: 11-06-2026

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Abstract: ***Background:*** Liver cirrhosis is associated with several cardiopulmonary complications, including Hepato-pulmonary syndrome (HPS) and porto pulmonary hypertension (POPH), which may lead to significant right ventricular (RV) structural and functional alterations. Early detection of these abnormalities using noninvasive echocardiographic techniques may improve patient evaluation and follow-up. ***Aim:*** To detect intrapulmonary vascular dilatation (IPVD) in cirrhotic patients using contrast echocardiography (bubble test) and to assess the relationship between Porto pulmonary hypertension and the right ventricular–pulmonary artery (RV–PA) coupling index using the TAPSE/mPAP ratio , To evaluate the predictive value of right ventricular (RV) echocardiographic parameters for a positive bubble test in patients with liver cirrhosis . ***Methods:*** This case-control study included patients , known have liver cirrhosis and age- and sex-matched healthy controls. Patients with congenital heart disease, significant valvular disease, pulmonary disease, heart failure, or poor echocardiographic windows were excluded. Conventional echocardiography was performed to assess right-sided cardiac parameters including RV dimensions, right atrial area (RAA), right atrial volume index (RAVI), fractional area change (FAC), TAPSE, and mean pulmonary artery pressure (mPAP). RV–PA coupling was evaluated using the TAPSE/mPAP ratio. Contrast-enhanced echocardiography with agitated saline was used to detect IPVD. ***Results:*** Positive bubble tests suggestive of IPVD were identified in 28% of cirrhotic patients. Suspected POPH based on echocardiographic findings was observed in 32% of cases. Cirrhotic patients demonstrated significantly increased RAA, RAVI, and RV dimensions compared with controls, while FAC remained preserved. The TAPSE/mPAP ratio was significantly reduced, indicating early RV–PA uncoupling and impaired RV adaptation to increased pulmonary vascular load. A significant association was also found between advancing age and reduced TAPSE/mPAP ratio. ***Conclusion:*** Liver cirrhosis is associated with early subclinical cardiopulmonary changes, including IPVD and possible POPH. Echocardiography, particularly contrast echocardiography and the TAPSE/mPAP ratio, represents a valuable noninvasive tool for early detection of pulmonary vascular and RV functional abnormalities in cirrhotic patients.

Keywords: liver cirrhosis, bubbles test (agitated saline),protopulmonary shunt, portopulmonary hypertenstion, Right ventricular indeces Coupling, index (TAPSE / mPAP),

INTRODUCTION

Liver Cirrhosis is a pathological process that represents the last stage of any chronic liver disease. It is marked by fibrosis and alteration of normal hepatic tissue into irregular, abnormal nodules, known as regenerative nodules. This transformation is irreversible and affects the whole liver. Histologically, cirrhosis is considered an all-or-nothing diagnosis, although clinically it is classified as compensated or decompensated. Decompensated cirrhosis, which is identified by the presence of ascites, variceal hemorrhage, encephalopathy, or jaundice, is a complication that results from the main consequence of cirrhosis: portal hypertension and liver failure

{1}.Hepatopulmonary syndrome (HPS) is vasodilation in the pulmonary circulation leads to arterial hypoxemia, the main sign of hepato pulmonary syndrome. Normal pulmonary capillaries are 8 µm wide, and red blood cells, which are slightly less than 8 µm wide, pass through them one at a time, helping oxygenate the blood. In hepato pulmonary syndrome, the pulmonary capillaries can be as wide as 500 µm, allowing red blood cells to travel through them in groups of several cells. Because of this, many red blood cells don't get oxygen, which is like a right-to-left shunt {2}. Epidemiology : HPS is thought to be present in between 4% and 32% of cases of liver cirrhosis. The incidence of HPS in individuals assessed for LT is approximately 10–30%. HPS is usually detected in the sixth decade of life, exhibiting no significant association with gender, the a etiology of underlying liver disease, or the Model for End-Stage Liver Disease (MELD). The determined five-year survival rate was 20% for individuals with HPS, in contrast to 32–63% for individuals without HPS. {4},

Intra-pulmonary vascular dilatation (IPVD) and intra-pulmonary shunting are relatively frequent findings among patients with liver cirrhosis and portal hypertension. Several Middle Eastern studies evaluated the prevalence of pulmonary vascular abnormalities using contrast-enhanced echocardiography.

An Iraqi study conducted among patients with chronic liver disease and portal hypertension demonstrated intrapulmonary vascular dilatation in approximately 36.6% of cirrhotic patients using contrast echocardiography {5} .

Similarly, an Iranian study reported pulmonary shunting in 23.7% of patients with liver cirrhosis. {6}. Furthermore, an Egyptian study demonstrated intrapulmonary vascular dilatation in approximately 20% of cirrhotic patients {7} .

This study aims to --detect intrapulmonary vascular shunt in patients with liver cirrhosis using contrast echocardiography (bubbles test).

--To evaluate the correlation between Porto-pulmonary hypertension in patients with liver cirrhosis and the right ventricular-pulmonary artery (RV-PA) coupling index (TAPSE/mPAP).

--To evaluate the predictive value of right ventricular (RV) echocardiographic parameters for a positive bubble test in patients with liver cirrhosis

MATERIALS AND METHODS

2.1. Study design.

The study was designed as cross sectional , case- control study conducted to evaluated echocardiographic parameters in patients with liver cirrhosis compared with healthy controls .

2.2 .Data setting and collection time .

This study was done at Mirjan Medical City , Babil Health Directorate , Babylon , Iraq , in collaboration with the Gastrointestinal center at the same institution . Data collection took period over a six-month , from December 2025 to May 2026, within the echocardiography unit.

This study selected 50 subjects and divided into two groups .The first group comprised 25 individuals known have liver cirrhosis. The second group comprised 25 healthy adults who served as controls with the same age , BMI . The average age for each group was documented,.

2.3. Inclusion criteria:

Group 1 included patients with known liver cirrhosis.
Group 2 consisted of healthy control subjects without any chronic disease, matched to Group 1 by age and sex.
Informed consent was obtained from all participants.

2.4 .Exclusion criteria:

Subjects were excluded if they had congenital heart disease, significant valvular lesions, significant pulmonary disease, heart failure, or a poor echocardiographic window…

2.6 Ethical Approval.

Ethical approval was obtained from the Ethics Committee, College of Medicine, University of Babylon.
Informed consent was obtained from all patients before examination, and all data were anonymized using coded names in accordance with the principles of the Declaration of Helsinki.

2.7 Echocardiographic assessment .

Transthoracic echocardiographic (TTE) examinations were conducted with patients initially connected to an electrocardiogram (ECG) and positioned in the left lateral decubitus position, with the left arm extended below the head. All examinations used echocardiography devices, a Philips . Affiniti 70 C equipped with an S5-1 probe. And Vivid E9-GE, (XD clear GE vingmed-ultrasound Horten, Norway in 2012, LCD17 with Phased array M5Sc type probe with a frequency of 1.4 – 4.6MHZ and harmonic imaging for the 2DE imaging Measurements and image acquisition adhered to the guidelines established by the European Association of Cardiovascular Imaging (EACVI) and the American Society of Echocardiography (ASE) {21}

Figure 2.1 : Echocardiographic Philips ,Affiniti 70 C device equipped with an S5-1 probe

2.8 The method .

Tricuspid annular plane systolic excursion (TAPSE) :

Tricuspid annular plane systolic excursion (TAPSE) is assessed using the right ventricular (RV)-focused apical four-chamber view, which evaluates the longitudinal function of the right ventricle.
The M-mode cursor was positioned through the lateral tricuspid annulus, orientated in accordance with the direction of annular motion.
The recordings were acquired at a medium to fast sweep speed to provide accuracy.
TAPSE was determined by measuring the total systolic excursion of annular motion toward the apex, using a vertical measurement from leading edge to leading edge , TAPSE normal value is > 1.70 cm {21} , As showed in Figure 2.2 .

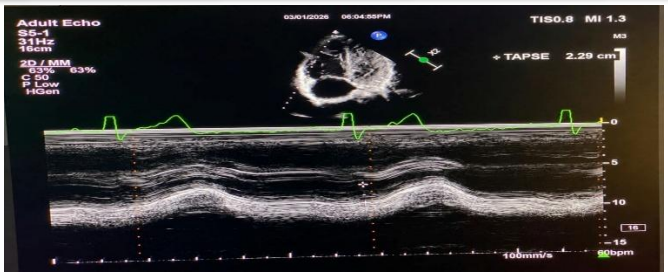


Figure 2.2 : Measurement of TAPSE

Peak systolic lateral annular velocity (S`) :

S', which represented the longitudinal systolic velocity of the tricuspid annulus, was measured using the RV-focused apical four-chamber view. The TDI sample volume was placed at the lateral aspect of the annulus. The Doppler beam was parallel to the longitudinal motion of RV free wall, and the highest systolic velocity was recorded . as in Figure 2.3 .

A normal s' velocity is greater than 9.5 cm/s . {21 }.

Figure 2.3 : measurement of right ventricular S`

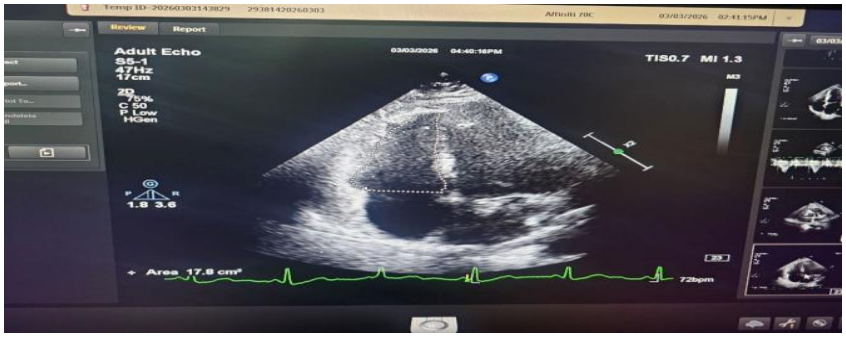
Right ventricular (RV) fractional area change (FAC) :

An indicator of global RV contractile function, was measured in the apical four-chamber view by evaluating the change from RV end-diastolic area to end-systolic area

The RV endocardium was traced beginning at the lateral tricuspid annulus, continuing along the right ventricular free wall to the apex, and then along the interventricular septum to the medial tricuspid annulus. Liked in Figure 2.4.

According to American Society of Echocardiography (ASE) guidelines, a normal RV fractional area change (FAC) >35 %

RV FAC % =(RVEDA – RVESA) RVEDA) ×100% {21 } .



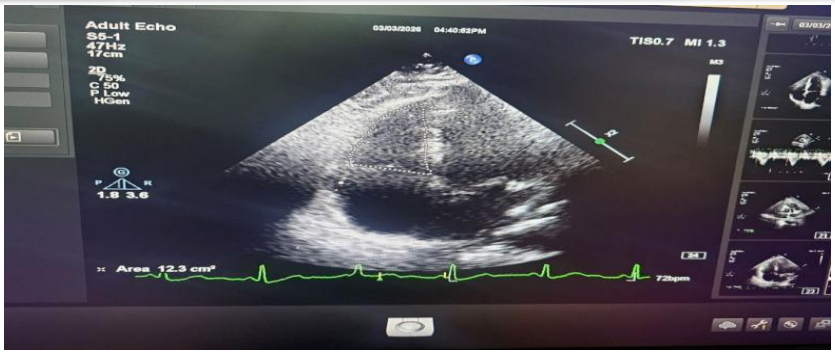


Figure 2.4 : Measurement of FAC of RIGHT VENTRICULAR .

Pulmonary acceleration time :

Pulmonary acceleration time (PAT) is a dependable noninvasive technique for estimating mean pulmonary artery pressures, especially useful when it is difficult to acquire or accurately interpret velocities of the tricuspid regurgitation jet. PAT is assessed using a pulsed-wave Doppler cursor placed just proximal to the pulmonary valve at end-expiration, starting from the onset of flow to the peak pulmonary flow velocity in the parasternal short-axis view of the pulmonary artery bifurcation. , as showed in Figure 2.5 . The right ventricular outflow tract acceleration time (RVOTAccT) reflects the time spent for flow to accelerate from initial to peak velocity. This time is reduced in pulmonary hypertension (PH) due to higher vascular impedance.

PAT > 120 ms is considered normal {22}.

Figure 2.5 : Measurement of pulmonary acceleration time .

Mean pulmonary artery pressure (mPAP) .

is estimated by calculating pulmonary acceleration time (AT) using the formula:
mPAP = 79 - (0.45 × AT).
If AT is less than 120 ms, mPAP is calculated using the equation:
mPAP = 90 - (0.62 × AT),
in accordance with ASE guidelines ,mPAP > 20 considered elevated pulmonary pressure . {21}.

Right ventricular dimension :

Right ventricular (RV) dimensions are measured in the RV-focused apical four-chamber view at end-diastole. The basal RV diameter is obtained at the maximal transverse dimension in the basal one-third of the right ventricle, the mid-cavity diameter is measured at the middle third of the RV cavity, and the longitudinal dimension is measured from the plane of the tricuspid annulus to the RV apex. As displayed in figure 2.6,
RV dilatation is defined as a basal diameter >41 mm or a mid-cavity diameter >35 mm. {21} .

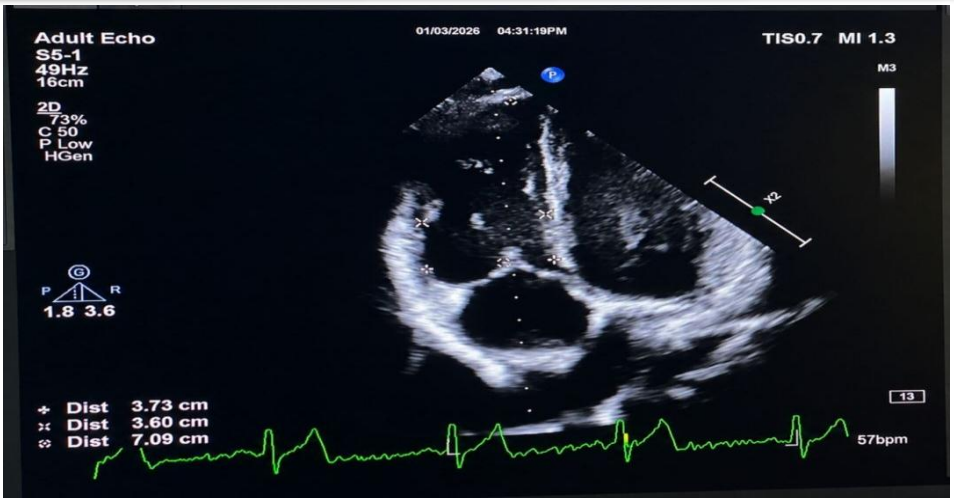


Figure 2.6 : Measurement of Right ventricular dimensions (basal , mild and length In RV-focused apical four-chamber view at end-diastole.

Right Atrium Area and Volume :
Right atrial area (RA area and volume) was measured in the apical four-chamber view at end-systole , just before the tricuspid valve opening, when the right atrium reaches its maximal size

The atrial endocardial border is traced carefully, excluding the area of the inferior vena cava, superior vena cava, and right atrial appendage. As manifested in figure 2.7
An RA area greater than or 18 cm² is considered enlarged. {23}.

The RA volume was calculated using the single-plane Simpson's disk method. The right atrial volume index (RAVI) was then calculated by dividing the measured right atrial volume by body surface area (BSA). A RAVI value >30 mL/m² is considered enlarged {21 }.

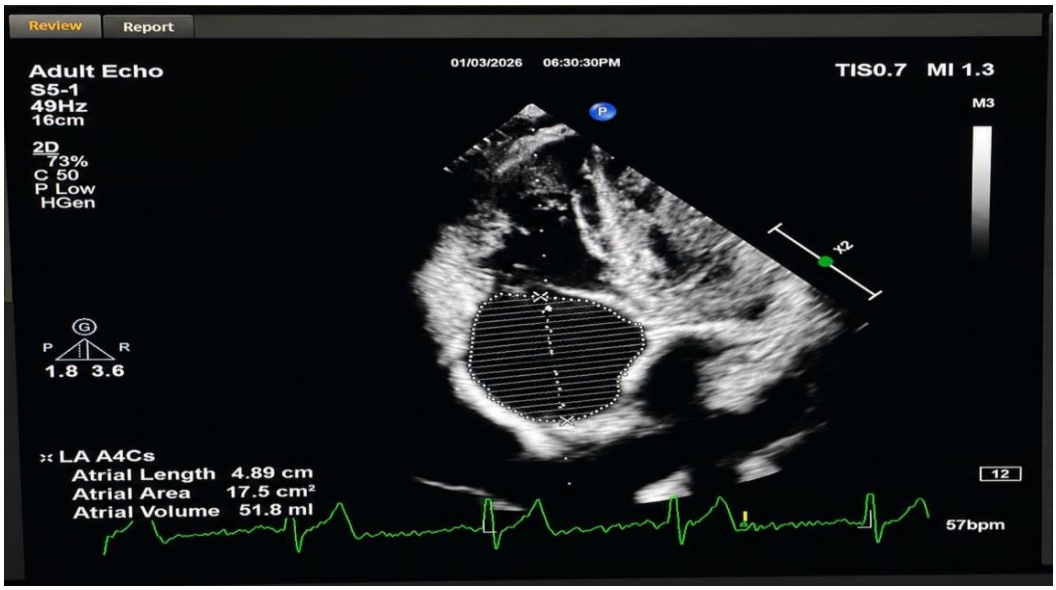


Figure 2.7 : Measurement of Right Atrial area, RAV .

Bubbles test :
Initially, we explained the test to the patient and then obtained their consent to proceed.
A 20-gauge intravenous cannula was inserted into the antecubital vein to quickly infuse a bolus of agitated saline that fully opacifies the right atrium. It was positioned on the right side to facilitate the left lateral decubitus position to improve echocardiographic views.
Taking either the apical 4-chamber or subcostal view, by a three-way stopcock, we mixed 9 ml of normal saline with 1 ml of room air , directing the mixture between two empty syringes to generate micro bubbles detectable by ultrasonography.

The agitated saline was administered via a peripheral intravenous cannula by one operator, while a second operator performed a simultaneous two-dimensional (2D) echocardiography. This imaging demonstrated the presence of micro bubbles from the agitated saline in the right side of the heart, and we subsequently observed their appearance in the left side of the heart after 4, 6, or 8 cardiac cycles. {24}.as manifested in Figure 2.8 .

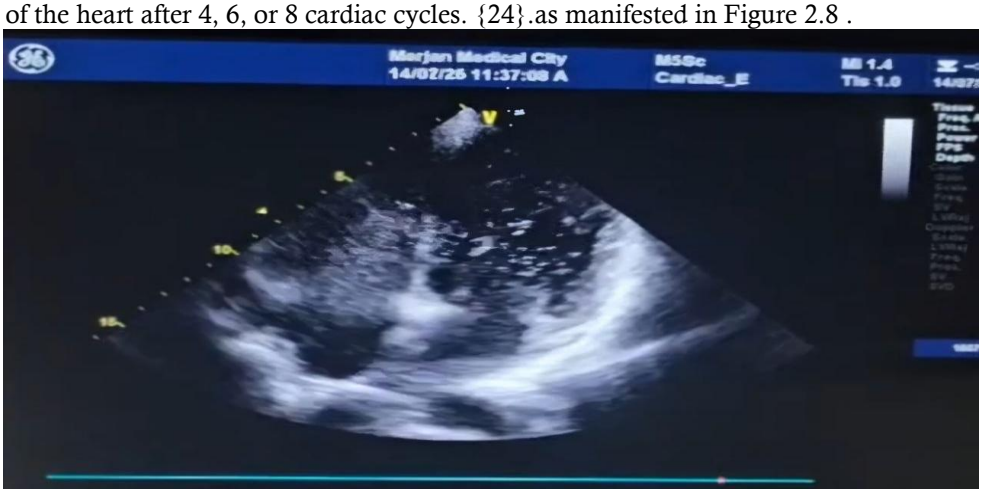


Figure 2.8 : appearance of micro bubbles in left side of heart after 6 cardiac cycle .

Data analysis

Statistical analysis was carried out using SPSS version 27. Categorical variables were presented as frequencies and percentages. Continuous variables were presented as (Means ± SD). Student t-test was used to compare means between two groups. Pearson Chi-square test was used to find the association between categorical variables. Pearson correlation coefficient (r) was used to assess relationship between two continuous variables. P value ≤ 0.05 was considered as significant.

RESULTS

Table 1: Distribution of patients with liver cirrhosis according to socio-demographic characteristics including age and sex. Mean age of patients was (54.92 ± 11.04) years. Older patient was 72.0 years and younger patient was 35.0 years. Patients with age (< 50.0 years) represent only 7 patients (28.0%). More than half of patients were males (N=13, 52.0%).

Table 1: Distribution of patients with liver cirrhosis according to socio-demographic characteristics (N=25)

Socio-demographic characteristics	Number	%
Age		
< 50 years	7	28.0%
50-60 years	9	36.0%
≥ 60 years	9	36.0%
Total	25	100.0%
Sex		
Male	13	52.0%
Female	12	48.0%
Total	25	100.0%

Figure 3.1: Distribution of patients with liver cirrhosis according to bubble test including (positive and negative). Patients with positive bubble test represent only 7 patients (28.0%) and patients with negative bubble test represent 18 patients (72.0%).

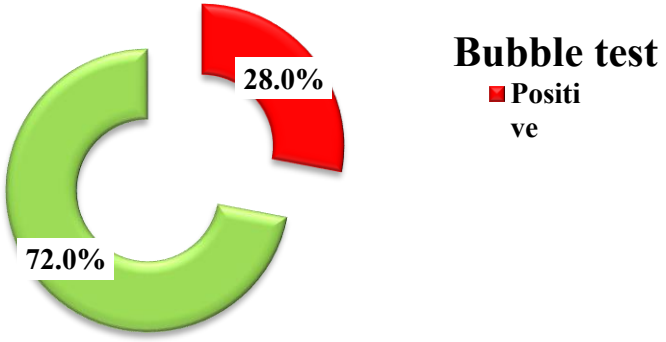


Figure 3.1 : Distribution of patients with liver cirrhosis according to bubble test (N=25)

Figure 3.2 : Distribution of patients with liver cirrhosis according to echocardiographic parameters including (high probability ,low probability). Patients with high probability represent only 8 patients (32.0%) and patients with low probability represent 17 patients (68.0%).

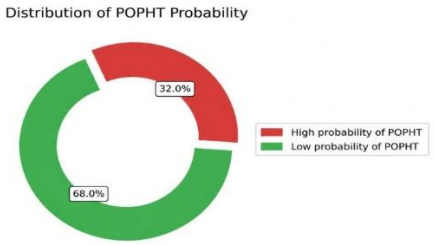


Figure 3.2: Distribution of patients with high probability of POPHT according to echocardiographic parameters .(N=25)

Table 2: The comparison between patients with liver cirrhosis and control group according to socio-demographic characteristics including age and sex. There was no significant mean differences of age between patients with liver cirrhosis in comparison to control group. There was no significant association between liver cirrhosis and sex of patient.

Table 2: The comparison between patients with liver cirrhosis and control group according to socio-demographic characteristics (N=50)

Study variables	Study group		P-value
	Liver cirrhosis (N=25)	Control group (N=25)	
Age (years)	54.92 ± 11.04	53.72 ± 12.51	0.721
Sex			
Male	13 (52.0)	13 (52.0)	1.000
Female	12 (48.0)	12 (48.0)	
Total	25 (100.0)	25 (100.0)	

- The mean differences of Right Atrial Volume Index (RAVI) and right atrial area (cm^2) according to study group including (liver cirrhosis and control group). There was significant mean elevation of Right Atrial Volume Index (RAVI) and right atrial area (cm^2) among patients with liver cirrhosis in comparison to control group. As showed in Figure (3.3, 3.4)

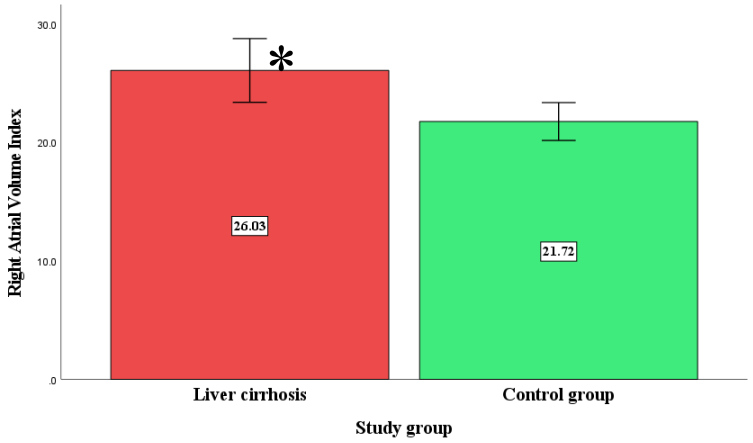


Figure 3.3: Significant mean elevation of Right Atrial Volume Index (RAVI) among patients with liver cirrhosis in comparison to control group (P=0.009*)

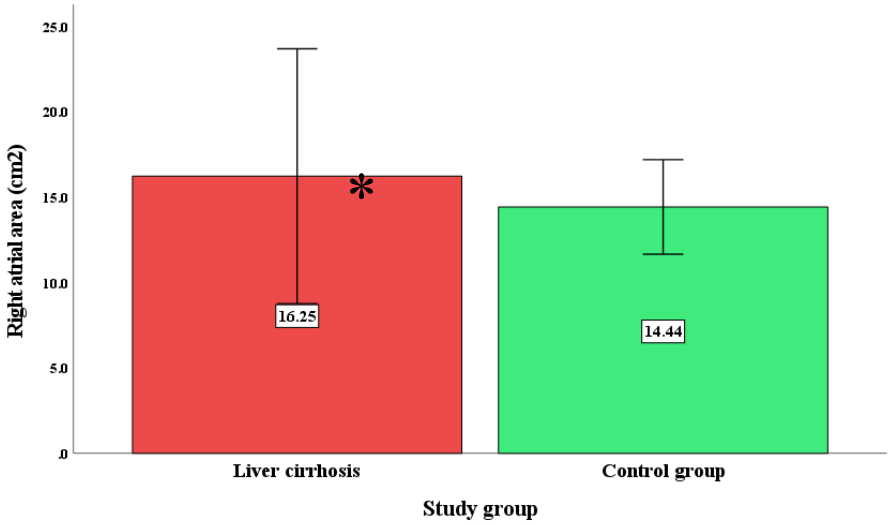


Figure 3.4: Significant mean elevation of Right atrial area (cm^2) among patients with liver cirrhosis in comparison to control group (P=0.031*)

Table 3: The mean differences of echocardiographic markers including (TAPSE (mm), FAC (%), S`1, S`2, RV Basal (mm), RV Mid (mm) and RV Length (mm) according to study group including (liver cirrhosis and control group). There was significant mean elevation of TAPSE (mm), RV Basal (mm) and RV Mid (mm) among patients with liver cirrhosis in comparison to control group.

Table 3: : The mean differences of echocardiographic markers according to study group (N=50)

Echocardiographic markers	Study group		P-value
Echocardiographic markers	Study group		P-value
	Liver cirrhosis (N=25)	Control group (N=25)	
TAPSE (mm)	24.22 ± 2.93	22.08 ± 2.34	**0.006***
FAC (%)	38.68 ± 4.49	39.76 ± 2.91	0.318
S`1	13.40 ± 3.10	12.20 ± 2.16	0.119
S`2	13.34 ± 2.71	12.38 ± 1.74	0.145
RV Basal (mm)	37.52 ± 4.28	31.80 ± 2.69	**<0.001***
RV Mid (mm)	30.91 ± 3.77	28.64 ± 2.66	**0.018***
RV Length (mm)	68.68 ± 3.99	68.16 ± 2.81	0.597

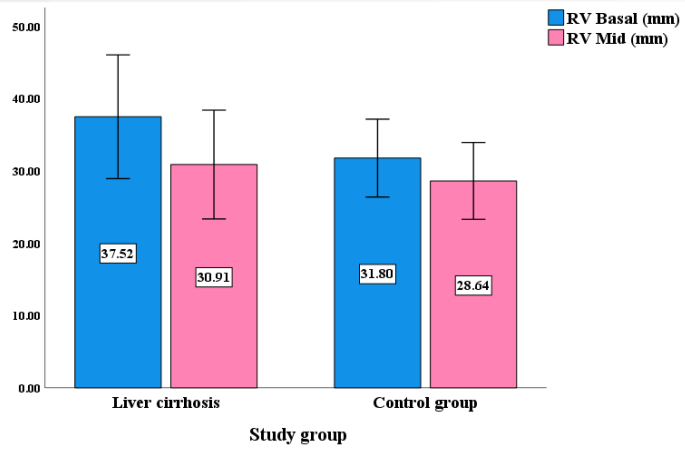


Figure 3.5: Significant mean elevation of RV Basal (mm) and RV Mid (mm) among patients with liver cirrhosis in comparison to control group (P<0.001* and P=0.018*)

- The mean differences of mPAP (mmHg), TAPSE / mPAP according to study group including (liver cirrhosis and control group). There was significant mean elevation of mPAP (mmHg) among patients with liver cirrhosis in comparison to control group. There was significant mean reduction of TAPSE / mPAP among patients with liver cirrhosis in comparison to control group.
. As showed in Figure (3.6 , 3.7) .

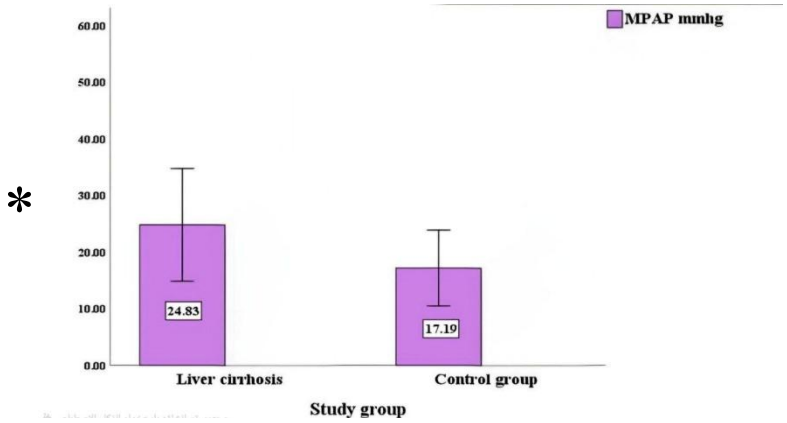


Figure 3.6: Significant mean elevation of mPAP (mmHg) among patients with liver cirrhosis in comparison to control group (P<0.001*)

Figure 3.7: Significant mean reduction of TAPSE / mPAP among patients with liver cirrhosis in comparison to control group (P<0.001*)

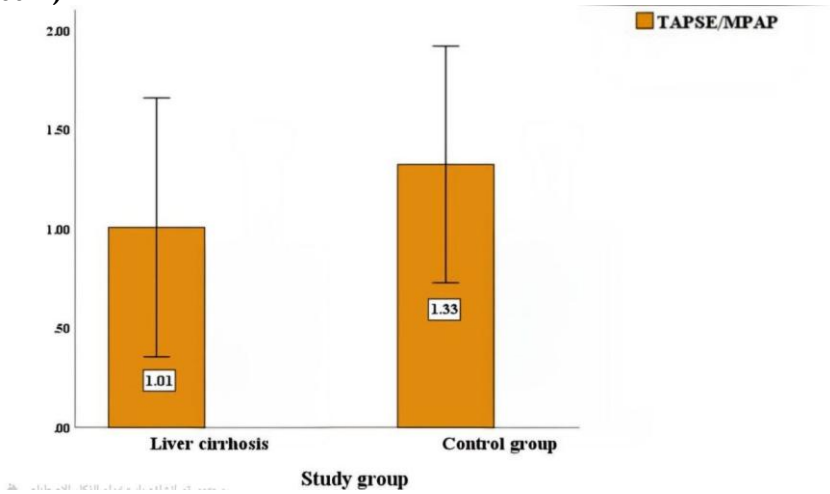


Table 4: The correlation between age of patient (years) and study markers including (TAPSE / mPAP) among patients with Liver cirrhosis. There was significant negative linear correlation between age of patient (years) and TAPSE / mPAP among patients with liver cirrhosis

Table 4: The mean differences of TAPSE / mPAP and TAPSE / PASP according to sex of patient with liver cirrhosis (N=25)

Study markers	Sex		P-value
	Male (N=13)	Female (N=12)	
TAPSE / mPAP	1.04 ± 0.35	0.98 ± 0.31	0.629

Table 5: The correlation between Right Atrial Volume Index and study markers including (TAPSE /mPAP) among patients with Liver cirrhosis. There was no significant correlation between Right Atrial Volume Index and TAPSE / mPAP among patients with liver cirrhosis

Table 5: The correlation between age of patient and study markers including (TAPSE / MPAP) among patients with Liver cirrhosis (N=25)

Study markers	Age of patient (years)	
	R	P-value
TAPSE / mPAP	-0.485	0.014*

DISCUSSION

Liver cirrhosis is usually associated with complex cardio-pulmonary alterations that occur due to hyper dynamic circulation, pulmonary vascular changes, and a intra-pulmonary shunt, all of which may affect the right side of the heart. Recently non-invasive echocardiographic parameters have been useful for assessing the Right ventricular – pulmonary artery (RV-PA) coupling index as a marker of RV adaption to pulmonary vascular load in cirrhotic patients. In our analysis, we found that 28% of patients with liver cirrhosis have a positive bubble test, characterized by an appearance of delayed micro-bubbles of agitated saline on the left side of the heart after six cardiac cycles following Right atrial opacification, suggesting intra-pulmonary vascular dilatation (IPVD). The findings demonstrate the existence of intra-pulmonary vascular dilatation (IPVD), resulting from elevated production of vasodilators, such as nitric oxide, in the context of liver cirrhosis. The vascular alterations result in a ventilation-perfusion imbalance and an intra-pulmonary shunt. However, IPVD alone does not confirm the diagnosis of hepato-pulmonary syndrome (HPS), which necessitates the evaluation of arterial hypoxemia using arterial blood gas analysis (ABG). These findings are consistent with Santos et al. (2024) in which 32% of patients demonstrated IPVD {25}, potentially advancing to HPS. While Verstraeten et al. (2026) documented a prevalence of Hepato-pulmonary Syndrome (HPS) of roughly 17% among patients referred for liver transplantation. {26}. The relatively high prevalence identified in this study may be related to the use of contrast echocardiography without arterial blood gas measurements to diagnose arterial hypoxemia. Moreover, contrast echocardiography is a highly sensitive diagnostic technique for detecting subclinical IPVD .

Dzikowska-Diduch et al. (2024) finding was supports that IPVD may manifest without hypoxemia as an initial phase of pulmonary vascular involvement in cirrhotic patients {27} .

Porto-pulmonary hypertension is a type of pulmonary hypertension linked with portal hypertension that results from liver dysfunction, which reduces the hepatic clearance of vasoactive agents like endothelin, serotonin, and inflammatory mediators. These substances induced vasoconstriction and endothelial remodeling, thereby elevating PVR and mPAP and increasing RV afterload. In our study, the prevalence of suspected Porto-pulmonary hypertension (POPHT) in patients with liver cirrhosis was 32%, based on echocardiographic measures. Huang Ds et al. (2026) and Gupta A et al. (2022) , they were found this rate ranged from 1.6% to 9.3%, where the diagnosis was confirmed by right heart catheterization RHC {28,29}.

Our findings are close to Kumar A .et al. (2024) that reporting a prevalence of 29.5% when echocardiography is used as a screening modality {30} . The similarities and differences between our results and earlier studies support the utility of echocardiography as a screening modality for identifying suspected subclinical Porto-pulmonary hypertension in patients with liver cirrhosis; however, the echocardiographic findings may overestimate the prevalence compared with right heart catheterization, which remains the cornerstone diagnostic method for POHT. However, this outcome may indicate the sensitivity of non-invasive echocardiographic examination in detecting the potential for subclinical pulmonary vascular alterations, suggestive of POPHT rather than definitively confirming the diagnosis via

right heart catheterization.

Our analysis , revealed RAA and RAVI parameters were significantly increased in patients with liver cirrhosis, which may reflected right atrial remodeling and dilation .Theses finding may related to chronic hemodynamic alteration that associated with liver cirrhosis, including increased right side filling pressures and possible pulmonary vascular changes . Consequently, a persistent increase in R.V pressure may lead to backward transmission pressure and progression to RA, resulting in RA dilatation and elevated right atrial pressure RAP , similar observation was revealed in the study by Gupta A et al. (2022) , who reported increased pulmonary artery pressure and echocardiographic manifestation of right sided involvement in cirrhotic patient with POPHT {28} .

These findings in line with observation by Zhang K et al. study that documented the effect of POPHT on RA, including remodeling, chamber dilatation in patient with end stage liver cirrhosis {31} .

Furthermore, patients with liver cirrhosis usually have hyper dynamic circulation, with systemic vasodilation, elevated cardiac output, and increased venous return to the atrium. These hemodynamic changes increase R.V. preload linked to pulmonary vascular alterations, resulting in right ventricular remodeling prior to affecting right ventricular systolic function.

This pathophysiology correlates with our findings: RV dimensions were markedly greater in patients with liver cirrhosis compared to controls. Although Fractional area changes FAC is an indicator of RV systolic function, it remained preserved ,not significant (P values = 0.318) . In addition : we observed that RV S′ displayed no significant difference between the studied groups.(P=0.145). In contrast, Nasr FM et al. (2015) .observed significantly increased tricuspid annular S′ velocity in cirrhotic patients, which may be due to the hyper-dynamic circulation and increased cardiac output that occur with liver cirrhosis. {32} .. And ,In line with Zhang K et al. (2019) study , that founded the right ventricular remodeling in patients with end stage liver cirrhosis have preserved systolic function was reported. {30}

Whereas Enenche AA et al. (2024) research documented RV dilation and remodeling associated with a significant reduction in FAC. {33 }

This may be explained by right ventricular structural changes that develop before systolic dysfunction becomes obvious. This disparity may be explained by variability in disease severity, disease duration, patient selection and the degree of concomitant hemodynamic changes between the studied groups .

Overall, these analyses suggest that RV dilatation in cirrhotic patients manifests as an early sub-clinical compensatory response to hyper-dynamic circulation and altered pulmonary hemodynamics rather than established R.V. failure.

In our study, we observed a significantly increase in Tricuspid annular plane systolic excursion TAPSE among cirrhotic patients, which may have resulted from hyper-dynamic circulation, leading to systemic vasodilation and increased venous return, thereby augmenting RV preload and increasing longitudinal RV motion associated with liver cirrhosis.

This result coincides with Celiker Guler E et al. (2023) study that documented sub-clinical changes in RV performance due to hyper-dynamic circulation and altered pulmonary hemo-dynamics {34} .

In the present study , this ratio of TAPSE / mPAP was statically significantly reduced (the ability of RV contractility to adapt to increased pulmonary afterload). Fortuni F et al. (2023) studies have demonstrated the clinical importance of the TAPSE / mPAP ratio as a surrogate marker of the right ventricular- pulmonary arterial coupling index, reflecting the ability of R.V. contractility relative to PA load {35}.

Importantly Silic V et al . (2025) . were found mPAP may be elevated in patients with liver cirrhosis secondary to hyper-dynamic circulation, increased cardiac output , and changes in pulmonary hemodynamics, which may not necessarily represent true pulmonary hypertension {36}. Therefore, the TAPSE/mPAP ratio may provide a more comprehensive assessment of R.V. adaptation rather than depend on isolated conventional parameters alone. Accordingly, this ratio serves as a sign for early RV-PA uncoupling and sub-clinical cardio-pulmonary involvement in patients with liver cirrhosis. Since it's a newly emerging parameter ,the studies about this ratio are limited globally, especially regarding Porto-pulmonary hypertension in liver cirrhosis and there are no similar studies within the country and region to compare with.

The current study , show significant negative correlation between age and the TAPSE/mPAP ratio, which may indicate a gradual deterioration in right ventricular-pulmonary artery coupling with advancing age. This can be attributed by age-associated alterations in cardio-pulmonary hemodynamics, including increasing pulmonary vascular stiffness and a gradual decrease in right ventricular functional reserve. Furthermore : it is related to the chronic hemodynamic alterations associated with prolonged hepatic cirrhosis. Also ; we observed no correlation between TAPSE/mPAP

ratio and Right atrial volume index

At present ,there are no studies support or against this correlation in patients have Porto-pulmonary hypertension.

In the present study, there were no statistically significant differences in age and sex distribution between cirrhotic patients and control group . This similar demographic finding across groups reduces the potential confounding effects of age- and sex-related cardio-pulmonary vascular changes in cirrhotic patients on echocardiographic findings.

Therefore, all echocardiographic findings are more likely related to the pathophysiological effects of liver cirrhosis rather than to demographic differences between the studied group.

CONCLUSION

- This research supports the role of echocardiographic study as a noninvasive tool for detecting early sub-clinical cardio-pulmonary abnormalities and identifying cirrhotic patients who may benefit from further diagnostic evaluation for HPS , POPHT .

-.Elevated TAPSE in patients with liver cirrhosis may reflect hyper-dynamic circulation, which could raise suspicion of HPS, especially in patients presenting hypoxemia or related clinical symptoms. Thus , further evaluation with an agitated contrast saline echocardiographic (bubbles test) may be warranted .

-Right-sided dilation may raise suspicion of POPHT , which occurred due to pressure overload in a patient with liver cirrhosis , requiring further assessment of pulmonary hemodynamics.

-TAPSE /mPAP was a useful non-invasive echocardiographic marker for assessment of the right ventricular –pulmonary arterial coupling index; its reduction represented RV –PA uncoupling. - TAPSE /mPAP was associated with advancing age, which may contribute to the gradual deterioration of the R.V-P.A. coupling index in elderly patients.

LIMITATIONS :

Limited study time and small number of available patients , which impacted patient recruitment and data collection; thus , the findings may not represent the entire population of patients with liver cirrhosis and should be interpreted with caution.

-Limited previous research is available in the country or neighboring countries that addresses the RV-PA coupling index (TAPSE/mPAP ratio) in patients with liver cirrhosis, to compare with the present findings.

-A limited invasive hemodynamic method (RHC) to confirm pulmonary hypertension and R.V-P.A coupling could not be established.

REFERENCES

1 : Goldman L, Schafer AI, editors. Goldman-Cecil Medicine. 27th ed. Philadelphia: Elsevier; 2024. Chapter 139, p. 1035.

2 : Goldman L, Schafer AI, editors. Goldman-Cecil Medicine. 27th ed. Philadelphia: Elsevier; 2024. Chapter 139, p. 1037.

3 : Shah A, Jacob I, Rao K, et al. The Bubble Test for Diagnosis of Hepatopulmonary Syndrome. J Acute Care. 2024;3(2):101-104

4 : Than NN. Pulmonary Complications of Liver Cirrhosis: A Concise Review. In: Rodrigo L, editor. Liver Cirrhosis - Update and Current Challenges

5 : Almohana S. Prevalence of clinically significant hepatopulmonary syndrome among patients with chronic liver disease and portal hypertension. Al-Kindy Coll Med J. 2011;7(1):61-66.

6 : Al Mahtab M, Al Fayez NQ, Helmy A. Prevalence and predictors of hepatopulmonary syndrome in patients with liver cirrhosis. Hepat Mon. 2015;15(3):e15627. doi:10.5812/hepatmon.15627.

7 : El Makarem MAA, Hamam AM, Elakad A, Ali A, Abd Elkader M, Sayed AF, et al. Hepatopulmonary syndrome: prevalence and predictors in Egyptian cirrhotic patients. Tropical Gastroenterology. 2011;32(1):25-30.

8 : Raevens S, Geerts A, Van Steenkiste C, Verhelst X, Van Vlierberghe H. Hepatopulmonary syndrome. Clin Liver Dis (Hoboken). 2022;19(4):162-166. doi:10.1002/cld.1214.

9 : Zaka AZ, Khungar V. New updates on hepatopulmonary syndrome. J Intensive Care Soc. 2025;26(1):94-101. doi:10.1177/17511437241276058.

10 :Grilo-Bensusan I, Pascasio-Acevedo JM. Hepatopulmonary syndrome: What we know and what we would like to know. World J Gastroenterol. 2016 Jul 7;22(25):5728-5741. doi:10.3748/wjg.v22.i25.5728.

11: Iaconi M, Maritti M, Ettorre GM, Tritapepe L. Echocardiographic evaluation in patient candidate for liver transplant: from pathophysiology to hemodynamic optimization. J Anesth Analg Crit Care. 2024;4:75. doi:10.1186/s44158-024-00211-0.

12 : Krynytska I, Marushchak M, Mikolenko A, Smachylo I. Differential diagnosis of hepatopulmonary syndrome (HPS). J Pre Clin Clin Res. 2017;11(2):139-143. doi:10.26444/jpccr/74603.

13 : Xu H, Cheng B, Wang R, Ding M, Gao Y. Portopulmonary hypertension: Current developments and future perspectives. Hepatology Liver Res. 2022;6(1):10-20. doi:10.1016/j.livres.2022.02.002.

14: Krowka MJ, Fallon MB, Kawut SM, Fuhrmann V, Heimbach JK, Ramsay MA, et al. International Liver Transplant Society Practice Guidelines: Diagnosis and Management of Hepatopulmonary Syndrome and Portopulmonary Hypertension.

Transplantation. 2016 Jul;100(7):1440-1452. doi:10.1097/TP.0000000000001229.
15 : Benz F, Mohr R, Tacke F, Roderburg C. Pulmonary complications in patients with liver cirrhosis. Journal of Translational Internal Medicine. 2020;8(3):150-158. doi:10.2478/jtim-2020-0024. PMID: 33062591; PMCID: PMC7534492.
16 : Mukherjee M, Rudski LG, Addetia K, Afilalo J, D'Alto M, Freed BH, et al. Guidelines for the echocardiographic assessment of the right heart in adults and special considerations in pulmonary hypertension: Recommendations from the American Society of Echocardiography. J Am Soc Echocardiogr. 2025;38(3):141-186. doi:10.1016/j.echo.2025.01.006. PMID:40044341.
17 : He Q, Huang W, Zhang P, et al. Clinical usefulness of right ventricle-pulmonary artery coupling in cardiovascular disease. J Cardiovasc Dev Dis. 2023;10(4):166. doi:10.3390/jcdd10040166.
18: Stassen J, De Keulenaer G, Kaiser R, Herbots L, D'Alto M, Claus P, et al. Right ventricular-pulmonary artery coupling in cardiac surgery candidates: a prospective observational cohort study. ESC Heart Fail. 2022 Jun;9(3):1968-1978. doi:10.1002/ehf2.13857. PMID: 35266319; PMCID: PMC9065855.
19 : Fortmeier V, Lachmann M, Körber MI, Unterhuber M, Schöber AR, Stolz L, et al. Sex-related differences in clinical characteristics and outcome prediction among patients undergoing transcatheter tricuspid valve intervention. JACC Cardiovasc Interv. 2023;16(11):1270-1282. doi:10.1016/j.jcin.2023.01.378.
20 : Pelletier KJ. A quick and reliable mental formula to calculate the BSA of a patient. J Extra Corpor Technol. 2022 Sep;54(3):255-256.
21 ; Mukherjee M, Rudski LG, Addetia K, Afilalo J, D'Alto M, Freed BH, et al. Guidelines for the echocardiographic assessment of the right heart in adults and special considerations in pulmonary hypertension: Recommendations from the American Society of Echocardiography. J Am Soc Echocardiogr. 2025;38(3):141-186. doi:10.1016/j.echo.2025.01.006.
22 : 16.2.2.1 Pulmonary acceleration time to estimate pulmonary pressure. In: Thomas JD, editor. 123sonography Echo Book. Vienna: 123sonography; [cited 2026 May 27].
23 : Rudski LG, Lai WW, Afilalo J, Hua L, Handschumacher MD, Chandrasekaran K, et al. Guidelines for the echocardiographic assessment of the right heart in adults: a report from the American Society of Echocardiography. J Am Soc Echocardiogr. 2010;23(7):685-713
24 : Bernard S, Churchill TW, Namasivayam M, Bertrand PB. Agitated saline contrast echocardiography in the identification of intra- and extracardiac shunts: connecting the dots. Journal of the American Society of Echocardiography. 2021;34(1):1-12. doi:10.1016/j.echo.2020.09.018.
25: Santos AA, Silva Júnior GB, Daher EDF. Hepatopulmonary syndrome in liver cirrhosis: pathophysiology, diagnosis, and treatment. Brazilian Journal of Implantology and Health Sciences. 2024;6(2):1408-1417. doi:10.36557/2674-8169.2024v6n2p1408-1417.
26: Verstraeten M, De Clercq M, De Craemer H, Verhelst X, Lefere S, Devisscher L, et al. Liver transplantation for hepatopulmonary syndrome: A systematic review and meta-analysis. JHEP Reports. 2026;8:101659. doi:10.1016/j.jhepr.2025.101659.
27 : Dzikowska-Diduch O, Biederman A, Kurzyna M, et al. Echocardiographic Screening of Liver Transplant Candidates for Pulmonary Hypertension and Hepatopulmonary Syndrome. Journal of Clinical Medicine. 2024;13(22):6990. doi:10.3390/jcm13226990.
28 : Huang DS, Ramsay MAE, Kawut SM, et al. Long-Term Outcome of Pulmonary Artery Hypertension Associated With Portal Hypertension. Pulmonary Circulation. 2026. Available from: PubMed Central
29 : Gupta A, Rao S, Sharma P, et al. Prevalence and Clinical Features of Portopulmonary Hypertension Among Patients With Hepatic Cirrhosis. Cureus. 2022;14(5):e24868. doi:10.7759/cureus.24868.
30: Kumar A, Sharma P, Singh R, et al. Clinical Features and Prevalence of Pulmonary Hypertension in Chronic Liver Disease. Healthcare Bulletin. 2024. Available from: Healthcare Bulletin
31 : Zhang K, Braun A, von Koeckritz F, Schmuck RB, Teegen EM, Cuspidi C, Heinzel F, Pieske B, Tadić M. Right Heart Remodeling in Patients with End-Stage Alcoholic Liver Cirrhosis: Speckle Tracking Point of View. J Clin Med. 2019;8(9):1285. doi:10.3390/jcm8091285. PMCID: PMC6780282.
32 : Nasr FM, Metwaly A, Abdel Khalik A, Darwish H. Cardiac dysfunction in liver cirrhosis: a tissue Doppler imaging study from Egypt. Electron Physician. 2015;7(4):1135-1143. doi:10.14661/2015.1135-1143..
33 : Enenche AA, Kweki AG, Aiwuyo HO, et al. Echocardiographic Assessment of Right Ventricular Function in Patients With Liver Cirrhosis. Cureus. 2024;16(4):e57410. doi:10.7759/cureus.57410. PMCID: PMC11062624.
34 : Celiker Guler E, Omaygenc MO, Naki DD, Yazar A, Karaca IO, Korkut E. Isolated subclinical right ventricle systolic dysfunction in patients after liver transplantation. J Clin Med. 2023;12(6):2289. doi:10.3390/jcm12062289
35: Fortuni F, Ciliberti G, Zilio F. Right Ventricular–Pulmonary Arterial Coupling: So You Think You Can Tell. JACC Cardiovasc Interv. 2023;16(12):1536–1537. doi:10.1016/j.jcin.2023.05.007.
36 : Silić V, Vuković J, Radić M, et al. Contrasting Pathophysiology and Implications for Liver Transplantation in Hepatopulmonary Syndrome and

Portopulmonary Hypertension. Journal of Clinical Medicine. 2025;15(1):72 doi:10.3390/jcm15010072.

