

Liver stiffness measurement for non-invasive assessment of central venous pressure in patients with heart failure: A multicentre pilot study

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Aims

Central venous pressure (CVP) is an important variable in assessing heart failure (HF) patients. However, invasive CVP measurement using right heart catheterization is associated with potential complications, and accurate measurement requires careful attention to technique. In this multicentre pilot study, we aimed to evaluate whether non-invasively measured liver stiffness can be used to assess CVP in patients with HF.

Methods and results

Patients aged 18 to 85 years with a history of HF (or left ventricular ejection fraction [LVEF] $\leq 40\%$) who required central venous line placement with CVP measurement were enrolled in an open-label study. Patients underwent simultaneous invasive catheter CVP measurement and non-invasive liver stiffness measurement (LSM) using vibration-controlled transient elastography (VCTE). The primary endpoint was the agreement between CVP and LSM-derived CVP ($-5.9 + 6.8 \times \ln[\text{LSM}]$) in the supine position. Among the 38 patients who completed the study, 34 (89.5%) were male, the mean age was 63.8 years, and the median LVEF was 24.5%. CVP correlated with LSM-derived CVP (Spearman $r = 0.53$, $p < 0.001$). Bland–Altman analysis demonstrated a mean difference (measured CVP minus LSM-derived CVP) of 0.11 mmHg (95% confidence interval -1.31 , 1.54). LSM identified clinically significant CVP elevation (> 10 mmHg) with an area under the curve of 0.83. An LSM threshold > 10 kPa yielded a sensitivity of 0.73 and a specificity of 0.78, correctly classifying CVP (> 10 or ≤ 10 mmHg) in 76% of patients.

Conclusions

Liver stiffness measurement is a promising non-invasive surrogate for CVP in patients with HF. Future studies are warranted to validate these findings and to assess the role of LSM for the screening, diagnosis, monitoring, and prognostic stratification of patients with HF.

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Graphical Abstract

Liver stiffness measurement for non-invasive assessment of central venous pressure in heart failure

Can non-invasively measured liver stiffness (LSM) be used to assess central venous pressure (CVP) in patients with HF?

Patients

Inclusion criteria:

- history of HF or LVEF $\leq 40\%$
- clinical indication for CVP measurement

Exclusion criteria:

- primary liver disease or cirrhosis

Right heart
catheterization



CVP in mmHg

Vibration-Controlled
Transient
Elastography

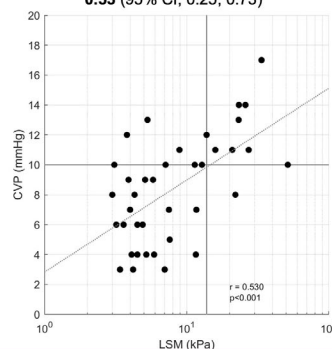


LSM in kPa

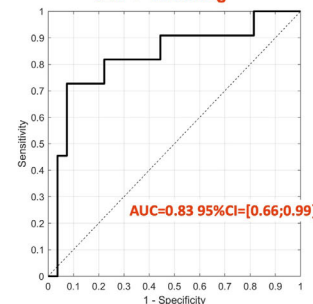
Correlation between CVP and LSM

Spearman correlation coefficient:

0.53 (95% CI, 0.25, 0.73)



Performance of LSM to diagnose CVP > 10 mmHg



	Accuracy	Sens.	Spe.
LSM > 10 kPa	76%	73%	78%
LSM > 13.3 kPa	87%	73%	93%

Patient characteristics

- 38 patients (M 34), mean age 64 yrs
- Mean BMI 30 kg/m²
- CVP: Mean 8.4 mmHg, Median 8.5 mmHg
- LSM: Mean 11.2 kPa, Median 6.4 kPa

Take home message

- LSM is a promising, non-invasive marker of CVP in HF
- Potential utility for screening, monitoring, and risk stratification
- Further validation in larger, diverse cohorts is needed

Liver stiffness measurement for central venous pressure assessment. AUC, area under the curve; BMI, body mass index; CI, confidence interval; CVP, central venous pressure; HF, heart failure; LSM, liver stiffness measurement; LVEF, left ventricular ejection fraction.

Keywords

Central venous pressure • Heart failure • Liver stiffness • Non-invasive assessment • Right heart catheterization • Vibration-controlled transient elastography

Introduction

Central venous pressure (CVP) assessment plays a significant role in the management of patients with heart failure (HF) by providing an estimate of cardiac preload, which reflects volume status and right ventricular function.^{1–4} The CVP is also correlated with kidney venous pressure, one of the key determinants of glomerular filtration rate.⁵ Although the gold standard for evaluating CVP is invasive measurement with a catheter that is advanced in the superior vena cava, this procedure requires attention to technical details, and it may be associated with complications.^{6–9} Moreover, CVP cannot be assessed consistently and repeatedly in all patients. Therefore, non-invasive CVP assessment methods have been investigated, including liver stiffness measurement (LSM) as a surrogate for CVP.^{10–15}

Vibration-controlled transient elastography (VCTE) is a reliable, fast (<4 min), standardized, and non-invasive method to measure liver stiffness, which serves as an indicator of liver fibrosis and cirrhosis.¹⁶ Its use is recommended in clinical practice guidelines to assess prognosis and guide treatment decisions in patients with liver disease.¹⁷ It has been shown that LSM is useful to diagnose porto-sinusoidal vascular liver disease, a chronic vascular abnormality associated with liver congestion and portal hypertension without cirrhosis.¹⁸ The pathophysiology of bidirectional heart–liver–kidney interactions in HF is complex and associated with abnormalities in liver biomarkers and unfavourable prognosis.^{19–22} In HF, liver congestion is the result of passive venous congestion, as CVP elevation in right-sided HF is transmitted to the hepatic (central) veins of the liver.²³ Small studies in patients with decompensated HF, congenital heart disease or recipients of

durable left ventricular assist devices have demonstrated a good correlation between invasive CVP measurement and VCTE assessment of liver stiffness.^{15,24–27} These findings open the possibility that a quantitative estimation of CVP based on non-invasive LSM could be developed and applied in clinical practice.

In this multicentre pilot study, we aimed to evaluate whether non-invasively measured liver stiffness can be used to assess CVP in patients with HF in five European centres.

Methods

Patients

Patients aged 18 to 85 years with a history of HF or known to have a left ventricular ejection fraction (LVEF) of 40% or lower, who required central venous line placement to measure CVP, and provided informed consent, were enrolled in this multicentre open-label study. Major exclusion criteria included mechanical ventilation, infection or severe life-threatening disease (for patients enrolled during an admission); significant pulmonary disease; oxygen saturation <95%; myocardial infarction, unstable angina or cardiac surgery within 3 months, cardiac resynchronization therapy device implantation within 3 months, or percutaneous transluminal coronary artery intervention within 1 month prior to inclusion; severe mitral or tricuspid regurgitation or any moderate valvular stenosis or moderate aortic or pulmonary regurgitation at screening; primary liver disease or cirrhosis; significant ocular disease (due to the potential use of the Trendelenburg position); kidney disease with an estimated glomerular filtration rate <30 ml/min/1.73 m² (as estimated by the simplified Modification of Diet in Renal Disease equation) at inclusion. Full eligibility criteria are listed in online supplementary Table Appendix S1.

The study protocol was reviewed and approved by the respective Institutional Review/Ethics boards.

Interventions and follow-up

Patients were assessed in the catheterization laboratory. Patients underwent simultaneous invasive catheter CVP measurement and non-invasive LSM assessment (Guided VCTE, FibroScan, Echosens, Paris, France),²⁸ first after 10 min in the supine position and subsequently after 10 min in the Trendelenburg position. All study participants underwent invasive CVP measurement as part of standard care. The procedure was performed in experienced centres, following recommended practices across participating sites, including zeroing at the mid-axillary line with patients positioned at 45°, in accordance with current clinical guidelines.

Liver stiffness was measured using VCTE with a FibroScan 430 Mini device (Echosens, Paris, France) equipped with the Guided VCTE feature, which demonstrates higher success rate, shorter examination times, and better performance in patients with a body mass index (BMI) >35 kg/m² compared to standard VCTE.²⁸

Operators were trained as recommended by the manufacturer. During the procedure (Figure 1), the operator positioned the tip of the FibroScan probe in an intercostal position in front of the right lobe of the liver with the aid of the embedded Guided VCTE indicators. A minimum of 10 valid measurements were required. The final liver stiffness value was the median of all valid measurements. Liver stiffness examinations with an interquartile range/median ratio below 30% were considered valid.²⁹ Operators performing LSM were blinded to CVP values.

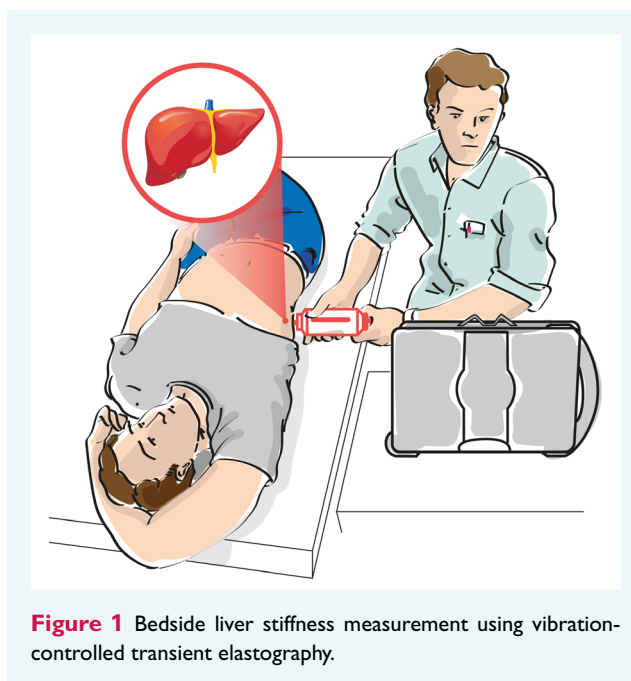


Figure 1 Bedside liver stiffness measurement using vibration-controlled transient elastography.

Liver stiffness measurement-derived CVP (CVP_{LSM}) was estimated using the previously validated model developed by Taniguchi et al.,²⁴ where CVP_{LSM} is calculated according to the following equation: $CVP_{LSM} = -5.9 + 6.8 \times \ln(LSM)$. In this model, LSM (expressed in kilopascals) is incorporated through its natural logarithm to account for the non-linear relationship between liver stiffness and CVP. This approach was selected based on its prior validation in patients with HF and aims to provide a non-invasive quantitative estimate of CVP.

Echocardiography and N-terminal pro-B-type natriuretic peptide (NT-proBNP) measurements were not systematically performed as part of the study. These measurements were performed at the local institutions, and the most recent values available in patient records were used, where available.

During a follow-up visit scheduled 6–8 days following the intervention, patients were assessed for the occurrence of any adverse events.

Endpoints

The primary endpoint was the agreement between CVP and LSM-derived CVP in the supine position.

Secondary efficacy endpoints included the agreement between CVP and LSM-derived CVP in the Trendelenburg (exploratory assessment), the correlation between CVP and LSM, the sensitivity and specificity of LSM to detect CVP elevations >10 mmHg,³⁰ factors associated with CVP elevation, and the relationships between LSM and inferior vena cava (IVC) diameter, LVEF and NT-proBNP level.

Safety endpoints were the occurrence of adverse events related to LSM and any serious adverse events from informed consent through the follow-up visit.

Statistical analysis

Continuous data were summarized by the mean, standard deviation (SD), median, interquartile range, minimum and maximum. Categorical data were shown as absolute and relative frequencies (numbers and percentages). Estimates and associated 95% confidence intervals (CI)

are presented. Unless stated otherwise, two-sided p -values of <0.05 were considered statistically significant. No adjustments to the significance level for multiple testing was made. Statistical tables, figures, and listings were produced using SAS release 9.1 or later (SAS Institute, Inc., Cary, NC, USA), R (R Core Team, 2020) or other validated statistical software.

The agreement between CVP and LSM-derived CVP was assessed using the Spearman's and Pearson's correlation coefficients, intraclass correlation coefficient and Bland–Altman plot.

Sensitivity and specificity were estimated using a receiver-operating characteristic (ROC) curve. Discrimination between elevated and non-elevated CVP was evaluated using the area under the ROC curve (AUC). The agreement between CVP and LSM was assessed using Spearman's rank correlation coefficient.

The sensitivity and specificity of LSM >10 kPa—a cut-off value proposed by Elkrief *et al.*¹⁸ in patients with chronic vascular diseases, and closely aligned with the 10.6 kPa threshold identified by Taniguchi *et al.*²⁴ in their seminal study on LSM-based CVP estimation—were calculated to assess its ability to detect clinically significant CVP elevation.

Factors associated with elevated LSM or elevated CVP were determined with Wilcoxon rank sum tests or Chi-square tests as appropriate. Agreements between NT-proBNP, echocardiography parameters and LSM were assessed with Spearman's rank correlation coefficients.

Results

Between 22 May and 14 November 2024, 39 patients were enrolled at five centres located in Poland ($n = 4$, 36 patients) and Romania ($n = 1$, 3 patients). One patient lacking a valid CVP measurement was excluded from the analysis. All liver stiffness examinations had an interquartile range/median ratio below 30%, and the applicability of VCTE was 100%. Among the 38 patients who completed the study, 34 (89.5%) were male and mean age was 63.8 years. Patient characteristics and their medical history are described in Table 1. Guideline-directed medical therapies were widely used across the cohort, with high rates of beta-blockers (94.7%), mineralocorticoid receptor antagonists (81.6%), and sodium–glucose cotransporter 2 inhibitors (86.8%). One patient had elevated alanine aminotransferase (≥ 50 U/L), and no patient had elevated aspartate aminotransferase (≥ 50 U/L).

Central venous pressure, LSM and echocardiographic results are summarized in Table 2. Patients in the supine position had a mean CVP of 8.39 ± 3.57 mmHg and a mean LSM of 11.18 ± 10.54 kPa. Most patients had reduced LVEF (median 24.5% [20.0–35.0%]).

Patients with LSM >10 kPa were younger ($p = 0.04$) but otherwise had similar clinical characteristics and treatment profiles compared to those with LSM ≤ 10 kPa (Table 1).

Primary endpoint: association of liver stiffness measurement-derived central venous pressure with central venous pressure in the supine position

A positive correlation was observed between invasively measured CVP and LSM-derived CVP calculated according to the Taniguchi *et al.*'s formula in the supine position (Figure 2). The Spearman

correlation coefficient was 0.53 (95% CI 0.25, 0.73), the Pearson correlation was 0.58 (95% CI 0.32, 0.76) and the intraclass correlation coefficient was 0.55 (95% CI 0.28, 0.74). The Bland–Altman plot showed a mean difference (measured CVP – LSM-derived CVP) of 0.11 mmHg (95% CI -1.31 , 1.54).

In a sensitivity analysis, the correlation between CVP and LSM-derived CVP remained consistent across obesity status, with a Pearson correlation of 0.52 in obese and 0.70 in non-obese patients (p for interaction = 0.43).

Evaluation in the Trendelenburg position

The correlation between CVP and LSM-derived CVP in the Trendelenburg position was assessed in the first 19 patients enrolled in the study. The Spearman correlation coefficient between invasively measured CVP and LSM-derived CVP calculated according to the Taniguchi *et al.*'s formula in the Trendelenburg position was 0.38 (95% CI -0.08 , 0.71). Due to difficulties in measuring CVP and LSM simultaneously in the Trendelenburg position, evaluations in this position were discontinued after the first 19 patients.

Association of liver stiffness measurement with central venous pressure in the supine position

A correlation between CVP and LSM in the supine position was observed, as indicated by a Spearman correlation coefficient of 0.53 (95% CI 0.25, 0.73) and a Pearson correlation coefficient of 0.55 (95% CI 0.29, 0.74) (Figure 3).

Liver stiffness measurement exhibited a good discriminatory ability for detecting clinically significant CVP elevation (CVP >10 mmHg), with an AUC of 0.83 (95% CI 0.66, 0.99) (Figure 4). According to Youden's index, the optimal LSM cut-off value for detecting an elevated CVP was 13.3 kPa, with a sensitivity of 0.73, a specificity of 0.93, a negative predictive value of 0.89, and a positive predictive value of 0.80. At the optimal threshold of 13.3 kPa, LSM accurately predicted CVP classification in 86.8% of patients, with 2 false positives, 3 false negatives, 8 true positives, and 25 true negatives.

The cut-off of LSM >10 kPa had a sensitivity of 0.73 and a specificity of 0.78 for detecting an elevated CVP. At the threshold of 10 kPa, LSM correctly classified 29 of 38 patients (76.3%), with 6 false positives, and 3 false negatives, 8 true positives, and 21 true negatives. Notably, among the six false positives, three patients had a CVP of exactly 10 mmHg.

Factors associated with elevated liver stiffness measurement and elevated central venous pressure

The following factors were significantly associated with LSM >10 kPa in univariable analysis: CVP, maximal IVC diameter, IVC collapsibility index, E/A ratio, left ventricular end-systolic diameter (LVESD), and LVEF (Table 3). In multivariable analysis, CVP (odds ratio 1.76 per 1 mmHg, 95% CI 1.24, 2.97), along with LVEF, remained independently associated with LSM >10 kPa.

Table 1 Patient characteristics and medical history

Patient characteristics	All patients (n = 38)	LSM >10 kPa (n = 14)	LSM ≤10 kPa (n = 24)	p-value
Age (years), median (Q1–Q3)	63.0 (59.0–71.0)	60.0 (55.5–64.2)	64.5 (62.0–74.8)	0.04
Age >65, n (%)	13 (34.2)	3/14 (21.4)	10/24 (41.7)	0.36
Male sex, n (%)	34 (89.5)	14/14 (100.0)	20/24 (83.3)	0.29
BMI (kg/m ²), median (Q1–Q3)	28.2 (26.1–32.3)	27.9 (26.4–30.5)	29.0 (26.0–32.5)	0.69
BMI <25, n (%)	8 (21)	3/14 (21.4)	5/24 (20.8)	0.52
BMI 25–30, n (%)	15 (39.5)	7/14 (50.0)	8/24 (33.3)	
BMI >30, n (%)	15 (39.5)	4/14 (28.6)	11/24 (45.8)	
NYHA class prior to screening, n (%)				0.57
I	1 (2.6)	0/14 (0)	1/24 (4.2)	
II	15 (39.5)	4/14 (28.6)	11/24 (45.8)	
III	17 (44.7)	8/14 (57.1)	9/24 (37.5)	
IV	5 (13.2)	2/14 (14.3)	3/24 (12.5)	
Pulmonary congestion at screening, n (%)	18 (47.4)	7/14 (50.0)	11/24 (45.8)	1
Medical history, n (%)				
Diabetes	15 (39.5)	6/14 (42.9)	9/24 (37.5)	1
Hypertension	27 (71.1)	10/14 (71.4)	17/24 (70.8)	1
Hypercholesterolaemia	30 (78.9)	10/14 (71.4)	20/24 (83.3)	0.65
Ischaemic heart disease	19 (50.0)	8/14 (57.1)	11/24 (45.8)	0.74
Atrial fibrillation	18 (47.4)	6/14 (42.9)	12/24 (50.0)	0.93
Pacemaker	2 (5.3)	1/14 (7.1)	1/24 (4.2)	1
Implantable cardioverter-defibrillator	13 (34.2)	4/14 (28.6)	9/24 (37.5)	0.84
Cardiac resynchronization therapy	3 (7.9)	0/14 (0)	3/24 (12.5)	0.45
Medication, n (%)				
ACEI/ARB	13 (34.2)	5 (35.7)	8 (33.3)	1
ARNi	18 (47.4)	5 (35.7)	13 (54.2)	0.45
Beta-blockers	36 (94.7)	14 (100)	22 (91.7)	0.72
MRA	31 (81.6)	11 (78.6)	20 (83.3)	1
SGLT2i	33 (86.8)	13 (92.9)	20 (83.3)	0.73
Loop diuretics	32 (84.2)	13 (92.9)	19 (79.2)	0.51
Laboratory findings at screening, median (Q1–Q3)				
Haemoglobin (g/dl)	13.87 (12.50–15.50)	13.9 (12.8–14.8)	13.4 (12.5–15.5)	0.68
Leucocyte count (10 ⁹ /L)	7.095 (5.800–8.050)	6.9 (5.3–7.7)	7.3 (5.9–8.4)	0.13
Sodium (mmol/L)	140.0 (138.0–141.0)	139.2 (137.2–140.8)	140.5 (138.8–141.5)	0.29
Potassium (mmol/L)	4.17 (3.80–4.50)	4.0 (3.8–4.3)	4.2 (3.9–4.5)	0.24
Creatinine (μmol/L)	99.010 (83.098–121.111)	114.8 (97.0–125.2)	96.4 (80.1–104.7)	0.12
Urea (mmol/L)	7.576 (5.994–10.490)	8.0 (5.3–10.5)	7.2 (6.8–9.8)	0.70
Aspartate aminotransferase (U/L)	27.8 (22.0–33.0)	32.0 (24.0–33.0)	26.4 (22.0–30.0)	0.31
Alanine aminotransferase (U/L)	27.0 (18.0–35.0)	22.0 (16.8–32.1)	27.5 (18.8–35.5)	0.41
Total bilirubin (μmol/L)	17.10 (13.68–27.37)	24.7 (15.1–34.9)	16.8 (12.1–19.6)	0.07
INR	1.20 (1.00–1.30)	1.2 (1.1–1.3)	1.1 (1.0–1.3)	0.28
Albumin (mmol/L)	0.572 (0.527–0.647)	0.6 (0.6–0.6)	0.6 (0.5–0.6)	0.95
eGFR (ml/min/1.73 m ²)	60.5 (51.0–79.0)	58.5 (53.5–65.8)	67.5 (50.5–84.5)	0.59
Laboratory findings available from patient's files	n = 27	n = 10	n = 17	
NT-proBNP (pg/ml), mean ± SD	5478.9 ± 5865.7	8053.9 ± 8051.5	3964.2 ± 3586.6	0.16
NT-proBNP (pg/ml), median (Q1–Q3)	3432.6 (1461.8–6740.2)	4518.5 (3072.5–10 543.0)	2277.5 (1199.9–6407.0)	0.16

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNi, angiotensin receptor–neprilysin inhibitor; BMI, body mass index; eGFR, estimated glomerular filtration rate; INR, international normalized ratio; LSM, liver stiffness measurement; MRA, mineralocorticoid receptor antagonist; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; Q, quartile; SD, standard deviation; SGLT2i, sodium–glucose cotransporter 2 inhibitor.

Liver stiffness measurement was the only variable significantly associated with CVP >10 mmHg in univariable analysis (Table 3).

Linear models

Liver stiffness measurement was also found to be correlated with maximal IVC diameter ($r = 0.61$, 22 patients) and LVEF ($r = -0.56$). The correlation with NT-proBNP ($r = 0.36$) was weaker. No correlation between LSM and BMI was observed, as indicated by a Spearman correlation coefficient of 0.00 (95% CI -0.32 , 0.32) and a Pearson correlation coefficient of -0.11 (95% CI -0.42 , 0.21).

In univariable linear regression, both LSM ($p = 0.0003$) and NT-proBNP ($p = 0.03$) were significantly associated with CVP, while other parameters such as IVC maximal diameter ($p = 0.06$)

and E/A ratio ($p = 0.07$) did not reach significance. In multivariable analysis, LSM remained independently associated with CVP (beta 0.19, 95% CI 0.09, 0.28; $p = 0.0003$), whereas NT-proBNP was not ($p = 0.12$).

Safety

No adverse events related to the measurement of LSM were reported during follow-up.

Discussion

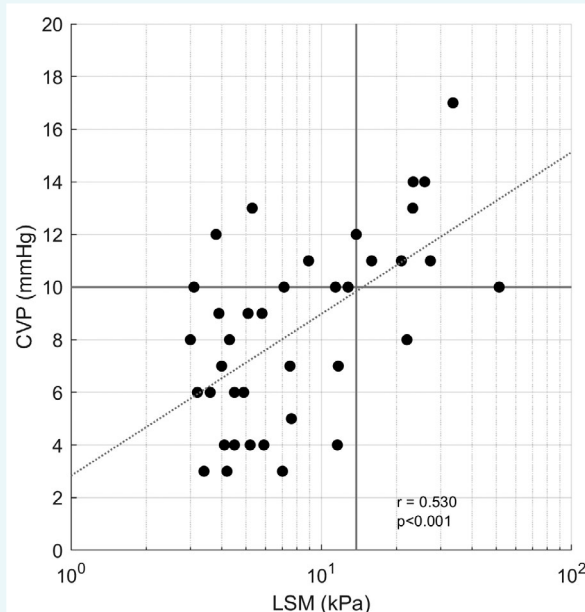
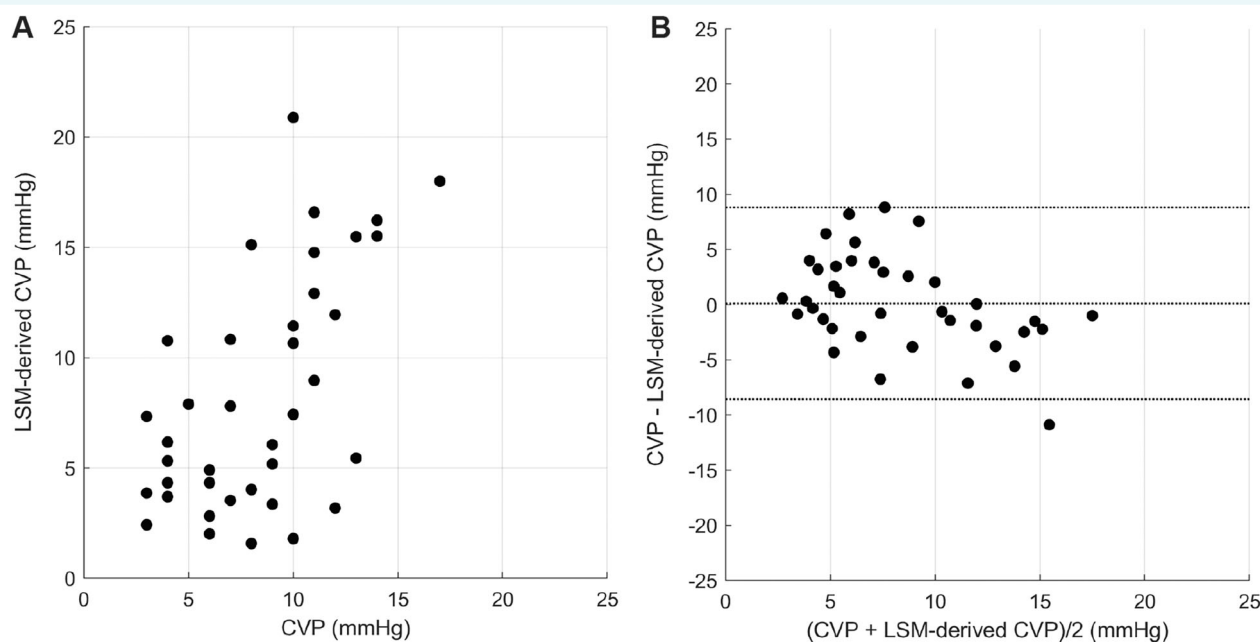
In this multicentre pilot study conducted in 38 patients with HF across five European centres—most of whom had HF with

Table 2 Central venous pressure, liver stiffness measurements and echocardiographic measurements

Central venous pressure (CVP)	
CVP (mmHg), mean $\pm$ SD	8.39 $\pm$ 3.57
CVP (mmHg), median (Q1–Q3)	8.50 (6.00–11.00)
Extremes (min–max)	3.0–17.0
CVP >10 mmHg, n (%)	11 (29)
Liver stiffness measurement (LSM)	
LSM (kPa), mean $\pm$ SD	11.2 $\pm$ 10.5
LSM (kPa), median (Q1–Q3)	6.4 (4.2–13.6)
Extremes (min–max)	3.1–51.4
LSM >10 kPa, n (%)	14 (37)
Echocardiography findings available from patient's files	
Most recent LVEF (%)	
Median (Q1–Q3)	24.5 (20.0–35.0)
Mean $\pm$ SD	29.4 $\pm$ 13.2
Most recent IVC diameter (mm), n = 22	
Median (Q1–Q3)	24.9 (21.3–27.2)
Mean $\pm$ SD	23.7 $\pm$ 5.1
Most recent IVC collapsibility, n = 22	
Median (Q1–Q3)	0.3 (0.1–0.5)
Mean $\pm$ SD	0.4 $\pm$ 0.3

IVC, inferior vena cava; LVEF, left ventricular ejection fraction; Q, quartile; SD, standard deviation.

reduced ejection fraction (HFrEF)—LSM-derived CVP was found to be significantly correlated with invasively measured CVP in the supine position, with excellent feasibility (no invalid measurements and consistently good measurement quality). LSM demonstrated good discriminatory ability for detecting clinically significant CVP

**Figure 3** Correlation between liver stiffness measurement (LSM) and invasively measured central venous pressure (CVP) in the supine position. Spearman's rank correlation coefficient: 0.53 (95% confidence interval 0.25, 0.73).**Figure 2** Agreement between central venous pressure (CVP) and liver stiffness measurement (LSM)-derived CVP according to the Taniguchi *et al.*'s formula. (A) Correlation between invasively measured CVP in the supine position and LSM-derived CVP (Taniguchi *et al.*'s formula): Spearman correlation coefficient: 0.53 (95% confidence interval [CI] 0.25, 0.73); intraclass correlation coefficient: 0.55 (95% CI 0.28, 0.74). (B) Bland–Altman plot: mean difference 0.11 mmHg (95% CI –1.31, 1.54); lower limit of agreement: –8.38 mmHg (95% CI –10.85, –5.92); upper limit of agreement: 8.61 mmHg (95% CI 6.14, 11.08).

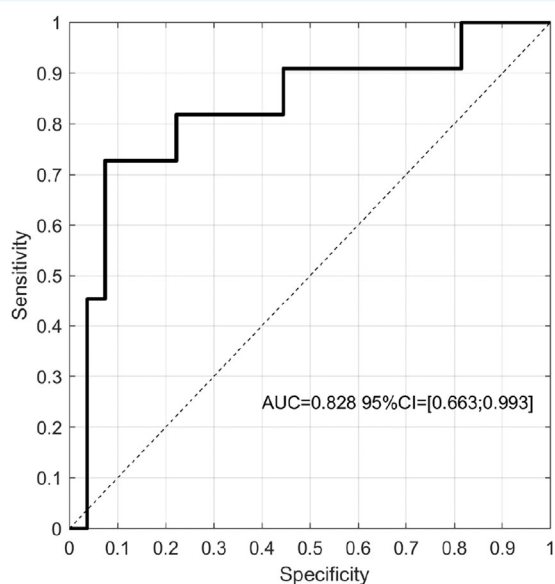


Figure 4 Discriminatory ability of liver stiffness measurement (LSM) for detecting clinically significant central venous pressure (CVP) elevation (CVP >10 mmHg). According to the Youden's index, the optimal LSM cut-off value for detecting an elevated CVP was 13.3 kPa, with a sensitivity of 0.73 and a specificity of 0.93.

elevation (>10 mmHg), with an AUC of 0.83. Using an LSM threshold of >10 kPa, CVP was correctly classified as above or below 10 mmHg in 76% of patients (Graphical Abstract). Our findings are consistent with previous clinical studies that explored the relationship between liver stiffness and CVP using VCTE,^{24–27} acoustic radiation force impulse imaging,^{31,32} and shear wave elastography.³³ They also confirm earlier experimental work with VCTE, notably by Millonig *et al.*,³⁴ who demonstrated that liver stiffness is directly influenced by CVP. This strong biological basis further supports the plausibility of using LSM as a non-invasive surrogate for CVP, given that hepatic congestion mechanically increases liver stiffness in a dynamic and reversible manner, closely reflecting CVP changes.

A moderate correlation ($r = 0.53$) was found between invasively measured CVP and LSM-derived CVP calculated according to the Taniguchi *et al.*'s formula. However, this correlation was notably weaker than that reported in the original study by Taniguchi *et al.*²⁴ ($r = 0.95$). This discrepancy was anticipated, as validation studies typically yield lower correlation coefficients than those observed in seminal, model-development cohorts. In addition, several factors may explain the difference, including the small sample sizes and differences in patient characteristics between the two studies. For instance, patients in our study had a mean BMI of 29.6 kg/m² and 39.5% had a BMI over 30 kg/m²; in contrast, patients in the test and validation groups of the study by Taniguchi *et al.*, had a mean BMI of 22.1 and 21.9 kg/m², respectively. This difference is particularly important, as obesity is known to pose

Table 3 Clinical and echocardiographic factors associated with liver stiffness measurement >10 kPa versus ≤10 kPa, and with central venous pressure >10 mmHg versus ≤10 mmHg

	N	LSM >10 kPa (n = 14)		LSM ≤10 kPa (n = 24)		p-value*
		Median (Q1–Q3) or n (%)	n	Median (Q1–Q3) or n (%)	n	
CVP (mmHg)	38	11 (10–12.8)	14	6.5 (4–9)	24	0.001
Mitral regurgitation	38	6 (42.9)	14	7 (29.2)	24	0.61
Tricuspid regurgitation	38	5 (35.7)	14	5 (20.8)	24	0.53
Maximal IVC diameter (mm)	22	27.3 (27–29.1)	11	22.3 (16.2–24)	11	0.001
IVC collapsibility index	22	0.2 (0.1–0.4)	11	0.6 (0.2–0.7)	11	0.03
E/A ratio	19	1.8 (1.6–2.8)	5	0.9 (0.8–1.1)	14	0.01
LVEDD (mm)	35	59.5 (51.8–65.5)	14	53 (38–59)	21	0.02
LVEF (%)	38	20.0 (18.2–22.8)	14	30.5 (24–41.2)	24	0.001
	N	CVP >10 mmHg (n = 11)		CVP ≤10 mmHg (n = 27)		p-value*
		Median (Q1–Q3) or n (%)	n	Median (Q1–Q3) or n (%)	n	
LSM (kPa)	38	20.9 (11.4–24.6)	11	5.1 (4–7.6)	27	0.002
Mitral regurgitation	38	5 (45.5)	11	8 (29.6)	27	0.58
Tricuspid regurgitation	38	5 (45.5)	11	5 (18.5)	27	0.19
Maximal IVC diameter (mm)	22	27.0 (23.4–28.0)	8	23.9 (19.1–26.8)	14	0.21
IVC collapsibility index	22	0.5 (0.2–0.6)	8	0.2 (0.1–0.5)	14	0.76
E/A ratio	19	1.3 (1.1–2.6)	3	0.9 (0.8–1.3)	16	0.18
LVEDD (mm)	35	56.0 (48.0–65.0)	11	55.5 (39.8–59.2)	24	0.43
LVEF (%)	38	22.0 (18.5–32.0)	11	27.0 (20.0–35.0)	27	0.36

CVP, central venous pressure; E/A, early (E) to late (A) ventricular filling velocity; IVC, inferior vena cava; LSM, liver stiffness measurement; LVEF, left ventricular ejection fraction; LVEDD, left ventricular end-systolic diameter; Q, quartile.

*Wilcoxon rank sum test or chi-square test.

technical challenges for LSM, potentially affecting measurement accuracy and reliability. Interestingly, LSM was not correlated with BMI, reinforcing its specificity for venous congestion rather than obesity-related hepatic stiffness—as observed in other contexts such as non-alcoholic steatohepatitis. Furthermore, a sensitivity analysis stratified by obesity status showed that LSM-derived CVP remained correlated with invasively measured CVP in both obese and non-obese patients, with no significant interaction. These findings support the potential generalizability of LSM as a non-invasive marker of CVP, regardless of BMI.

No meaningful correlation was observed between invasively measured CVP and LSM-derived CVP, calculated using the Taniguchi *et al.*'s formula, when patients were assessed in the Trendelenburg position. This finding may be explained by the high compliance of the hepatic vasculature, which can passively expel up to 50% of its blood volume in this position, thereby making LSM an unreliable surrogate for CVP measurement under these conditions.

The optimal LSM cut-off value identified based on the data from this study was 13.3 kPa, with a sensitivity of 0.73 and a specificity of 0.93. Using a cut-off value of 10.6 kPa, Taniguchi *et al.* found a sensitivity and specificity of 0.85 and 0.93, respectively.²⁴ For clinical simplicity, we propose an LSM threshold of >10 kPa, yielding a sensitivity of 0.73 and a specificity of 0.78 in our cohort. Using this cut-off, six patients were classified as false positives and three as false negatives; notably, three of the false positives had a CVP of exactly 10 mmHg, suggesting borderline cases. From a HF perspective, false positives could lead to unnecessary diuretic therapy, while false negatives might delay decongestive strategies. However, the majority of patients were correctly classified, reinforcing that LSM could serve as a useful adjunct to standard congestion assessment. In addition, in multivariable analysis, CVP remained independently associated with LSM, supporting its role as a primary driver of liver stiffness in this setting. Taken together, and considering the inherent limitations of existing non-invasive markers as well as the invasive nature of direct CVP measurement, LSM appears to be a promising complementary tool—although it should not be used in isolation and cannot be considered interchangeable with invasive CVP assessment.

A correlation between LSM and IVC diameter was observed, with a magnitude similar to that seen with CVP, whereas the correlation with NT-proBNP levels was weaker. These findings are of particular interest, as all these parameters can be obtained through non-invasive methods, unlike the invasive measurement of CVP. An advantage of LSM over blood biomarkers or echocardiographic parameters is its ability to be repeated very frequently, with immediate results obtained in less than 4 min, and with the procedure easily performed by a trained nurse, for example. Further studies with larger sample sizes are warranted to confirm these associations and to assess their potential applicability in clinical practice.

Vibration-controlled transient elastography is a promising tool for the assessment and monitoring of patients with suspected or confirmed HF, with three major advantages: (1) non-invasiveness, (2) reliability and standardization, and (3) ease of use (it can be performed by allied health professionals at the bedside without extensive training or specific ultrasound skills). Further research is

needed to investigate the role and clinical applications of liver stiffness assessment in the management of HF. Soloveva *et al.*³⁵ found significant correlations of changes in LSM with changes in clinical congestion and weight emphasizing that LSM reflects congestion in decompensated HF and could be used as a non-invasive method for quantification and monitoring of congestive hepatopathy.

Limitations

Despite the multicentre design, the study included a small number of patients, the majority of whom had reduced LVEF. It was a pilot study, and a validation study is planned very soon.

The proportion of patients with a CVP >10 mmHg was 29%, reflecting a relatively low prevalence of liver congestion.

The clinical indications for CVP measurement were not recorded, as procedures were performed at the discretion of the investigators. This limits the characterization of the clinical context.

Gamma-glutamyl transferase and alkaline phosphatase were not available, limiting full hepatic assessment. However, as only one patient had elevated alanine aminotransferase and none had elevated aspartate aminotransferase, no patient showed significant hepatocellular injury.

Moreover, our study did not include a systematic assessment of certain clinical or imaging markers of congestion—such as peripheral oedema, jugular venous distension, pulmonary artery systolic pressure, or the venous excess ultrasound (VExUS) score—which could have provided complementary insights into patients' volume status.

Echocardiography findings and natriuretic peptide levels were obtained retrospectively and were not available in all cases. Therefore, the comparison between the FibroScan and these non-invasive methods should be interpreted with caution.

Due to sample size constraints, we were only able to explore the impact of BMI on the association between LSM and CVP. Future studies with larger and more diverse populations should evaluate whether other patient characteristics, such as sex, LVEF, or HF aetiology, influence the accuracy and applicability of LSM for estimating CVP.

Lastly, we did not perform repeated LSM to monitor treatment efficacy. In patients with acute decompensated HF, inadequate decongestion on discharge is associated with increased morbidity and mortality.³⁶ Nevertheless, many patients are discharged with residual congestion due to the lack of an objective measurement of HF. At least four studies compared admission and discharge VCTE LSM in patients admitted for acute decompensated HF and found a significant decrease in LSM after diuresis.¹³ Many studies are ongoing to confirm and extend the findings of this pilot study, including investigations assessing the utility of LSM to monitor changes during decongestive therapy or to predict outcomes following acute decompensation. Future work should also focus on validating LSM in prospective cohorts, comparing or integrating it with echocardiographic parameters or VExUS-based congestion scores, and evaluating its performance in broader populations, including patients with preserved ejection fraction.

Conclusion

Liver stiffness measurement is a promising non-invasive surrogate for CVP in patients with HF, in a population mostly composed of HFrEF, and might provide a novel opportunity for bedside or remote assessment of vascular congestion/central vascular filling pressures. Future studies are warranted to validate these findings and to assess the role of LSM for the screening, diagnosis, monitoring, and prognostic stratification of HF patients.

Supplementary Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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