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HEPATOBILIARY

Liver stiffness obtained by ElastPQ ultrasound shear wave elastography independently determines mean right atrial pressure

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Abstract

Purpose We aimed to investigate the relationship between right atrial pressure (RAP) and liver stiffness (LS) determined by liver elastography (LE) during cardiac resynchronization therapy (CRT) in patients with heart failure (HF) and conventional pacemaker (PM) implantation in patients without HF.

Methods 60 patients with HF who underwent CRT and 60 patients without HF who underwent PM were enrolled. Routine echocardiography and laboratory examinations were performed. Systolic, diastolic, and mean RAP measurements were performed inversely during PM implantation and LS measurement with ElastPQ technique.

Results Systolic, diastolic, and mean RAP, left ventricular (LV) systolic-diastolic, right ventricular (RV) diastolic and left atrial diameters, tricuspid regurgitation pressure gradient, and RV-myocardial performance index (MPI) values were significantly higher in patients with HF ($p < 0.05$ each-one). LV ejection fraction and tricuspid annular plane systolic excursion values were significantly lower in patients with HF group ($p < 0.05$ each-one). LS values and inspiratory (Ins) and expiratory inferior vena cava (IVC) diameters were significantly higher in the patients with HF ($p < 0.05$ each-one). Mean RAP was found to be closely related to LS value, Ins-IVC diameter, RV-MPI, and NT-proBNP levels. LS value and Ins-IVC diameter were found to determine patients with mean RAP > 5 mmHg and > 10 mmHg. When the cut-off value of LS was taken as 7 kPa, it was found that the mean RAP > 10 mmHg with 89.6% sensitivity and 87.5% specificity.

Conclusions The non-invasive LS value determined by LE independently determines the mean RAP in patients with and without HF. According to our study results, > 7 kPa value for LS determined in liver US may be predictive for increased mean RAP.

Keywords Liver stiffness · Heart failure · Right atrial pressure

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Introduction

Anamnesis, physical examination, Postero-anterior chest X-ray, electrocardiography and natriuretic peptide (NT-proBNP), biochemical parameters, and echocardiography are used in the follow-up and treatment of heart failure with reduced ejection fraction (HFrEF) patients [1]. In a recent study, we also reported that liver stiffness (LS) value increases with the New York Heart Association (NYHA) class in patients with heart failure (HF) and therefore the LS value obtained by liver elastography (LE) can be used as follow-up parameters in patients with HF [2].

In HFrEF patients, right atrial pressure (RAP) is very important in evaluating volume status and diuretic therapy. Increased RAPs are directly responsible for congestive symptoms. Right heart evaluation is performed by echocardiographic examination in HF patients [1]. Invasive right atrial (RA), right ventricular (RV), and pulmonary artery pressure measurement are not routinely recommended. In advanced decompensated patients, invasive measurement parameters are used for volume status. In patients with HF, maximal tricuspid regurgitant jet and the tricuspid systolic gradient, breathing-related collapse, inferior vena cava (IVC) size, and RAP are considered subjectively [3].

When HFrEF physiopathology is considered, (i) Left ventricular (LV) end-diastolic pressure increases due to decreased LV ejection fraction (EF), (ii) followed by left atrial (LA) pressure increase, (iii) followed by pulmonary capillary wedge pressure (PCWP) increase, (iv) pulmonary artery pressure increases, (v) RV end-diastolic pressures from the right heart pressures and RAP increase, (vi) increased peripheral hepatic congestion increased jugular venous pressure (JVP) and pretibial edema due to increased RAP, and (vii) liver has a rigid fibrous or non-elastic capsule that cannot expand adequately and tissue stiffness increases due to congestive hepatomegaly (Fig. 1). This increased tissue stiffness can also be measured objectively with LE methods. In HF patients, congestive parameters: pretibial edema, hepatomegaly, hepato-jugular reflux, and JVP increase are subjective parameters that vary from person to person and over time. However, the LS value given by the average of ten measurements with LE is an objective parameter. It is totally associated with the measurement method and right-side filling pressures. In the light of this described physiopathology and our previous study, we thought that invasive RAPs might be closely related to LS measurement.

Therefore, in our study, we aimed to investigate the relationship between RAP and LS obtained by LE method during cardiac resynchronization therapy (CRT) in patients with HF and conventional pacemaker (PM) implantation in patients without HF.

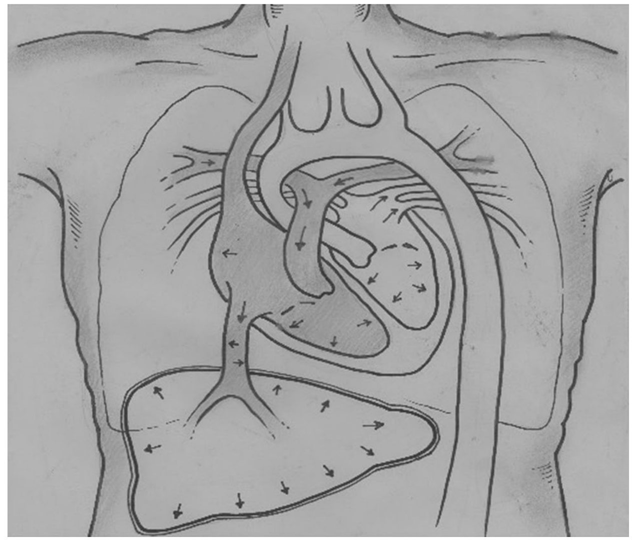

Fig. 1 When heart failure reduced ejection fraction physiopathology is considered, (i) LV diastolic end-pressure increases due to decreased LVEF, (ii) followed by LA pressure increase, (iii) followed by PCWP increase, (iv) pulmonary artery pressure increases, (v) RV diastolic end pressures from the right heart pressures and RA filling pressures increase, (vi) increased peripheral hepatic congestion increased JVP and pretibial edema due to increased RAP, and (vii) liver has a rigid fibrous or non-elastic capsule that cannot expand adequately and tissue stiffness increases due to congestive hepatomegaly

Methods

Study population

This prospective study included 60 patients (34 males, 26 females, mean age 59.2 ± 9.9 years) who were under medical treatment according to the NYHA class II-IV, and HFrEF (EF ≤ =40%), who applied to the cardiology clinic and who underwent CRT implantation and 60 controls (32 males, 28 females and mean age 58.0 ± 7.9 years) with a LVEF ≥ 50% planned for conventional PM implantation NYHA class I with symptomatic bradycardia similar to age and sex. Severe renal failure (eGFR < 30 ml/kg/1.73 m^2), history of known acute or chronic liver disease, presence of hepatitis B or C, regular alcohol use (> 20 g/day) or alcohol addiction, severe heart valve disease, portal hypertension (HT), inflammatory diseases, hematologic diseases, active thyroid disease, cancer and/or pregnancy suspicion, and patients who did not wish to be included in the study were excluded. The study was conducted according to the recommendations of the Human Subjects Biomedical Research Helsinki Declaration, and the institutional ethics committee approved the protocol. Voluntary consent forms were explained in detail, and all patients were included in the study after written informed consent was obtained. After all patients were included in the study, detailed history and physical examination were performed. Subsequently, basal demographic characteristics of all groups were questioned for age, gender, and ischemic etiology for HF, presence of HT, diabetes mellitus (DM), active smoking, hyperlipidemia, and coronary artery disease. Pulse rate, systolic blood pressure, and diastolic blood pressure were recorded. Body mass index (BMI) was calculated by measuring weight and height.

Biochemical parameters

Blood samples were taken in the supine position from an antecubital vein of the patients after rested for 20 min. Blood samples were collected in biochemical tubes containing ethylenediaminetetraacetic acid. Whole blood cell count was performed. The samples were centrifuged at 4000 rpm for 10 min at 0 °C. Blood urea nitrogen, creatinine, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and triglycerides were measured using automated laboratory methods (Abbott Aeroset, MN, USA) and using appropriate commercial kits (Abbott). Uric acid, hs-CRP, and NT-proBNP levels were also measured using an automated chemistry analyzer (Abbott Aeroset, MN, USA) with appropriate commercial kits (Abbott).

Echocardiographic evaluation

Echocardiography examinations were done with EPIQ 7 (Philips Healthcare Andover MA, USA). Images was taken according to the guidelines of the American Echocardiography Society when the patients were monitored and left-sided, a standard short and parasternal long axis was obtained, as well as apical 5, 4, and 2 chambers and at least three consecutive cycles [4]. Parasternal long axis M-mode examination revealed LV diastolic and systolic dimensions (LVd and LVs) and left atrial diastolic (LAd) dimension. The LVEF was calculated by the modified Simpson method from apical four and two chambers [5]. Tricuspid regurgitation pressure gradient (TRPG) was calculated by the Bernoulli equation over the peak flow rate of tricuspid regurgitation. RV diastolic diameter and tricuspid annular plane systolic excursion (TAPSE) was measured from a RV focused apical four-chamber view. RV isovolumic contraction time (ICT), isovolumic relaxation time (IRT), and ejection time (ET) were measured five times with pulse wave Doppler for RV-myocardial performance index measurement (MPI). RV-MPI was calculated with (ICT + IRT)/ET formulas after the mean values of five measurements were obtained [6].

Liver ultrasonography

All patients underwent liver ultrasound (US) screening using a high-resolution USG device (Philips EPIQ 7), using a 1–5 MHz high-resolution convex probe (Philips Health Care, Bothell, WA, USA). Inspiratory and expiratory IVC (Ins-IVC and Exp-IVC) diameters were measured by using US in hepatic long axis. The antero-posterior IVC diameters were calculated in long axis by placing the probe in the subxiphoid region. At least three Ins-IVC and Exp-IVC diameter measurements were taken and their average was calculated. ElastPQ technique is a point shear wave elastography (pSWE) assessment, which was used for LS measurements, while the patient is in lateral decubitus position. During hepatic US, least possible compression was applied with the probe, which was maintained in a constant position. During the procedure, subjects were asked to pause breathing for a few seconds to minimize hepatic movement occurring with respiration. First conventional hepatic US images were obtained, then the target area was determined, and the measurements were taken after the region of interest (ROI) was positioned on the target (Fig. 2a, b). Gray scale imaging was performed for finding an appropriate measurement area, and at least 1 cm depth of the liver capsule was measured. The ROI was placed perpendicular to the liver capsule. ROI was positioned perpendicular to an area containing no vascular structures and bile ducts or space occupying lesions. The maximum ROI target distance was 8 cm in our study, with a constant ROI box dimension of 1–0.5 cm. The compression during the imaging was maintained as low as possible, to avoid mechanical pressure on the liver. In each subject, ten valid measurements from different hepatic parenchymal segments were obtained and their average was calculated. Firstly, three measurements were taken from the intercostal space from different regions of the right upper hepatic lobe (segment VII-VIII). Subcostal approach was followed by three further measurements from the right lower hepatic lobe (segment V–VI). Then, four more measurements were taken from the left medial (segment IV) and the left lateral (segment II–III) hepatic lobe. During the LS measurements if there is a patient (cuff, breathing and cough etc.) or operator (overpressure, not holding the probe fixed) condition that affects the measurement value and when the measurement has low reliability, the measurement is accepted as 0.00 kPa and the mean measurement is not taken into account and a reliable measurement is obtained again. The results were expressed in terms of kPa. Subjects were stratified into two groups as those with or without LF, based on LS value. Subjects were evaluated by a two well experienced radiology specialists for conventional, Doppler, and SWE examinations. Specialists had more than 5 years of experience in SWE studies and at least 500 SWE procedures in a year. All USG examination time was approximately 25–30 min.

Right atrial pressure measurement

Patients with and without HFrEF were immediately enrolled in the electrophysiology laboratory for CRT or conventional

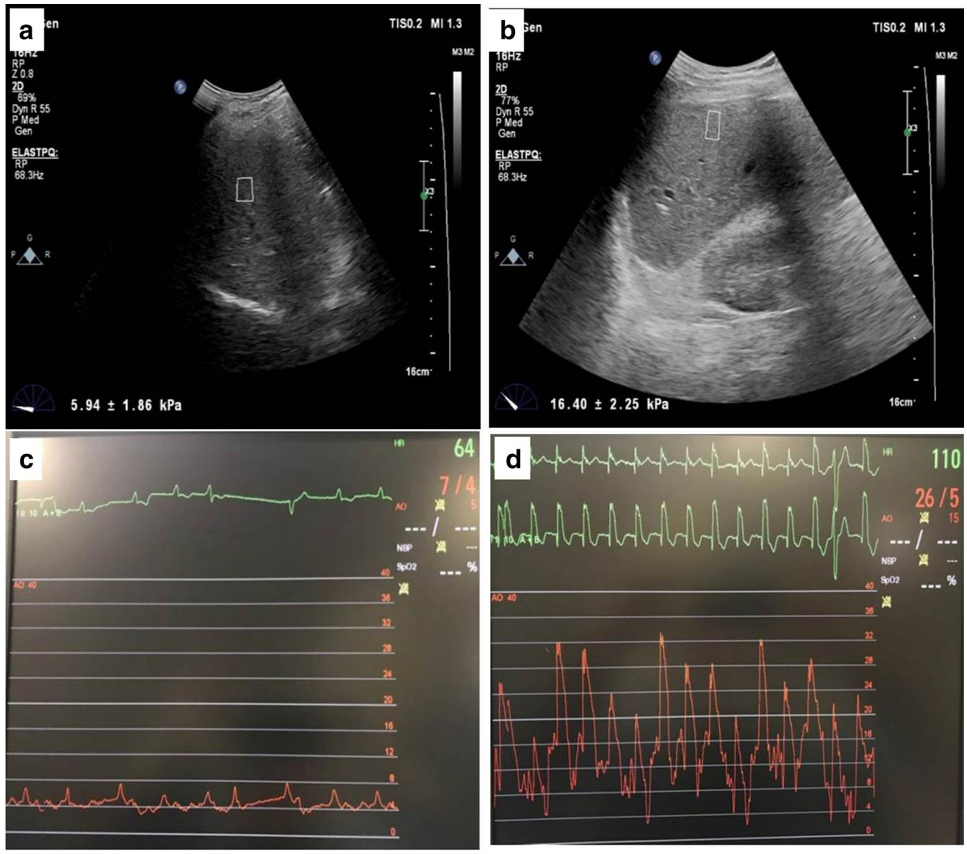

Fig. 2 **a** Liver stiffness measurement by liver elastography was 4.59 ± 0.92 kPa in the patient with heart failure reduced ejection fraction with (**c**) a mean right atrial pressure 5 mmHg. **b** Liver stiffness measurement by liver elastography was 16.40 ± 2.25 kPa in the patient with heart failure reduced ejection fraction with (**d**) a mean right atrial pressure 15 mmHg

PM immediately after measurement of LS by using abdominal US. Three left subclavian vein punctures were performed to the patients who were planned to undergo CRT implantation and two punctures for patients who were planned to undergo conventional PM implantation. After the puncture, Medtronic Attain Command Sheath (Mounds View USA) was released to RA. Before pressure measurement, long sheath was clarified in RA and free from contact with the wall. Then, systolic, diastolic, and mean pressure measurements were obtained (Fig. 2c, d). Pressure measurement was recorded two times from three different localizations of the upper, middle and lower regions of RA. Systolic, diastolic, and mean RAP were calculated by taking the average of six measurements.

Statistical analyses

For all analyses SPSS 20.0 statistical software pack (Chicago, IL, USA) was used. The variables were divided into groups: continuous and categorical. Kolmogorov–Smirnov test was used for normal distribution of the continuous variables. Continuous variables were expressed as mean ± standard deviation if they were normally distributed, but should be expressed as median (range) if not. Categorical variables were expressed as numbers and percentages. Continuous variables that showed normal distribution were compared using the Student t test, whereas the Mann–Whitney *U* test was used for samples without normal distribution. The Chi square (χ^2) test was used to compare categorical variables. The kappa coefficient was used to examine the interobserver, intraobserver variability of echocardiography, and ultrasound parameters. In univariate analyses, the parameters which were significantly different in patients with RA pressures were determined. Then a logistic regression analysis was performed to determine the independent markers among patients with mean RAP > 5 mmHg and > 10 mmHg showing differences. Parameters associated with mean RAP were determined with univariate Pearson's and Spearman's correlation analyses. Statistically significant parameters were included in a linear regression analysis, and the parameters having the closest association with the mean RAP were identified. A *p* level of < 0.05 was considered statistically significant.

Results

The mean RAP and LS measurements were successfully obtained from all patients with HF and control subjects included in the study. Cohen kappa values that evaluate interobserver and intraobserver variability were over 90% for all echocardiography parameters, and LS. The study data were compared and divided into two groups. The variables related to the mean RAP value were determined. In addition, the parameters that determined patients independently with mean RAP values > 5 mmHg and > 10 mmHg were determined.

Demographic, clinical and laboratory data

When compared with demographic data of patients with and without HF, it was found to be similar in age and sex. DM frequency and pulse rate were higher in patients with HF, and BMI was found to be lower in patients with HF. Other demographic and clinical parameters were similar (Table 1). Laboratory parameters blood urea nitrogen (BUN), creatinine, uric acid, NT-proBNP, and hs-CRP levels were found to be higher in patients with HF (Table 1). HDL cholesterol levels were lower in patients with HF (Table 1).

Right atrial pressure, liver ultrasonography, and echocardiography data

When the RA pressure measurements of the patients were examined, the systolic, diastolic, and mean RAP measurements were higher in patients with HF (Table 2). When the echocardiographic parameters of the patients were examined, the LVd, LVs, LAd, RVd, TRPG, and RV-MPI values were significantly higher in patients with HF than without HF group. (Table 2). LVEF and TAPSE values were significantly lower in patients with HF group. (Table 2). When the US findings were compared, it was found that the LS values and Ins-IVC, Exp-IVC diameters were significantly higher in patients with HF (Table 2).

Parameters related to mean right atrial pressure

In the Univariate analysis, demographic, clinical, laboratory, echocardiography, and USG parameters related to mean RAP were summarized in Table 3. A linear regression analysis was performed with these parameters that were significantly associated with mean RAP (Table 3). The mean RAP value was found to be closely correlated with LS value, Ins-IVC diameter, RV-MPI, and NT-proBNP levels, respectively (Table 3). Very close relationship between mean RAP, and LS value is shown in Fig. 3.

Table 1 The clinic, demographic, laboratory, and medical treatment findings according to patients with and without heart failure

Variable	Patients without HF $n = 60$	Patients with HF $n = 60$	p
Age (year)	58.0 ± 7.9	59.2 ± 9.9	0.490
Sex (male/female)	32/28	34/26	0.856
Hypertension, *n* (%)	30 (50%)	33 (55%)	0.715
Diabetes mellitus, *n* (%)	11 (18.3%)	30 (50%)	< 0.001
Current smoker, *n* (%)	22 (36.7%)	19 (31.7%)	0.701
Hyperlipidemia, *n* (%)	5 (8.3%)	7 (11.7%)	0.762
Coronary artery disease, *n* (%)	15 (25%)	20 (33%)	0.094
Systolic blood pressure (mmHg)	122 ± 15	120 ± 16	0.801
Diastolic blood pressure (mmHg)	75 ± 12	79 ± 13	0.744
Pulse (bpm)	75.8 ± 9.6	79.4 ± 10.1	0.048
Body mass index (kg/m^2)	28.4 ± 5.2	26.3 ± 5.4	0.027
Total cholesterol (mg/dL)	189 ± 47	177 ± 61	0.257
Low-density lipoprotein cholesterol (mg/dL)	128 ± 38	116 ± 42	0.136
High-density lipoprotein cholesterol (mg/dL)	41 ± 10	37 ± 15	0.049
Triglycerides (mg/dL)	197 ± 119	224 ± 158	0.301
Aspartate aminotransferase (u/L)	23.7 ± 8.2	28.0 ± 17.1	0.086
Alanine aminotransferase (u/L)	22.4 ± 12.9	24.3 ± 16.0	0.492
Blood urea nitrogen (mg/dL)	30.8 ± 9.4	46.6 ± 22.6	< 0.001
Creatinine (mg/dL)	0.79 ± 0.2	1.01 ± 0.3	< 0.001
Uric acid	5.52 ± 1.4	6.59 ± 2.2	0.002
High sensitive C reactive protein (mg/dL)	0.97 ± 1.7	2.35 ± 2.4	0.001
N-terminal pro-brain natriuretic peptide (pg/mL)	172 ± 176	3654 ± 3855	< 0.001

Table 2 Right atrial pressure measurement, liver ultrasound, and echocardiographic findings according to patients with and without heart failure

Variable	Patients without HF $n=60$	Patients with HF $n=60$	p
Right atrium systolic pressure (mmHg)	6.3 ± 1.8	14.4 ± 4.4	< 0.001
Right atrium diastolic pressure (mmHg)	3.8 ± 1.6	6.5 ± 3.1	< 0.001
Right atrium mean pressure (mmHg)	4.9 ± 1.5	10.1 ± 3.4	< 0.001
Left ventricular diastolic dimension (mm)	47.6 ± 5.1	62.6 ± 3.6	< 0.001
Left ventricular systolic dimension (mm)	31.2 ± 4.2	52.9 ± 4.3	< 0.001
Left ventricular ejection fraction (%)	60.3 ± 5.1	27.1 ± 5.2	< 0.001
Left atrium diastolic dimension (mm)	35.9 ± 4.1	42.6 ± 4.1	< 0.001
Right atrium diastolic dimension (mm)	35.8 ± 4.0	42.4 ± 4.2	< 0.001
Right ventricular diastolic dimension (mm)	30.1 ± 2.2	36.2 ± 4.4	< 0.001
Tricuspid annular plane systolic excursion (mm)	19.5 ± 1.9	15.3 ± 1.4	< 0.001
Tricuspid regurgitation pressure gradient (mmHg)	19.2 ± 3.3	37.1 ± 6.3	< 0.001
Right ventricular—myocardial performance index	0.29 ± 0.1	0.35 ± 0.1	< 0.001
Expiratory inferior vena cava diameter (mm)	9.3 ± 1.9	16.8 ± 4.8	< 0.001
Inspiratory inferior vena cava diameter (mm)	11.8 ± 2.0	18.2 ± 5.0	< 0.001
Liver stiffness (kPa)	4.24 ± 1.3	9.0 ± 3.5	< 0.001

Table 3 The parameters associated with right atrium mean pressure

	Univariate analyze		Multivariate analyze	
	p	r	p	β
Pulse (bpm)	0.004	0.258	0.159	0.073
Blood urea nitrogen (mg/dL)	< 0.001	0.367	0.771	0.016
Creatinine (mg/dL)	< 0.001	0.399	0.038	0.112
Uric acid	0.011	0.240	0.35	0.05
NT-proBNP (pg/mL)	< 0.001	0.424	0.309	0.061
LVd dimension (mm)	< 0.001	0.608	0.021	0.138
LVs dimension (mm)	< 0.001	0.665	0.004	0.174
LVEF (%)	< 0.001	− 0.684	0.002	− 0.190
LAd dimension (mm)	< 0.001	0.677	0.279	0.079
RVd dimension (mm)	< 0.001	0.739	0.288	0.098
TAPSE (mm)	< 0.001	− 0.719	0.013	− 0.198
TRPG (mmHg)	< 0.001	0.851	< 0.001	0.404
RV-MPI	< 0.001	0.852	0.002	0.343
Exp-IVC diameter (mm)	< 0.001	0.626	0.001	0.186
Ins-IVC diameter (mm)	< 0.001	0.662	< 0.001	0.245
Liver stiffness (kPa)	< 0.001	0.865	< 0.001	0.484

Exp-IVC expiratory inferior vena cava, *Ins-IVC* inspiratory inferior vena cava, *LVd* left ventricular diastolic, *LVEF* left ventricular ejection fraction, *LVs* left ventricular systolic, *NT-proBNP* N-terminal pro-brain natriuretic peptide, *RVd* right ventricular diastolic, *RV-MPI* Right ventricular—myocardial performance index, *TAPSE* tricuspid annular plane systolic excursion, *TRPG* tricuspid regurgitation pressure gradient, $R^2_{\text{Adjusted}} = 0.738$ in multivariate analyze

Parameters associated with slightly increased right atrial pressure (> 5 mmHg) and significantly increased right atrial pressure (> 10 mmHg)

Increased mean RAP was accepted as > 5 mmHg. In univariate analysis, demographic, clinical, laboratory, echocardiography, and USG parameters related to slightly elevated LS were evaluated by multivariate logistic regression analysis. LS value and Ins-IVC diameter was found to determine patients independently with mean RAP > 5 mmHg (Table 4). The same analyses were performed to determine patients with significantly increased mean RAP (> 10 mmHg). It was found that pulse rate, LS values, and Ins-IVC diameters independently determined patients with mean RAP > 10 mmHg (Table 4).

ROC analysis for liver stiffness measurement in the determination of a significantly increased right atrial pressure (> 10 mmHg)

In the ROC analysis of the LS values for the significantly elevated RAP detection, it was found that the area under the ROC curve for the LS value was 0.929 (0.874–0.984) and statistically significant ($p < 0.001$). When LS value was taken as 7 kPa, it was found that mean RAP was > 10 mmHg with 89.6% sensitivity and 87.5% specificity (Fig. 4). The area under the ROC curve for Ins-IVC diameter was 0.853 (0.771–0.935) and found to be statistically significant ($p < 0.001$). It was found that when the limit value of Ins-IVC diameter was taken as 14 mm, it was predicted to have mean RAP value > 10 mmHg with 85.4% sensitivity and 81.9% specificity (Fig. 4).

Fig. 3 Scatter plot diagram of the relationship of right atrial mean pressure with liver stiffness

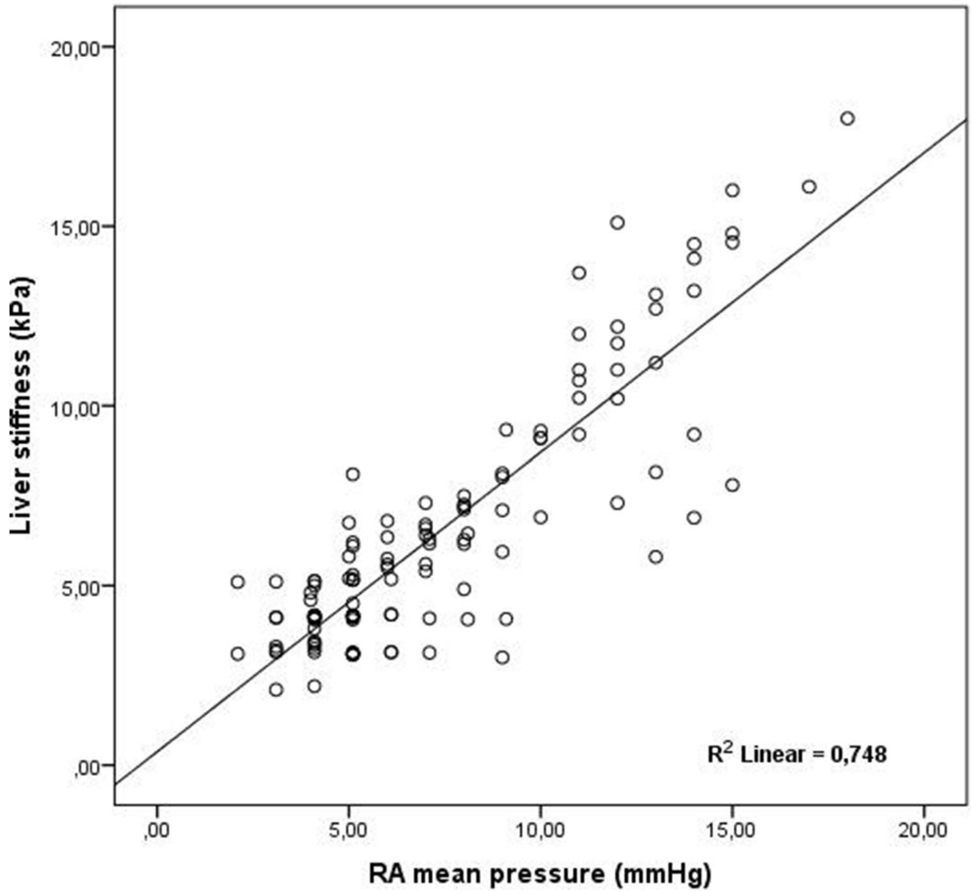

Table 4 Independent parameters for occurrence of mean right atrial pressure > 5 mmHg, and > 10 mmHg

	Odds ratio	95% confidence interval	*p*
Mean RAP > 5 mmHg			
Ins-IVC diameter (mm)	1.318	1.039–1.672	0.023
Liver stiffness (kPa)	3.286	1.702–6.343	< 0.001
Mean RAP > 10 mmHg			
Ins-IVC diameter (mm)	1.350	1.045–1.744	0.022
Liver stiffness (kPa)	5.088	2.184–11.853	< 0.001

Ins-IVC inspiratory inferior vena cava, *RAP* right atrial pressure

Discussion

The main finding of this study is that LS values in patients with HFrEF determine the mean RAP value better and independent than all other parameters. When taken as the limit value of > 7 kPa for LS, it determines patients with mean RAP > 10 mmHg in HFrEF patients with acceptable sensitivity and specificity. Due to this close relationship, LS measurement for monitoring in patients with HFrEF can be used as a new HF follow-up parameter.

Liver US is not used in the routine follow-up of patients with HF. Only in patients with HF associated liver diseases, liver US can be performed in the evaluation of abdominal symptoms and signs and for hepatosteatosis. The latest HF guideline recommends the measurement of IVC diameter in the US study for the assessment of volume status of the patients with a low level of evidence (Class IIb and Level C) [1]. There is no information on the LS measurement in the same guideline. LS measurement is mainly used in hepatology clinics and the LS value determined with LE is closely related to LF [7, 8]. In recent years, studies have also reported increased LS levels in HF patients [9–16]. As a result of these studies, it was thought that LS value could be used in the follow-up and treatment of patients. This important development has attracted our attention. Especially considering the pathophysiology of HFrEF (Fig. 1), right heart volume and pressures should be closely related to LS. At the same time, with the evolving technology of US devices and increased accessibility of LE examination, the LS measurement has been routinely applicable to all patients with HFrEF. Pretibial edema, hepatomegaly, and

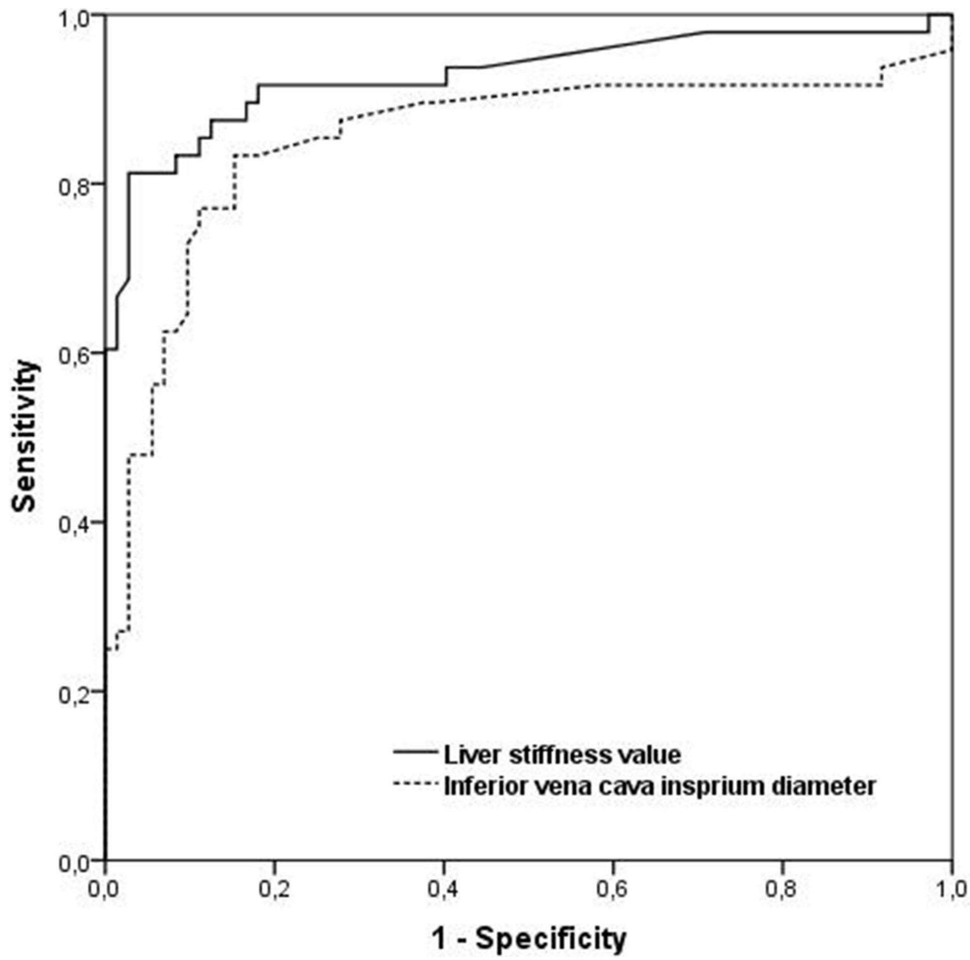

Fig. 4 ROC curve analysis to determine the predictive value of liver stiffness and inspiratory inferior vena cava diameter for right atrial mean pressure > 10 mmHg

increased JVP are the subjective parameters of the congestion parameters in patients with HF and vary from person to person and over time. For this reason, the LS value obtained by LE with at least ten different measurement means can be a new follow-up parameter which can objectively indicate the congestion state.

Non-invasive RAP detection will provide important information for follow-up and treatment of volume in patients with HF. In patients with HF, the objective relationship between the LS value and the invasively measured RAP was shown clearly in the study conducted by Taniguchi et al. [10] in 2014. In previous studies, the relationship between LS and RAP measured by echocardiography is shown. In another study, a similar finding was also demonstrated in patients with acute decompensated HF and decrease in LS value with medical treatment was shown [11]. In a study by Taniguchi T et al., mechanical transient elastography was used as LS examination technique. In this invasive study, the LS value obtained by mechanical transient elastography was compared with the right-sided filling pressure, and it was reported that it could be calculated by estimating right-sided filling pressure (mmHg) = − 5.8 + 6.1 × ln [LS (kPa)] [11]. We did not use this formula because different kPa values are obtained with new model devices. In addition, mechanical transient elastography device was used in this invasive study and the probability of successful measurement was reported to be 60%. [11]. In our study, high-resolution USG device and ElastPQ technique, which is one of the latest point SWE examination technology system was used. LS value was successfully obtained from all patients. Although there are different LE measurement methods, the most important features of the ElastPQ technique used in our study are the ease of use, the ability to take high rates of measurement, and the high strength in predicting liver pathology [17, 18]. The most important differences of our study from the study by Taniguchi et al. [11] are the RAP measurement technique and patient number included in the study. In the previous study, although patients with HF in different etiologies were evaluated, in our study, HFrEF patients with NYHA class II-IV with CRT indication were taken. In addition, NYHA class I control group were included so the findings have become more meaningful. In addition, RAP was measured in our study and RA was measured as anatomically clear in the catheter laboratory and therefore more clear RAP measurement was obtained than the previous study.

Different limit values have been taken in different studies related to increased mean RAP. To the best our knowledge mean RAP > 5 mmHg is known as increased RA pressure. Therefore, in our study, mean RAP > 5 mmHg was considered as slightly increased RA pressure and > 10 mmHg as significantly increased RA pressure [19]. In the literature, LS value has been reported to determine increased RAP (> 10 mmHg) [10, 11]. In echocardiography, RAP evaluation can be performed noninvasively during cardiac function evaluation. However, RAP evaluation predicted by IVC diameters and respiratory variation is semi-quantitative, and can be misleading in intermediate cases, especially RAP values of 5–10 mmHg [20]. In addition, patients with respiratory problems and tricuspid insufficiency are difficult to assess [20]. In the same study, when the LS limit value of 10.6 kPa was taken, it was found to be useful in determining the presence of RAP > 10 mmHg with 85% sensitivity and 93% specificity [10]. However, in this invasive study, patients with HF with all EF values were included. In our study, LS values were evaluated in the determination of patients with significantly increase RAP (> 10 mmHg). LS value, pulse rate, and Ins-IVC diameter was found to independently determine patients with RAP > 10 mmHg. When the cut-off value of LS was taken as 7 kPa, it was found that the mean RAP was > 10 mmHg with 89.6% sensitivity and 87.5% specificity.

In patients with HF, different limit values are given for increased LS due to different patient groups. LS limit value ≥ 7 kPa was taken in previous studies and the two recent studies [11, 12]. In another recent study on patients with HFrEF, patients with isolated HFrEF were taken for the first time and the ElastPQ method LS measurement was used. The mean and median LS values of all patients with HF included in the study were 7.77 ± 3.07 kPa and 7.20 kPa, respectively. [2]. In this study in which the patients with HFrEF underwent CRT implantation, when the ROC analysis was performed for the LS value in the determination of patients with increased mean RAP > 10 mmHg, LS cut-off value was determined as 7 kPa with the best sensitivity and specificity. This finding further clarified that in patients with HF, the value of > 7 kPa should be used for the increased LS value. In addition, every 1 kPa increase in LS value was found to increase the probability of mean RAP > 10 mmHg by 5.1 times.

Our study has some important limitations. First of all, we performed invasive RAP measurement in our study. This has been done due to a medical condition that should be considered in the RA with another indication. We did not include HFrEF patients with NYHA class I, so the relationship between LS and RAP in this group is unknown. All patients in our study were receiving optimal treatment according to their clinical status and NHYA class. Therefore, the effect of current therapy on LS was not evaluated. It has been shown that there is a decrease in LS with medical and surgical treatment especially in some diseases [21, 22]. Patients with renal and hepatic failure were excluded from the study. These two conditions are common in patients with HF, and our data cannot be used in this patient group. Since only patients with HFrEF were included and the ElastPQ technique was used, no comparison for limit value could be made with another study. In patients with HF, LS measurement is also a prognosis parameter with congestion [9, 11]. However, patients were not followed-up in terms of prognosis in our study. In previous studies, it is recommended to take measurements from the right hepatic lobes because the measurements of the left hepatic lobe are higher than the right hepatic lobe and also the measurements taken from the right lobe are related to liver fibrosis [23, 24]. However, our study is different from previous studies. We hypothesized that an increase in central venous pressure caused an increase in LS in patients with HF without liver pathology. The pathophysiology of this condition is different from all studies in the literature. For this reason, we took measurements from both right and left hepatic lobes. However, we did not evaluate whether there was any difference between the measurements taken from the right and left hepatic lobes. Whether the effect of central venous pressure increase on the right and left lobes is different can be another subject of study.

In conclusion, the non-invasive LS value of liver US determines the average mean RAP independently in patients with and without HF. LS measurement was thought to be a cheap, simple, and non-invasive follow-up parameter that could be used to adjust the volume status and the dose of diuretic therapy in the routine follow-up of patients with HF. According to previous studies and our study results, > 7 kPa value for LS determined in liver US may be predictive for increased mean RAP. However, it was concluded that the results obtained in our study should be strengthened by new studies involving multicentric patients, including larger and different patient groups.

Compliance with ethical standards

Conflict of interest There is no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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