Circulation Reports
Circ Rep 2022; 4: 166–172
doi:10.1253/circrep.CR-21-0155

ORIGINAL ARTICLE
Heart Failure

Gallbladder Wall Thickness-Based Assessment of Organ Congestion in Patients With Heart Failure

Takahiro Sakamoto, MD; Kazuhiko Uchida, MD, PhD; Akihiro Endo, MD, PhD; Hiroyuki Yoshitomi, MD, PhD; Kazuaki Tanabe, MD, PhD

Background: Diffuse gallbladder (GB) wall thickening is caused by elevated systemic venous pressure, such as heart failure (HF). This study investigated the relationship between GB wall thickness (WT) and HF, and the prognostic impact of GBWT.

Methods and Results: This prospective study included 116 patients with HF and 11 healthy controls. Among the 116 patients, 30 with GBWT measurements in the postprandial state or a history and/or signs of GB disease were excluded. The remaining 86 patients had significantly higher GBWT than the controls (median [interquartile range {IQR}] 2.0 [1.7–2.4] vs. 1.3 [1.1–1.6] mm, respectively; P<0.001). GBWT was significantly correlated with B-type natriuretic peptide (r=0.386, P<0.001), left atrial volume index (r=0.452, P<0.001), and tricuspid annular plane systolic excursion (r=–0.311, P=0.006). GBWT also exhibited a stepwise increasing relationship with increasing HF stage (Stage B, 22 patients, median [IQR] 1.8 [1.7–2.1] mm; Stage C, 60 patients, 2.0 [1.8–2.5] mm; and Stage D, 4 patients: 4.0 [3.5–4.5] mm). In Stage C or D HF patients, 11 hospitalizations for HF were observed over a median follow-up of 303 days (IQR 125–394 days). Furthermore, the rate of hospitalization events for HF was significantly higher in the high (≥3 mm) than low GBWT group (P=0.007).

Conclusions: GBWT can be used to assess organ congestion in patients with HF.

Key Words: Gallbladder wall; Heart failure; Organ congestion; Ultrasonography

In heart failure (HF) that occurs because of compensatory failure of cardiac pump function, blood flow remains upstream of the ventricles, consequently causing high filling pressure (i.e., congestion) and impairing organ function.[1] As a result, pulmonary congestion and pulmonary edema occur when the blood flow remains upstream of the left ventricle (left-sided HF) because of an increase in left atrial pressure; however, congestion of the organs in the abdominal cavity occurs when the blood flow remains upstream of the right ventricle (RV; right-sided HF). Left-sided HF is usually associated with high left ventricular (LV) filling pressure and has been well assessed using echocardiography as a non-invasive method.[2] In fact, increasing severity of diastolic dysfunction is associated with an increased risk of cardiovascular events and death.[3] Organ congestion due to right-sided HF is also a common manifestation, and its prognostic value has been well recognized and reported. Residual congestion commonly occurs despite providing adequate medical treatment, resulting in poor survival outcomes.[4] Organ congestion can now be evaluated using extracardiac ultrasound, which is considered a novel technique.[5] In particular, liver stiffness on elastography at admission and discharge has been found to reflect prognosis in patients with HF.[6,7]

In addition to the conditions mentioned above, diffuse gallbladder (GB) wall thickening has been found to be related to conditions with elevated portal or systemic venous pressures, such as cirrhosis and HF.[8] Although the thickness of the GB wall depends on the degree of GB distention, 3 mm is regarded as the upper limit of normal.[9] Given these findings, we hypothesized that GB wall thickness could be an indicator of congestion and the severity of HF. The aim of this study was to identify the relationships between GB wall thickness and HF, demonstrating the prognostic impact of GB wall thickness in patients with HF.

Methods

Patients and Protocol

This prospective study included 116 patients with pre-HF or HF and 11 healthy controls. The study was conducted at Masuda Red Cross Hospital between July 2018 and

Received December 9, 2021; accepted December 10, 2021; J-STAGE Advance Publication released online January 6, 2022 Time for primary review: 1 day

Division of Cardiology, Shimane University Faculty of Medicine, Izumo (T.S., A.E., K.T.); Division of Cardiology, Masuda Red Cross Hospital, Masuda (T.S., K.U.); and Department of Clinical Laboratory, Shimane University Hospital, Izumo (H.Y.), Japan

K.T. is a member of *Circulation Reports*' Editorial Team.

Mailing address: Takahiro Sakamoto, MD, Division of Cardiology, Shimane University Faculty of Medicine, 89-1 Enya-cho, Izumo 693-8501, Japan. E-mail: t.saka@med.shimane-u.ac.jp

ISSN-2434-0790

Table 1. Grading Scale for Investigator-Assessed Signs and Symptoms of Congestion

Signs/symptoms	Scale			
	0	1	2	3
Dyspnea	None	Seldom	Frequent	Continuous
Orthopnea	None	Seldom	Frequent	Continuous
Fatigue	None	Seldom	Frequent	Continuous
JVD (cmH_2O)	≤6	6–9	10–15	≥15
Rales	None	Bases	<50%	>50%
Edema	Absent/trace	Slight	Moderate	Marked

JVD, jugular venous distention.

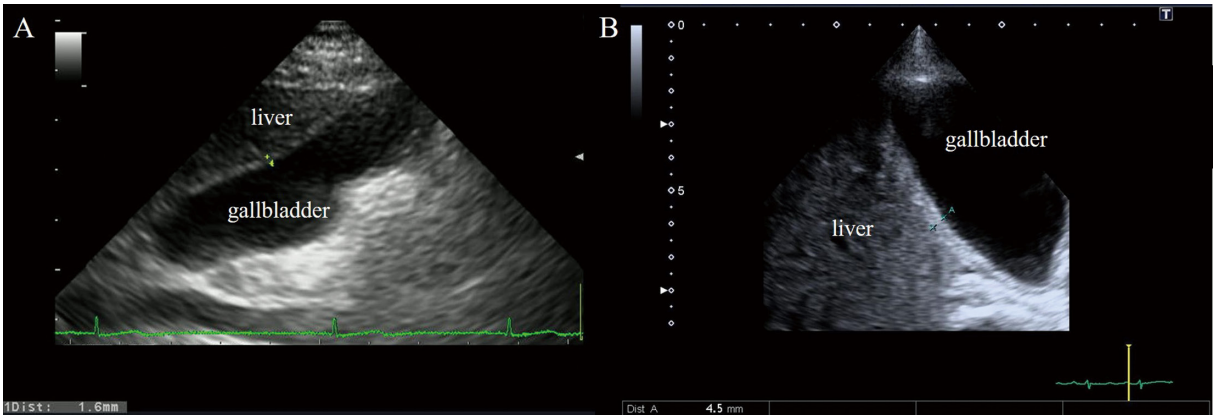

Figure 1. Gallbladder wall thickness measured using a sector scan in a patient in the supine position after echocardiography. Measurements of the (**A**) normal gallbladder wall and (**B**) diffuse gallbladder wall thickening are noted.

June 2019. HF was defined as a clinical syndrome of signs and/or symptoms caused by a structural and/or functional cardiac abnormality, which is corroborated by elevated natriuretic peptide levels and/or objective evidence of pulmonary or systemic congestion.[10] Pre-HF (Stage B) was diagnosed in patients without current or prior signs and/or symptoms of HF but with evidence of structural heart disease, abnormal cardiac function, or elevated natriuretic peptide levels. HF (Stage C) was diagnosed in patients with current or prior signs and/or symptoms of HF caused by a structural and/or functional cardiac abnormality. Advanced HF (Stage D) was diagnosed in patients based on the following characteristics: (1) severe signs and/or symptoms of HF at rest; (2) recurrent hospitalizations despite guideline-directed management; (3) refractory to or intolerant of guideline-directed management; and (4) requiring advanced therapies, such as consideration for transplant, mechanical circulatory support, or palliative care. Among the 116 HF patients, 30 with GB wall thickness measurements in the postprandial state, a history and/or signs of GB disease on ultrasonography, or acute decompensated HF were excluded. The patients included in this study were outpatients who were in a stable condition or inpatients at the time of discharge. None of the patients included in this study had a history or signs of liver disease, a previous diagnosis of chronic liver disease, hepatic ultrasound data indicating liver surface nodularity (a sign of severe fibrosis or ascites), anti-hepatitis C antibody positivity, or hepatitis B surface antigen reactivity. The healthy controls had no history or signs of cardiac, liver, or GB disease.

GB wall thickness was compared between the 11 healthy controls and the 86 patients with pre-HF or HF. The relationships between GB wall thickness, measured by ultrasound, and clinical characteristics (echocardiography, laboratory tests, and composite congestion score [CCS]) were investigated in the 86 patients with pre-HF or HF (Stage B, 22 patients; Stage C, 60 patients; and Stage D, 4 patients). The CCS was calculated by summing the individual scores (**Table 1**).[4] All data were collected on the same day, and GB wall thickness was compared among patients with Stage B, C, and D HF. Furthermore, 64 patients with Stage C or D HF were followed up for hospitalization for HF from the date of GB wall thickness measurement until August 2019.

The study protocol conformed to the principles outlined in the Declaration of Helsinki and was approved by the Masuda Red Cross Hospital Ethics Committee (Approval no. 49). Informed consent was obtained from all participants prior to their inclusion in the study.

Ultrasonography for GB Wall Thickness, Laboratory Tests, and Echocardiography

Ultrasonography allows direct visualization of the GB wall due to its superficial location.[11] Moreover, it has been reported to be an accurate modality for the measurement of GB wall thickness.[12] Usually, the GB wall presents with

Table 2. Baseline Characteristics of Participants

	HF (n=86)	Control (n=11)
Age (years)	75 [66–84]	71 [67–71.5]
Male sex	55 (64)	6 (56)
Body mass index (kg/m²)	22 [20–24]	23 [20–24]
SBP (mmHg)	116 [101–137]	–
Heart rate (beats/min)	72 [63–79]	–
NYHA Class I/II/III/IV (n)	56/19/7/4	–
HF Stage A/B/C/D (n)	0/22/60/4	
Medical history		
Hypertension	64 (74)	–
Diabetes	23 (27)	–
Dyslipidemia	40 (47)	–
Chronic kidney disease	43 (50)	–
Atrial fibrillation	32 (37)	–
HF etiology		
Ischemia	19 (22)	–
Valvular heart disease	14 (16)	–
Cardiomyopathy	30 (35)	–
Hypertension	12 (14)	–
Others	11 (13)	–
Medications		
ACEI or ARB	57 (66)	–
β-blocker	50 (58)	–
Mineral corticoid receptor antagonists	30 (35)	–
Diuretics	47 (55)	–

Unless indicated otherwise, values are presented as the median [interquartile range] or n (%). ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; HF, heart failure; NYHA, New York Heart Association; SBP, systolic blood pressure.

Table 3. Laboratory Data, Echocardiography Findings, and Composite Congestion Score in Heart Failure Patients (n=86)

Laboratory data	
Hemoglobin (g/dL)	12 [11–14]
Platelet (×10³/μL)	21 [18–25]
T-Bil (mg/dL)	0.7 [0.5–0.9]
AST (U/L)	22 [19–27]
ALT (U/L)	18 [13–26]
γ-GTP (U/L)	26 [18–53.5]
ALP (U/L)	231 [192–293]
eGFR (mL/min/1.73 m²)	45 [29–67]
Sodium (mEq/L)	140 [138–143]
BNP (pg/mL)	182 [77–421]
Echocardiography	
LVEDV (mL)	76 [59–102]
LVSDV (mL)	32.5 [26–56.75]
LVEF (%)	52 [38–62]
LAVI (mL/m²)	40 [30–52]
E/A	0.8 [0.7–1.3]
E/e'	12 [9–16]
LVOT-VTI (cm)	17 [13–22]
TRPG (mmHg)	23 [18.5–28.5]
Maximum IVC diameter (mm)	13 [11–16]
TAPSE (mm)	17 [14–20]
Pulsed Doppler S wave (cm/s)	10 [8.5–12]
RVFAC (%)	36 [28–44]
MR III/IV	5 (6)
TR III/IV	11 (13)
CCS	0 [0–1]

Values are expressed as the median [interquartile range] or n (%). A, late transmitral flow velocity; ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BNP, B-type natriuretic peptide; CCS, composite congestion score; E, early transmitral flow velocity; E/e', ratio of peak mitral E wave velocity to peak early diastolic myocardial velocity at septal and lateral position recorded using tissue Doppler imaging; eGFR, estimated glomerular filtration rate; γ-GTP, γ-glutamyl transpeptidase; IVC, inferior vena cava; LAVI, left atrial volume index; LVEDV, left ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume; LVEF, left ventricular ejection fraction; LVOT-VTI, left ventricular outflow tract-velocity time integral; MR, mitral regurgitation; RVFAC, right ventricular fractional area change; TAPSE, tricuspid annular plane systolic excursion; T-Bil, total bilirubin; TR, tricuspid regurgitation; TRPG, tricuspid regurgitation peak gradient.

1 hyperechogenic layer, or with an inner hypoechogenic layer and an outer hyperechogenic layer. A normal GB wall on ultrasonography appears as a thin echogenic rim ≤3 mm in size. Important differentials for GB wall thickening include cholecystitis, adenomyomatosis, and wall thickening due to GB carcinoma.[8] To avoid these confounders, patients with a history and/or signs of GB disease were excluded from this study.

In this study, sonographers experienced in measuring GB wall thickness measured the GB using a sector scan in patients in the supine position after echocardiography (**Figure 1**). All GB ultrasound examinations were conducted on an adequately distended GB on fasting because pseudo-thickening due to physiologic contraction can occur in the postprandial state.[13,14]

On the same day as the GB wall thickness measurement, on-site laboratory tests were performed, including routine tests, such as liver function tests and measurement of B-type natriuretic peptide (BNP) concentrations. Echocardiography was also performed by experienced sonographers who were blinded to all other data, as per the recommendations of the American Society of Echocardiography and the European Association of Cardiovascular Imaging.[15] The LV ejection fraction (LVEF) was calculated from the apical 4- and 2-chamber views using the biplane method of disks. Similarly, left atrial volume was measured from standard apical 2- and 4-chamber views at end-systole. The left atrial volume index (LAVI) was calculated by dividing the left atrial volume by body surface area. Peak early (E) and late (A) diastolic velocities were measured from transmitral flow velocity curves, whereas early diastolic (e') myocardial velocities were obtained from tissue Doppler imaging of the mitral annulus at the septal position. Furthermore, the LV outflow tract velocity time integral was calculated by placing the pulsed Doppler sample volume in the outflow tract below the aortic valve and recording the velocity. From the subcostal view, the diameter of the inferior vena cava (IVC) was measured within 3 cm of the right atrium–IVC junction during passive respiration. Moreover, the tricuspid annular plane systolic excursion (TAPSE), pulsed Doppler S wave, and RV fractional area change (RVFAC) were measured from an RV-focused apical 4-chamber view. Mitral regurgitation and tricuspid regurgitation (TR)

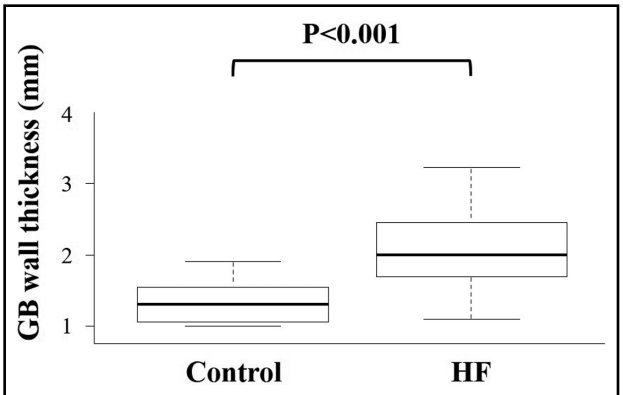

Figure 2. Gallbladder (GB) wall thickness in the control and heart failure (HF) groups. The boxes show the interquartile range, with the median value indicated by the horizontal line; whiskers show the range.

were graded using a 4-point scale based on color-flow Doppler images.

Statistical Analysis

Continuous variables are expressed as the median with interquartile range (IQR), and were compared using the Mann-Whitney test. Categorical variables are expressed as numbers and percentages of patients. Relationships between GB wall thickness and other variables were assessed by Spearman's rank correlation analyses, and event-free survival was estimated using the Kaplan-Meier method, wherein group differences were compared by the log-rank test. For assessment of intra- and interobserver reliability of measurement of GB wall thickness, intraclass correlation coefficients (ICCs) were computed.

All statistical analyses were performed using SPSS for Windows version 23.0 (SPSS Inc., Chicago, IL, USA) and EZR version 1.54 (Saitama Medical Centre, Jichi Medical University, Saitama, Japan), a graphical user interface for R version 4.0.3 (R Foundation for Statistical Computing, Vienna, Austria).[16] Two-sided P≤0.05 was considered statistically significant.

Results

Baseline Characteristics

Participants' baseline characteristics are presented in **Table 2**. Laboratory data, echocardiography findings, and CCS are summarized in **Table 3**. Age, sex, and body mass index were comparable between the HF and control groups. Sodium-glucose cotransporter 2 inhibitors, angiotensin receptor-neprilysin inhibitors, and ivabradine were not approved for use in Japan during the study period.

GB Wall Thickness in Patients With HF

GB wall thickness was significantly higher in the HF than control group (2.0 [1.7–2.4] vs. 1.3 [1.1–1.6] mm, respectively; P<0.001; **Figure 2**). The ICC for intraobserver variability for Observers 1 and 2 was 0.993 (95% confidence interval [CI] 0.976–0.998) and 0.990 (95% CI 0.961–0.999), respectively. The ICC for interobserver variability was 0.988 (95% CI 0.952–0.997). GB wall thickness among HF patients was significantly correlated with alkaline phosphatase concentrations (r=0.325, P=0.004), BNP concentrations (r=0.386, P<0.001), LAVI (r=0.452, P<0.001), the E/A ratio (r=0.337, P=0.009), the TR peak gradient (TRPG; r=0.280, P=0.013), maximum IVC diameter (r=0.243, P=0.025), TAPSE (r=−0.311, P=0.006), and pulsed Doppler S wave (r=−0.308, P=0.008; **Table 4**). GB wall thickness was correlated with increasing HF stage (Stage B: 1.8 [1.7–2.1] mm; Stage C: 2.0 [1.8–2.5] mm; and Stage D: 4.0 [3.5–4.5] mm) and BNP tertiles (first tertile [BNP ≤99 pg/mL]: 2.0 [1.7–2.1] mm; second tertile [99 pg/mL < BNP ≤ 340 pg/mL]: 2.0 [1.6–2.5] mm; and third tertile [340 pg/mL < BNP]: 2.4 [2.0–3.3] mm; **Figure 3A**,**B**). The GB wall thickness of patients with ≥2 hospitalizations in 1 year was significantly greater than that of patients with no hospitalizations (P=0.013; **Figure 3C**).

Table 4. Relationship Between Gallbladder Wall Thickness and Clinical Characteristics

	GB wall thickness	
	R	P value
Laboratory data		
Hemoglobin	−0.133	0.227
Platelet	0.055	0.622
T-Bil	0.034	0.765
AST	−0.029	0.799
ALT	0.054	0.626
γ-GTP	0.162	0.144
ALP	0.325	0.004
eGFR	−0.148	0.280
Sodium	−0.068	0.540
BNP	0.386	<0.001
Echocardiography		
LVEDV	0.048	0.662
LVESV	0.130	0.232
LVEF	−0.192	0.077
LAVI	0.452	<0.001
E/A	0.337	0.009
E/e'	0.179	0.128
LVOT-VTI	−0.021	0.876
TRPG	0.280	0.013
Maximum IVC diameter	0.243	0.025
TAPSE	−0.311	0.006
Pulsed Doppler S wave	−0.308	0.008
RVFAC	−0.149	0.235
CCS	0.202	0.063

Abbreviations as in Table 3.

GB Wall Thickness and Clinical Outcomes

During a median follow-up of 303 days (IQR 125–394 days), there were 11 hospitalizations for HF. Upon dividing 64 patients with Stage C or D HF into 2 groups, based on 3 mm as the upper limit of normal GB wall thickness, Kaplan-Meier analysis showed that the group with high GB wall thickness (≥3 mm) had a significantly higher incidence of hospitalization events for HF (P=0.007, log-rank test; **Figure 4**).

Discussion

In this study, GB wall thickness on ultrasonography could be used as an indicator of organ congestion in patients

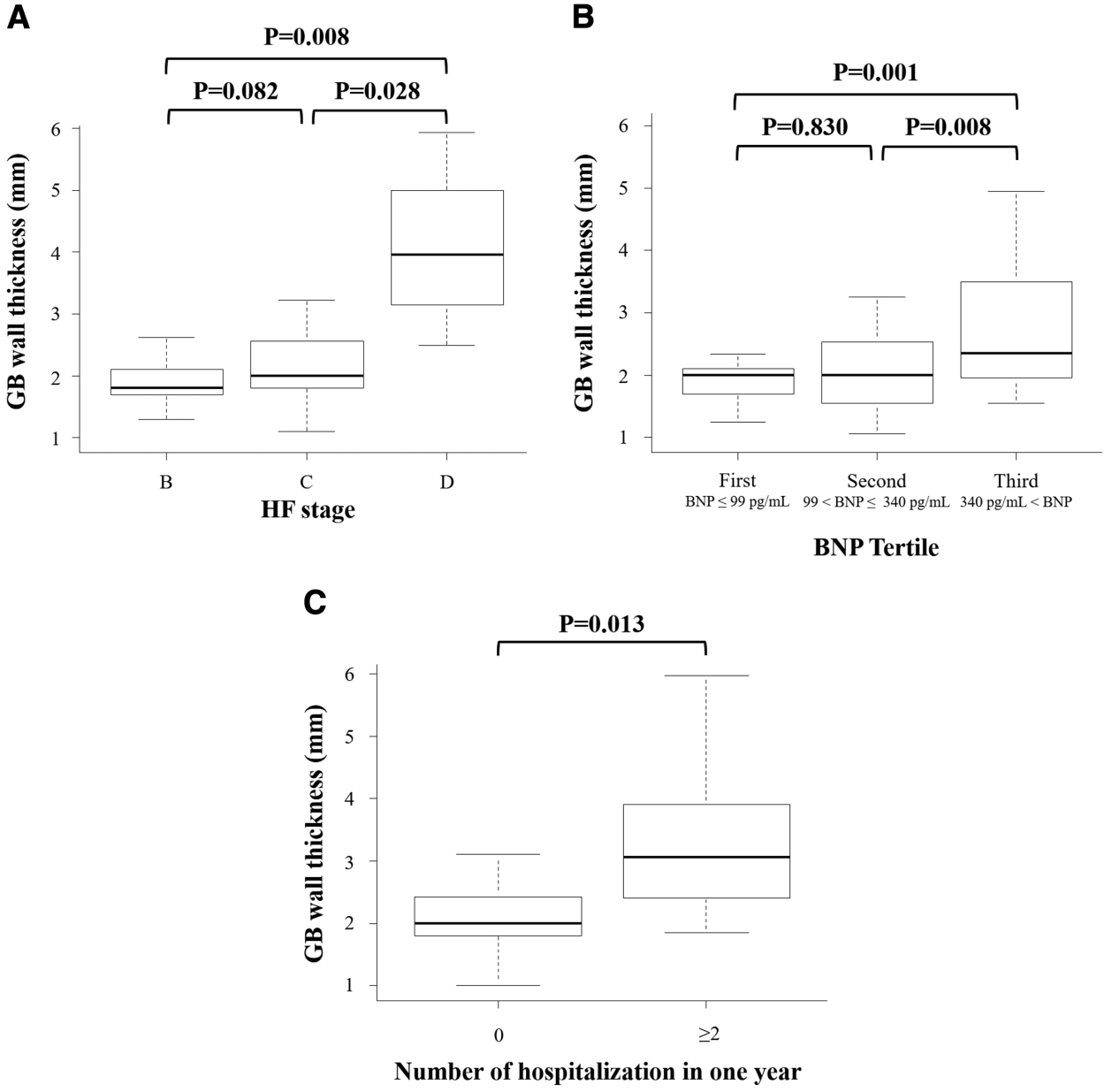

Figure 3. (**A**,**B**) Gallbladder (GB) wall thickness according to heart failure (HF) stage (**A**) and B-type natriuretic peptide (BNP) tertiles (**B**). (**C**) GB wall thickness in patients with no hospitalizations and those with ≥2 hospitalizations in 1 year. The boxes show the interquartile range, with the median value indicated by the horizontal line; whiskers show the range.

with HF. This study has 4 major findings: (1) GB wall thickness was significantly greater in the HF than control group; (2) BNP, maximum IVC diameter, TRPG, TAPSE, and pulsed Doppler S wave, which is used as a marker for organ congestion and assessment of RV systolic function on echocardiography, were significantly correlated with GB wall thickness in patients with HF; (3) GB wall thickness was positively correlated with HF stage; and (4) the group with high GB wall thickness (≥3 mm) had a significantly higher incidence of hospitalization events for HF. To the best of our knowledge, this is the first clinical study to measure GB wall thickness and investigate its relationship with the cardiovascular system of patients with HF.

Edema of the GB Wall

The GB is a hollow, pear-shaped viscus with thin and regular walls located in the GB fossa between liver segments IV and V, an area devoid of visceral peritoneum.[17] The GB is divided into the infundibulum, body, and fundus, and its walls comprises 4 layers: (1) a mucosa formed by simple columnar epithelium and basal lamina; (2) a second layer comprising irregular muscular tissue; (3) a third layer constituted by loose connective tissue; and (4) a final layer formed by the serosa.[16] Although the exact

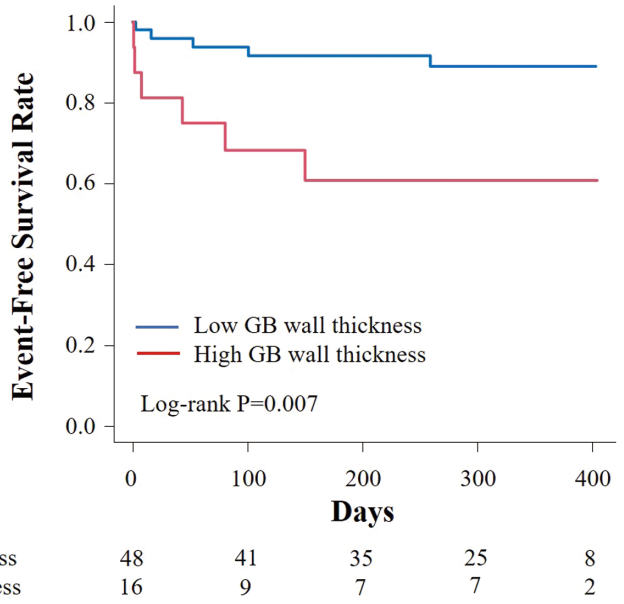

Figure 4. Kaplan-Meier plot of event-free (hospitalization for heart failure) survival in patients in high (≥3 mm) and low gallbladder (GB) wall thickness.

pathophysiological mechanism underlying edema of the GB wall remains uncertain, it is considered secondary to elevated portal venous pressure, elevated systemic venous pressure, decreased intravascular osmotic pressure, or a combination of these factors. In fact, determining edema in the second layer of the GB wall has been associated with the preservation of the hyperechogenic appearance of the mucosa.[8,17] On echography, edema of the GB wall can be visualized as thickening of the wall. Because echocardiographic findings for edema of the GB wall can easily be misdiagnosed as cholecystitis, careful evaluation of clinical symptoms and imaging findings is necessary.[18]

In the present study, the GB wall thickness in patients with HF was related to the maximum IVC diameter and TRPG, whereas it was negatively associated with TAPSE and pulsed Doppler S wave, as manifested by RV systolic function. Regarding parameters of left-sided HF, GB wall thickness was related to both LAVI and the E/A ratio, suggesting that GB wall thickness in patients with HF was influenced by both RV function and elevated LV filling pressure. Left-sided HF often causes post-capillary pulmonary hypertension due to increased LV filling pressure and World Health Organization Group 2 pulmonary hypertension, and usually indicates a poor prognosis; therefore, recognition of biventricular HF is important.[10] As shown in **Figure 3**, GB wall thickness increased with increasing HF stage, possibly reflecting these aforementioned factors. GB wall thickness was also related to alkaline phosphatase in patients with HF; this could be because cholestasis is observed with elevated alkaline phosphatase concentrations in the setting of venous congestion.[1]

Non-Invasive Estimation of Organ Congestion on Ultrasound

Residual congestion in the organs of patients with HF has been shown to be associated with prognosis. Therefore, understanding the presence of residual congestion may indicate further therapeutic interventions. In ultrasonography, although organ congestion has been evaluated based on elastography assessment of liver stiffness, this measurement method is time consuming and difficult to learn. In contrast, estimation of organ congestion by measuring the thickness of the GB wall is relatively easy to learn and can be performed in a relatively short period of time. However, because GB wall thickness depends on the degree of GB distension, it should be noted that the measurement of GB wall thickness should be performed on an empty stomach. Moreover, GB disease can affect the measurement of GB wall thickness and GB wall thickness cannot even be measured in patients after cholecystectomy. In the present study, there was a significant difference in GB wall thickness between the HF and control groups; however, it should be noted that the median GB wall thickness in the HF group was approximately 2 mm, which is within the normal range. If GB wall thickness is above the upper limit of normal, as shown in **Figure 3**, the possibility of hospitalization for HF is high. This method, namely using ultrasound to measuring GB wall thickness, may have the unique advantage of easily providing additional information on organ congestion and estimating the stage in patients with HF.

Interaction Between the Heart and Other Organs in Patients With HF

In clinical practice, dysfunction of the heart and other organs may coexist in the setting of their respective diseases because of complex interactions. Assessment of organ congestion via extracardiac ultrasound may facilitate an understanding of the interaction between the heart and other organs, as observed between the heart and kidney in cardiorenal syndrome. Regarding the cardiac-gallbladder connection, Barie and Eachempati reported that congestive HF was associated with acute acalculous cholecystitis.[19] Further studies are warranted to explore this connection.

Study Limitations

This study has some limitations. First, the sample size was small, with relatively few events, posing a potential risk of

model overfit. Second, we were not able to compare GB wall thickness at admission and discharge. Third, there was no comparison of GB wall thickness and central venous pressure, measured by right heart catheterization. Fourth, GB wall thickness was measured after the echocardiogram had been performed by the same sonographers. This may have affected measurements of GB wall thickness. Finally, it should be noted that in this study GB wall thickness was measured using a sector scan, which is different from a convex scan, the usual method for measuring GB wall thickness on ultrasonography.

Conclusions

In conclusion, the results of this study suggest that GB wall thickness measured using a sector scan was associated with congestion in patients with HF, possibly indicating an advantage because it can be measured in conjunction with echocardiography. Despite the limitations noted above, we conclude that GB wall thickness can be used to assess organ congestion and estimate the stage in patients with HF.

Acknowledgments

The authors gratefully acknowledge the assistance of Yasuharu Tokuda in performing the ultrasounds in this study.

Sources of Funding

This study did not receive any specific funding.

Disclosures

K.T. is a member of *Circulation Reports*' Editorial Team. The other authors have no conflicts of interest to declare.

IRB Information

This study was approved by the Masuda Red Cross Hospital Ethics Committee (Reference no. 49).

Data Availability

The deidentified participant data will not be shared.

References

1. Harjola VP, Mullens W, Banaszewski M, Bauersachs J, Brunner-La Rocca HP, Chioncel O, et al. Organ dysfunction, injury and failure in acute heart failure: From pathophysiology to diagnosis and management. A review on behalf of the Acute Heart Failure Committee of the Heart Failure Association (HFA) of the European Society of Cardiology (ESC). *Eur J Heart Fail* 2017; **19:** 821–836.
2. Nagueh SF, Smiseth OA, Appleton CP, Byrd BF 3rd, Dokainish H, Edvardsen T, et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography: An update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr* 2016; **29:** 277–314.
3. Brucks S, Little WC, Chao T, Kitzman DW, Wesley-Farrington D, Gandhi S, et al. Contribution of left ventricular diastolic dysfunction to heart failure regardless of ejection fraction. *Am J Cardiol* 2005; **95:** 603–606.
4. Ambrosy AP, Pang PS, Khan S, Konstam MA, Fonarow GC, Traver B, et al. Clinical course and predictive value of congestion during hospitalization in patients admitted for worsening signs and symptoms of heart failure with reduced ejection fraction: Findings from the EVEREST trial. *Eur Heart J* 2013; **34:** 835–843.
5. Sakamoto T, Tanabe K. Assessment of organ congestion in patients with heart failure by ultrasonography. *J Echocardiogr*, doi:10.1007/s12574-021-00541-w.
6. Saito Y, Kato M, Nagashima K, Monno K, Aizawa Y, Okumura Y, et al. Prognostic relevance of liver stiffness assessed by transit elastography in patients with acute decompensated heart failure. *Circ J* 2018; **82:** 1822–1829.
7. Taniguchi T, Ohtani T, Kioka H, Tsukamoto Y, Onishi T, Nakamoto K, et al. Liver stiffness reflecting right-sided filling pressure can predict adverse outcomes in patients with heart failure. *J Am Coll Cardiol Imaging* 2018; **12:** 955–964.
8. Breda Vriesman AC, Engelbrecht MR, Smithuis RH, Puylaert JBCM. Diffuse gallbladder wall thickening: Differential diagnosis. *Am J Roentgenol* 2007; **188:** 495–501.
9. Zissin R, Osadchy A, Shapiro-Feinberg M, Gayer G. CT of a thickened-wall gallbladder. *Br J Radiol* 2003; **76:** 137–143.
10. Bozkurt B, Coats AJS, Tsutsui H, Abdelhamid CM, Adamopoulos S, Albert N, et al. Universal definition and classification of heart failure. *J Card Fail* 2021; **27:** 387–413.
11. Gupta P, Marodia Y, Bansal A, Kalra N, Kumar-M P, Sharma V, et al. Imaging-based algorithmic approach to gallbladder wall thickening. *World J Gastroenterol* 2020; **26:** 6163–6181.
12. Gupta P, Kumar M, Sharma V, Dutta U, Sandhu MS. Evaluation of gallbladder wall thickening: A multimodality imaging approach. *Expert Rev Gastroenterol Hepatol* 2020; **14:** 463–473.
13. American Institute of Ultrasound in Medicine. AIUM practice guideline for the performance of an ultrasound examination of the abdomen and/or retroperitoneum. *J Ultrasound Med* 2008; **27:** 319–326.
14. Runner GJ, Corwin MT, Siewert B, Eisenberg RL. Gallbladder wall thickening. *Am J Roentgenol* 2014; **202:** W1–W12.
15. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: An update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr* 2015; **28:** 1–39.e14.
16. Kanda Y. Investigation of the freely available easy-to-use software 'EZR' for medical statistics. *Bone Marrow Transplant* 2013; **48:** 452–458.
17. Barbosa ACR, Souza LRMF, Pereira RS, D'Ippolito G. Gallbladder wall thickening at ultrasonography: How to interpret it? *Radiol Bras* 2011; **44:** 381–387.
18. Matsui Y, Hirooka S, Kotsuka M, Yamaki S, Kosaka H, Yamamoto T, et al. Prognosis in patients with gallbladder edema misdiagnosed as cholecystitis. *JSLS* 2019; **23:** e2019.00022.
19. Barie PS, Eachempati SR. Acute acalculous cholecystitis. *Gastroenterol Clin North Am* 2010; **39:** 343–357.