Optimal timing of echocardiography for heart failure inpatients in Japanese institutions: OPTIMAL Study

Tanaka, Hidekazu ; Nabeshima, Yosuke ; Kitano, Tetsuji ; Nagumo, Sakura ; Tsujiuchi, Miki ; Ebato, Mio ; Mataki, Hiroyuki ; Takada, Masanori ;…

ORIGINAL RESEARCH ARTICLE

Optimal timing of echocardiography for heart failure inpatients in Japanese institutions: OPTIMAL Study

Hidekazu Tanaka[1]*, Yosuke Nabeshima[2], Tetsuji Kitano[2], Sakura Nagumo[3], Miki Tsujiuchi[3], Mio Ebato[3], Hiroyuki Mataki[4], Masanori Takada[5], Taichi Hayashi[6], Daisuke Sato[7], Yoko Miyasaka[8], Keiko Araki[9], Noriaki Iwahashi[10], Masaaki Takeuchi[11], Satoshi Nakatani[12] and OPTIMAL investigators

[1]*Division of Cardiovascular Medicine, Department of Internal Medicine, Kobe University Graduate School of Medicine, Kobe, Japan;* [2]*Second Department of Internal Medicine, University of Occupational and Environmental Health, School of Medicine, Kitakyusyu, Japan;* [3]*Division of Cardiology, Showa University Fujigaoka Hospital, Yokohama, Japan;* [4]*Division of Cardiology, Kobe Century Memorial Hospital, Kobe, Japan;* [5]*Division of Cardiology, Medical Corporation Kawasaki Hospital, Kobe, Japan;* [6]*Department of Cardiovascular Medicine, Faculty of Medicine and Graduate School of Medicine, Hokkaido University, Sapporo, Japan;* [7]*Department of Cardiovascular Medicine, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan;* [8]*Division of Cardiology, Department of Medicine II, Kansai Medical University, Hirakata, Japan;* [9]*Department of Cardiology, Hiratsuka Kyosai Hospital, Hiratsuka, Japan;* [10]*Division of Cardiology, Yokohama City University Medical Center, Yokohama, Japan;* [11]*Department of Laboratory and Transfusion Medicine, Hospital of University of Occupational and Environmental Health, School of Medicine, Kitakyushu, Japan;* [12]*Division of Cardiology, Saiseikai Senri Hospital, Osaka, Japan*

Abstract

Aims   Guidelines for the diagnosis and treatment of acute and chronic heart failure (HF) provided by the European Society of Cardiology state that echocardiography is recommended for the assessment of the myocardial structure and function of subjects with suspected HF including HF with reduced (HFrEF), mid-range (HFmrEF), and preserved ejection fraction (HFpEF) as class I of recommendation and level C of evidence. However, the impact of timing of echocardiography on survival for hospitalized HF patients or the prevalence of echocardiography during their stay has not yet been fully investigated. Therefore, we designed and conducted a prospective multicentre study, Optimal Timing of Echocardiography for Heart Failure Inpatients in Japanese Institutions (OPTIMAL) study, to investigate and evaluate the prevalence of echocardiography during the in-hospital stay of HF patients, and the impact of timing of echocardiography on their survival.

Methods and results   OPTIMAL was based on a nationwide, prospective, multicentre registry at 10 institutions in Japan endorsed by the Japanese Society of Echocardiography. A total of 601 patients hospitalized with HF were enrolled between August 2016 and July 2018 at the participating centres. Their mean age was 73.9 ± 13.0 years, left ventricular ejection fraction was 37.0% (26.0–50.0), and 256 patients (42.6%) were female. Admission echocardiography (admission echo) was categorized as either standard or point-of-care echocardiography performed within 3 days of admission, as was pre-discharge echocardiography (pre-discharge echo) within 3 days of discharge. The primary endpoint was defined as cardiovascular death over a median follow-up period of 18.9 months (9.3–26.5 months). Admission echo was performed for 476 patients (79.2%) and pre-discharge echo for 216 patients (35.9%). The primary endpoint of cardiovascular death occurred in 65 patients (10.8%). Kaplan–Meier curve findings indicated that survival of patients with pre-discharge echo was significantly better than that of patients without it (log-rank $P < 0.001$), and the same findings were obtained for patients with HFrEF, HFmrEF, and HFpEF. However, survival of patients with and without admission echo was similar (log-rank $P = 0.33$).

Conclusions   This OPTIMAL study prospectively showed the importance of pre-discharge echo for hospitalized HF patients. Careful attention is needed regarding the haemodynamic status of HF patients by administering pre-discharge echo to avoid HF re-hospitalization after discharge, and pre-discharge echo may provide additional information for deciding the appropriate discharge time. Our findings may thus offer a new insight into the management of hospitalized HF patients.

Keywords   Heart failure; Echocardiography; Survival; Pre-discharge echocardiography

Received: 22 June 2020; Revised: 18 August 2020; Accepted: 15 September 2020
*Correspondence to: Hidekazu Tanaka, Division of Cardiovascular Medicine, Department of Internal Medicine, Kobe University Graduate School of Medicine, 7-5-2, Kusunoki-cho, Chuo-ku, Kobe 650-0017, Japan. Tel: +81-78-382-5846; Fax: +81-78-382-5859.
Email: tanakah@med.kobe-u.ac.jp

Introduction

Heart failure (HF) is a global pandemic affecting at least 26 million people worldwide and still increasing in prevalence.[1] HF health expenditures are considerable and will increase dramatically owing to ageing populations. Despite the significant advances in therapies and prevention, mortality and morbidity are still high, and quality of life remains poor. The reported prevalence, incidence, mortality, and morbidity rates show geographic variations, depending on the different aetiologies and clinical characteristics observed among patients with HF. Projections are even more alarming, however, with total costs expected to increase by 127% between 2012 and 2030.[2] Echocardiography is the most useful and widely available examination for diagnosing patients with suspected HF. It provides immediate information on chamber volumes, ventricular systolic and diastolic function, wall thickness, valve function, and pulmonary hypertension.[3–6] This information is crucial for establishing a diagnosis and determining appropriate treatment. Furthermore, guidelines for the diagnosis and treatment of acute and chronic HF provided by the European Society of Cardiology (ESC) state that echocardiography is recommended for the assessment of the myocardial structure and function of subjects with suspected HF. Such an assessment is then used to establish a diagnosis of either HF with reduced ejection fraction (EF) (HFrEF), HF with mid-range EF (HFmrEF), or HF with preserved EF (HFpEF) as class I of recommendation and level C of evidence.[7] In addition, echocardiography is recommended, also as class I of recommendation and level C of evidence, for various other purposes, including the assessment of left ventricular (LV) EF (LVEF), valvular heart disease, and pulmonary artery pressure of HF patients.[7] In addition to standard routine echocardiography, point-of-care echocardiography as a quick bedside method has recently been reported to be useful for the evaluation of cardiac findings.[8–10] Thus, echocardiography can measure multiple, clinically important parameters of HF patients' cardiac function, including haemodynamic status and LV function, volumes, and mass. However, the impact of timing of echocardiography on survival for hospitalized HF patients or the prevalence of echocardiography during their stay has not yet been fully investigated. Therefore, we designed and conducted a prospective multicentre study, Optimal Timing of Echocardiography for Heart Failure Inpatients in Japanese Institutions (OPTIMAL) study, to investigate and evaluate the prevalence of echocardiography during the in-hospital stay of HF patients, and the impact of timing of echocardiography on their survival.

Methods

OPTIMAL was based on a nationwide, prospective, multicentre registry at 10 institutions in Japan endorsed by the Japanese Society of Echocardiography (Principal Investigator: Hidekazu Tanaka). A total of 601 patients hospitalized with HF and who met the Framingham criteria[11] were enrolled between August 2016 and July 2018 at the department of cardiology in each participating centre. There were no specific exclusion criteria for this study. The trial was registered with the University Hospital Medical Information Network (UMIN) Clinical Trials Registry (registration number: UMIN000024450) and conforms to the principles outlined in the Declaration of Helsinki. The protocol was approved by the institutional review board at each of the participating centres, and written informed consent was obtained from all patients.

Study protocol

After informed consent form was obtained at admission, the decision on timing of echocardiography was left to the attending physicians in each participating centre during the hospital stay. In-hospital care and post-discharge care for HF were based on the way at each of the participating centres. The number of times both standard echocardiography (standard echo) and point-of-care echocardiography (point-of-care echo) were performed during hospital stay was determined. Standard echo was defined as routinely performed echocardiography and point-of-care echo as a quick bedside echocardiography method for the evaluation of any cardiac findings obtained at each of the participating centres. Admission echocardiography (admission echo) was determined as either standard echo or point-of-care echo performed within 3 days after admission. Similarly, pre-discharge echocardiography (pre-discharge echo) was determined as either standard echo or point-of-care echo performed within 3 days before discharge. Furthermore, the following blood examinations were performed at admission: blood urea nitrogen (BUN), creatinine, estimated glomerular filtration rate (eGFR), and either B-type natriuretic peptide (BNP) or N-terminal pro-B-type natriuretic peptide (NT-proBNP). BNP was converted into a logarithmic scale (Log BNP) according to its distribution, while NT-proBNP was converted into log BNP using the formula proposed by Nabeshima *et al*.[12]

Echocardiographic examination

Echocardiography was performed with commercially available ultrasound systems at each of the participating centres. Standard echocardiographic measurements were obtained in accordance with the current guidelines of the European Association of Cardiovascular Imaging.[13] All echocardiographic examinations were performed by senior echocardiologists or sonographers.

Definition of primary endpoint

The primary endpoint was defined as cardiovascular death over a median follow-up period of 18.9 months (9.3–26.5 months).

Statistical analysis

Continuous variables were expressed as mean values with standard deviation for normally distributed data and as medians with inter-quartile range for non-normally distributed data. Categorical variables were expressed as frequencies and percentages. The parameters of the two subgroups were compared by using Student t-test or Mann–Whitney U-test according to data distribution. Proportional differences were evaluated with Fisher's exact test. Survival curves of freedom from cardiovascular death were determined with the Kaplan–Meier method, and cumulative event rates were compared by using the log-rank test. The associations of parameters with cardiovascular death were identified using a Cox proportional-hazards model in univariate and multivariate analyses. Variables with a univariate value of $P < 0.10$ were incorporated into the stepwise selection. For all steps, a P-value of <0.05 was considered statistically significant. All the analyses were performed with commercially available software (MedCalc software version 18.1.1; MedCalc Software, Mariakerke, Belgium).

Results

Patient characteristics

The baseline clinical and echocardiographic characteristics of the 601 patients are summarized in *Table 1*. Their median age was 73.9 ± 13.0 years, LVEF was 37.0% (26.0–50.0), and 256 patients (42.6%) were female. In accordance with the ESC guidelines,[7] 323 patients (53.7%) were diagnosed with HFrEF, 102 (17.0%) with HFmrEF, 169 (28.1%) with HFpEF, and seven (1.2%) with unknown HF phenotypes. Of 601 patients, 395 patients (66%) were newly diagnosed HF, and the remaining 206 patients (34.3%) had a history of hospitalized HF.

In-hospital data

The mean length of in-hospital stay was 19.0 days (13.0–29.0). The frequency of standard echo and point-of-care echo administration was 2.0 ± 1.1 times and 0.7 ± 1.2 times, respectively, while the frequency for either standard echo or point-of-care echo was 2.7 ± 1.6 times. Admission echo was performed for 476 patients (79.2%) and pre-discharge

Table 1 Baseline clinical and echocardiographic data of patients

	Patients (n = 601)
Clinical data	
Age, years	73.9 ± 13.0
Gender (female), n (%)	256 (42.6)
Body mass index, kg/m^2	23.1 ± 4.7
Ischaemic aetiology, n (%)	182 (30.3)
Blood examination	
BUN, mg/dL	30.3 ± 17.6
Creatinine, mg/dL	1.8 ± 1.9
eGFR, mL/min/1.73 m^2	43.8 ± 23.6
Log BNP	2.8 ± 0.4
Electrocardiogram, n (%)	
Sinus rhythm	343 (57.1)
Atrial fibrillation	191 (31.8)
Ventricular pacing	46 (7.7)
Others	21 (3.5)
HF phenotypes, n (%)	
HFrEF	323 (53.7)
HFmrEF	102 (17.0)
HFpEF	169 (28.1)
Unknown	7 (1.2)
Echocardiographic parameters at admission	
LV end-diastolic diameter, mm	53 ± 10
LV end-systolic diameter, mm	42 ± 13
IVSTd, mm	10 ± 2
PWTd, mm	10 ± 2
LV mass index, g/m^2	128 ± 40
LV end-diastolic volume, mL	138 ± 68
LV end-systolic volume, mL	91 ± 57
LVEF, %	37 (26–50)
Left atrial volume index, mL/m^2	59 ± 30
E/e'	21 ± 10
TR-PG, mmHg	34 ± 14
MR ≥ moderate, n (%)	152 (36.1)
AR ≥ moderate, n (%)	37 (8.8)
AS ≥ moderate, n (%)	38 (9.0)
In-hospital data	
Length of stay, days	19.0 (13.0–29.0)
Frequency of standard echo, times	2.0 ± 1.1
Frequency of point-of-care echo, times	0.7 ± 1.2
Frequency of either standard or point-of-care echo, times	2.7 ± 1.6
Admission echo, n (%)	476 (79.2)
Pre-discharge echo, n (%)	216 (35.9)

AR, atrial regurgitation; AS, atrial stenosis; BUN, blood urea nitrogen; e', spectral pulsed-wave Doppler-derived early diastolic velocity from the septal mitral annulus; E, peak early diastolic mitral flow velocity; Echo, echocardiography; eGFR, estimated glomerular filtration rate; HF, heart failure; HFmrEF, heart failure with mid-range ejection fraction; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; IVSTd, interventricular septal thickness end-diastole; Log BNP, logarithmic scale of B-type natriuretic peptide; LV, left ventricular; MR, mitral regurgitation; PWTd, posterior wall thickness end-diastole; TR-PG, tricuspid regurgitation pressure gradient.
Values are mean ± standard deviation for normally distributed data, and median and inter-quartile range for non-normally distributed data, or n (%). Echocardiographic data at admission were available in 421 patients with standard admission echocardiography.

echo for 216 patients (35.9%). The frequency distribution for 'standard echo', 'point-of-care echo', and 'either standard echo or point-of-care echo' during in-hospital stay is shown in *Figure 1*.

Primary endpoint

The primary endpoint of cardiovascular death occurred in 65 patients (10.8%). *Table 2* shows the clinical and echocardiographic parameters for patients with and without cardiovascular death. Cardiovascular death was more likely to occur in patients who were older and had lower body mass index, higher BUN, lower eGFR, higher log BNP, higher frequency of ventricular pacing, and lower LVEF than patients without cardiovascular death. It was noteworthy that the frequency of pre-discharge echo for patients with cardiovascular death was significantly lower than that for patients without (16.9% vs. 38.2%, $P < 0.001$), while the frequency of admission echo for patients with and without cardiovascular death was similar (73.8% vs. 79.9%, $P = 0.33$). In addition, the Kaplan–Meier curve indicated that survival of patients with pre-discharge echo was significantly better than that of patients without pre-discharge echo (log-rank $P = 0.0005$; *Figure 2*). Similar findings were observed for patients with HFrEF, HFmrEF, and HFpEF (*Figure 3*). On the other hand, survival of patients with admission echo was similar to that of patients without admission echo (log-rank $P = 0.22$; *Figure 4*).

Comparison of data for patients with and without pre-discharge echo

Table 3 shows a comparison of the baseline clinical and echocardiographic parameters for patients with and without pre-discharge echo. Patients with pre-discharge echo were likely to have lower prevalence of female, lower BUN, shorter length of hospital stay, and higher frequency of either standard or point-of-care echo than patients

without pre-discharge echo. *Table 4* shows a Cox proportional-hazards model in univariate and multivariate analyses for the associations with cardiovascular death including parameters with significant differences between patients with and without pre-discharge echo. Pre-discharge echo was a powerful independent parameter for predicting cardiovascular death in multivariate Cox proportional-hazards analyses.

Discussion

Our OPTIMAL study has clarified the prevalence of both standard echo and point-of-care echo during in-hospital stay, and the association of optimal timing of echocardiography during in-hospital stay with cardiovascular death for hospitalized HF patients in Japan. The main findings of this prospective multicentre study pertain to the following: (i) the frequency of echocardiography, whether standard echo or point-of-care echo, was 2.7 ± 1.6 times during hospital stay; (ii) admission echo was performed for 79.5% of patients, but pre-discharge echo for only 34.8%; and (iii) the survival of patients with pre-discharge echo was significantly better than that of patients without pre-discharge echo, whereas the survival of patients with and without admission echo was similar.

Echocardiography for heart failure patients

HF is a clinical syndrome characterized by typical symptoms that may be accompanied by a structural and/or functional cardiac abnormality, resulting in a reduced cardiac output and/or elevated intracardiac pressures at rest or during

FIGURE 1 Distribution of the frequency of 'standard echo', 'point-of-care echo', and 'either standard echo or point-of-care echo' during in-hospital stay.
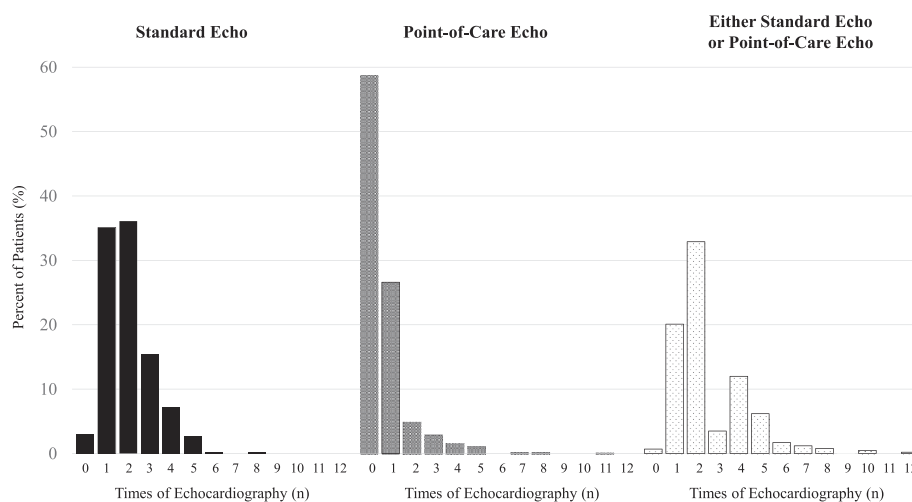
Table 2 Comparison of baseline clinical and echocardiographic data of patients with and without cardiovascular death

	Patients with cardiovascular death ($n = 65$)	Patients without cardiovascular death ($n = 536$)	P-value
Clinical data			
Age, years	78.6 ± 11.2	73.3 ± 13.1	0.002
Gender (female), n (%)	29 (44.6)	227 (42.4)	0.79
Body mass index, kg/m^2	21.6 ± 3.9	23.3 ± 4.8	0.008
Ischaemic aetiology, n (%)	26 (40.0)	156 (29.1)	0.06
Blood examination			
BUN, mg/dL	38.8 ± 22.1	29.3 ± 16.8	<0.001
Creatinine, mg/dL	2.0 ± 1.6	1.8 ± 1.9	0.29
eGFR, mL/min/1.73 m^2	35.0 ± 21.3	44.9 ± 23.7	0.002
Log BNP	2.9 ± 0.4	2.8 ± 0.4	0.012
Electrocardiogram, n (%)			
Sinus rhythm	32 (49.2)	311 (58.0)	0.19
Atrial fibrillation	20 (30.8)	171 (31.9)	0.89
Ventricular pacing	10 (15.4)	36 (6.7)	0.02
Others	3 (4.6)	18 (3.4)	0.72
HF phenotypes, n (%)			
HFrEF	35 (53.8)	288 (53.7)	1.0
HFmrEF	14 (21.5)	88 (16.4)	0.38
HFpEF	12 (18.5)	157 (29.3)	0.08
Unknown	4 (6.2)	3 (0.6)	0.003
Echocardiographic parameters at admission			
LV end-diastolic diameter, mm	54 ± 11	53 ± 11	0.54
LV end-systolic diameter, mm	50 ± 14	42 ± 12	0.10
IVSTd, mm	10 ± 3	10 ± 2	0.76
PWTd, mm	10 ± 2	10 ± 2	0.09
LV mass index, g/m^2	130 ± 41	128 ± 39	0.79
LV end-diastolic volume, mL	146 ± 93	137 ± 65	0.31
LV end-systolic volume, mL	100 ± 66	90 ± 56	0.20
LVEF, %	31 (24–43)	38 (26–51)	0.02
Left atrial volume index, mL/m^2	64 ± 27	58 ± 30	0.22
E/e'	19 ± 11	18 ± 8	0.28
TR-PG, mmHg	37 ± 13	33 ± 14	0.05
MR ≥ moderate, n (%)	21 (32.3)	131 (24.4)	0.18
AR ≥ moderate, n (%)	5 (7.7)	37 (6.9)	1.0
AS ≥ moderate, n (%)	9 (13.8)	38 (7.1)	0.08
In-hospital data			
Length of stay, days	21.0 (13.0–35.0)	19.0 (13.0–29.0)	0.37
Frequency of standard echo, times	1.7 ± 1.2	2.0 ± 1.1	0.02
Frequency of point-of-care echo, times	1.2 ± 2.0	0.7 ± 1.1	0.001
Frequency of either standard or point-of-care echo, times	2.8 ± 2.3	2.7 ± 1.5	0.49
Admission echo, n (%)	48 (73.8)	428 (79.9)	0.33
Pre-discharge echo, n (%)	11 (16.9)	205 (38.2)	<0.001

Values are mean ± standard deviation for normally distributed data, and median and inter-quartile range for non-normally distributed data, or n (%). Echocardiographic data at admission were available in 421 patients with standard admission echocardiography. Abbreviations as in *Table 1*.

FIGURE 2 Kaplan–Meier curve indicating that survival of patients with pre-discharge echo was significantly better than that of patients without pre-discharge echo.

Number at risk
Patients **with** pre-discharge echo
216   173   115   26
Patients **without** pre-discharge echo
385   268   168   48
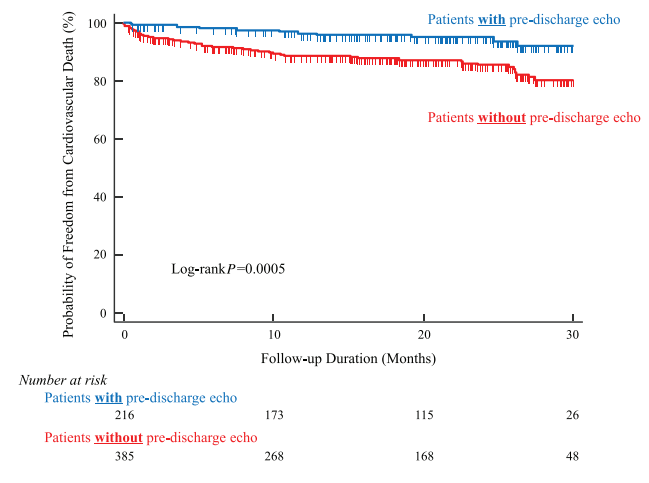
stress. As a rapid and accurate modality, echocardiography can provide non-invasive detection and a more accurate definition of the haemodynamic and morphologic changes associated with HF. Echocardiography also seems to be as good as catheter-based techniques for managing therapy and improving outcomes without the risks and cost of invasive measures.[14] Haemodynamic data such as intracardiac pressure measurements are very important information for the management of HF patients but has traditionally required invasive methods, whereas echocardiography can be a non-invasive substitute. Furthermore, echocardiography plays an important role in the management of HF patients, including those with HFrEF, HFmrEF, and HFpEF, and is, according to current ESC guidelines, a class I recommendation for the assessment of myocardial structure, cardiac function, valvular heart disease, and pulmonary artery pressure in HF.[7] Although echocardiography has been proven to be useful for the management of HF patients for the abovementioned reasons, the impact of its timing or frequency on survival for hospitalized HF during their stay remains uncertain. On the basis of findings from the Nationwide Inpatient Sample study in the USA, Papolos *et al.* reported that the use of echocardiography was associated with lower odds of inpatient mortality including patients hospitalized for acute myocardial infarction, cardiac dysrhythmia, acute cerebrovascular disease, congestive HF, and sepsis.[15] In addition, point-of-care echo for HF patients, which is a quick bedside echocardiography performed by cardiologists or attending physicians, is, according to recent reports, as effective as routine standard echo.[8–10] Although point-of-care echo is simply a quick echocardiography method, it can provide important information about HF, such as the status of preload, afterload, cardiac contractility, diastolic function, and valvular disease.

FIGURE 3 Kaplan–Meier curve indicating that survival of HFrEF, HFmrEF, and HFpEF patients with pre-discharge echo was significantly better than that of patients without pre-discharge echo. HF, heart failure; HFmrEF, HF with mid-range ejection fraction; HFpEF, HF with preserved ejection fraction; HFrEF, HF with reduced ejection fraction.
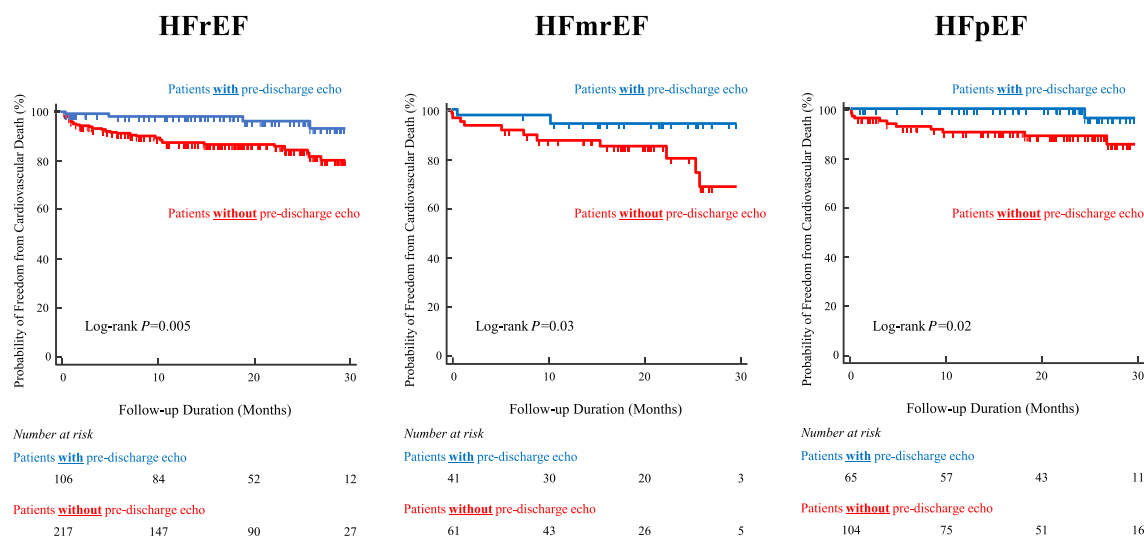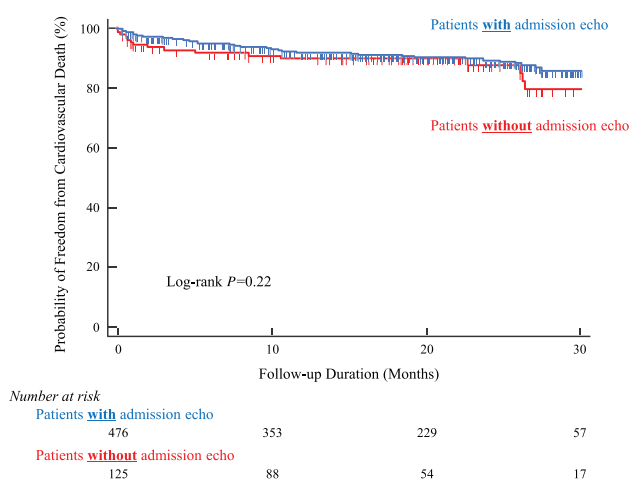

FIGURE 4 Kaplan–Meier curve indicating that survival of patients with admission echo was similar as compared with that of patients without admission echo.

Impact of pre-discharge echo on survival of hospitalized heart failure patients

Our study prospectively showed that performance of pre-discharge echo was associated with better patient survival irrespective of HF phenotypes after discharge, but not for those who had undergone admission echo only. Pre-discharge echo results, unlike those of admission echo, reflect treatment response in terms of LV filling pressure reduction, the degree of haemodynamic stability, HF progression, and the severity of underlying diastolic dysfunction.

Thus, pre-discharge echo makes it possible to verify whether patients have responded well to the HF therapy or not. The information of therapeutic regimen at discharge such as dose of diuretics or the need for cardiac devices was not part of this study so that impact of pre-discharge echo on post-discharge care for HF in patients with pre-discharge echo may not be uniform at each participating centre. However, pre-discharge echo for HF patients may be widely expected positive impact on outcome as follows based on this trial. If patients who did not respond well to the HF therapy were confirmed by pre-discharge echo such as dilated inferior vena cava or high trans-tricuspid pressure gradient, further administration of diuretics or other intensive treatment for HF may be considered. Yang *et al.* previously reported that pre-discharge echo is important for hospitalized HF patients.[16] They retrospectively studied 267 hospitalized HF patients to investigate the utility of admission echo (within 2 days of admission) or pre-discharge echo (within 7 days of discharge) for predicting major adverse cardiovascular events. They showed that several pre-discharge echo parameters were associated with major adverse cardiovascular events for both HFrEF and HFpEF patients; however, none of the admission echo parameters were associated with such events. They therefore concluded that pre-discharge echo should be recommended for hospitalized HF patients to provide more information about their status.

In addition, the length of hospital stay in patients with pre-discharge echo was significantly shorter than that in patients without pre-discharge echo in this study. Because patients with pre-discharge echo were more

Table 3 Comparison of baseline clinical and echocardiographic data of patients with and without pre-discharge echo

	Patients with pre-discharge echo (n = 216)	Patients without pre-discharge echo (n = 385)	P-value
Clinical data			
Age, years	74.1 ± 13.0	73.8 ± 13.0	0.77
Gender (female), n (%)	98 (45.4)	225 (58.4)	0.002
Body mass index, kg/m²	23.4 ± 4.7	22.9 ± 4.7	0.20
Ischaemic aetiology, n (%)	59 (27.3)	123 (31.9)	0.27
Blood examination			
BUN, mg/dL	28.1 ± 16.5	31.5 ± 18.2	0.02
Creatinine, mg/dL	1.6 ± 1.6	1.9 ± 2.0	0.07
eGFR, mL/min/1.73 m²	45.5 ± 22.4	42.9 ± 24.2	0.21
Log BNP	2.8 ± 0.4	2.8 ± 0.4	0.08
Electrocardiogram, n (%)			
Sinus rhythm	121 (56.0)	222 (57.7)	0.73
Atrial fibrillation	73 (33.8)	118 (30.6)	0.47
Ventricular pacing	19 (8.8)	27 (7.0)	0.52
Others	3 (4.6)	18 (3.5)	0.04
HF phenotypes, n (%)			
HFrEF	106 (49.1)	217 (56.4)	0.09
HFmrEF	41 (19.0)	61 (15.8)	0.38
HFpEF	65 (30.1)	104 (27.0)	0.36
Unknown	4 (1.9)	3 (0.8)	0.43
Echocardiographic parameters at admission			
LV end-diastolic diameter, mm	53 ± 10	53 ± 10	0.97
LV end-systolic diameter, mm	42 ± 13	43 ± 12	0.72
IVSTd, mm	10 ± 2	10 ± 2	0.48
PWTd, mm	10 ± 2	10 ± 2	0.79
LV mass index, g/m²	129 ± 39	128 ± 40	0.89
LV end-diastolic volume, mL	141 ± 68	136 ± 69	0.42
LV end-systolic volume, mL	92 ± 59	90 ± 56	0.72
LVEF, %	38 (27–51)	36 (25–50)	0.18
Left atrial volume index, mL/m²	58 ± 33	60 ± 28	0.59
E/e′	18 ± 8	18 ± 9	0.28
TR-PG, mmHg	34 ± 14	33 ± 14	0.58
MR ≥ moderate, n (%)	50 (23.1)	102 (26.5)	0.38
AR ≥ moderate, n (%)	15 (6.9)	27 (6.9)	1.0
AS ≥ moderate, n (%)	15 (6.9)	32 (8.3)	0.64
In-hospital data			
Length of stay, days	17.5 (13.0–25.0)	21.0 (14.0–32.0)	0.004
Frequency of standard echo, times	2.3 ± 1.0	1.8 ± 1.2	<0.001
Frequency of point-of-care echo, times	0.7 ± 1.3	0.7 ± 1.2	0.48
Frequency of either standard or point-of-care echo, times	2.9 ± 1.4	2.6 ± 1.7	0.004
Admission echo, n (%)	180 (83.3)	296 (76.9)	0.07

Values are mean ± standard deviation for normally distributed data, and median and inter-quartile range for non-normally distributed data, or n (%). Echocardiographic data at admission were available in 462 patients with standard admission echocardiography. Abbreviations as in Table 1.

Table 4 Univariate and multivariate Cox proportional-hazards analysis

	Univariate analysis			Multivariate analysis		
Variables	HR	95% CI	P-value	HR	95% CI	P-value
Gender (female)	0.98	0.68–1.41	0.915			
BUN	1.02	1.01–1.02	0.002	1.02	1.01–1.03	0.001
Length of stay	1.00	0.98–1.02	0.777			
Frequency of standard echo	0.58	0.41–1.41	0.004			
Frequency of either standard or point-of-care echo	1.18	0.99–1.41	0.061			
Admission echo	1.26	0.61–2.60	0.525			
Pre-discharge echo	0.20	0.06–0.63	0.006	0.38	0.20–0.73	0.004
Admission echo and pre-discharge echo	2.68	0.89–8.05	0.080			

BUN was the data at admission. Other abbreviations as in Table 1. CI, confidential interval; HR, hazard ratio.

likely to have higher frequency of either standard or point-of-care echo during the hospital stay, the frequent echo for HF may also contribute to reduce the length of hospital stay.

Clinical implications

The clinical course of HF is generally chronic and progressive. HF often manifests as acute HF and then progresses to compensated, chronic HF. Patients with established HF show chronic progression and may have repeated episodes of acute decompensated HF. Repeated acute exacerbations gradually lead to the development of more severe HF, from Stage C HF to Stage D HF. Attending physicians thus need to prevent repeated acute exacerbations for HF patients. The I-PRESERVE Trial with 4128 patients with New York Heart Association functional class II to IV HF and LVEF > 45% enrolled reported that 55% of the patients needed at least one hospital admission after discharge.[17] Moreover, they showed that cumulative mortality of patients without re-hospitalization for HF after discharge was much better than that for patients with at least one re-hospitalization for HF after discharge. The findings of this trial thus support the results of our study that careful attention is needed regarding the haemodynamic status of HF patients by administering pre-discharge echo to avoid HF re-hospitalization and to lead to a positive impact of outcome after discharge. Also, pre-discharge echo may provide additional information for deciding the appropriate discharge time to avoid HF re-hospitalization after discharge.

Study limitations

Several limitations this study should be addressed. First, the length of stay for HF patients in Japan was long as compared with that in other countries owing to the differences in reimbursement and participation in inpatient disease management programmes. Global hospitalized HF registries revealed the median length of stay ranges from 4 to 20 days with a median length of stay of approximately 4 days,[17] but a median length of stay of 21 days as reported according to the Japanese ATTEND registry.[17,18] As the median length of stay in this study was as long as 19 days, this may have affected the timing and the prevalence of echocardiography during in-hospital stay for HF patients. Second, evaluation of the association of specific parameters of pre-discharge echo with cardiovascular death was not part of this study. The multivariate Cox proportional hazard analysis used in a retrospective study by Yang *et al.* showed that several specific parameters of pre-discharge echo were associated with major adverse cardiovascular events after discharge for patients with HFrEF and HFpEF.[16] Thus, further prospective studies to evaluate the association of specific parameters of pre-discharge echo with cardiovascular death will be needed to augment our findings. Finally, this registry did not enrol consecutive hospitalized HF patients in each participating centre so that some extent bias regarding enrolment of patients may occur between the participating centres. Less biased study with consecutive hospitalized HF patients will be needed to validate our findings.

Conclusions

This OPTIMAL study prospectively showed the importance of pre-discharge echo for hospitalized HF patients. Our findings may thus offer a new insight into the management of hospitalized HF patients.

Conflict of interest

None declared.

References

1. Ponikowski P, Anker SD, AlHabib KF, Cowie MR, Force TL, Hu S, Jaarsma T, Krum H, Rastogi V, Rohde LE, Samal UC. Heart failure: preventing disease and death worldwide. *ESC Heart Fail* 2014; **1**: 4–25.
2. Writing Group M, Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, Das SR, De Ferranti S, Després JP, Fullerton HJ, Howard VJ. Heart disease and stroke statistics—2016 update: a report from the American Heart Association. *Circulation* 2016; **133**: e38–e360.
3. Marwick TH, Raman SV, Carrio I, Bax JJ. Recent developments in heart failure imaging. *JACC Cardiovasc Imaging* 2010; **3**: 429–439.
4. Garbi M, McDonagh T, Cosyns B, Bucciarelli-Ducci C, Edvardsen T, Kitsiou A, Nieman K, Lancellotti P, On behalf of the EACVI Imaging Task Force. Appropriateness criteria for cardiovascular imaging use in heart failure: report of literature review. *Eur Heart J Cardiovasc Imaging* 2015; **16**: 147–153.
5. Gimelli A, Lancellotti P, Badano LP, Lombardi M, Gerber B, Plein S, Neglia D, Edvardsen T, Kitsiou A, Scholte AJHA, Schroder S, Cosyns B, Gargiulo P, Zamorano JL, Perrone-Filardi P. Non-invasive cardiac imaging evaluation of patients with chronic systolic heart failure: a report from the European Association of Cardiovascular Imaging (EACVI). *Eur Heart J* 2014; **35**: 3417–3425.
6. Klaeboe LG, Edvardsen T. Echocardiographic assessment of left ventricular systolic function. *J Echocardiogr* 2019; **17**: 10–16.
7. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JGF, Coats AJS, Falk V, González-Juanatey JR, Harjola VP, Jankowska EA, Jessup M, Linde C, Nihoyannopoulos P, Parissis JT, Pieske B, Riley JP, Rosano GMC, Ruilope LM, Ruschitzka F, Rutten FH, van der Meer P, ESC Scientific Document Group. 2016

ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur Heart J* 2016; **37**: 2129–2200.

8. Ultrasound guidelines: emergency, point-of-care and clinical ultrasound guidelines in medicine. *Ann Emerg Med* 2017; **69**: e27–e54.

9. Moore CL, Copel JA. Point-of-care ultrasonography. *N Engl J Med* 2011; **364**: 749–757.

10. Boyd JH, Sirounis D, Maizel J, Slama M. Echocardiography as a guide for fluid management. *Crit Care* 2016; **20**: 274.

11. McKee PA, Castelli WP, McNamara PM, Kannel WB. The natural history of congestive heart failure: the Framingham study. *N Engl J Med* 1971; **285**: 1441–1446.

12. Nabeshima Y, Sakanishi Y, Otani K, Higa Y, Honda M, Otsuji Y, Takeuchi M. Estimation of B-type natriuretic peptide values from N-terminal proBNP levels. *J UOEH* 2020; **42**: 1–12.

13. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, Flachskampf FA, Foster E, Goldstein SA, Kuznetsova T, Lancellotti P, Muraru D, Picard MH, Rietzschel ER, Rudski L, Spencer KT, Tsang W, Voigt JU. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *Eur Heart J Cardiovasc Imaging* 2015; **16**: 233–270.

14. Capomolla S, Ceresa M, Pinna G, Maestri R, La Rovere MT, Febo O, Rossi A, Paganini V, Caporotondi A, Guazzotti G, Gnemmi M. Echo-Doppler and clinical evaluations to define hemodynamic profile in patients with chronic heart failure: accuracy and influence on therapeutic management. *Eur J Heart Fail* 2005; **7**: 624–630.

15. Papolos A, Narula J, Bavishi C, Chaudhry FA, Sengupta PP. U.S. hospital use of echocardiography: insights from the Nationwide Inpatient Sample. *J Am Coll Cardiol* 2016; **67**: 502–511.

16. Yang LT, Kado Y, Nagata Y, Otani K, Otsuji Y, Takeuchi M. Timing on echocardiography and blood laboratory test is important for future outcome association in hospitalized heart failure patients. *J Cardiol* 2018; **71**: 71–80.

17. Carson PE, Anand IS, Win S, Rector T, Haass M, Lopez-Sendon J, Miller A, Teerlink JR, White M, McKelvie RS, Komajda M, Zile MR, McMurray JJ, Massie B. The hospitalization burden and post-hospitalization mortality risk in heart failure with preserved ejection fraction: results from the I-PRESERVE Trial (Irbesartan in Heart Failure and Preserved Ejection Fraction). *JACC Heart Fail* 2015; **3**: 429–441.

18. Sato N, Kajimoto K, Keida T, Mizuno M, Minami Y, Yumino D, Asai K, Murai K, Muanakata R, Aokage T, Sakata Y, Mizuno K, Takano T, on behalf of the ATTEND Investigators. Clinical features and outcome in hospitalized heart failure in Japan (from the ATTEND Registry). *Circ J* 2013; **77**: 944–951.