Response of Jugular Venous Pressure to Exercise in Patients With Heart Failure and Its Prognostic Usefulness

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Jugular venous pressure (JVP) has been established for the assessment of central venous pressure in patients with heart failure (HF), but data are limited regarding the response of JVP to exercise because of its complicated methods. Simplifying the estimation of JVP may be applied in such situations. JVP was assessed before and after the 6-minute walk test (6MWT) in 81 patients with HF using a simple method by which the JVP was considered high when the internal jugular venous pulsation on the right side was visually identified above the right clavicle in the sitting position. The primary outcome was a composite of cardiovascular death and hospitalization for worsening HF. None of the patients exhibited high JVP before the 6MWT and 11 patients (14%) had a high JVP after. The 6MWT distances were lower in patients with a high JVP after the 6MWT (338 ± 114 m) than those in patients without a high JVP (417 ± 78 m, p = 0.04). During a follow-up period of 13.4 ± 6.9 months, 11 patients died and 8 patients were hospitalized for worsening HF. The incidence of adverse cardiac events was higher in patients with a high JVP after the 6MWT (64%) than in patients without a high JVP after (64% vs 17%; hazard ratio, 7.52; 95% confidence interval, 2.69 to 20.83; p <0.001). In conclusion, high JVP after exercise was associated with exercise intolerance and poor prognosis. The response of JVP to exercise using this simple technique of physical examination may be a new approach for patients with HF for risk assessment. **(Am J Cardiol 2020;125:1524−1528)**

Physical examination is essential even in the era of advanced imaging and laboratory techniques. In the management of patients with heart failure (HF) in particular, assessment of the jugular venous pressure (JVP) is important for the assessment of central venous pressure.[1] A high JVP is independently associated with adverse outcomes in patients with HF,[2] but assessment of JVP is inadequately performed in clinical practice because of its complicated methods (i.e., vertical distance measurement between the sternal angle and the top of the jugular vein at 45° position).[3,4] More recently, attention has been paid to simplifying the estimation of JVP, by which the right internal jugular vein above the right clavicle is visually assessed in the sitting position − either visible or not visible.[5] This simple technique can also be applied to JVP assessment after exercise. The objectives of this study were to assess the response of JVP to exercise, and its clinical significance in patients with HF.

Methods

This study consisted of 81 patients with HF (59 inpatients and 22 outpatients) who underwent cardiac rehabilitation and the 6-minute walk test (6MWT) at Matsushita Memorial Hospital between September 2017 and July 2019. A diagnosis of HF was made based on the guidelines for diagnosis and treatment of acute and chronic HF.[6] Exclusion criteria were subjective symptoms of HF within the past week, severe valvular heart diseases, being unable to walk >200 m, untreated severe arrhythmias, severe left ventricular outflow tract obstruction, and active myocarditis.[7] The causes of HF were ischemic heart disease in 22 patients, dilated cardiomyopathy in 15, valvular heart diseases in 14, arrhythmias in 10, hypertrophic cardiomyopathy in 7, hypertensive heart disease in 5, and others in 8. This study was approved by the ethics committee of Matsushita Memorial Hospital and written consent was received from all patients.

Patient characteristics, including age, height, weight, body mass index, resting heart rate, the presence of comorbidities (hypertension, diabetes, dyslipidemia, and atrial fibrillation), and medicines (beta blockers, angiotensin converting enzyme inhibitor/angiotensin receptor blockers, and diuretics) were investigated by reviewing medical records. Furthermore, levels of plasma brain natriuretic peptide, serum hemoglobin, and serum albumin were examined. The estimated glomerular filtration rate was calculated according to the formula by the Japanese Society of Nephrology.[8] The geriatric nutritional risk index was calculated as follows: 14.89 × serum albumin (g/mL) + 41.7 × (body weight in kilograms/22 × square of height in meters).[9]

The 6MWT was conducted in accordance with the guidelines of the American Thoracic Society.[10] In brief, all patients were instructed to walk the corridor from one end to the other at their own pace, as many times as possible within 6 minutes.

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The rating of perceived exertion scale, heart rate before and after the 6MWT, and maximum walk distance were measured. The 6MWT was performed before discharge for patients who started cardiac rehabilitation during hospitalization, whereas outpatients underwent 6MWT as an initial assessment of cardiac rehabilitation.

The JVP was examined just before and after 6MWT without breath control in the sitting position. It was considered high when the internal jugular venous pulsation on the right side was visually identified above the right clavicle.[5] Although the external jugular vein, compared with the internal jugular vein, is easier to visualize, the internal jugular vein on the right side was assessed because of its features, including a larger vessel and lack of competent valves with a straight line to the superior vena cava and right atrium.[11] Interobserver agreement for the presence or absence of a high JVP was assessed in 36 patients.

Handgrip strength was measured for both the left and right hands in a standing position using a dynamometer (Grip-D handgrip dynamometer, Takei Scientific Instruments, Tokyo, Japan) in units of kilograms.[12] In brief, patients were instructed to hold the dynamometer at thigh level and encouraged to exert the strongest possible force. The average of 2 measurements for the left and right maximum grip strengths was used for the present analysis. Quadriceps isometric strength was also measured using a hand held dynamometer (μtas; ANIMA, Tokyo, Japan).[13] In brief, patients sat on a bench, and the dynamometer was fixed to a rigid bar. Five-second maximal isometric voluntary contractions of the quadriceps were measured twice for both legs with the knee joint angle fixed at 90° of flexion. The highest strength values on the left and right sides were averaged, and expressed as an absolute value as well as relative value to body weight. The 1-leg standing time was measured using a digital mirror (Panasonic Digital Mirror, Panasonic, Osaka, Japan). In brief, patients were instructed to maintain the standing position with their eyes open for a maximum time of 60 seconds, and the time until the lower limbs other than the support side touched the floor was measured. The average of the maximum times on the left and right legs was used for the present analysis.

Echocardiography was performed using echocardiography equipment (Vivid E9; GE Healthcare, Milwaukee, Wisconsin) by a standard method.[14] The left ventricular ejection fraction, left ventricular end-diastolic and end-systolic diameter, left atrial diameter, left atrial volume index, mitral valve E wave peak velocity, and septal mitral annular early peak velocity (E') were measured by tissue Doppler imaging. The maximum and minimum diameters of the inferior vena cava at rest and during sniffing were measured. The degree of tricuspid regurgitation (none to severe), the peak velocity of tricuspid regurgitation, and the tricuspid regurgitation pressure gradient were measured by the Doppler method.

All patients were followed up from the 6MWT. Patient information was obtained from available medical records and interviews with the patients and/or their physicians in charge. The primary outcome was a composite of cardiac death and hospitalization for worsening HF requiring initiation of intravenous treatment with inotropic, vasodilator, and/or diuretics, mechanical ventilation, or circulatory support.

Categorical variables were compared by the chi-square test or Fisher's exact test as appropriate. Continuous variables were expressed as the mean ± standard deviation and were compared using the Student's *t* test. Time-to-event data were evaluated with the use of Kaplan-Meier estimates and Cox proportional-hazards models, stratified according to JVP response to exercise. Cox models were used to calculate hazard ratios, 95% confidence intervals (CI), and p values. A 2-sided $p < 0.05$ was considered significant. The Cohen's kappa coefficient was used to assess the interobserver agreement for JVP response to exercise.

Results

None of the patients had a high JVP before the 6MWT and all the patients completed the 6MWT without complication. After the 6MWT, 11 patients (14%) had a high JVP. There were no significant differences in the causes of HF between patients with and without a high JVP after the 6MWT ($p = 0.62$; e.g., 27% vs 27% with ischemic heart disease and 19% vs 18% with dilated cardiomyopathy). The presence of a high JVP was significantly associated with a higher incidence of atrial fibrillation, lower levels of hemoglobin, and lower geriatric nutritional risk index (Table 1).

Patients with a high JVP after the 6MWT, compared with those without, had significantly higher left ventricular end-diastolic and end-systolic diameters, higher maximum and minimum diameters of the inferior vena cava, and higher peak velocity and pressure gradient of tricuspid regurgitation (Table 2). The 6MWT distances were significantly lower in patients with a high JVP after the test than those in patients without a high JVP (Table 2). There were no significant between-group differences in other physical functions such as quadriceps isometric strength or one-leg standing time (Table 2).

Follow-up data on the outcome were available for all patients. During a follow-up period of 13.4 ± 6.9 months, 19 patients (23%) developed cardiac events. Of patients with a high JVP after the 6MWT, 5 died and 2 were hospitalized for worsening HF. Of patients without a high JPV after the 6MWT, 6 died and 6 were hospitalized for worsening HF. The incidence of a composite of cardiac death and hospitalization for worsening HF (the primary outcome) was higher in patients with a high JVP after the 6MWT than in those without (64% vs 17%; hazard ratio, 7.52; 95%CI, 2.69 to 20.83; $p < 0.001$), as shown in Figure 1. The incidence of cardiac death did not significantly differ between the 2 groups (18% vs 7%; hazard ratio, 4.11; 95%CI, 0.74 to 22.72; $p = 0.10$).

In 36 patients in which interobserver agreement was assessed, disagreement regarding the presence or absence of a high JVP was observed in 2 patients. The Cohen's kappa coefficient was calculated as 0.89 (excellent agreement).

Discussion

We assessed the JVP before and after the 6MWT using a simple method (i.e., visibility of the right internal jugular vein above the right clavicle in the sitting position) in 81 patients with HF. The new development of high JVP after the 6MWT was significantly associated with decreased exercise capacity and adverse cardiac events.

Table 1
Characteristics of the patients at baseline

Variable	Overall (n = 81)	High JVP		p
		Present (n = 11)	Absent (n = 70)	
Age (years)	71 ± 10	75 ± 7	70 ± 10	0.11
Men	61%	63%	61%	0.89
Height (cm)	161 ± 10	161 ± 10	161 ± 11	0.97
Body weight (kg)	61 ± 12	58 ± 13	61 ± 12	0.42
Body mass index (kg/m^2)	23 ± 3	22 ± 4	23 ± 3	0.30
Resting heart rate (beats/min)	71 ± 11	72 ± 11	71 ± 11	0.87
Hypertension	60 (74%)	9 (81%)	51 (73%)	0.74
Diabetes mellitus	27 (33%)	7 (64%)	20 (40%)	0.11
Dyslipidemia*	30 (37%)	5 (45%)	25 (36%)	0.57
Atrial fibrillation	26 (32%)	7 (64%)	19 (27%)	0.04
Brain natriuretic peptide (pg/mL)	229.7 ± 238.2	355.4 ± 256.6	209.7 ± 230.5	0.10
Hemoglobin (g/mL)	13.2 ± 2.1	11.6 ± 2.4	13.4 ± 2.4	0.02
Albumin (g/mL)	3.9 ± 0.5	3.8 ± 0.7	4.0 ± 0.4	0.39
eGFR (mL/min/1.73 m^2)	50.7 ± 17.1	42.4 ± 15.9	51.9 ± 17.1	0.07
Geriatric nutritional risk index	102 ± 10	93 ± 11	104 ± 10	0.02
Medications				
Beta blockers	58 (72%)	9 (82%)	49 (70%)	0.39
Angiotensin-converting enzyme inhibitors/angiotensin receptor blockers	26 (28%)	3 (33%)	23 (72%)	0.72
Diuretics	52 (72%)	8 (63%)	44 (72%)	0.72

eGFR = estimated glomerular filtration rate; JVP = jugular venous pressure.

Data are means ± standard deviation or number (%).

* Dyslipidemia was defined as low-density lipoprotein cholesterol ≥140 mg/dL, high-density lipoprotein cholesterol <40 mg/dL, triglycerides ≥150 mg/dL, or use of cholesterol-lowering medications.

Table 2
Echocardiography and physical functions

Variable	Overall (n = 81)	High JVP		p
		Present (n = 11)	Absent (n = 70)	
Echocardiography data				
Left ventricular ejection fraction (%)	47 ± 16	40 ± 17	48 ± 15	0.19
Left ventricular end-diastolic diameter (mm)	51 ± 10	59 ± 10	51 ± 9	0.02
Left ventricular end-systolic diameter (mm)	40 ± 12	48 ± 12	39 ± 12	0.04
Left atrial diameter (mm)	41 ± 6	42 ± 7	41 ± 7	0.83
Left atrial volume index (ml/m^2)	56 ± 23	58 ± 28	56 ± 23	0.86
E/e'	17 ± 8	17 ± 8	17 ± 8	0.91
Inferior vena cava				
Maximum diameter (mm)	14 ± 4	19 ± 6	14 ± 4	0.02
Minimum diameter (mm)	8 ± 4	12 ± 6	7 ± 3	0.02
Tricuspid regurgitation grade				0.06
Mild	48 (59%)	5 (45%)	43 (53%)	
Moderate	26 (32%)	3 (27%)	23 (28%)	
Severe	7 (9%)	3 (27%)	4 (5%)	
Peak velocity of tricuspid regurgitation (m/s)	2.4 ± 0.5	2.9 ± 0.7	2.3 ± 0.5	0.03
Tricuspid regurgitation pressure gradient (mm Hg)	25 ± 11	36 ± 17	23 ± 8	0.03
6MWT				
Distance (meters)	406 ± 88	338 ± 114	417 ± 78	0.04
Maximum heart rate (beats/min)	111 ± 24	108 ± 38	112 ± 21	0.75
Rest rating of perceived exertion scale	10 ± 2	11 ± 1	10 ± 2	0.29
Peak rating of perceived exertion scale	13 ± 1	13 ± 1	13 ± 1	0.57
Hand grip strength (kg)	29 ± 10	24 ± 9	30 ± 10	0.11
Quadriceps isometric strength (%body weight)	49 ± 2	45 ± 1	50 ± 2	0.35
One leg standing time (seconds)	30 ± 23	17 ± 16	32 ± 23	0.07

E/e' = peak mitral inflow early velocity to tissue Doppler E' ratio of the intraventricular septum; JVP = jugular venous pressure; 6MWT = 6-minute walk test.

Data are the median ± standard deviation or number (%).

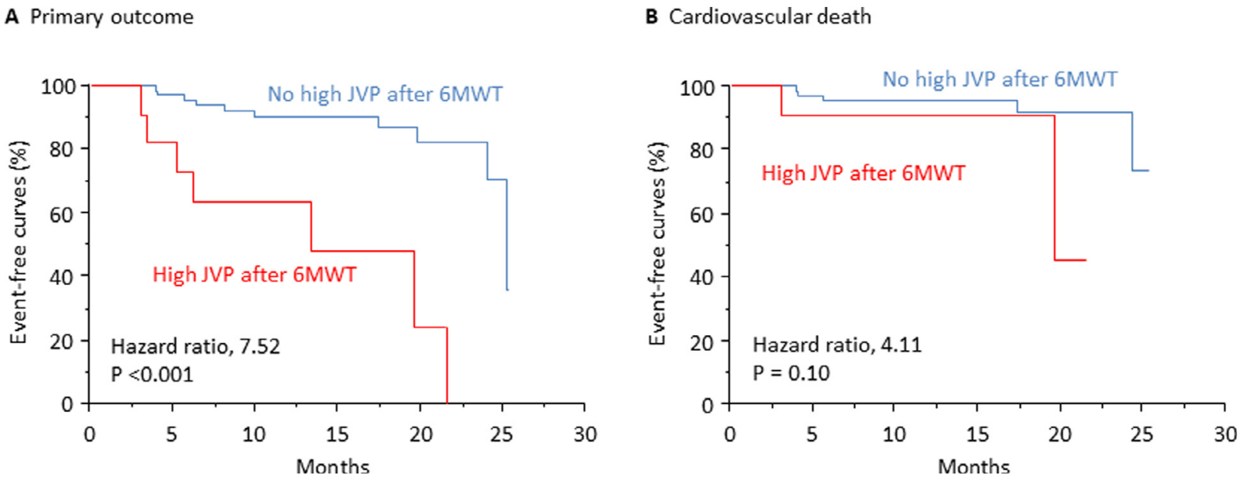

Figure 1. Cardiovascular outcomes. The primary outcome was a composite of cardiovascular death and hospitalization for worsening HF. Event rates were based on Kaplan-Meier estimates. On Cox proportional-hazards models stratified according to the response of the JVP to exercise, the 95% confidence interval of the hazard ratio was 2.69 to 20.83 for the primary outcome (Panel A) and 0.74 to 22.72 for cardiovascular death (Panel B).

The main finding of our study is that a high JVP developed after exercise in 14% of our patients with HF who did not have a high JPV before exercise. This is not surprising because in a study of HF patients who underwent upright treadmill exercise testing with hemodynamic monitoring, pulmonary vascular resistance frequently increased during exercise.[15] Although the JVP has been commonly used as an objective end point in the management of patients with HF,[3] caution is needed because it has been mostly assessed only at rest due to methodological limitations. Data are limited regarding the response of JVP to exercise in patients with HF. In our study, simplifying the estimation of JVP[5] made it possible to assess the response of JVP to exercise. As all our HF patients with a high JVP after exercise had a normal JVP before exercise, JVP as assessed by the conventional technique or only at rest may be undervalued for risk assessment of HF.

Another notable finding of this study is that high JVP after exercise was significantly associated with exercise intolerance and poor outcomes in patients with HF. As exercise intolerance results in a poor quality of life and a poorer prognosis,[16] it is intuitive that HF patients who had a high JVP after exercise have a higher risk than HF patients who did not. Our results suggest that the response of JVP to exercise, as compared with the conventional JVP assessment at rest, will provide additional information for the risk stratification of patients with HF. Precise recognition of high-risk patients with HF is needed because many medical and interventional treatments should be considered for such patients not only to improve their outcomes, but also to reduce the increasing socioeconomic burden.[17]

In the present study, the 6MWT was used to assess exercise capacity. Although cardiopulmonary exercise testing is generally regarded as the gold standard for the evaluation of exercise capacity, the 6MWT has been more widely used in clinical practice for HF patients because of its patient-friendly profile and similar prognostic value to cardiopulmonary exercise testing.[18] As the JVP assessment used in this study was simple, this technique can also be applied even for patients who are incapable of completing the 6MWT because a high JVP may be easily recognized even during walking. In addition, exercise may be discontinued when a high JVP is noted during low-grade exercise. Physical examination with this simple method may be considerably useful and practical for the management of patients with HF.

The exact mechanisms of the association of a high JVP after the 6MWT in our study remain unclear, but a high central venous pressure may be due to worsening left-sided HF after the 6MWT. Chronic increases in left-sided pressures were reported to be frequently and reliably transduced to the pulmonary circulation and the right ventricle.[19] This may be supported by the echocardiographic findings of our study. Patients with a high JVP after 6MWT, compared with those without, had higher left ventricular end-diastolic and end-systolic diameters, findings indicative of higher ventricular strain. In addition, inferior vena cava diameters and pressure gradient of tricuspid regurgitation were higher in patients with a high JVP than in those without, findings suggestive of more stress on the pulmonary circulation and right ventricle.

The current study has several limitations. First, it was conducted at a single center on highly selected patients. Therefore, the results may not be generalizable to the global HF population. Second, high JVP was visually assessed (i.e., qualitatively rather than quantitatively) before and after the 6MWT; it is unclear whether the timing and degree of the new onset during 6MWT provides more useful information for the management of patients with HF. Third, there are many determinants of the 6MWT other than cardiac function in patients with HF, such as peripheral vascular function and mental condition,[7] none of which were assessed in our study. Lastly, there are patients in whom JVP may be difficult to access for different reasons, such as body habitus or obesity, although the JVP was able to be assessed for all patients in our study.

In conclusion, a high JVP after the 6MWT, which was assessed by visibility of the right internal jugular vein above the right clavicle in the sitting position, was associated with exercise intolerance and poor outcomes in patients with HF. The response of JVP to exercise using this simple technique of physical examination may be a new approach for patients with HF for risk assessment.

Author Contribution

Kenichi Kasai: Data curation, Methodology, and Writing. Tatsuya Kawasaki: Conceptualization, Writing - Reviewing and Editing. Shingo Hashimoto, Shiho Inami, and Atsushi Shindo: Visualization and Investigation. Hirokazu Shiraishi: Supervision. Satoaki Matoba: Supervision.

Disclosures

The authors have no conflicts of interest to disclose.

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1. Constant J. Jugular pressure and pulsations. In: Constant J, ed. Beside Cardiology. 5th edn. Philadelphia: Lippincott Williams & Wilkins; 1999:67–93.
2. Drazner MH, Rame JE, Stevenson LW, Dries DL. Prognostic importance of elevated jugular venous pressure and a third heart sound in patients with heart failure. *N Engl J Med* 2001;345:574–581.
3. McGee SR. Physical examination of venous pressure: a critical review. *Am Heart J* 1998;136:10–18.
4. Chua Chiaco JM, Parikh NI, Fergusson DJ. The jugular venous pressure revisited. *Cleve Clin J Med* 2013;80:638–644.
5. Sinisalo J, Rapola J, Rossinen J, Kupari M. Simplifying the estimation of jugular venous pressure. *Am J Cardiol* 2007;100:1779–1781.
6. Tsutsui H. Guidelines for Diagnosis and Treatment of Acute and Chronic Heart Failure. (JCS 2017/JHFS 2017). http://www.j-circ.or.jp/guideline/pdf/JCS2017_tsutsui_h.pdf. Accessed September 27, 2019.
7. Nohara R. Guidelines for Rehabilitation in Patients with Cardiovascular Disease (JCS 2012). http://www.j-circ.or.jp/guideline/pdf/JCS2012_nohara_h.pdf. Accessed September 27, 2019.
8. Ando Y, Ito S, Uemura O, Kato T, Kimura G, Nakao T, Hattori M, Fukagawa M, Horio M, Mitarai T. Japanese Society of Nephrology. CKD clinical practice guidebook. The essence of treatment for CKD patients. *Clin Exp Nephrol* 2009;13:191–248.
9. Cereda E, Pedrolli C. The geriatric nutritional risk index. *Curr Opin Clin Nutr Metab Care* 2009;12:1–7.
10. ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. ATS statement: guidelines for the six-minute walk test. *Am J Respir Crit Care Med* 2002;166:111–117. Erratum in: *Am J Respir Crit Care Med* 2016;193:1185.
11. Lipton B. Estimation of central venous pressure by ultrasound of the internal jugular vein. *Am J Emerg Med* 2000;18:432–434.
12. Gatt I, Smith-Moore S, Steggles C, Loosemore M. The takei handheld dynamometer: an effective clinical outcome measure tool for hand and wrist function in boxing. *Hand (N Y)* 2018;13:319–324.
13. Kamiya K, Masuda T, Tanaka S, Hamazaki N, Matsue Y, Mezzani A, Matsuzawa R, Nozaki K, Maekawa E, Noda C, Yamaoka-Tojo M, Arai Y, Matsunaga A, Izumi T, Ako J. Quadriceps strength as a predictor of mortality in coronary artery disease. *Am J Med* 2015;128:1212–1219.
14. Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, Picard MH, Roman MJ, Seward J, Shanewise JS, Solomon SD, Spencer KT, Sutton MS, Stewart WJ, Chamber quantification writing group; American Society of Echocardiography's Guidelines and Standards Committee; European Association of Echocardiography. recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. *J Am Soc Echocardiogr* 2005;18:1440–1463.
15. Butler J, Chomsky DB, Wilson JR. Pulmonary hypertension and exercise intolerance in patients with heart failure. *J Am Coll Cardiol* 1999;34:1802–1806.
16. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JG, Coats AJ, Falk V, González-Juanatey JR, Harjola VP, Jankowska EA, Jessup M, Linde C, Nihoyannopoulos P, Parissis JT, Pieske B, Riley JP, Rosano GM, Ruilope LM, Ruschitzka F, Rutten FH, van der Meer P, Authors/Task Force Members; document reviewers. 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 J Heart Fail* 2016;18:891–975.
17. Giannitsi S, Bougiakli M, Bechlioulis A, Kotsia A, Michalis LK, Naka KK. 6-minute walking test: a useful tool in the management of heart failure patients. *Ther Adv Cardiovasc Dis* 2019:1753944719870084.
18. Forman DE, Fleg JL, Kitzman DW, Brawner CA, Swank AM, McKelvie RS, Clare RM, Ellis SJ, Dunlap ME, Bittner V. 6-min walk test provides prognostic utility comparable to cardiopulmonary exercise testing in ambulatory outpatients with systolic heart failure. *J Am Coll Cardiol* 2012;60:2653–2661.
19. Economides E, Stevenson LW. The jugular veins: knowing enough to look. *Am Heart J* 1998;136:6–9.