

Title	Two cases showing alterations of the order of tricuspid and mitral valve opening during loading manipulations : a new approach for quick assessment of stress-induced left ventricular filling pressure elevation			
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Instructions for use

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1	Two cases showing alterations of the order of tricuspid and mitral valve opening during
2	loading manipulations: a new approach for quick assessment of stress-induced left
3	ventricular filling pressure elevation
4	
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25	Running head: Quick assessment of elevated LV filling pressure during loading manipulations
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28	
29	Funding/Grants: None
30	

31 Case 1

32	A 78-year-old woman was referred to our hospital to diagnose the etiology of left ventricular (LV)
33	systolic dysfunction. Echocardiography showed reduced LV ejection fraction (36%) with diffuse
34	hypertrophy. Precise observation of the motion of atrioventricular valves (AVV) revealed a unique
35	sequence in early-diastolic opening: the tricuspid valve (TV) opened earlier than the mitral valve
36	(MV) (Fig. 1a, Video 1). Pressure recording revealed normal mean pulmonary capillary wedge
37	pressure (PCWP) of 6 mmHg (v-wave: 8 mmHg) at rest, but it dramatically increased to 36 mmHg,
38	with an increase in the v-wave (53 mmHg) during supine bicycle exercise (Fig. 1b). Also, mean
39	right atrial pressure (RAP) increased during exercise (6 to 12 mmHg) but it was less than the
40	change in PCWP (Fig. 1c). Consistently, simultaneous echocardiography with the pressure
41	recording showed increased ratio of early-diastolic transmitral flow velocity to septal mitral annular
42	velocity (E/e') (17 to 26). Interestingly, the order of early-diastolic AVV opening changed to earlier
43	opening of the MV (Fig. 1d, Video 2).
44	Case 2
45	A 79-year-old woman with atrial fibrillation after transcatheter aortic valve implantation underwent

46 invasive hemodynamic and echocardiographic assessment due to exertional dyspnea.

- 47 Echocardiography demonstrated normal LV ejection fraction (69%) without any transcatheter heart
- 48 valve dysfunction. At baseline, AVV opened simultaneously (Fig. 1e, Video 3), and PCWP/RAP
- 49 was 14/7 mmHg, respectively. During passive leg raise, the v-wave of PCWP increased from 19 to

50	24 mmHg, resulting in increased mean PCWP of 17 mmHg (Fig. 1f) (RAP was somewhat
51	increased to 10 mmHg [Fig. 1g]), whereas slight increase in echocardiographic E velocity (95 to
52	108 cm/s) and constantly normal septal E/e' (9 to 8) were observed. In contrast, early-diastolic MV
53	opening became earlier than TV (Fig. 1h, Video 4).
54	Discussion
55	Impaired LV diastolic reserve is an occult sign of heart failure and a predictor of its adverse
56	outcomes [1]. While the early-diastolic opening of TV precedes that of MV in normal condition,
57	once left atrial (LA) pressure elevates, the opening of MV becomes early and precedes TV opening
58	resulted from the early crossover of LA and LV pressures [2-4]. In case 1, E/e' increased along with
59	the elevated PCWP during exercise, and the order of AVV opening was also altered. Meanwhile, in
60	case 2, E/e' did not track the increase of PCWP during leg lifts, but the order of AVV correctly
61	changed. Because E velocity depends on the early-diastolic LA to LV pressure difference [5],
62	increase in E velocity might have been gentle due to increase of LV minimal pressure despite the
63	increased LA v-wave. These cases underline the potential usefulness of the stress-induced alteration
64	of the order of early-diastolic AVV opening to detect impaired LV diastolic function reserve.
65	However, further studies including a larger sample, ideally using simultaneous catheterization-
66	echocardiographic testing, are needed to confirm our findings.

67	De	clarations
68	Etl	nical statements All procedures followed were in accordance with the ethical standards of the
69	res	ponsible committee on human experimentation (institutional and national) and with the Helsinki
70	De	claration of 1964 and later versions. Informed consent was obtained from all patients for being
71	inc	luded in the study.
72		
73	Co	nflict of interest Michito Murayama, Hiroyuki Iwano, Ko Motoi, Suguru Ishizaka, Shingo
74	Tsu	ijinaga, Toshiyuki Nagai, and Toshihisa Anzai declare that they have no conflicts of interest.
75		
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91 FIGURE CAPTION

92	Figure	1
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93	Two-dimensio	onal echocard	diographic	images at	echocardiography	laboratory (a	a, e), pulmonary
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- 94 capillary wedge pressure (PCWP) waveforms (b, f), right atrial pressure (RAP) waveforms (c, g),
- 95 and corresponding echocardiographic images (d, h) during loading manipulations in case 1 and
- 96 case 2. Note that earlier opening of the MV (yellow asterisks) was observed along with the marked
- 97 elevation of v-wave of PCWP (arrow heads) during the loading manipulation in both cases. LV, left
- 98 ventricle; RV, right ventricle; MV, mitral valve; TV, tricuspid valve.
- 99

100 Supplemental Video 1. Order of tricuspid and mitral valve opening at rest in case 1

101 During slow playback, we can appreciate the earlier opening of tricuspid valve.

102

103 Supplemental Video 2. Order of tricuspid and mitral valve opening during exercise in case 1

104 During slow playback, we can appreciate the earlier opening of mitral valve.

105

106 Supplemental Video 3. Order of tricuspid and mitral valve opening at rest in case 2

107 During slow playback, we can notice that both atrioventricular valves open almost simultaneously.

108

109 Supplemental Video 4. Order of tricuspid and mitral valve opening during passive leg lifts in

110 case 2

- 111 During slow playback, we can appreciate the earlier opening of the mitral valve on the first and
- third beat whereas both valves open almost simultaneously in the second beat. This image was
- judged as mitral valve opening first. When beat-to-beat variability was observed, six to nine beats
- 114 were used, and the majority result was used for the final judgment.



CW rit





PCW rit(a/v/m)





Baseline at Laboratory

RV

10

LV





