



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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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**

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25 **Running head:** Quick assessment of elevated LV filling pressure during loading manipulations

26

27 **Conflict of interest:** None to declare.

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 **Declarations**

68 **Ethical statements** All procedures followed were in accordance with the ethical standards of the  
69 responsible committee on human experimentation (institutional and national) and with the Helsinki  
70 Declaration of 1964 and later versions. Informed consent was obtained from all patients for being  
71 included in the study.

72

73 **Conflict of interest** Michito Murayama, Hiroyuki Iwano, Ko Motoi, Suguru Ishizaka, Shingo  
74 Tsujinaga, Toshiyuki Nagai, and Toshihisa Anzai declare that they have no conflicts of interest.

75

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90

91 **FIGURE CAPTION**

92 **Figure 1.**

93 Two-dimensional echocardiographic images at echocardiography laboratory (**a, e**), pulmonary  
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

112 third beat whereas both valves open almost simultaneously in the second beat. This image was

113 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.



