Paradoxical increase in E/e' during severe central hypovolemia in healthy humans

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Introduction: The ratio of mitral blood inflow to mitral annular tissue velocity in early diastole (E/e’) is widely used as an index of left ventricular (LV) diastolic dysfunction. Theoretically, it is considered that e’ can correct the effect of LV relaxation on E, and thus E/e’ can be applied for the prediction of LV filling pressures in patients with cardiac diseases. However, recent guidelines indicate that E/e’ may not provide a reliable estimate of filling pressures in healthy subjects. Indeed, previous studies have reported that E/e’ did not decrease during acute central hypovolemia because both E and e’ are similarly reduced by low preload conditions. However, it is possible that E/e’ did not decrease since central hypovolemia were not critical in the previous studies.

Purpose: The purpose of the present study was to clarify the change of E/e’ during severe central hypovolemia induced by lower body negative pressure.

Methods: Twelve healthy men (25±5 years old) underwent 2D Doppler and 3D echocardiography during graded lower body negative pressure (LBNP) up to presyncope. We measured LV diastolic function indices by 2D echocardiography including septal and lateral mitral annular early diastolic velocities (e’), and early (E) and late (A) mitral inflow velocities. In addition, we measured LV function indices by 3D echocardiography including end-diastolic volume (EDV), end-systolic volume (ESV), stroke volume (SV), ejection fraction (EF), global longitudinal strain (GLS), global circumferential strain (GCS), twist and peak untwisting rate. We compared echocardiography indices before LBNP (Baseline) with those at maximal LBNP (LBNPmax) and at half of the maximal LBNP (LBNP1/2max).

Results: E/e’ (Baseline: 5.8±0.8, LBNP1/2max: 5.4±1.0, LBNPmax: 7.8±2.3, mean±SD, p<0.01, ANOVA) did not change at the LBNP1/2max but increased only at the LBNPmax. E (80±11, 59±10, 62±12 cm/sec, p<0.01) and E/A (2.2±0.8, 1.5±0.5, 1.0±0.3, p<0.01) decreased at the LBNP1/2max as compared to baseline but did not change from LBNP1/2max to LBNPmax. e’ (14.1±2.0, 11.1±1.5, 8.2±2.2 cm/sec, p<0.01) decreased in response to LBNP. LV EF (62±3, 55±5, 43±9 %, p<0.01), LV GLS (-20.5±2.8, -17.6±2.7, -13.6±4.7 %, p<0.01), and LV GCS (-31.2±3.7, -26.8±3.3, -19.4±5.3 %, p<0.01) decreased in response to LBNP. LV twist (15.2±5.1, 14.5±5.4, 20.9±7.7 °, p<0.01) and LV peak untwisting rate (-138±42, -164±50, -245±88 °/cm, p<0.01) increased only at the LBNPmax.

Conclusion: The present study for the first time showed that E/e’ paradoxically increased during acute severe hypovolemia in healthy humans. This paradox was likely caused by well-preserved E, while e’ decreased in response to acute severe central hypovolemia. The present finding also showed that peak untwisting rate was increased at severe central hypovolemia, suggesting that the well-preserved E may be caused by high pressure gradient from left atrium to LV induced by enhanced LV untwisting suction function.
Key results of this study

The change of indexes of left ventricular diastolic function during severe central hypovolemia

Values are mean±SD. *P<0.05 vs. Baseline, †P<0.05 vs. LBNP1/2max.
LBNP: Lower Body Negative Pressure
The change of indexes of left ventricular diastolic function during severe central hypovolemia

- **E (cm/sec)**

- **Peak Untwisting Rate (°/cm)**

Values are mean ± SD. *P<0.05 vs. Baseline, †P<0.05 vs. LBNP1/2max.
LBNP: Lower Body Negative Pressure

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