2P-266

Quantitative Evaluation of Anesthesia Depth and Myocardial Infarction Impact on Mitral Annular Velocity in Rats Using Tissue Doppler Imaging.

組織ドプラを用いたラットの麻酔深度と心筋梗塞が僧帽弁輪速度に与える影響の定量的評価

〇Takuya Akashi, Mina Matsumoto, Yoshizo Fukuda, Ayahito Kimura　〇赤司　卓也, 松本　美奈, 福田　好造, 木村　恵人
NISSEI BILIS Co., Ltd., Shiga Laboratory　日精バイリス株式会社　滋賀研究所

Introduction

Left ventricular function in rat heart failure models has been assessed by echocardiography using left ventricular ejection fraction in Motion mode (M-mode) , left ventricular inflow velocity in pulsed Doppler mode (D-mode), and maximum mitral annular translation velocity in tissue Doppler imaging mode (TDI-mode). It has been widely reported about usage of isoflurane (ISO) and mixed ketamine/xylazine anesthesia for the assessment of left ventricular function. We evaluated whether medetomidine-midazolam-butorphanol (MMB) anesthesia could serve as an alternative to ISO anesthesia (Experiment 1). In addition, we examined temporal changes in left ventricular function under MMB anesthesia in rat myocardial infarction model (Experiment 2).

Materials & Methods

This study was conducted as approved by the Institutional Animal Care and Use Committee of NISSEI BILIS Co., Ltd., Shiga Laboratory.

Anesthesia

MMB Anesthesia (subcutaneous injection)

Drug	Dose（mg/kg）	
	Low（L MMB）	High（H MMB）
Medetomidine (Kyoritsu Seiyaku Corp.)	0.075	0.15
Midazolam (Sandoz K.K.)	1.0	2.0
Butorphanol (Meiji Seika Pharma Co., Ltd)	1.25	2.5

ISO Anesthesia (inhalation)

2.0～3.0%, 2.5 L/min

Echocardiography

Device: Vivid S6、GE Healthcare

Parameters

- M-mode: diastolic left ventricular internal dimension (LVIDd), systolic left ventricular internal dimension (LVIDs), left ventricular ejection fraction (LVEF), left ventricular fractional shortening (%FS), and heart rate (HR)
- D-mode: early diastolic filling velocity (E), atrial systolic velocity (A), and early diastolic filling velocity to atrial contraction velocity ratio (E/A)
- TDI-mode**:** septal early diastolic mitral annular tissue velocity (e'), septal atrial systolic mitral annular tissue velocity (a'), and peak systolic myocardial velocity (s')

Analysis

Individual data were calculated on the average of values from three consecutive cardiac cycles. E/e' was calculated from the E and e' waves.

Experiment 1

Animals

Male Wistar rats (Japan SLC, Inc.), 12 or 7 weeks old

Groups	n	Anesthesia	Echocardiography	
			Age	Imaging mode
ISO	6	Isoflurane (one day after L MMB evaluation)	7 weeks old	M-mode
L MMB		L MMB		
H MMB	2	H MMB	12 weeks old	

Experiment 2

Animals

Male Wistar rats (Japan SLC, Inc.), 7 weeks old

Group design

Five animals underwent complete coronary artery ligation (MI) under H MMB anesthesia, and three animals with no apparent left ventricular wall motion were allocated to the MI group.

Groups	n	Anesthesia	Echocardiography	
			Time point	Imaging mode
Normal (intact animal)	6	L MMB	MI Day28	M-mode D-mode TDI-mode
MI	3		MI Day7 MI Day14 MI Day28	

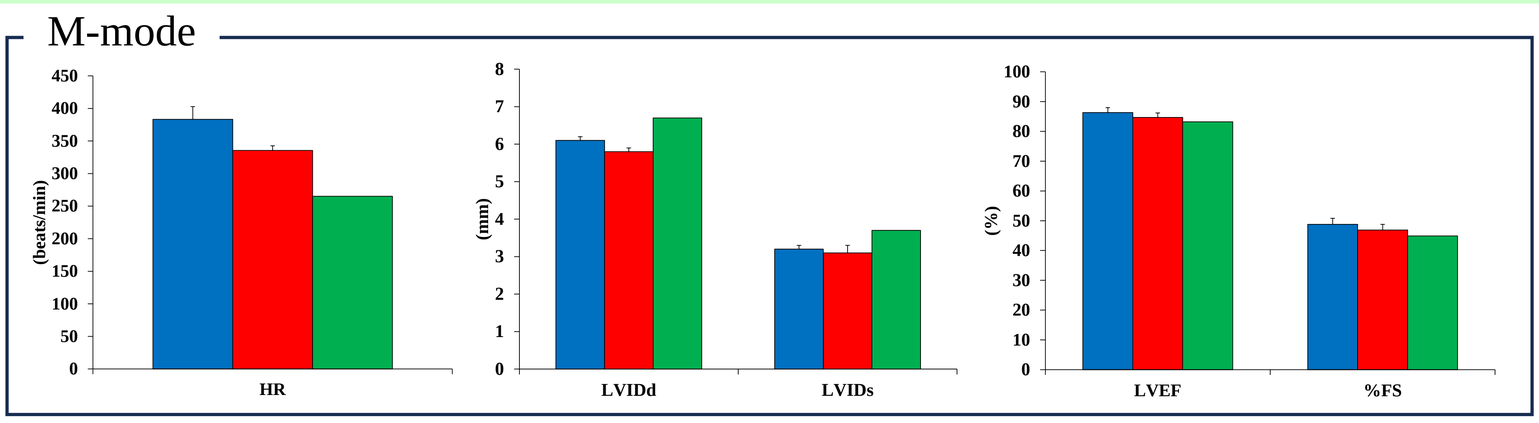
Left heart cardiac catheterization

- Time point: MI Day 28
- Number of animals : MMB; n=2, MI; n=3
- Methods

  A Miller catheter (SPR-215, Millar Instruments) was inserted into the left ventricular through the right carotid artery to measure LVEDP and recorded on a Labchart 8 (AD Instruments) via a polygraph system (RMT-1000, Nihon Kohden Corp.).

Results & Discussions

Experiment 1



Experiment 1: Comparison of MMB and ISO anesthesia

Standard group	Comparative group	HR	LVIDd	LVIDs	LVEF	%FS
ISO	L MMB	↓	→	→	→	→
	H MMB	↓↓	↑	↑	→	→

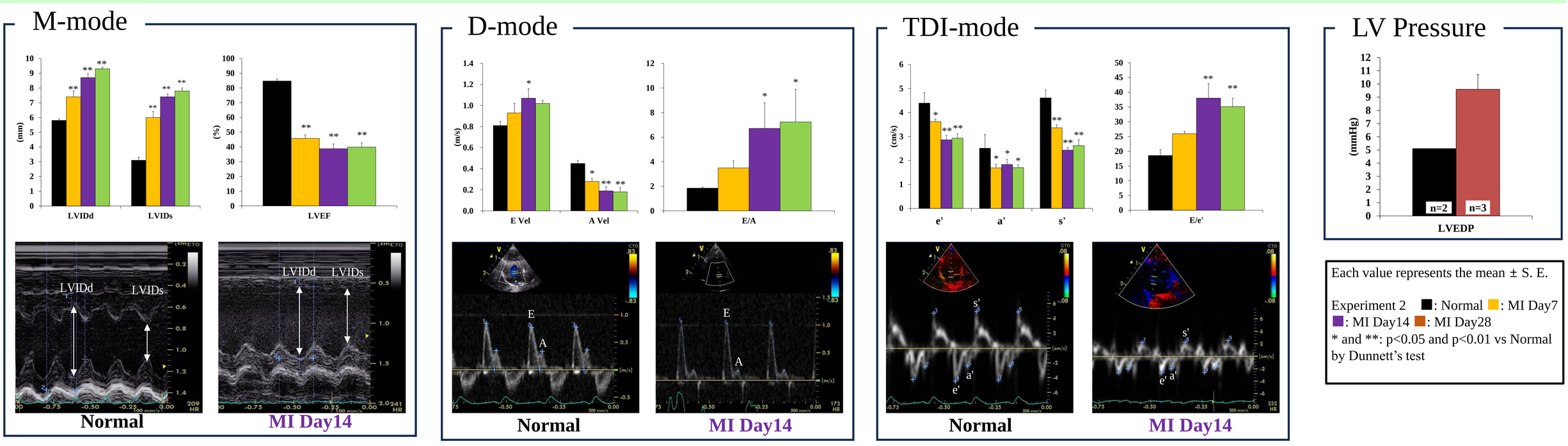
→: no change, ↑: increased, ↓: decreased

L MMB anesthesia was available as an anesthetic for left ventricular function evaluation.

Each value represents the mean ± S. E.

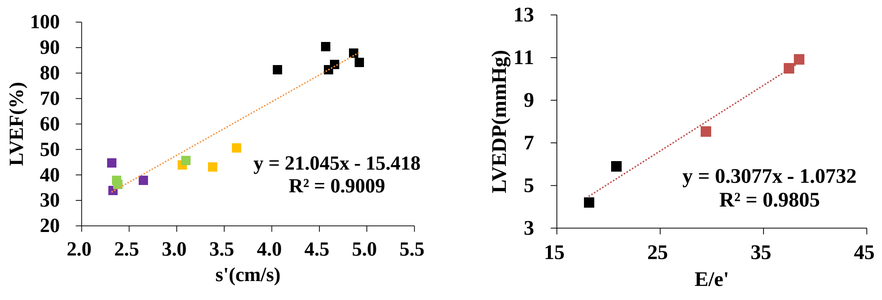
Experiment 1 ■: ISO ■: L MMB ■: H MMB
No significant difference between ISO and L MMB groups.

Experiment 2



Each value represents the mean ± S. E.

Experiment 2 ■: Normal ■: MI Day7 ■: MI Day14 ■: MI Day28
* and **: p<0.05 and p<0.01 vs Normal by Dunnett's test



Strong positive correlations were observed between LVEF and s', as well as between LVEDP and E/e'.

Experiment 2: Sequential changes in left ventricular function in a rat MI model

Measurement parameters												
Standard group	Comparative group	M-mode			D-mode			TDI-mode				LV Pressure
		EF	LVIDd	LVIDs	E Vel	A Vel	E/A	e'	a'	s'	E/e'	LVEDP
Normal	MI	↓ Day 7-28			↓ Day 14	↓ Day 7-28	↑ Day 14-28	↓ Day 7-28			↑ Day 14-28	↑ Day 28

→: no change, ↑: increased, ↓: decreased

Conclusion

Based on these results, MMB anesthesia proved to be viable for left ventricular function assessment, enabling measurements of left ventricular ejection fraction, left ventricular inflow velocity waveform, and maximum mitral annular translation velocity. Furthermore, it was possible to observe the temporal progression of cardiac dysfunction in the myocardial infarction model.

COI：disclosure information :We have no financial relationship to disclose for our presentation contents.