Cardiac Magnetic Resonance Imaging Without General Anesthesia in Mice

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INTRODUCTION

As new genetically engineered models of cardiovascular disease are developed, in vivo phenotyping remains a challenge. Echocardiography (Echo) can be performed in real time in conscious mice, but is encumbered by acquisition in limited planes, necessitating assumptions about cardiac shape. Cardiovascular magnetic resonance imaging (CMR) yields superior visualization and quantitative accuracy, but requires immobilization of the mouse for image acquisition – typically with general anesthesia. All general anesthetics are cardio-depressant [1] which introduces a confounding variable into phenotyping studies [2,3]. The purpose of this study was to determine whether CMR can be performed reliably using deep sedation and to assess its impact on image quality and cardiac function compared to traditional anesthesia protocols.

METHODS

Echo was performed under light sedation with midazolam (0.15 mg s.c.), which has previously been shown to have no cardio-depressant effect compared to unsedated mice, in 6 normal mice and in 4 mice with ischemic heart failure (CHF). Subsequently, each mouse underwent two sessions of CMR on a Varian Unity/INOVA 4.7 T horizontal bore scanner (Varian Inc., Palo Alto, CA) equipped with a 38 mm diameter quadrature RF coil and physiologic monitoring system for cardiac triggering (SA Instruments, Stony Brook, NY). The imaging protocol consisted of axial and oblique coronal localizers followed by an ECG-gated short-axis multi-slice cine spoiled gradient echo pulse sequence covering the entire left ventricle (LV) throughout the cardiac cycle with parameters TR/TE = 6.0/3.4 ms, flip angle = 15°, 0.2 x 0.2 x 1 mm^3 voxels, 256 x 128 matrix, 7-9 short-axis slices, yielding 15-20 cine frames per cardiac cycle depending on the heart rate.

The first CMR session utilized deep sedation with a combination of morphine (4.5 mg/kg s.c.) and midazolam (9 mg/kg s.c.). The second session occurred one week later and applied general anesthesia using 1% isoflurane administered via nose cone. In both sessions, mouse body temperature was maintained with an external warm air source. Quantification of cardiac volumes and mass were computed using Simpson's Rule applied to manual tracings of left ventricular borders at end-systole and end-diastole.

RESULTS

All 10 mice survived the three consecutive imaging sessions. Image quality was comparable and sufficient for quantitative analysis in all cases (Figure 1). Table 1 displays the set of CMR-derived morphological and functional parameters for each sedation regimen. Deep sedation with midazolam + morphine resulted in significantly higher, more physiological heart rate and ejection fraction (LVEF) compared to measurements made during general anesthesia with isoflurane. The mean decrements in heart rate from light sedation for Echo in normal mice were 32 min^{-1} and 147 min^{-1} for deep sedation and isoflurane respectively ($p < 0.01$). LV mass was highly reproducible between CMR scans, with mean absolute difference between scans of 4 mg in normal mice and 2 mg in CHF mice.

DISCUSSION

CMR performed under deep sedation with morphine and midazolam yielded comparable image quality and significantly less artifactual depression of heart rate and LVEF compared to CMR performed under general anesthesia with 1% isoflurane. This regimen is advantageous over traditional anesthesia protocols for assessment and quantitation of cardiovascular function with CMR.

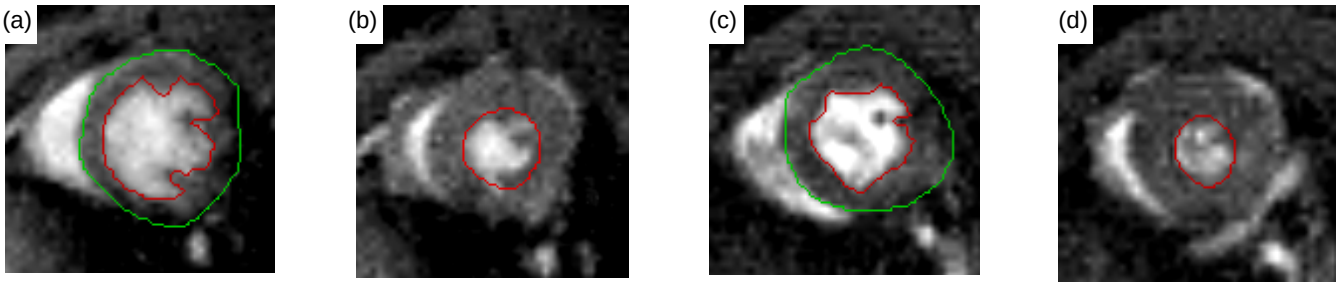

Figure 1. Representative end-diastolic (a,c) and end-systolic (b,d) frames from mouse with normal cardiac function under general anesthesia (a,b) and deep sedation (c,d).

Table 1: Image-derived LV parameters (mean ± SE)

	Normal (Echo, light sedation)	*Normal (MRI, isoflurane)*	*Normal (MRI, deep sedation)*	*CHF (Echo, light sedation*	*CHF (MRI, isoflurane)*	*CHF (MRI, deep sedation)*
Heart Rate (min^{-1})	†615 ± 25	468 ± 7	†583 ± 30	515 ± 49	447 ± 120	544 ± 80
LVEF (%)	†94 ± 1	60 ± 4	†79 ± 4	27 ± 8	23 ± 6	24 ± 5
LV Mass (mg)	N/A	66 ± 6	67 ± 7	N/A	137 ± 26	135 ± 25

† Significant difference versus isoflurane ($p < 0.01$)

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