

A Dataset from Echocardiographic Assessment of Cardiac Function in Mice after Myocardial Infarction

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ABSTRACT

Open-access datasets for cardiac remodelling after myocardial infarction in any species have not been reported, and this limits the development of systems approaches in medicine. In this paper, we present a dataset from echocardiographic assessment of male C57BL mice that were subjected to acute myocardial infarction. We present measurements that show the deterioration of global left ventricular (LV) function, regional function, development of LV dilation and hypertrophy. At the same time, we present measurements showing the degree of cardiac injury as well as the development of pulmonary congestion. Importantly, LV dilation—a hallmark of cardiac remodelling—does not develop in all subjects, and this is only partly explained by the degree of cardiac injury.



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Overview

Despite the advances in current treatments, a substantial proportion of patients fail to recover after acute myocardial infarction resulting in heart failure.¹ The main cause of this failure to recover is the development of cardiac remodelling, a process that leads to a series of structural and functional changes in the viable myocardium. Although progress has been made in understanding the pathophysiology of cardiac remodelling, we are still unable to predict disease progress and lack effective treatments tailored to the needs of the specific patient.² This is due to the complex pathophysiology of the cardiac remodelling that requires a systems medicine approach through the integration of multiple data types, as well as to the complexi-

ties inferring information from such data.³ To date, open-access datasets for cardiac remodelling have not been reported in any species, and this limits the development of systems medicine approaches. Our group has worked for many years in this area aiming to determine novel pathophysiological insights and therapeutic interventions using *in vivo* models of myocardial infarction in mice and rats.⁴⁻⁷ In this report, we present an echocardiographic dataset from male C57BL mice that were subjected to acute myocardial infarction. Part of this data has been used in previously published works that investigated the role of thyroid hormone receptor alpha 1 in cardiac remodelling, as well as the role of thyroid hormone as new therapeutic approach in this process.⁷⁻⁸

Methods

Animals

Male C57BL mice were maintained on a 12 h light/dark cycle and fed with a standard chow ad libitum. Mice were handled in accordance with the Guide for the Care and Use of Laboratory Animals published by the US National Institutes of Health Guide (NIH Pub. No. 83-23, Revised 1996).

Experimental model of myocardial infarction in mice

Myocardial infarction was induced by ligation of the left coronary artery. Mice were anesthetized with sevoflurane inhalation in a closed chamber, intubated and ventilated via a tracheal cannula using a constant-volume rodent ventilator (Harvard Apparatus, Inspira, 100 breaths/min, 0.1ml/10g tidal volume). Anaesthesia was maintained by inhalation of sevoflurane (3-4%). Left thoracotomy was performed at the fourth intercostal space followed by pericardiotomy. Left coronary artery was then ligated with a 8-0 silk round-bodied suture. The heart was quickly returned to the chest cavity, the chest was closed and mice were allowed to recover using assist mode ventilation. Atelectasis was prevented by using positive end-expiratory pressure at the end of the surgical procedure. Body temperature was maintained at 37°C by using a heating blanket (Harvard Homeothermic Blanket, 50-7061). The animals were left to recover for three weeks after myocardial infarction. The same procedure was followed for sham-operated animals, but the coronary artery was not ligated. Animals were 12-16 weeks old at the time of surgical procedure. A total of 16 animals were subjected to sham-operation, while 15 animals were subjected to coronary artery ligation (CAL).

Experimental procedure

Three weeks after the surgical procedure, mice were anaesthetized with ketamine hydrochloride and midazolam, subjected to echocardiography analysis, and the heart and lungs were removed. Left ventricle (LV) and right ventricle (RV) of the heart and lung weight (LW) were measured for each animal. Scar LV tissue was dissected out. The area of the scar tissue was measured in mm² and the weight in mg. The ratio of lung weight to body weight (LW/BW in mg/mg) was used to assess the development of pulmonary congestion after myocardial infarction.

Echocardiography

Short and long-axis images were acquired using a digital ultrasound system (Vivid 7 version Pro, GE Healthcare) with the 14.0-MHz i13L probe. A large number of consecutive measurements were performed and analysed by two independent operators. All measurements were averaged for at least 3 consecutive cardiac cycles. Left ventricular (LV) internal diameter at the diastolic phase, LV internal diameter at the systolic phase, posterior wall thickness at the diastolic phase and the ejection fraction (EF %) were measured. EF % was calculated using the Simpson equation. EF % was used to determine the global contractile LV function. Systolic velocity of the posterior wall radial displacement (SVPW) was also measured. SVPW was measured from two-dimensional guided M-mode recordings obtained at the midventricular level. SVPW was calculated according to the following formula: $V = ds/dt$, where 'V' represents velocity, 's' – the distance, and 't' represents time.

Data Records

The data in the accompanying spreadsheet is organised in the following columns:

- A:** It shows the ID of the subject.
- B:** It shows the intervention that the animals were subjected to. It includes two options – either sham-operation or coronary artery ligation (CAL).
- C:** It shows the duration of the time in weeks between the intervention and evaluation of measurements. All measurements were performed three weeks after the surgical procedure.
- D:** It shows body weight of animals in grams at the time of surgery.
- E:** It shows body weight of animals in grams at the day of sacrifice.
- F:** It shows the left ventricular (LV) end-diastolic diameter in cm that was measured by echocardiography.
- G:** It shows the left ventricular end-systolic diameter in cm that was measured by echocardiography.
- H:** It shows the left ventricular posterior wall thickness in cm that was measured by echocardiography.

- I:** It shows the maximum distance from the basis to the apex of the left ventricle in cm (called long axis) that was measured by echocardiography.
- G:** It shows the left ventricular ejection fraction in percentages that was measured by echocardiography using the Simpson equation.
- K:** It shows the systolic velocity of the left ventricular posterior wall in cm/sec that was measured by echocardiography.
- L:** It shows the left ventricular end-diastolic volume in ml that was measured by echocardiography using the Simpson equation.
- M:** It shows the left ventricular end-systolic volume in ml that was measured by echocardiography using the Simpson equation.
- N:** It shows the Wall tension index (WTI) defined as the ratio of (LV end-diastolic diameter)/ 2* (left ventricular posterior wall thickness). WTI was measured in order to indirectly assess myocardial wall stress.
- O:** It shows the heart rate in beats per min that was measured during echocardiography.
- P:** It shows the left ventricular weight in grams.
- Q:** It shows the weight of the scar tissue of the left ventricle in grams. Animals subjected to sham operation did not have a scar.
- R:** It shows the area of the scar tissue of the left ventricle in mm². Animals subjected to sham operation did not have a scar.
- S:** It shows the wet lung weight in grams.
- T:** It shows the right ventricular (RV) weight in grams.

Use and potential reuse

The publication of well-structured data from the level of the cardiac cell to the level of the heart could form the basis for the development of a holistic approach to integrate different advances into a unified model of heart function and disease.³ Thus, open-access datasets referring to the process of cardiac remodelling after myocardial infarction could be valuable tools in understanding the adaptation of the heart to stress through the development of computational models.⁹ Furthermore, modelling the response of the heart after myocardial infarction could predict recovery of function or development of heart failure and serve as a useful tool both for developing new

therapies and evaluating current treatments. In other fields, such as electrophysiology, computational models have now been developed for a variety of animal species, allowing representation of species-specific propensity for arrhythmia.¹⁰ However, models of the human cardiac myocyte that have been developed are constrained by limited available experimental data and have restricted applications.¹¹⁻¹³

The dataset published in this paper was created after acute myocardial infarction was induced in mice by ligation of the left coronary artery. Within three weeks after myocardial infarction, the cardiac function was evaluated by echocardiography. In this data paper, we present measurements that show the deterioration of global LV function (ejection fraction), regional function (systolic velocity of posterior wall), development of LV dilation (LV end-diastolic diameter and volume) and hypertrophy (LV weight and posterior wall thickness). At the same time, we present measurements showing the degree of cardiac injury (as assessed by the scar weight and area) as well as the development of pulmonary congestion (wet lung weight and RV weight). It is interesting to note that as it happens in humans, the development of LV dilation (a hallmark of cardiac remodelling) does not appear in all subjects and this is only partly explained by the degree of cardiac injury.

Conclusions

In conclusion, we present a dataset from echocardiographic assessment of male C57BL mice that were subjected to acute myocardial infarction for 3 weeks. Similar datasets could be used to create an *in silico* disease model for heart failure after myocardial infarction and help to overcome the difficulty in extrapolating pre-clinical data to predict clinical efficacy.

Data Files

The data described in this paper is presented in an openly accessible spreadsheet: "01301_Mice_Myocardial_Infarction.xlsx".

The file is available also in the Open Document Spreadsheet format.

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