

T400-Series Surgical Protocol

Mouse Myocardial Infarction Model

Generally this procedure is performed in adult mice > 10 weeks of age. However, it is possible to perform the surgery on younger animals.

PRE-SURGERY

1. The mouse is weighed under aseptic conditions.
2. Pre-operatively buprenorphine is given at 0.1 mg/kg s.c.
3. Anesthesia is induced by placing the mouse in an induction box filled with isoflurane 4-5%. When the anesthetic state is achieved, the mouse is intubated using a blunt needle (19 gauge) and connected to a Hugo Sachs rodent ventilator (type: Minivent, 250µl stroke volume, 4 Hz) while breathing isoflurane (1.5-2%). If gas anesthesia is not possible the mouse can be anesthetized by ketamine (100 mg/kg i.m.) xylazine (5 mg/kg s.c.). Sodium pentobarbital is not used because the use of this agent is associated with higher mortality.
4. The anterior thorax is shaved and disinfected with iodine.
5. If available, two electrodes are placed subcutaneously to monitor the ECG during the procedure.

SURGERY

1. The skin is incised (parasternal) at the level of the left third and fourth ribs.
2. The pectoral muscles are dissected with two fine forceps and retracted gently with 6-0 silk to free the location where the thoracotomy will be made.
3. The thorax is entered about 2 mm lateral of the sternum with small forceps by making a hole through the intracostal muscles and pleura. The opening is enlarged by cutting the intracostal muscles a bit further. For this purpose, the muscles are lifted with small forceps. Care should be taken to not damage the lungs.
4. The wound is opened about 6 mm with a mouse retractor (Fine Science Tools). An absorption triangle is wet in sterile 0.9% NaCl and used to push the lungs gently aside. With two fine forceps the pericardium is opened.
5. Using a microscope, the left anterior descending coronary artery is identified.

ACKNOWLEDGEMENT

J. Debets, A. Brouns, Dr. B. Janssen, Department of Pharmacology and Toxicology, Cardiovascular Research Institute Maastricht, Universiteit Maastricht, Maastricht, The Netherlands

SUMMARY

- Weigh mouse
- Induce anesthesia
- Shave anterior thorax
- Intubate mouse (19-gauge tube)
- Connect to rodent ventilator (200 ml per stroke, 240 strokes per minute)
- Open skin and retract muscles
- Enter thorax between 3rd-4th rib
- Cut intracostal muscles
- Pull lungs away with absorption sponge
- Place and pull ligature 6-0 prolene ligature around the coronary artery
- Close the thorax
- Press chest to restore negative pressure and release muscles
- Close the skin
- Keep the mouse warm while recovering.
- Give buprenorphine (0.4 mg/kg i.p) when mouse is waking up.

Mouse Myocardial Infarction Model Cont.

6. A prolene 6-0 ligature is placed around the coronary artery just above the site where the artery splits into two smaller branches (Fig. 1). When the ligature is tightened, the apex of the heart should lose some of its red color. The ECG should also show marked differences now. If the ligature is placed too high upstream, then the circumflex artery can also be occluded and this may be associated with increased acute mortality. In our experience, lidocaine is not effective as anti-arrhythmic agent here.
7. The wound is closed as follows:
 - a. Two ligatures (silk 5-0) are placed around the third and fourth ribs.
 - b. The absorption sponge is taken out and the chest is closed with these ligatures.
 - c. The 6-0 silk ligatures that were placed around the muscles are now released. Make sure that the muscles cover the wound.
 - d. The chest is pressed to restore negative pressure.
 - e. The skin is then closed with 5-0 silk.

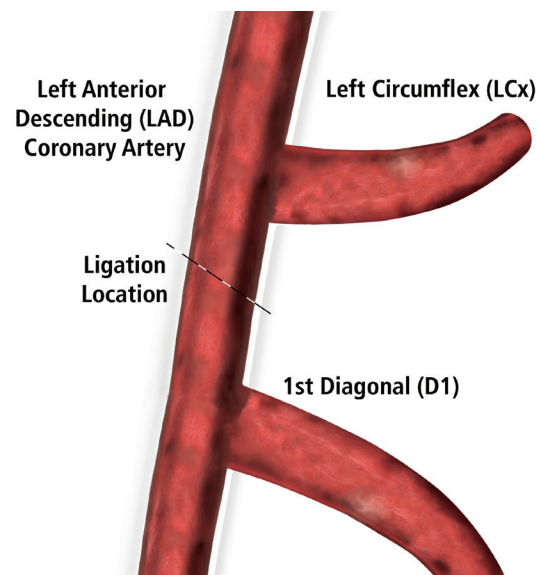


Fig. 1: Schematic drawing of the mouse heart viewed from the ventral site. The ligation is placed just above the bifurcation of the LAD into the 1st Diagonal Branch but after the Circumflex artery originates. When the ligation is placed too high LCx will be ligated too and most of the animals will die.

RECOVERY

1. The ECG is monitored regularly during the first 5-10 minutes after the end of the surgical procedure. Then the isoflurane is stopped and the tube is removed from the trachea.
2. The mouse is allowed to recover for 24 h in a warm environment (28°C). Extra oxygen may help too.
3. 6-24 hours later the s.c. injection of buprenorphine is repeated for additional analgesia (0.1 mg/kg).

In general about 30% of the MI mice die within the first 24 hrs. Sham-operated animals do recover quickly. Cardiac wound healing lasts about 2 weeks.

REFERENCES

The functional and structural consequences of this procedure including the ischemia / reperfusion variant as well as effects of strain differences are described in more detail in:

- Lutgens et al. Cardiovascular Research 41: 586-593, 1999
 Janssen et al. Am J Physiol Regulatory Integrative Comp Physiol 282: R928-R935, 2002;
 De Celle et al. Exp Physiol 89: 605- 615, 2004
 van den Borne et al. Cardiovascular Research 84: 273-282, 2009



www.transonic.com

Transonic Systems Inc. is a global manufacturer of innovative biomedical measurement equipment. Founded in 1983, Transonic sells "gold standard" transit-time ultrasound flowmeters and monitors for surgical, hemodialysis, pediatric critical care, perfusion, interventional radiology and research applications. In addition, Transonic provides pressure and pressure volume systems, laser Doppler flowmeters and telemetry systems.

AMERICAS

Transonic Systems Inc.
 34 Dutch Mill Rd
 Ithaca, NY 14850
 U.S.A.
 Tel: +1 607-257-5300
 Fax: +1 607-257-7256
 support@transonic.com

EUROPE

Transonic Europe B.V.
 Business Park Stein 205
 6181 MB Elsloo
 The Netherlands
 Tel: +31 43-407-7200
 Fax: +31 43-407-7201
 europe@transonic.com

ASIA/PACIFIC

Transonic Asia Inc.
 6F-3 No 5 Hangsiang Rd
 Dayuan, Taoyuan County
 33747 Taiwan, R.O.C.
 Tel: +886 3399-5806
 Fax: +886 3399-5805
 support@transonicasia.com

JAPAN

Transonic Japan Inc.
 KS Bldg 201, 735-4 Kita-Akitsu
 Tokorozawa Saitama
 359-0038 Japan
 Tel: +81 04-2946-8541
 Fax: +81 04-2946-8542
 info@transonic.jp