A Case Report of Acute Cardiac Tamponade Creation in a Macaque: Echo-Guided Catheter Manipulation to Perforate Coronary Artery

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ABSTRACT

Although acute cardiac tamponade is one of the major problems in clinical practice, a suitable animal model is still lacking. We tried to create acute cardiac tamponade in macaques by echo-guided catheter manipulation. A 13-year-old male macaque was anesthetized, and a long sheath was inserted into the left ventricle via the left carotid artery under the guidance of transthoracic echocardiography. The sheath was then inserted into the orifice of the left coronary artery to perforate the proximal site of the left anterior descending branch. A cardiac tamponade was successfully created. Injection of diluted contrast agent into the pericardial space via a catheter made it possible to clearly distinguish between the hemopericardium and the surrounding tissues on postmortem computed tomography. This procedure did not need an X-ray imaging system during catheterization. Our present model would help us examine the intrathoracic organs in the presence of acute cardiac tamponade.

Key words acute cardiac tamponade; animal model; transthoracic echocardiography; echo-guided; postmortem computed tomography

Complications of cardiopulmonary resuscitation (CPR) are occasionally encountered in the field of forensics or emergency medicine.[1–5] One of the complications is pericardial rupture associated with CPR in the presence of acute cardiac tamponade,[2, 5] the mechanisms of which remains unclear. Several studies have been conducted on animals[6, 7] and humans[8, 9] to evaluate internal cardiac pressure and vasculatures during cardiac arrest, cardiac tamponade, and CPR. Rodents and swine are mainly used for animal studies; however, the quadrupedal animals have significantly different thoracic structures from bipedal humans and may not accurately reflect CPR performed on humans. In this study, we tried to create an acute cardiac tamponade in a macaque by echo-guided catheter manipulation as a model that could be used for the validation of the mechanical load applied to the thorax and intrathoracic organs during CPR in the presence of cardiac tamponade.

EXPERIMENTAL PROCEDURES

All experimental procedures were approved by the institutional guidelines for animal experiments of the Oita University Animal Ethics Committee (approval number 1651001). All animal experiments should comply with the ARRIVE guidelines and should be carried out in accordance with the National Research Council's Guide for the Care and Use of Laboratory Animals. A thirteen-year-old male macaque (weighing 2.9 kg) was purchased from Japan SLC, Inc. (Hamamatsu, Japan) and reared in an appropriate environment according to the guidelines of Oita University until the experiment. To reduce the number of laboratory animals in accordance with ethical guidelines for laboratory animals, this study was scheduled when macaques planned to be used for multiple experiments were euthanized.

Catheterization was performed at the Surgical Operation Laboratory for Innovation and Education, Research Promotion Institute, Faculty of Medicine, Oita University. Anesthesia was induced to the macaque with intramuscular injection of ketamine hydrochloride (Ketalar; Daiichi Sankyo Co. Ltd., Tokyo, Japan) at 20 mg/kg body weight and midazolam (Dormicum; Astellas Pharma Inc., Tokyo, Japan) at 2 mg/kg, followed by another intramuscular injection of 0.05 mg/

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Abbreviations: Ao, aorta; CPR, cardiopulmonary resuscitation; CT, computed tomography; ECG, electrocardiogram; LA, left atrium; LV, left ventricle; TTE, Transthoracic echocardiography

kg of atropine sulfate (Atropine Sulfate Injection; Mitsubishi Tanabe Pharma Co. Ltd., Osaka, Japan). The macaque was orotracheally intubated with a 3.5-mm tube, and the surgical depth of anesthesia was maintained with 2–4% sevoflurane (Sevoflurane; Pfizer Japan Inc., Tokyo, Japan) in oxygen. A normal four-limb electrocardiogram (ECG) was monitored to visualize the electrical activity of the macaque heart, and SpO_2 was monitored to check its respiratory condition. An intravenous route was maintained from the right femoral vein, and normal saline was given at the dose of 5 mL/min. Left common carotid artery catheterization via cutdown was performed, which included a direct needle puncture and insertion of a 4-Fr catheter sheath. After an 8-Fr SL0 sheath (S643M, St. Jude Medical, St. Paul, Minnesota, the US) was exchanged with the 4-Fr catheter sheath, a guide wire was moved forward until premature ventricular contraction occurred, followed by the SL0 sheath. Transthoracic echocardiography (TTE) (ARIETTA 70 with a S31 probe; Hitachi Ltd., Tokyo, Japan) was used to confirm the position of the SL0 sheath in the left ventricle (LV). Under TTE guidance, the top of the SL0 sheath was directed toward the posterior wall of the LV, and the SL0 sheath was pulled out into the sinus of Valsalva. The SL0 sheath was cannulated into the left anterior descending artery, resulting in penetration into the coronary artery. Since complete cardiac arrest takes time when only a cardiac tamponade was created, the macaque was finally euthanized with an intravenous injection of potassium chloride (20 mEq Kit; Terumo Co. Ltd., Tokyo, Japan) to apply a humane endpoint.

After confirming cardiac arrest by ECG, postmortem CT was performed with a 16-channel multidetector row CT (Emotion16 (2010); Siemens, Munich, Germany) at the Imaging Center for Basic Medicine, Faculty of Medicine, Oita University. To separate thoracic organs and pericardial hemorrhage, contrast agent Omnipaque®350 (Daiichi-Sankyo Co. Ltd., Tokyo, Japan) was diluted 0.73 times with normal saline to achieve a specific gravity of 1.05, the same as the specific gravity of blood, and used. The CT value of the diluted contrast agent was estimated to be 330 HU, and the volume of the pericardial cavity was estimated to be 10 mL. Based on these value, 6 mL of blood in the pericardial cavity was withdrawn and the same volume of diluted contrast was injected instead into the pericardial cavity through the SL0 sheath to target the CT value of 120 HU for contrast agent in a typical angiogram. After injecting contrast, chest compression was applied for 30 seconds to allow the blood in the pericardial space to mix well with the contrast, and then CT imaging was performed in helical scan mode, 110 kV, 150 mA and 0.6 s/rotation, and 0.75-mm sections.

RESULTS

TTE revealed acute accumulation of pericardial effusion (Fig. 1a, orange arrowheads) and the position of the 8-Fr SL0 sheath in the pericardial space (Fig. 1a, red arrowheads). Once blood leaked into the pericardial space, the heart rate rose once and then became bradycardic with a sudden decline of SpO_2. Postmortem enhanced-CT showed clear optical separation of the heart and pericardial effusion by CT value of 50 HU and 120–500 HU, respectively, without artifacts due to the contrast. The cardiac tamponade was 5.19 × 4.93 cm with a heart sized 3.92 × 3.86 cm (Fig. 1b). An autopsy was performed immediately after postmortem CT. There were no injuries to the ribs or sternum. While no pericardial tear was identified, a hemopericardium (12 mL) was identified within the pericardium. The heart did not show any ventricular wall rupture. The left coronary artery was perforated at the proximal portion of the left anterior descending branch. Other viscera did not exhibit any significant pathological abnormalities macroscopically.

DISCUSSION

Animal studies of CPR have been performed on quadrupeds such as mice, rats, and swine.[6, 7] There are significant differences in the position, structure, and strength of the thorax and intrathoracic organs between bipedal animals such as humans and macaques and quadrupedal animals used in animal experiments. In bipedal animals, the bottom of the heart is supported by the diaphragm, and the pericardium supporting the heart is thick and strong. On the other hand, the bottom of the heart is supported by the thorax and the pericardium is thin in quadrupeds.[10] Additionally, the thorax of a quadruped is strong enough to support the force exerted by its forelegs, while the thorax of a biped is more flexible.[11] Considering these structural differences, it is necessary to use bipedal animals such as macaques for experiments to accurately determine the stress and mechanical response of the thorax and the thoracic organs such as heart and pericardium during CPR in humans.

We successfully created acute cardiac tamponade in macaque using an echo-guided procedure. Our protocol did not require an X-ray imaging system, making it possible to conduct this protocol in animal facilities even without any radioprotection. Several candidate puncture sites in the heart were considered to establish acute cardiac tamponade. The right atrium or right ventricle is the easiest to access via the jugular vein; however,

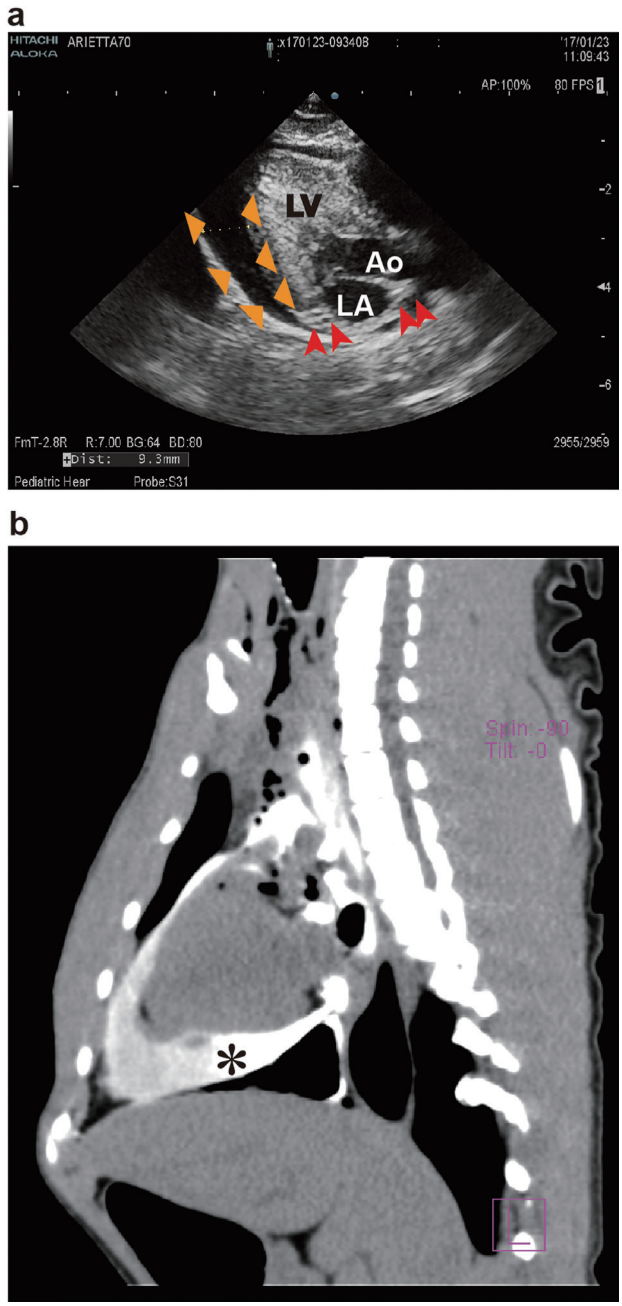

Fig. 1. (a) A TTE view just after construction of a cardiac tamponade model in a macaque. An 8-Fr SL0 catheter sheath was introduced into the aorta in a retrograde manner. The SL0 sheath in the aorta could be observed clearly using TTE (red arrowheads). The sheath perforated the coronary artery to develop cardiac tamponade (orange arrowheads). (**b**) Sagittal plane of postmortem CT image was obtained after establishing cardiac tamponade in a macaque. Contrast clearly indicated pericardial blood leakage (*). Ao, aorta; LA, left atrium.

accomplishing cardiac tamponade takes time due to low pressure in the right chambers of the heart (20–40 mmHg). The left atrium is difficult to access without intracardiac ultrasound or X-ray imaging. Although it was possible to approach the LV without any special settings, its wall thickness is about 8mm, which makes perforation difficult even with a Brockenbrough needle. We succeeded in easily perforating the coronary artery using SL0 sheath alone in this study. If perforation could not be achieved with a catheter alone, it can be achieved with a Brockenbrough needle through an SL0 sheath placed at the orifice of coronary artery. It should be noted that when using a Brockenbrough needle, perforation of the pericardium does not result in cardiac tamponade.

We simulated the postmortem conditions in acute cardiac tamponade in a macaque, which suitably reflected the clinical features from the onset of tamponade to death. As blood leaked into the pericardial cavity, the heart rate rose once and then slowed down. Finally, cardiac arrest occurred with rapid SpO_2 depression. This model can thus be used to study how intra-thoracic organs respond to mechanical stress during chest compression in the presence of cardiac tamponade. We also obtained postmortem CT images to help visualize pathological abnormalities or CPR-related changes. Since the CT attenuation value of the blood immediately after death would be nearly equal to that of the myocardium,[12, 13] we used a contrast agent to separate the two more reliably. Contrast medium generally has a higher specific gravity than blood and will precipitate dorsally when administered during circulatory arrest. It is recommended that the specific gravity of the contrast agent be as close as possible to that of blood to allow the contrast agent to diffuse into the pericardial cavity.

This model might be useful for further understanding the pathophysiology of acute cardiac tamponade by simulating a clinical situation. Combined with postmortem CT, it is also possible to observe the shape and the deformation of the intrathoracic organs in detail and to estimate the mechanical load on the organs. There were case reports in which CPR was performed in the presence of cardiac tamponade, and the cardiac tamponade was lifted by pericardial rupture, saving the patient's life.[2] An accurate understanding of the mechanical responses of intrathoracic organs may lead to the development of effective CPR methods for patients with cardiac tamponade, which has a high mortality rate.

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The authors declare no conflict of interest.

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