

# A simple method of placing a coronary sinus catheter through the femoral vein in miniature swine

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Received December 8, 2015; Accepted December 9, 2016

DOI: 10.3892/etm.2017.4158

**Abstract.** The aim of the present study was to evaluate the feasibility of placing a coronary sinus (CS) catheter through the femoral veins of miniature swine. A total of 16 male domestic pigs (3-4 months old,  $25\pm 2$  kg) were used. Firstly, the anatomic structure of the CS ostium of swine heart was observed at different angles under X-ray. The guide wire and Cobara catheter were subsequently advanced into the right atrium through the femoral vein. Subsequently, the guide wire was retracted behind the fix curve of the Cobara catheter and the catheter bent spontaneously in the absence of supporting guide wire following retraction. The catheter was then gently rotated clockwise to direct the catheter tip to the left allowing the catheter to easily be placed in the CS ostium. This method was associated with a short procedure time: The time on separation of the blood vessels was  $15.5\pm 5.8$  min and the time of radiation exposure was  $112\pm 20$  sec. The success rate of placing the catheter to CS ostium was 100%. Only one pig experienced a hematoma after the sheath was pulled out. All swine recovered without serious complications, such as perforation of coronary vein and pericardial tamponade. Therefore, this method of placing CS catheter is simple, safe and reliable, which may offer help for related research.

## Introduction

Pigs have similar coronary artery anatomical features to humans, thus pigs are often used in coronary intervention studies as an ischemia/reperfusion model through the use of balloon obstruction (1), coronary microemboli model (2) and coronary slow flow model (3) through microsphere injection. Pigs are also used in electrophysiological and pacemaker studies such as in radiofrequency ablation (4) and cardiac

resynchronization therapy (CRT) research (5). Placing a coronary sinus (CS) catheter or electrode in the coronary sinus ostium is an essential technique in these studies. However, placing CS catheters in swine remains a challenging technique for researchers. Previous studies have collected metabolic and hemodynamic measurements data through CS catheters with the open-chest technique in pigs (6-11), and have demonstrated that the aforementioned method is linked with complicated operation procedures and heavy traumatic injury in swine. A number of novel techniques have been developed to place the CS catheter in swine. Hilbert *et al* (12) introduced a method utilizing fluoroscopy and a high-density electroanatomical mapping catheter to verify the CS anatomy to facilitate CS catheter placement. Neizel *et al* (13) reconstructed the cardiac venous system in pigs using magnetic resonance imaging and performed magnetic resonance-guided placements of CS catheters in swine. Nazarian *et al* (14) used a flexible steerable fiber optic infrared endoscope to visualize the CS ostium and branches in closed-chest dogs. However, such methods require high-end equipment, which is not available in all laboratories. Therefore, in the present study, the efficacy of a simple CS catheter placement method via the femoral vein in a closed-chest pig model was assessed.

## Materials and methods

**Animals.** A total of 16 male domestic pigs (3-4 months;  $25\pm 2$  kg) were used in this study, which were purchased from the Experimental Animal Center of Tongji Medical College, Huazhong University of Science and Technology (Wuhan, China). Aspirin ( $2-3$  mg/kg/day; Bayer China Co., Ltd., Shanghai, China) was mixed in the food three days prior to experimental studies. Animals were maintained in a conventional animal environment ( $21\pm 2^\circ\text{C}$ ;  $55\pm 10\%$  humidity), with a 12-h light/dark cycle (lights off at 19:30 h and no twilight period). Animals had free access to water and were fed three times per day in accordance with the Guide for the Care and Use of Laboratory Animals published by the US National Institute of Health (Bethesda, MD, USA) (15). Four animals were used in the pilot study for initial evaluation of the surgical technique and 12 animals were used in the main study. The study protocol was approved by the Tongji Medical

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**Key words:** coronary sinus, swine, femoral vein

College Council of the Animal Care Committee of Huazhong University of Science and Technology (Wuhan, China).

**Preoperative preparation and anesthesia.** The pigs fasted for 12 h prior to operation but had *ad libitum* access to drinking water until 4 h prior to operation. Pigs were anesthetized by an intramuscular injection of ketamine (15 mg/kg; Jiangsu Hengrui Medicine Co., Ltd., Lianyungang, China) combined with atropine (1 mg; Guangdong South China Pharmaceutical Co., Ltd., Guangzhou, China), then fixed in a supine position on the workstation. During the operation, 3–5 ml 3% pentobarbital sodium solution (Sigma-Aldrich; Merck Millipore, Darmstadt, Germany) was injected via ear marginal vein on demand to maintain the anesthesia state. Electrocardiogram and vital signs were continuously monitored. Oxygen saturation (SO<sub>2</sub>) was measured with a pulse oximeter attached to the ear of pigs.

**Evaluation of the surgical technique.** In the pilot study, four pigs were used to evaluate the feasibility of the surgical technique applied. A catheter was inserted into the CS through the jugular vein of the pigs; however, it took a long time to separate the neck vasculature due to the complexity of the anatomical structures. Therefore, the method of catheter insertion through the femoral vein was assessed during the pilot study and main study. Following routine disinfection, the muscle layer and the femoral sheath, femoral vein, *arteria cruralis* and nerve were carefully separated. A 5F vascular sheath (Cordis Corporation, Milpitas, CA, USA) was placed for arterial and venous access. Anticoagulation was induced with 200 IU/kg heparin sodium (Jiangsu Wanbang Biopharmaceuticals Co., Ltd., Xuzhou, China). The arterial sheath can be used for pressure monitoring, coronary angiography (16). The 5F pigtail catheter (Cordis Corporation, Milpitas, CA, USA) was advanced into the right atrium from the right femoral vein. Right atrium imaging was performed [right anterior oblique (RAO) 30°, anterior-posterior (AP) angle] to observe the CS opening and record right atrium pressure.

**Imaging analysis of pig heart.** Under the X-ray, the transparent triangle area in the pig hearts could not be clearly visualized at RAO 30°, left anterior oblique (LAO) 45°, AP angle, as it is in humans. In order to observe the structure of the right atrium and the CS ostium, the 5F pigtail catheter was advanced to the lower part of right atrium and radiography was performed (AP, RAO 30° angle) with a high pressure injector (20 ml/sec; 300 kPa; Auto injector 120S; Nemoto Co., Ltd., Tokyo, Japan). The CS ostium could clearly be detected at AP or RAO 30°, and the contours of CS could be clearly presented at the AP position (Fig. 1A and B).

**Radiation dose assessment.** All operations were performed by two experienced researchers. Radiation exposure time was recorded and the radiation dose received by the operator was detected using a Wearing X-ray detector provided by the Wuhan Center for Disease Prevention and Control.

## Results

**CS catheter placement method.** In the main experiment, a 5F guide wire (RF\*GA3513M; Terumo Corporation, Tokyo,

Japan) and Cobara catheter (RF\*DB55008M; Terumo Corporation, Tip curve L: Middle) were advanced into the right atrium through the femoral vein and the guide wire was retracted out of the catheter, which then spontaneously bent. CS ostium was generally located one width of a rib under the middle of long axis of the heart. Following gentle clockwise rotation of the catheter to the left, the catheter could be easily and smoothly placed into the CS ostium. Following successful placement, the characteristic swing sign could be visualized. Contrast medium was injected to confirm the successful placement of catheter inside the CS (Fig. 1C and D). Afterwards, CS blood sampling was performed (Fig. 1E and F).

**Reliability and safety evaluation.** This method was associated with a short procedure time (the time used on separation of the blood vessels was 15.5±5.8 min and the time of radiation exposure was 112±20 sec) and a success rate of 100%. Only one pig experienced a hematoma after the arterial sheath was pulled out. All swine recovered without serious complications, including perforation of coronary vein and pericardial tamponade. Additionally, this method had a low per capita irradiation dose (1.56±0.32 µGy) at each operation.

## Discussion

Cardiologists usually pay more attention to the arterial system of coronary circulation, and less to the coronary vein system. With the rapid development of interventional techniques in recent years, there is an increased requirement of CS placement of CS catheters, for example to determine the myocardial metabolic product in CS. Moreover, placing electrodes to the CS during electrophysiological examinations and left ventricular electrode placement in CRT also requires the placement of a CS catheter in selected patients. This technique is also necessary during retrograde stem cell transplantation through the CS route (17). It has been demonstrated that simultaneous coronary artery and CS perfusion facilitate myocardial preservation (18). As pigs are the ideal experimental animal model when investigating the heart, particularly in coronary intervention and electrophysiology pacemaker research field, an effective method for placing a CS catheter in swine is particularly important. The primary difficulty is that the catheter may pop out and injure the CS if the catheter is pushed directly without adjusting the direction. In some pigs, pushing catheters to distal CS is difficult. The current study demonstrated that if the guide wire can be fixed, and the direction of catheter gently adjusted, the majority of catheters can be advanced to the distal CS without injuring the CS. In addition, the COBARA catheter used in the present study is a 5F peripheral vessel operated catheter with soft tip; the probability of perforation is thus low. Moreover, placing the CS catheter through the femoral vein may reduce the operation time and avoid pneumothorax and hemothorax complications. This method may also significantly reduce the radiation dose the operator is exposed to.

Placing a catheter to the CS through the femoral vein in miniature pigs may also be useful in electrophysiology research in swine animal models. If an adjustable curved electrode is used and the direction of the catheter is gently

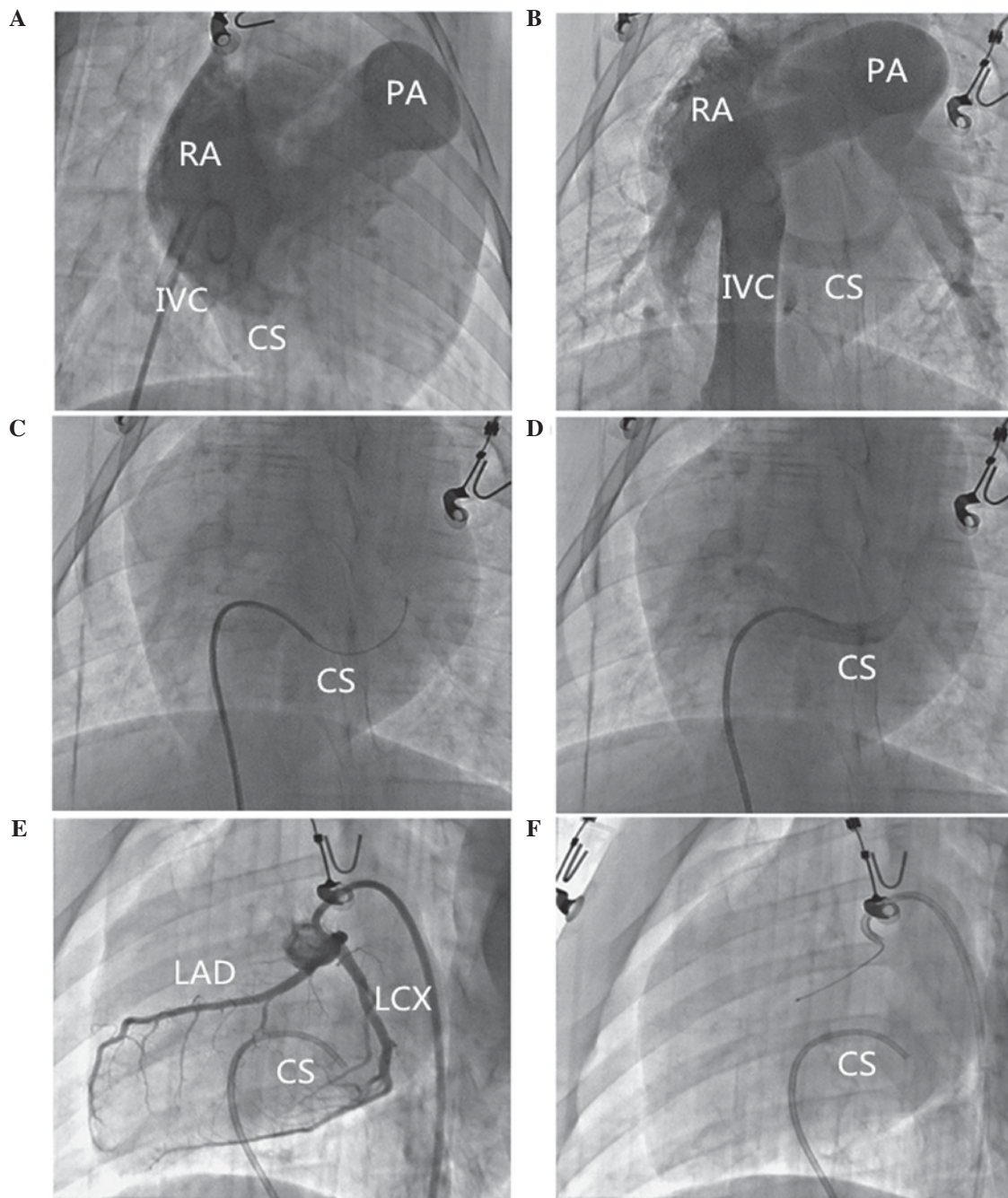


Figure 1. CS contours and catheter placement procedures. (A) Right atrium imaging (RAO 30°). (B) Right atrium imaging (AP). (C) Thread entry into the CS (AP). (D) CS imaging (AP). (E) Simultaneous placement of CS catheter and coronary arteriography (LAO 30°). (F) Simultaneous placement of CS catheter and guide wire in coronary (LAO 30°). RA, right atrium; PA, pulmonary artery; IVC, inferior vena cava; LAD, anterior descending branch; LCX, left circumflex; CS, coronary sinus; AP, anterior-posterior; LAO, left anterior oblique; RAO, right anterior oblique.

adjusted, the CS electrode could successfully be advanced to the distal CS.

Placing the CS catheter through the femoral vein in miniature pigs has the following advantages: i) Avoiding open chest and other complex surgical procedures, thus reducing trauma and the operating time; ii) does not require the support of endotracheal intubation and breathing machine ventilation when animals are under anesthetic; and iii) avoiding the jugular vein puncture-related pneumothorax and hemothorax complications. The groin hematoma complication observed in one of the pigs in the current study may be avoided by prolonged local oppression.

In conclusion, the method of lacing a catheter into the CS of swine assessed in the current study is simple, safe and reliable; it may be beneficial for scientific researchers using swine as animal models in related coronary studies.

#### Acknowledgements

The present study was supported by the National Natural Science Foundation of China (grant no. 81270266) and the Nature Science Foundation of Hubei Province (grant nos. 2014CFB365 and 2015CFA081).



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