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Transauricular intra-arterial and intravenous digital subtraction angiography for abdominal aortic aneurysm imaging in a rabbit model

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HIGHLIGHTS

- Correlations of DSA via ear vein and ear central artery to conventional DSA were good.
- Transauricular DSA shows good correlation to conventional DSA.
- Transauricular DSA can be used repeatedly with less invasiveness, and suitable for rabbit AAA follow-up study.

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ABSTRACT

Aim: The aim of this study was to evaluate transauricular digital subtraction angiography (DSA) as an alternative to conventional intra-arterial DSA for rabbit abdominal aortic aneurysm (AAA).
Materials and methods: AAA models were created in 8 New Zealand white rabbits by sewing vein patch. The diameters of aortic arteries were measured by DSA via ear vein and ear central artery. The common carotid artery (CCA) was exposed and cannulated for DSA as conventional angiography. Diameter size was measured and compared.
Results: Aortic diameters, tested by DSA via ear vein, ear central artery and CCA were 7.9 ± 1.2 mm, 7.8 ± 1.0 mm and 7.9 ± 1.1 mm respectively, with no significant differences. Angiography via CCA as standard procedure, correlation in aneurysm neck diameter was r = 0.93 for IVDSA and r = 0.96 for angiography via central artery ($P < 0.01$); Correlation in AAA diameter was r = 0.99 for IVDSA and r = 0.99 for angiography via central artery ($P < 0.0001$).
Conclusions: Transauricular DSA shows good correlation to conventional DSA, can be used repeatedly with less invasiveness, and suitable for rabbit AAA follow-up study.

1. Introduction

Abdominal aortic aneurysm (AAA) is a silent degenerative disease with life-threatening consequences, its pathogenesis is complex and not completely understood. Animal model of AAA is useful to study its pathogenesis and to evaluate effect of drug intervention. Diameter follow-up of AAA is quite necessary in animal study. It is generally known that digital subtraction angiography (DSA) is the gold standard for measurement of aneurysm diameter. In the studies of intracranial aneurysm in rabbit model, intravenous digital subtraction angiography (IVDSA) is often used to follow up aneurysm induced in common carotid artery (CCA), which can be carried out repeatedly without loss of access sites [1–6]. Also, angiography through the ear central artery can be used in rabbit aneurysm with the CCA origin to spare the femoral artery access sites [7,8]. However, in the studies of rabbit AAA, transverse diameters were often directly measured with micrometer or vernier calipers [9–11], which might caused significant measurement errors due to deformation and pulsation of artery. Conventional angiography was performed by way of a cannula inserted into the femoral artery [12–14] or carotid artery [11,15,16], however, this method was impossible due to the needs of ligating the femoral

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artery or carotid artery after catheter placement, and multiple time points were often needed in AAA follow-up study [6]. The femoral artery is accessed via a surgical cutdown, which needs a ligation or microsurgical closure of artery after operation and may limit repeated use of the same access for further procedure [7,17]. Sometimes, this procedure is time-consuming and technically difficult, with the possible complications of hematoma formation, wound infection and limb ischemia [18,19]. There was almost no usage of non-invasive or minimally invasive imaging alternatives for experimental AAA follow-up, such as IVDSA or DSA via ear central artery in rabbit AAA, except for previous reports [20–22]. The objective of this study was to evaluate transauricular DSA imaging via ear vein and ear central artery as an alternative to conventional intra-arterial DSA for depiction of anatomy and size of rabbit AAA.

2. Materials and methods

2.1. Ethics statement

Animal care followed the Chinese Community Standard for care and use of laboratory animals, and the protocols for animal experimentation was approved by the Animal Care and Use Committee of the China Medical University. All surgery was performed under sodium pentobarbital anesthesia, and all efforts were made to minimize suffering.

2.2. Creation of rabbit AAA

Eight New Zealand white rabbits, weighing 2.95 ± 1.01 kg, from our laboratory animal center were used to create AAA model. Animals were anesthetized with 30 mg/kg intravenous sodium pentobarbital. Rabbit was placed supine, the abdomen was approached by a midline laparotomy after local shaving and disinfection. A 1-cm segment of infrarenal abdominal aorta was isolated, and excised after the occlusion of its ends by vascular clamps. A segment of vena jugularis externa, 1 cm in length, was dissected and sewn to the ends of aorta with 9-0 polypropylene suture under microscope. Clamps were removed and circulation was restored (Fig. 1). Animal care followed the Chinese Community Standard for care and use of laboratory animals, and the protocols for animal experimentation were approved by the Animal Care and Use Committee of the China Medical University. All surgery was performed under sodium pentobarbital anesthesia, and all efforts were made to minimize suffering.

2.3. DSA via ear vein and ear central artery

Rabbits were anesthetized again 4 weeks after surgery. After placing the 19-gauge angiocatheters in the ear marginal vein and ear central artery, about 8 ml of iodinated contrast medium was infused quickly by manual injection. An external sizing device, 1 cm in length, was placed under the abdomen during DSA. The diameters of the aneurysm neck and AAA were measured in reference to this sizing device as previously reported [1,2,20,21,23,24]. Aneurysm was defined as an aortic diameter that was dilated at least 50% the diameter of aneurysm neck above.

2.4. Angiography via CCA

After finish of the tests above, the right CCA was exposed through a middle line incision along the trachea. A 18-gauge cannula was inserted, and a 5-F arterial sheath was introduced into the right CCA through the guiding wire. Under fluoroscopic guidance, a 5-F pig-tail angiographic catheter was placed in the proximal infrarenal abdominal aorta. Then, DSA was performed by manual injection of contrast medium.

2.5. Statistical analysis

Diameter data were expressed as means ± SD. Paired t-tests and one-way ANOVA were performed to identify the diameter differences (Prism 5.0, GraphPad Software, Inc., SanDiego, CA). The differences were considered statistically significant when $P < 0.05$.

3. Results

No animal died during operation and DSA imaging. All the sewn vein patches enlarged significantly and formed AAA with 68.6%–268.0% increase after 4 weeks. The rabbit ear vein and ear central artery were available and could be cannulated repeatedly. DSA through these approaches was performed successfully, and the resulting image quality is adequate for measuring the diameter exactly. However, DSA through CCA needs an exposure of artery by surgery and then puncture of the artery. It is not easy to introduce the 5-F arterial sheath into the narrow and very fragile CCA in rabbit. Sheathes were unable to be inserted successfully in 2 rabbits at first, DSA was performed successfully after second try in the left CCA. This method was invasive, but able to measure the diameter exactly (Fig. 2).

The effect of different DSA on the diameter measurement was shown in Fig. 3. Aneurysm neck diameters, tested by IVDSA, DSA via ear central artery and CCA, were 2.8 ± 0.4 mm, 2.8 ± 0.3 mm and 2.8 ± 0.3 mm, respectively, with no significant difference ($P = 0.97$). The corresponding diameters of AAA were 7.9 ± 1.2 mm, 7.8 ± 1.0 mm and 7.9 ± 1.1 mm, respectively. Differences were also not statistical significant ($P = 0.99$).

A good correlation was observed between the different imaging modalities. Angiography via CCA as standard procedure, correlation in aneurysm neck diameter was $r = 0.93$ for IVDSA and $r = 0.96$ for angiography via central artery ($P < 0.01$); Correlation in AAA diameter was $r = 0.99$ for IVDSA and $r = 0.99$ for angiography via central artery ($P < 0.0001$).

4. Discussion

It is known to all that DSA is considered the standard-of-reference tool for aneurysm diameter measurement. In this study, DSA through three different approaches, ear vein, ear central artery and CCA, was feasible in the measurement of AAA diameter in rabbits. Of which, Angiography via CCA is most invasive, the cannulated artery should be repaired or ligated after imaging, making this approach not available repeatedly in the diameter follow-up. In the studies of intracranial aneurysm, IVDSA was widely used to investigate the aneurysm originated from CCA in rabbits [1–5]. Ding et al. [25] reported that IVDSA can serve as an alternative method to intra-arterial DSA for rabbit aneurysm imaging.

IVDSA was performed successfully in rabbit AAA model in this experiment and previous studies [20,21]. Miskolczi et al. [7] reported that the contrast, injected via the ear marginal vein, is very much diluted and the resulting image contrast is poor. To our experience, the imaging figure achieved from IVDSA is of good quality, which is clear enough to measure the aorta diameter exactly if 6–8 ml of contrast medium was injected fast enough manually. Injection of contrast medium into the rabbit ear central artery quickly fills the external and CCA, results in retrograde flow to the aorta. Angiogram was of excellent quality when using the ear central artery injection method. These two kinds of angiography are less invasive and easy to carry out, and are useful to measure the aorta diameter in vivo and to show the whole infra-renal aorta. In

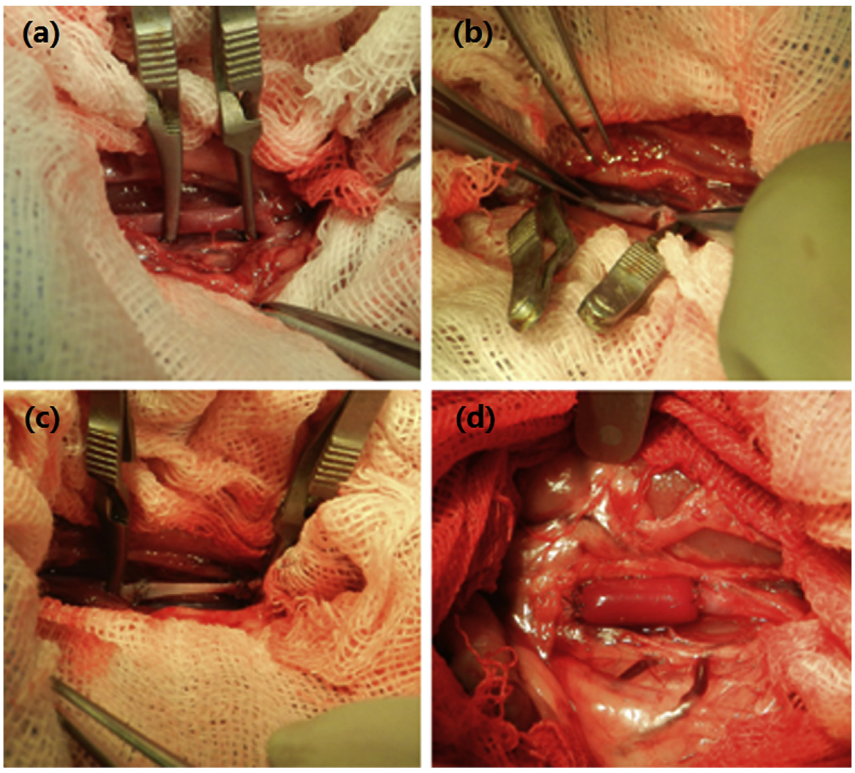

Fig. 1. The creation of rabbit AAA. **(a)** A infrarenal aorta segment was isolated and clamped. **(b)** A segment of vena jugularis externa was sewn to the ends of aorta with 9-0 polypropylene suture. **(c), (d)** Clamps were removed and circulation was restored.

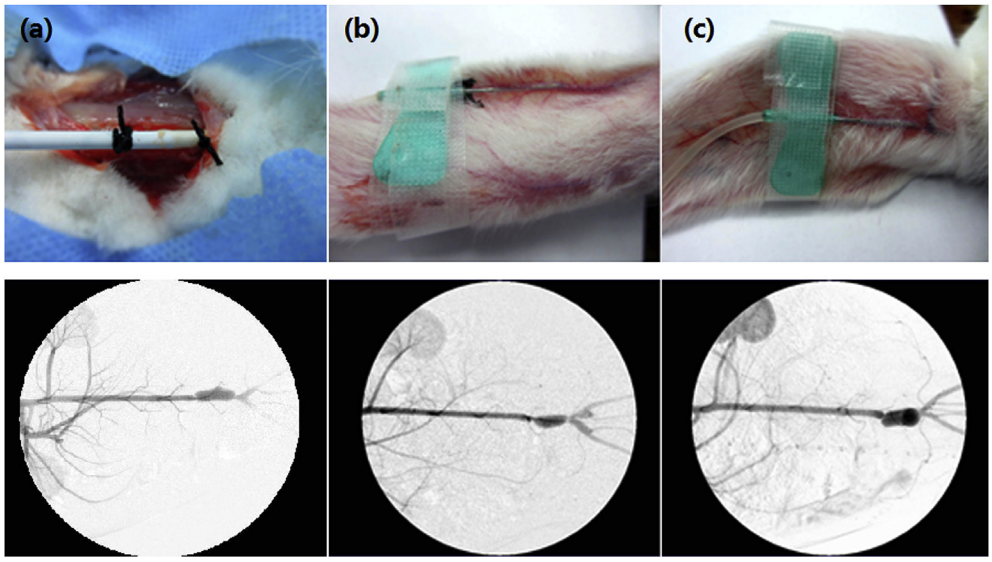

Fig. 2. Digital subtraction angiography was performed via CCA, ear vein and ear central artery for rabbit AAA.

addition, ear vein and central artery puncture can be repeated numerous times, angiography can be performed repeatedly in follow-up study.

IVDSA and DSA via ear central artery, as almost noninvasive methods, are able to test the inner diameter of AAA exactly and repeatedly, and are suitable to follow up AAA in rabbits. Moreover, Chang et al. [17] verified that rabbit hepatic artery angiography is feasible by introducing a 2.0-F microcatheter via the central auricular artery. Owing to omission of shaving and surgical cutdown, this method needs less procedure time than transfemoral arterial access. Transauricular arterial or venous access was also useful for cardiovascular experimental protocols in rabbits [26]. However, rabbit aorta was not shown clearly in transauricular arterial angiography, due to less contrast medium injected via a 2.0-F microcatheter manually. Microcatheter should be introduced to fine arteries, such as hepatic artery and iliac artery, then angiography was performed to investigate these arteries clearly.

In summary, our results demonstrate that IVDSA or angiography

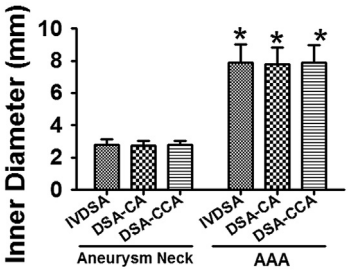

Fig. 3. Inner diameter measurement by IVDSA and DSA via ear central artery and CCA. *$P < 0.0001$, compared with diameter of aneurysm neck.

via central artery and CCA is feasible in rabbit AAA model. We observed a good correlation between these different imaging modalities. IVDSA and angiography via central artery are all suitable for accurate non-invasive measurement of aneurysm diameter and can serve as alternative imaging to conventional DSA.

Ethical approval

Animal care followed the Chinese Community Standard for care and use of laboratory animals, and the protocols for animal experimentation was approved by the Animal Care and Use Committee of the China Medical University. All surgery was performed under sodium pentobarbital anesthesia, and all efforts were made to minimize suffering.

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Author contribution

Study concept or design: Ke Xu; Xinwei Han.
Animal study: Yonghua Bi.
Data collection: Gang Wu.
Data analysis: Hongshan Zhong.
Writing the paper: Yonghua Bi.
Revise the paper: Zepeng Yu.

Conflicts of interest

None.

Guarantor

Xinwei Han.

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