

Intracranial Aneurysm Model for Detachable Coil Testing

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Intracranial aneurysm is major vascular disease which is life-threatening and challenging treatment. Detachable coil is one of the standard treatments. Because of little knowledge about it, the detachable coils were evaluated by various methods. Animal aneurysm models were also used to test this equipment. In the present study, sidewall aneurysms were created on common carotid arteries of Landrace-Yorkshire-Duroc swine. External jugular vein grafts were used as aneurysm sac. End-to-side anastomosis was done. Ten aneurysms were created successfully in 5 swine. There is no perioperative death. This animal aneurysm model is appropriated for coil testing especially in the histopathology aspect.

Keywords: Aneurysm model, Coil testing, Common carotid artery, Endovascular, Intracranial aneurysm, Sidewall aneurysm, Swine

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Intracranial aneurysms are one of the life-threatening major vascular diseases that found 3-8% of general population⁽¹⁻³⁾. The common presentation is subarachnoid hemorrhage that can cause mortality rate of 32-67% and 30-50% significant morbidity if the patients survive⁽⁴⁻⁷⁾. Surgical clipping and endovascular therapy, using detachable coils, were standard treatment^(8,9).

The detachable coils were first introduced by Gulielmi et al, in 1991^(10,11). This alternative treatment for intracranial aneurysms is considered as a new technique compared with open surgery and needs to be studied more. The animal aneurysm model for detachable coil testing is the value way to better understand about it in many aspects for example pathophysiology of aneurysms after coiling, the aneurysmal orifice coverage ability of each type of coils or even testing for new coils. Various species of animals were used in the intracranial aneurysm model

laboratory but only canine, rabbits and swine were commonly used for coil testing⁽¹²⁾. The decision of selecting one of them was depend on the purpose of the studies and facilities of the institutes.

In the present study, swine aneurysm model was reconstructed on their common carotid arteries with the purpose of evaluating endothelial cell proliferation of aneurysm after. The preparation, surgical technique and tips were described in detail. Furthermore, the characteristics of each kind of the animal aneurysm models for coil testing were reviewed and discussed in this present study.

Material and Method

All procedures were approved by Animal Care Committee of Juntendo University. Adult Landrace-Yorkshire-Duroc swine weighing 30-40 kg were obtained from the National Livestock Breeding Center Ibaraki station (Ibaraki, Japan). They were maintained on a 12-hour light/dark cycle with free access to food and water in the animal laboratory, Juntendo University, prior to operation.

Preparation

The swine were sedated by injecting 36.8 mg/kg ketamine hydrochloride (Daiichi Sankyo Co., Ltd.,

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Tokyo, Japan) and 5.3 mg/kg xylazine (Bayer Healthcare, Leverkusen, Germany) intramuscularly. Then they were transferred to the surgical bed and secured in supine position. Oxygen saturation and electrocardiogram were continuously monitored. Venous access was obtained from the auricular vein and maintained with normal saline. After endotracheal intubation, anesthesia was maintained with mechanical ventilator and inhalation of 1.5-2.0% isoflurane in 35% oxygen and 65% nitrogen at a rate of 5-6 L/minute. The endotracheal tube should be carefully secured because the operating time was long and sometimes we had to manipulate around the head of the swine.

Equipment

In the aneurysm model experiment, a lot of equipment was needed. We summarized the necessary equipment in Table 1.

Surgical procedure

Anterior neck of swine was prepped with povidone-iodine solution and draped in a sterile fashion. Approximately 10 centimeters midline incision was done. Self-retaining retractor was applied. Both of sternocleidomastoid muscles were carefully dissected along the anterior border. Common carotid arteries and external jugular veins were exposed (Fig. 1A). One of the external jugular veins was skeletonized. A three-centimeter vein graft was harvested and kept in normal saline. About 2 centimeters of the common carotid arteries were cleaned of adventitia on both sides and packed with gauze soaked with papaverine solution after that (Fig. 1B). Then the vein graft was divided into two segments equally and meticulously cleaned of adventitia on one end of each graft. After preparation of vein grafts and both sides of the common carotid arteries, sidewall aneurysm models were ready to be

created. It is better to perform the anastomosis procedure under surgical loupes. Two vascular slings were rolled twice around the proximal and distal sites of the carotid artery (Fig. 1B) and hanged up by pulling the lateral end of the vascular slings more than the medial end in manner to roll the lateral aspect of the common carotid artery upward. According to this technique, the aneurysm models will point laterally. Two vascular clamps were applied at both ends of the isolated common carotid artery segment. Approximately 3 mm diameter arteriotomy was created by using a surgical knife and aortic punch (Premium aortic punch; Teleflex Medical Japan, Tokyo, Japan). Then an end-to-side anastomosis between external jugular vein graft and common carotid artery was performed. The vein graft was sutured to both edges (proximal and distal) of the arteriotomy using 7-0 Prolene (Ethicon, Inc., Somerville, NJ). Running sutures were subsequently performed on both sides of the orifice until reaching the other edge. After complete anastomosis was done, a small surgical clip was applied to the distal side of the vein graft. Leakage points were checked by releasing the vascular clamp which was on the distal common carotid artery and repaired. Finally, dome size of the aneurysm model was adjusted by ligation with 2-0 silk (Fig. 2).

Angiography

After finishing creation of aneurysm models on both sides of common carotid arteries, angiography was performed in every swine. Transfemoral approach was performed using a 4Fr short sheath (Super sheath, Medikit, Miyazaki, Japan). A 4Fr diagnostic catheter (JNS Type I, Medikit) with a 0.035" angled hydrophilic guidewire (Radifocus Guidewire, Terumo, Tokyo, Japan) was navigated into the proximal common carotid arteries under fluoroscopy. Contrast media was injected to

Table 1. The necessary equipment in animal aneurysm model

Surgical equipment	Angiography equipment
Surgical Drapes	2-0 silk
Surgical Blades #11, #15	7-0 prolene
Mosquito clamp	Vascular slings
Self-retaining retractors	Aortic punch
Tooth forceps	Irrigation tip
Vascular forceps	Vascular clips
Needle holder	Microvascular set
Scissors	Papaverine solution
Electrocautery	Heparinized saline
	Angiography suite
	4Fr short sheath
	4Fr diagnostic catheter
	0.035" angled hydrophilic guidewire
	Contrast media

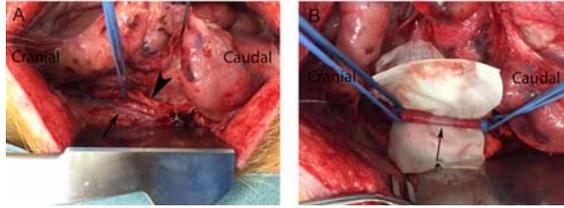


Fig. 1 Intraoperative view. (A) Right common carotid artery (arrow head) and external jugular vein (arrow) were exposed. (B) A segment of the common carotid artery was cleaned of adventitia (arrow).

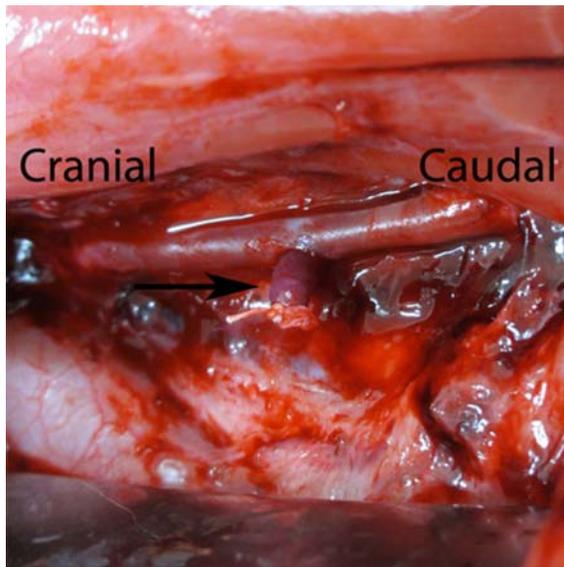


Fig. 2 Intraoperative view. The aneurysm model (arrow) after completely reconstructed.

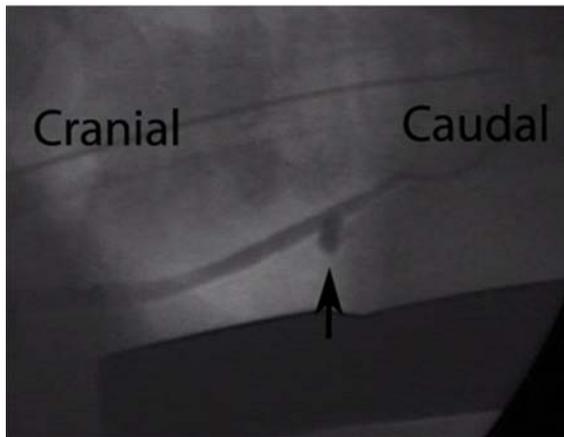


Fig. 3 Intraoperative angiography. Patency of the constructed aneurysm (arrow) was confirmed by intraoperative angiography.

confirm patency of the aneurysm models (Fig. 3).

Results

Ten side-wall aneurysms were created successfully in 5 swine. All of the aneurysm patency were confirmed by immediate angiography. All of them could be visualized by contrast injection via A 4Fr diagnostic catheter (JNS Type I, Medikit). The procedure was done in 120-150 minutes.

There were no perioperative complications (e.g. aneurysms rupture, anastomosis leakage or carotid thrombosis). No perioperative deaths occurred.

Discussion

Constructed sidewall aneurysm on common carotid arteries was one of the most popular intracranial aneurysm models⁽¹²⁾. This kind of animal experiment was introduced by the pioneer group, German and Black, in 1995⁽¹³⁾. Many technical variants were developed and introduced subsequently⁽¹³⁻¹⁷⁾. The procedure that was described in this paper was simplified and explained in detail. Therefore, it is beneficial for the researchers who do the same animal laboratory and surgeons who are not well experienced in vascular field.

Comparing bifurcation types and variants, lateral wall aneurysm models were less complicated in a surgical procedure. In addition, we can create 2 aneurysms in an animal. On the other hand, the hemodynamic character was not closely matched with an intracranial aneurysm in a human as the bifurcation model.

Various animals were used in the intracranial aneurysm model laboratory^(12,18). For coil testing purpose, swine and canine were generally appropriated because of large vessel size and long-term survival⁽¹⁹⁻²³⁾. Rabbits were also used for the same purpose^(23,24). But according to smaller vascular size, the interventional procedure requires multiple catheters⁽²⁵⁾. Moreover, mortality due to the adverse effect of anesthesia was high in rabbits with constructive aneurysm model⁽²⁶⁻²⁸⁾. The elastase-induced aneurysms, which limited to rabbits, were easy in handling with the exception of uncontrolled size of the aneurysms^(29,30). Although mice and rats were also popular for aneurysmal experiment, they have too small aneurysms that cause inappropriateness for endovascular interventions⁽¹²⁾. Hence, canine, swine and rabbits were commonly used for coil testing.

Unique healing ability of each kind of the

animal aneurysm models is one of the considerations. Swine which is nearly similar coagulation system to human seems to be the best choice to represent aneurysmal healing characteristic^(31,32). This is an important point that we use swine in our experiment. But it has tendency for spontaneous thrombosis, immediate embolization was recommended^(20,33,34). Dogs have intermediate obliteration ability whereas swine and rabbits have high and low ability of obliteration, respectively⁽¹²⁾. Neointima at the neck of aneurysm after coiling was thin especially in the bifurcation in dog models^(19,35-37). The rate of spontaneous thrombosis is low even long-term follow-up in dog models^(38,39). Rabbits have lesser propensity for healing and it has partial or complete coverage of thin endothelization across the aneurysm orifice⁽⁴⁰⁻⁴³⁾.

Bifurcation canine and rabbit models were frequently recurrent despite treated with various types of devices^(33,35,37,44,45). On the other hand, recurrence rate of lateral wall canine and rabbit model depends on the completeness of obliteration. If the aneurysms were completely occluded, the risk of recurrence was rare⁽³⁵⁾. Recurrence rate among elastase-induce models in rabbits was also rare if complete occlusion was done^(41,46,47). Swine aneurysm model have low tendency to recurrent⁽⁴⁸⁾.

According to the need of evaluating the endovascular equipment, the aneurysm model which is similar to human being is desired. Animal aneurysm models as mentioned above were the common way to evaluate the endovascular equipment. But the nature of each aneurysm models comparing to human should be further studied. It will provide some objective evaluation of choosing animal models using detachable coil testing in the future. Moreover, it will be helpful when we interpret the results.

Conclusion

In our study, swine, canine and rabbits are appropriate for detachable coil testing. The properties of each type are different in many aspects as discussed. The sidewall swine aneurysm model is appropriate to use for detachable coil testing in histopathology aspects.

What is already known on this topic?

As mention previously, this kind of animal experiment was introduced by the pioneer group, German and Black, in 1995⁽¹³⁾. In the recent previous literatures, the methodology was usually described in

short paragraph without discussion about the reasons of choosing the type of aneurysm model^(15,42,49).

What this study adds?

In this paper, details of surgical techniques, the preparation process and instrument were described. Additionally, the characteristics of several types of aneurysm model were reviewed and discussed, in purpose to help researchers choose the proper type of aneurysm model for their studies.

Potential conflicts of interest

None.

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แบบจำลองหลอดเลือดสมองโป่งพองสำหรับทดลองรักษาด้วยวิธีใส่ขดลวดทางการแพทย์

พีรพงศ์ เหลืองอากาศพงศ์, ฮิเดโนริ โออิชิ, ยาสุโอะ สุกะ, เคนจิ ยาโตมิ, ยูมิโกะ มิโตเมะ มิซึมา

หลอดเลือดสมองโป่งพองเป็นโรคที่มีความเสี่ยงต่อการเสียชีวิตมากและทำร้ายในด้านการรักษา รักษาด้วยวิธีใส่ขดลวดนั้นถือว่าเป็นหนึ่งในวิธีการรักษามาตรฐาน อย่างไรก็ตามยังมีความจำเป็นต่อศึกษาเกี่ยวกับคุณสมบัติของขดลวดชนิดต่าง ๆ ด้วยหลากหลายวิธี แบบจำลองหลอดเลือดสมองโป่งพองในสัตว์เป็นหนึ่งในวิธีทดสอบขดลวดด้วยเช่นกัน ในการศึกษานี้ได้จำลองหลอดเลือดสมองโป่งพองไว้ที่หลอดเลือดแดงคอมมอนคาโรติคของหนูพันธุ์ Landrace-Yorkshire-Duroc โดยตัดหลอดเลือดดำที่คอของหนู แล้วต่อเข้ากับด้านข้างของหลอดเลือดแดงคอมมอนคาโรติคแบบจำลองหลอดเลือดสมองโป่งพอง 10 อันถูกสร้างขึ้นในหนู 10 ตัว ไม่มีหนูเสียชีวิตระหว่างทดลอง จากการศึกษาพบว่าแบบจำลองหลอดเลือดสมองโป่งพองนี้เหมาะแก่การนำมาทดสอบขดลวดทางการแพทย์โดยเฉพาะอย่างยิ่งในด้านจุลพยาธิวิทยา
