Endovascular aneurysmal models at the external iliac artery of dogs

Poster No.: C-1851
Congress: ECR 2011
Type: Scientific Exhibit
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Keywords: Animal (veterinary) studies, Interventional vascular, Vascular, Catheter arteriography, Experimental, Ultrasound, Experimental investigations, Arterial access, Balloon occlusion, Aneurysms, Drugs / Reactions, Obstruction / Occlusion
DOI: 10.1594/ecr2011/C-1851

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Purpose

Establishing an aneurysm model using simple and easy operative techniques in comparatively larger animals is desirable for development of new IVR procedures.

We tried to develop an aneurysm model using the arteries of adult beagle dogs, a relatively large animal, and a simple and less complicated procedure of IVR. Specifically, we designed an aneurysm model that was difficult to rupture in the long term. Additionally, we histologically evaluated the generated aneurysm model and determined the factors that were necessary for creating more dilated aneurysmal model.
Methods and Materials

The present study was granted approval by the Tohoku University Animal Experiment Committee. Experimental animals consisted of 16 beagle dogs that weighed an average of 14.0 kg (range, 13.5-15.3 kg). The dogs were anesthetized with an intramuscular injection of ketamine (20 mg/kg body weight) and atropine sulfate (0.1 mg). Sodium pentobarbital (25 mg/kg; Nembutal R; Abott Laboratories, North Chicago, IL, USA) was used as a supplemental anesthetic.

We measured the inner diameter of the bilateral EIA using an echo. We fixed an adult beagle dog in the face-up position on an operating table. Sufficient anesthesia was provided after confirmation. After surgically exposing the right internal carotid artery (ICA), an 8-Fr introducer sheath (Medikit, Tokyo, Japan) was advanced into the descending aorta, followed by intravenous administration of heparin (loading dose 50 U/kg body weight and maintenance dose 300 U per hour).

Afterwards, we divided the dogs into following four groups.

# Balloon non-dilation group (n = 8)

We made a closed cavity with a double-balloon catheter (Selecon MP Catheter, Clinical Supply, Gifu, Japan) at the left EIA. In total, 2.5 ml elastase (4.42 U/mgP, 24 mgP/mL; Worthington Biochemical Corporation, Lakewood, NJ) was injected into the closed cavity, which was left unattended for 30 min (E group). As a control, we made a similar closed cavity with a double-balloon catheter at the right EIA and 2.5 ml of normal saline was injected into the cavity, which was also left unattended for 30 min (S group).

# Balloon dilation group (n = 8)

At a diameter of about 1.5 times that of the left EIA inner diameter measured in an echo, we expanded the left EIA with a 2-cm-long balloon catheter (Ultra-Thin Diamond; Boston Scientific/Medi-Tech) for vasodilatation. Expansion was performed ten times at 4 atm or 6 atm, each for 10 s. Afterward, we made a closed cavity with the double-balloon catheter in the extension of the left EIA, and then 2.5 ml elastase was injected into the closed cavity, which was left unattended for 30 min (B+E group). Likewise, we expanded the right EIA and made a closed cavity with the double-balloon catheter; then 2.5 ml of normal saline was injected into the cavity, which was left unattended for 30 min (B+S group).

After that it is the procedure that was common in non-balloon expansion group and balloon expansion group.
We performed abdomen aortography with a 5-F Cobra-type catheter, withdrew the sheath, and ligated the right internal carotid artery. Additionally, we performed adequate hemostasis and closed the wound.

Four weeks later, we measured the inner diameter of both sides of the EIA using an echo under anesthesia. We calculated the ratio of the postoperative inner diameter to the preoperative inner diameter and evaluated the dilatation of vessel inner diameter.

We exposed the left ICA, advanced a 7-Fr introducer sheath into the descending aorta, and performed abdomen aortography using a 5-F Cobra-type catheter.

Each dog was killed using an excessive quantity of Nembutal and exsanguinated; then both sides of the EIA were extracted. The EIA was immediately fixed in 10% formalin, and alcohol dehydration was performed a week later.

The mensuration technique of the outer diameter of the EIA: we measured the inner circumference and the outer circumference with image processing software: ImageJ (National Institutes of Health, Bethesda, MD, USA). We calculated the postoperative outer diameter of EIA from the inner and outer circumference ratio of the organization with the numerical value in the preoperative echo. For calculating the preoperative outer diameter of EIA, EIA wall-thickness of S group (contrast group) calculated from postoperative inner and outer diameter. It was assumed that a wall-thickness doesn't have the change in pre-operation and post-operation in S group. And then the preoperative inner diameter of each group added an average wall-thickness of S group into the preoperative each group's outer diameter of EIA.

By using the ratio of that postoperative outer diameter to that preoperative outer diameter, we evaluated the dilatation of vessel outer diameter.

Histological examination using hematoxylin-eosin (H&E) staining, Elastica-Masson (EM) staining, and immunostaining (CD3, CD20) was performed. We evaluated the following four characteristics during the histologic examination:

1. disappearance of the internal elastic lamina;
2. degeneration and disappearance of medial smooth muscle;
3. degeneration and disappearance of the external elastic lamina; and
4. neointimal thickening.

When the degeneration and disappearance of medial smooth muscle and the external elastic lamina were observed in more than 50% of all layers of the normal structure, this was assmued to be a change.
We measured the percentage of vessel perimeter in each histologic characteristic using ImageJ.

We evaluated the presence of CD20- or CD3-positive lymphocytes by immunostaining (CD3 as a marker of B cells and CD20 as a marker of T cells).

Statistical analysis was performed using the Statistical Package for the Social Sciences software, version 11.0 (SPSS Inc., Chicago, IL, USA).

We performed Scheffe's F test for multiple comparison official approval after having held Kruskal-Wallis authorization for analysis of inside diameter dilation rate and the histologic evaluation item at a significance level of $P<0.05$. 
Images for this section:

Fig. 0

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Fig. 0

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Double Balloon Catheter

Intra-arterial closed cavity is provided by dilataion of distal and proximal balloons.

The drug can be injected into the closed cavity through side holes.

Fig. 0

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Results

During the entire follow-up period, rupture of the EIA and death did not occur.

1. Vasodilation ratio of the external iliac arteries

The vasodilation ratio was the ratio of the postoperative inner diameter to the preoperative inner diameter. The ratios for the S, B+S, E, and B+E groups were 0.99±0.01#mean±SD#, 1.00±0.01, 0.96±0.03, and 1.13±0.09, respectively.

The vasodilation ratio was the ratio of the postoperative outer diameter to the preoperative outer diameter. The ratios for the S, B+S, E, and B+E groups were 1.01±0.01#mean±SD#, 1.05±0.01, 1.08±0.10, and 1.29±0.09, respectively.

The blood vessel inner and outer diameter was significantly dilated more in the B+E group compared to the other groups (P<0.05).

2. Histological examination.

1) Degeneration and disappearance of medial smooth muscle

Degeneration and disappearance of medial smooth muscle was observed in the B+S and B+E groups, but no significant difference was seen for other groups.

2) Degeneration and disappearance of the external elastic lamina

The degeneration and disappearance of external elastic lamina was observed only in groups using elastase(E group and B+E group). Compared to other groups, the B+E group demonstrated significant degeneration and disappearance of the external elastic lamina (P<0.05).

3) Disappearance of the internal elastic lamina

Disappearance of the internal elastic lamina in the E group was significantly pronounced compared to the S group (P<0.05). Similarly, in the B+E group, the disappearance of internal elastic lamina was significantly pronounced compared to the B+S group (P<0.05).

4) Neointimal thickening

Neointimal thickening was observed in the E group, B+S group and B+E group, but no significant difference was noted compared to each group.
5) Immunohistochemical examination

Immunohistochemical staining for CD3 and CD20 showed the lack of significant CD20- or CD3-positive lymphocytic infiltration.
Fig. 0

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Fig. 0

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Group B+E demonstrated significant dilatation compared to other groups ($p < 0.05$).

Fig. 0

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Group B+E showed significant dilatation compared to other groups ($p < 0.05$).

Fig. 0

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Disappearance of the internal elastic lamina

Group E was significantly higher than group S ($p < 0.05$). Group B+E was significantly higher than group B+S ($p < 0.05$).

Fig. 0

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The degeneration of medial smooth muscle was observed in group B+S and group B+E, but showed no significant difference.
Degeneration and disappearance of the external elastic lamina

Group B+E showed significant degeneration and disappearance of the external elastic lamina (p < 0.05).

Fig. 0

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Neointimal thickening was observed in group E, group B+S, and group B+E, but no significant difference was seen between any groups.

Fig. 0

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EIA showed **normal muscular artery findings.**

**Fig. 0**

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Neointimal thickening (▲) was recognized.
Disappearance of the internal elastic lamina (white arrow) was exhibited.
Degeneration and disappearance of medial smooth muscle (*) was seen.
Degeneration and disappearance of the external elastic lamina was not shown.
Slight neointimal thickening (blue arrow) was recognized.
Disappearance of the internal elastic lamina (white arrow) was exhibited.
Degeneration and disappearance of medial smooth muscle was not seen.
Degeneration and disappearance of the external elastic lamina (♦) were shown.
Neointimal thickening (▲) was recognized.
Disappearance of the internal elastic lamina (white arrow) was exhibited.
Degeneration and disappearance of medial smooth muscle (*) were seen.
Degeneration and disappearance of external elastic lamina (♦) were shown.

Fig. 0

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Conclusion

We established methods of experimental aneurysmal model at external iliac artery of adult beagle dogs by easy IVR technique without rupture.

To generate more dilated aneurysmal model, efficient degeneration and disappearance of elastic fiber is necessary.


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