Domuzlarda deneysel karotis bileşke anevrizma modeli ve literatür araştırması

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ÖZET

Amaç: Deneysel anevrizma modeli intrakranial anevrizmaların tedavisini değerlendirmek için üç ayrı nedenle kullanılmıştır. Bunlar; deneysel anevrizma oluşturulurken kazanılan pratik ve tecrübeler, karşılaştırılmalı çalışmaların ve yeni prosedürlerin yapılabilmesi ve yeni tedavi yöntemlerinin geliştirilmesidir. Bu çalışmada domuzlarda deneysel karotis bileşke anevrizması oluşturulmuş ve bu konudaki literatür çalışmalarının sunulması amaçlanmıştır.
Gereç ve Yöntem: Domuzlar üzerinde boyun bölgesinde karotis arter ve bileşkedeki dalları geçici anevrizma klipleri ile kapatılıp oval arter kesisi yapıldıktan sonra venöz damar grefti ile anastomoz yapılıp anevrizma oluşturuldu.
Sonuçlar: Karotis arter bileşkesinde 10 adet anevrizma oluşturuldu. Anevrizmaların büyüklüğü en az 4 mm olup, boyun genişliği en az 2 mm ölçüldü. Oluşturulan anevrizmaların sadece bir tanesi tromboze oldu.
Tartışma: Bu çalışmada deneysel arteriel bileşke anevrizması oluşturulurken bu modelin ve ayrıntılı literatür araştırmamızın endovasküler tekniklere ve anevrizma hemodinamiği için yapılan yeni çalışmalara ışık tutacağına ümit ediyoruz.
Anahtar kelimeler: Deneysel sakküler anevrizma, anjiografi, hayvan modeli

Experimental carotid bifurcation aneurysm model in the pig and review of the literature

ABSTRACT

Objective: Experimentally constructed aneurysms have been used in three ways in the evaluation of therapeutic methods for intracranial aneurysms: they may be used simply for the acquisition of skill through repeated practice of certain therapeutic procedures; in comparative studies of new and/or established procedures, and in the investigation, development, and refinement of new therapies. In this article a carotid artery bifurcation saccular aneurysm model is described in the pig and also we review the experimental applications of the aneurysms in the laboratory animals.
Methods: The cervical carotid and both bifurcation branches are occluded with temporary aneurysm clips for performance of an elliptical arteriotomy and anastomosis of the vein graft in the suscrofa pigs.
Results: 10 aneurysms were created at the carotid bifurcation of the pig. The lower limit on the size of the aneurysm in our study was 4 mm the lower limit of the size of the arteriotomy orifice was 2 mm. Only one aneurysm had thrombosed.
Conclusion: The surgical steps in the construction of this model are detailed and such a model is useful in studying aneurysm hemodynamics with various therapeutic modalities, and evaluating interventional techniques for the treatment of aneurysm
Keywords: Experimental saccular aneurysm, angiography, animal model

INTRODUCTION

Experimentally constructed aneurysm model allows for the investigation of the hemodynamic and physiologic changes that take place within bifurcation aneurysms in the setting of progressive vascular pathology as well as during the performance of various treatment modalities for peri-aneurysmal vascular pathology including treatment of the aneurysm itself. Intracranial saccular aneurysms remain a major cause of nontraumatic intracranial hemorrhage, with about 22-25% of cerebrovascular deaths following their rupture (1). Creation of such a model must demonstrate persistent aneurysmal patency, be reproducible, have minimal surgical morbidity and mortality

and be easy to use for experimental purposes.
Historically, many models of aneurysms have been developed (2-13). Experimental aneurysms, especially at arterial bifurcations, have been difficult to produce because of the surgical technique required, and aneurysm thrombosis.
In this study the design of carotid bifurcation aneurysm model is described in the pig and also the experimental applications of the aneurysms in the laboratory animals is reviewed.

MATERIALS AND METHODS

Ten susscrofa pigs weighing between 70-90 lbs. were induced, anesthesized and intubated with a telazol (0.8 mg /lb) mixture given via intramuscular injection. Anesthesia was then maintained with inhalational 2% isoflurane throughout the procedure. Intravenous access was established through an ear vein and IV normal saline given throughout the procedure. Temperature was maintained with a heating pad, vital signs were monitored with a femoral arterial line established via femoral cut-down, and a pulse ox-was placed on either the ear, or the tongue to monitor oxygenation. At the end of the procedure, all pigs were euthanized with euthasol (40 mg lb)
Utilizing sterile technique, a longitudinal incision was made in the right side of neck and dissection made in the plane lateral to the midline structures. The sternocleidomastoid muscle was reflected medially to allow the identification of the external jugular vein. 2 cm segment of the vein was exposed, dissected end isolated. Small branches were cauterized and sectioned. A 2 cm segment of the vein was isolated between two sutures and the vein sectioned to yield an open-ended venous pouch. A 4.0 silk ligature was placed around the open end of the venous graft to obtain a venous pouch. The vein graft was irrigated out with heparinized saline and adventitia along the edges of the cut end of the graft was denuded. The common carotid artery was then isolated deep to the cervical strap muscles and followed cephalad to its bifurcation. A 4 cm segment of the CCA was isolated and cleaned of adventitia. Any small branches were cauterized and sectioned. The internal carotid artery was always found to continue cephalad in the same plane as the common carotid artery, the external carotid artery always coursed laterally. Usually a small arterial branch of the internal carotid artery was found very close to but behind the carotid bifurcation. Depending on the size of this branch, it was occasionally cauterized and sectioned. Papaverine was used diligently to relieve vasoconstriction of the artery and its branches. Temporary aneurysm clips were then place on the common carotid artery. Utilizing the Carl Zeiss Universal S2 operating microscope, a 2-3 mm elliptical arteriotomy was then performed in the region of the bifurcation slightly eccentric to the anterior surface of the bifurcation. By varying the size of the arteriotomy and varying the length of the vein pouch, it was possible to produce narrow or wide necked aneurysms of various sizes (Fig 1& 2). The arteriotomy site was copiously irrigated with heparinized saline solution. Utilizing 7.0 prolene, two stay sutures were placed to oppose the edges of the venous graft to the arteriotomy site. The venous graft was then anastomosed to the bifurcation using a continuous 7.0 prolene (Fig 3). Vital signs and pulse oximetry were continually monitored throughout the procedure, and special care was taken not to disturb or injure the vagus nerve. Prior to placement of the last stitch, the temporary clips was removed from the branch artery to allow for back bleeding. The stitch was then placed, and subsequently all of the remaining temporary clips were removed from the ECA, CCA, and lastly ICA in a sequential fashion. The anastomosis was surveyed for any areas of leakage and if necessary a single interrupted stitch placed.

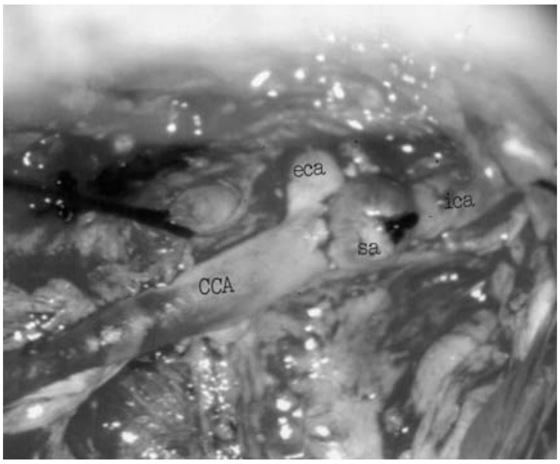

Fig 1: A bifurcation aneurysm is visualized. The internal carotid artery is in line with the common carotid artery. The external carotid artery courses laterally. CCA: Common carotid artery, ica: Internal carotid artery, sa: Saccular aneurysm.

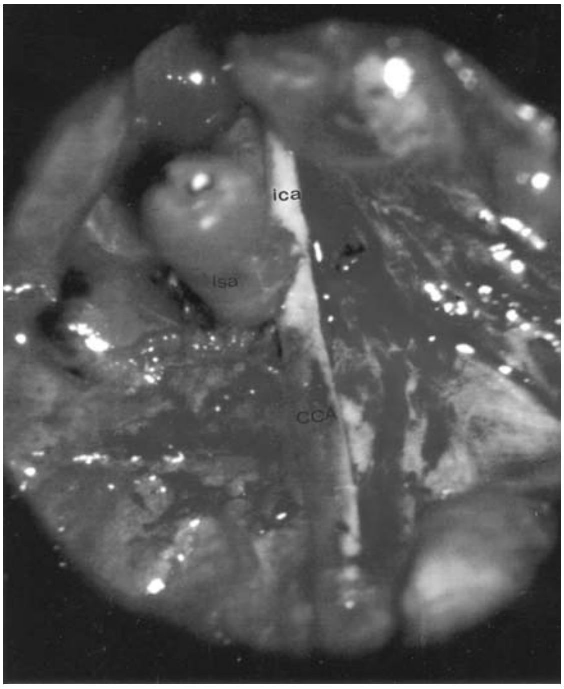

Fig 2: A large aneurysm has been created. Notice that the internal carotid artery is in line with the common carotid artery. CCA: Common carotid artery, lsa: Large saccular aneurysm, ica: Internal carotid artery.

Alternatively, for small areas of slow leakage, surgicel was placed around the anastomosis site. Once created, a Doppler probe was placed to check for pulsatile activity.The pig was then taken to the animal facilities angiography suite where within thirty minutes after creation of the aneurysm, a transfemoral angiogram was

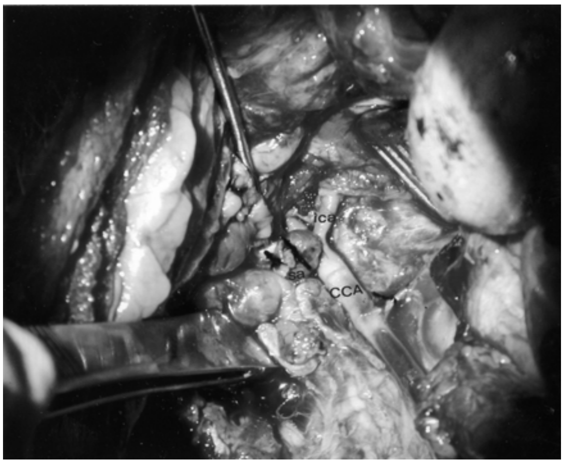

Fig 3: A right side carotid bifurcation aneurysm is visualized. CCA: Common carotid artery, sa: Saccular aneurysm, eca: External carotid artery, ica: Internal carotid artery.

Fig 4: An angiogram demonstrates patency of the bifurcation aneurysm. CCA: Common carotid artery, sa: Saccular aneurysm.

performed to access aneurysm patency (Fig. 4).

RESULTS

10 aneurysms were created at the carotid bifurcation of the pig utilizing this technique in our laboratory. It was our aim to create aneurysms that closely matched the morphological and hemodynamic characteristics of most intracranial berry aneurysms. One animal died after anastomosis secondary to anesthesia. Only one aneurysm had thrombosed by the time of angiography. Our aneurysm size to neck ratio was about 3:1. The lower limit on the size of the aneurysm in our study was 4 mm the lower limit of the size of the

arteriotomy orifice was 2 mm. The aneurysm that thrombosed was 4 mm in size with an orifice 2 mm. The time required for the dissection and anastomosis was never greater than 1.5 hrs. There was no associated morbidity. Vital signs remained stable in all pigs during the dissection and surgical procedure.

DISCUSSION

Four animal species (rabbit, rat, dog, swine) have been used for surgical construction of experimental aneurysms over the last 40 years (5,6,11,14,15,16,17,18,19). Advantages of rabbits include the similarity of the size of their common carotid arteries (where aneurysms are usually created) to the human proximal middle cerebral artery. Furthermore, the rabbit is one of the nonprimates whose thrombotic and thrombolytic profiles are most comparable to those of humans (20). The limitations of this animal as a model are that only one aneurysm is possible per animal and the high incidence of procedure-related mortality. The use of rats for experimental aneurysm formation has been advocated by Young and Yasargil particularly for development of skill in microsurgical techniques (19). The advantages of the rat are its low cost and the ability to produce accessible, sufficiently- sized carotid aneurysms. The rat carotid artery does not exhibit significant spasm in response to mechanical stimulation, which is probably an added factor in explaining the rarity of thrombosis (21). Dogs have been consistently used since the mid 1950s. Their ease of handling and reliable anesthesia contributes to their success as laboratory animals. The fibrinolytic system in canine blood is very active when compared to humans (15,18,22).

The great majority of human intracranial saccular aneurysms occur at arterial bifurcations. Paradoxically the literature contains many more descriptions of construction techniques for lateral aneurysms. Experimental aneurysms at arterial bifurcations have been difficult to produce because of high morbidity and aneurysm thrombosis (23). At least seven techniques for the construction of bifurcation aneurysms have been described. Stehbens was the firs to suture a vein pouch into the fork of the aortic bifurcation of the rabbit (11). Surgical construction of bifurcation aneurysms in large animals was first attempted by Roach (24,25). She developed the dog tail artery model by tying off this artery near its origin creating a cylindrical aneurysm at the aortic trifurcation. Currently, the surgical technique most commonly used for construction of experimental bifurcation aneurysms is that of Forrest and O'Reilly (Fig. 5), in which the left CCA is partially end-to-side anastomosed with the right CCA (23). A vein Pouch (from external jugular, anterior facial or posterior facial veins) is sutured to the notch formed by this anastomosis. Bifurcation aneurysms were constructed by Nishikawa et al. at a lingual- basilar artery anastomosis, using a vein patch or pouch (26). A success rate of only %23 was achieved due to considerable technical difficulties. Sekhar et al. (17) used a vein-pouch side-to-side anastomosis at the bifurcation of the common carotid artery (CCA) and the superior thyroid artery in the dog. Aneurysms of different sizes and shapes could be produced with this technique. Terminal aneurysms (simulating human basilar tip and internal carotid artery bifurcation aneurysms) were constructed by Strother et al. by end-to-end anastomosis of the right and left CCA in the dog (Fig. 6) (12). The proximal segment of the right CCA was then anastomosed end-to-side into the undersurface of the U formed by this linkage and a vein pouch was attached immediately above this anastomosis. This technique, however, resulted in significant angulation between the aneurysm sac and its parent artery, i.e., the stem, with resulting intra-aneurysmal stasis.

Bifurcation aneurysms are harder to construct surgically than side-wall aneurysm. A porcine model describing the

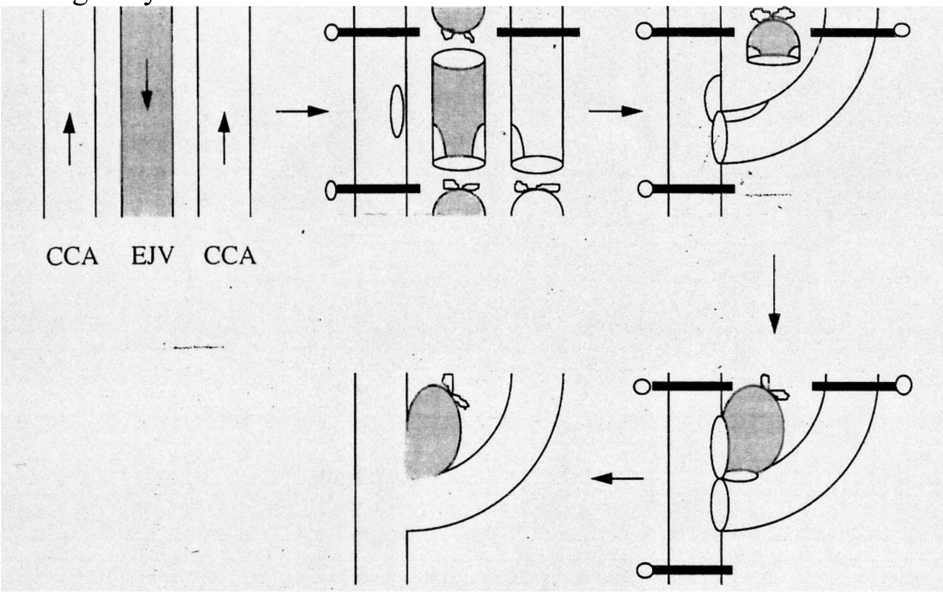

Fig 5: Surgical construction of bifurcation aneurysms according to Forrest and O'Reilly (23)

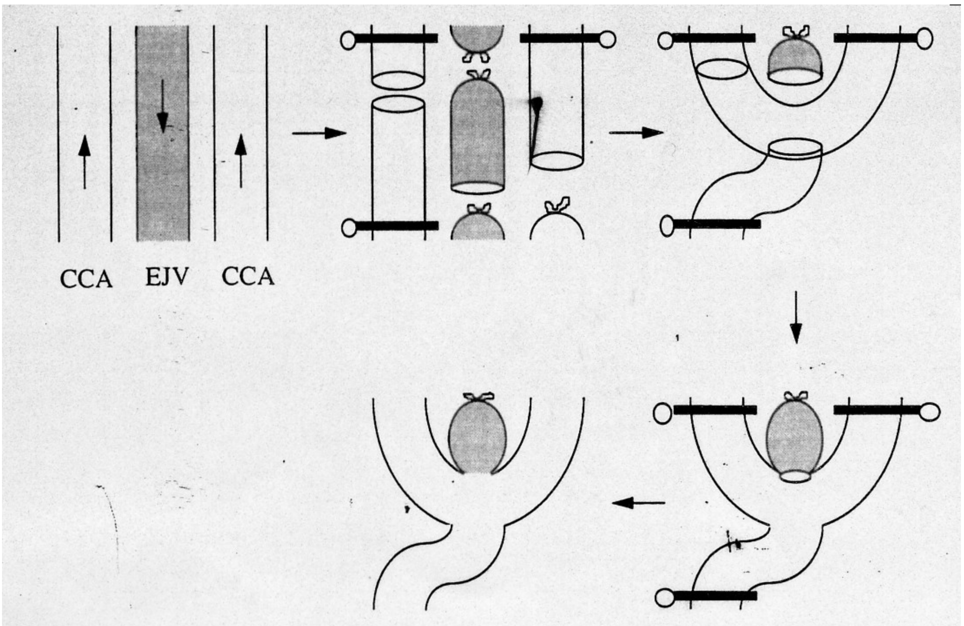

Fig 6: Surgical construction of terminal aneurysms according to Strother et al (12)

use of a venous pouch for the creation of a carotid bifurcation aneurysm model is reported. The model is reproducible, easy to perform, requires little time to perform, and demonstrates excellent patency rates when appropriate size to neck ratio is used. Such a model is useful in studying aneurysm hemodynamics, changes in aneurysm hemodynamics with various therapeutic modalities, and in evaluating interventional neurovascular techniques for the treatment of bifurcation aneurysms or vascular lesions with associated bifurcation aneurysms.

Most experimental aneurysms are constructed on the CCA. Multipl aneurysms may be constructed on one or both CCAs (14,27). Histologically, the resulting aneurysms show strong reparative processes, with marked polymorphonuclear infiltration of the aneurysm walls (1,28). According to Yong-Zhong et al this reaction arises from surrounding tissues in the neck, restricting the growth of the aneurysm sac. In addition, the muscles in the neck surrounding the CCA contract and relax, which provides a tight, limited space for the aneurysm (1,28). For this reason, Sadavisan et al. used the abdominal aorta to construct their aneurysms because it was felt that the pterional cavity is less restrictive than the neck (29). The femoral and renal arteries have also been used for the construction of aneurysms in dogs (30). The creation of an experimental aneurysm intracranially offers the advantages of studying growth, physical properties, and thrombosis of the lesion in a setting more realistically simulating that in humans (26). If experimental aneurysms could be constructed in subarachnoid space they would probably show fewer regenerative features and thinner and larger sac. Nishikawa et al constructed aneurysms at the site of a lingual- basilar artery anastomosis. Mortality was at %38.

Most of the surgical models, however, are flawed in that they do not recreate the normal hemodynamics encountered at the site of a true bifurcation aneurysm. The pig offers several advantages when constructing saccular aneurysm models. If animals in the 35-45 kg range are used, they are still easy to handle in the laboratory setting, and their neck vessels are similar in size to the middle cerebral arteries of the human. These vessels are, therefore, large enough to easily manipulate surgically, and aid the surgeon in developing skills with these size vessels when working in the human patient population. This makes it easier to extrapolate results of pathophysiological and therapeutic studies of porcine aneurysms to the human.

Experimentally constructed aneurysms have been used in three ways in the evaluation of therapeutic methods for intracranial aneurysms: they may be used simply for the acquisition of skill through repeated practice of certain therapeutic procedures; in comparative studies of new and/or established procedures, and in the investigation, development, and refinement of new therapies.

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