의학과 박사학위 논문

치료적 혈관 폐색을 위한 이중층 PVA 고분자 색전 코일의 개 혈관 모델에서의 효용성에 관한 실험적 연구

Polymeric embolization coil of bilayered PVA strand for therapeutic vascular occlusion: a feasibility study in canine experimental vascular models

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Polymeric embolization coil of bilayered PVA strand for therapeutic vascular occlusion: a feasibility study in canine experimental vascular models

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ABSTRACT

PURPOSE

The purpose of this study was to investigate the feasibility of PVA (polyvinyl alcohol) polymer coil as a new endovascular embolic agent and to gauge the related histologic response in a canine vascular model.

METHODS

PVA polymer coil was fabricated by cross-linking PVA and tantalum particles. Basic properties were then studied *in vitro* via swelling ratio and bending diameter. Normal renal segmental arteries and wide-necked aneurysms of carotid sidewalls served as canine vascular models. Endovascular PVA coil embolization of normal renal segmental arteries (n=20) and carotid aneurysms (n=8) was performed under fluoroscopic guidance in 10 dogs. Degree of occlusion was assessed immediately and at 4 weeks post-embolization by conventional and CT angiography. Histologic features were also graded at acute (Day 1: segmental arteries, 6; aneurysms, 4) and at chronic (Week 4: segmental arteries, 14; aneurysms, 4) phases post-embolization, assessing inflammation, organization of thrombus, and neointimal proliferation.

RESULTS

Swelling ratio declined as concentrations of cross-linking agent rose. Mean bending diameter was 2.05 mm (range, 0.86-6.25) in water at 37℃ and 2.29 mm (range, 0.94-6.38) in canine blood samples at 37℃. Occlusion of normal renal segmental arteries was sustained (Day 1: complete occlusion, 20; Week 4: complete occlusion, 14), whereas immediate outcomes in carotid aneurysms (Day 1: complete occlusion, 5; residual neck only, 3) were not sustained (Week 4: complete occlusion, 1; minor recanalization, 1; major recanalization, 2). At Week 4, chronic inflammatory cells predominated, with progressive organization of thrombus and fibrocellular ingrowth. All aneurysms bore full neointimal linings on the coil mass in chronic phase.

CONCLUSION

Vascular occlusion by PVA polymer coil proved superior in normal renal segmental arteries and feasible in surgically constructed carotid aneurysms (with packing densities ≥30%), constituting acceptable radiologic feasibility and histologic response.

Key words: PVA (polyvinyl alcohol), Polymer, Coil, Embolic agent, Endovascular embolization

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LIST OF ABBREVIATIONS

CT= computed tomography

F= French catheter scale (e.g. 1 mm= 3 F)

g= gram

mL= millilitre

PVA= polyvinyl alcohol

vol%= (volume of solute/volume of solution) x 100

wt%= (mass of solute / total mass of solution) x 100

INTRODUCTION

Endovascular embolization has become an important surgical alternative, particularly in the context of acute hemorrhage (1-4) or intracranial aneurysms. (3, 5, 6) Its potential in other disease states, such as arteriovascular malformation (AVM), (7, 8) hepatocellular carcinoma, (9) uterine myoma, (10) and metastatic malignancies, (11, 12) has fueled a search for novel embolic agents and improved endovascular techniques.

Delivery of metallic coil, whether stainless steel or platinum, is predictable and controllable, with superior radio-opacity. (1, 13-15) However, these materials are relatively costly, and their packing densities are low. (16, 17) Liquid embolic agents, including n-butyl cyanoacrylate (NBCA), polyvinyl alcohol (PVA), and dimethyl sulfoxide (Onyx®, EV3-MTI, Irvine, CA, USA) have superior packing densities but are difficult to handle, making delivery less reliable by comparison. (13, 14, 16) On the other hand, PVA particles have been widely used for reducing or blocking vascular flow pre-surgically in tumors or AVMs or urgent management of acute massive hemoptysis, (2, 7, 18) and their cost is relatively low. The drawbacks are their limited visibility and less controllable delivery. (19)

PVA (polyvinyl alcohol) is a biocompatible, nonbiodegradable, nontoxic, and noncarcinogenic constituent that has been used as a permanent embolic agent and has general medical and pharmaceutical utility. (2, 20, 21) PVA hydrogel is a hydrophilic polymer, which swells as water is absorbed. Bilayer PVA films, formed by PVA films of differing swelling ratios, yield various bending diameters and may be shaped into PVA coils, including bundles.

The purpose of this investigation was to study the feasibility of PVA polymer coil as an endovascular embolic agent in an experimental canine vascular model and gauge the related histologic response. PVA polymer coils were expected to show more predictable and controllable delivery with superior radio-opacity relative to the particulates, while having comparable packing density and lower cost to metallic coil. In addition, PVA polymer (like other polymer coils) has the potential for fewer artifacts on CT, compared with metallic coil. (22)

MATERIALS AND METHODS

The protocol for this investigation was approved by the Institutional Animal Care and Use Committee of the Clinical Research Institute, Seoul National University Hospital. Fabrication of cross-linked PVA hydrogel film was facilitated by the chemical cross-linking agent, glutaraldehyde. PVA hydrogel was prepared in mixture of 5 wt% (percentage by mass, mass of solute / total mass of solution x 100) PVA powder (Molecular weight 146,000-186,000 grams per mole, 99+% hydrolyzed; Sigma Aldrich, St. Louis, MO, USA) dissolved in distilled water, 50 wt% glutaraldehyde solution (Sigma Aldrich, St. Louis, MO, USA), and a catalyst mixture. The catalyst mixture comprised 10 vol% (percentage by volume, volume of solute/volume of solution x 100) aqueous acetic acid solution, 50 vol% aqueous methanol solution, and 10 vol% aqueous sulfuric acid solution. Radio-opacity was acquired by adding tantalum particles (200 nm each at 20 vol%). PVA hydrogel films with tantalum particles were prepared in mixture of PVA aqueous solution (1.95 g PVA in 20 mL distilled water) and tantalum aqueous suspension (6.40 g in 20 mL distilled water). The 50 wt% glutaraldehyde was added to the mixture with continuous stirring at 60 ℃ and 100 ℃ and then cooled to room temperature. The PVA solution with mixture was cast on a plastic substrate by use of micro-applicator. After drying the cast films at room temperature and a vacuum oven, PVA hydrogel film with radio-opacity was finally prepared. PVA film swelling ratios varied in accord with glutaraldehyde concentration.

Bilayer PVA films were formed by two adherent PVA hydrogel films of differing swelling ratios. Two PVA films were attached by using an adhesive solution which comprised PVA pre-gel solution, catalyst mixture, and glutaraldehyde, and reinfored by an application of heat and pressure. Bilayer PVA films were bendable, with concentration of cross-linking agent or specific PVA film combination (in 0.5, 1, 2, 3, and 6 wt%) determining bending diameters. Furthermore, bilayer PVA films could be cut/sized as needed into PVA coils (for our purposes: width, 0.4 mm; thickness, 0.1 mm; length, 50 mm).

In vitro studies

PVA hydrogel films were rated by swelling ratio, reflecting the corresponding level of cross-linking agent (0.5, 1, 2, 3, and 6 wt%). PVA hydrogel films 10 mm wide, 0.05 mm thick, and 10 mm long were evaluated in distilled water and in blood (venous whole blood from healthy dogs), both at 37℃. Bending diameters of PVA polymer coils 0.4 mm wide, 0.1 mm thick, and 50 mm long (**Figure 1**) were determined at various level of cross-linking agent (0.5+1, 0.5+2, 0.5+3, 0.5+6; 1+2, 1+3, 1+6, 2+3, 2+6; and 3+6 wt%). The volume of coils was also assessed in distilled water and in dog blood, both at 37℃.

In vivo studies

Ten adult mongrel dogs were used for *in vivo* studies. The dogs weighed 20-30 kg and were maintained on a standard laboratory diet. PVA polymer coil embolization of normal renal segmental arteries (n=20) was conducted in 10 dogs. Surgery to construct aneurysms and endovascular embolization were performed in four dogs. A total of eight wide-necked sidewall aneurysms were created in 8 common carotid arteries of 4 dogs. Venous grafts were acquired from each external jugular vein. End-to-side anastomosis was done in arteriotomy sites, forming aneurysmal orifices. Average size of constructed aneurysms was 10.5 mm (range, 3-17 mm).

Surgical construction of aneurysms and endovascular embolizations with PVA polymer coil were performed under general anesthesia, which was induced by intramuscular injection of ketamine hydrochloride, 20 mg (Ketalar; YuhanYanghang, Seoul, Korea) and xylazine hydrochloride, 40 mg (Rompun; Bayer Korea, Seoul, Korea) and maintained via mechanical ventilation (after endotracheal intubation) by an inhalation mixture of oxygen and isoflurane (Isoflo; Abbott Laboratories, Abbott Park, IL, USA) .

Embolization in canine vascular model

Pre-procedural CT angiography was performed to inspect the anatomy of carotid aneurysms generated and renal segmental arteries at baseline. Endovascular PVA polymer coil embolization was done 1 week after constructing aneurysms. Conventional angiography was performed using a digital

subtraction angiography system (Philips BV Pulsera; Philips Healthcare, Best, the Netherlands).

Under general anesthesia and with sonographic guidance, a 6-F introducer sheath was inserted into right and left common femoral arteries. A balloon-assisted technique was used for coil embolization of the wide-necked sidewall aneurysms. Two 6-F Envoy guiding catheters (Cordis Neurovascular, Miami, FL, USA) were placed unilaterally in the common carotid artery, one for coil delivery and the other for balloon catheterization (Scepter; MicroVention Inc, Tustin, CA, USA). A coaxial system was used, with a combination of 6-F Envoy guiding catheter and 5-F Davis or HN 5 catheter (A&A Medical Device, Seongnam, South Korea). The aneurysms were filled with PVA polymer coil via 5-F Davis or HN 5 catheter. Coil delivery was achieved through saline infusion via the 5-F catheters and/or 0.035-inch guide-wire push (Terumo Corp, Tokyo, Japan).

For the embolization of renal segmental arteries, a 6-F renal guiding catheter was placed in proximal renal artery and 5-F Davis catheters were coaxially placed in each segmental artery. PVA polymer coil was delivered as above.

Conventional angiography was done to assess the degree of occlusion immediately after coil embolization.

Degree of occlusion and follow-up

Renal segmental arterial occlusion was rated as either complete or partial immediately after embolization (n=20) and at 4 weeks (n=14) post-embolization. Complete occlusion was defined as the absence of renal parenchymal and renal arterial contrast by angiography. All else was considered partial occlusion.

Immediately after embolization of carotid sidewall aneurysms (n=8), degree of occlusion on angiography was rated as follows: (1) complete occlusion, (2) residual neck only, or (3) residual aneurysm. Complete occlusion was defined by dense packing of aneurysmal sac and neck with coils, with no contrast in aneurysmal sac. Residual neck only was defined by a coil-packed aneurysmal sac, with a small neck that retained contrast. Residual aneurysm was defined by a contrast-filled

aneurysmal sac. (23) At 4 weeks post-embolization (n=4), status of occlusion on angiography was assessed as follows: (1) complete occlusion (no opacification of aneurysm), (2) minor recanalization (slight opacification of aneurysmal neck), and (3) major recanalization (opacification of aneurysmal sac). (23) The migration, protrusion, or compaction of coil mass were rated at immediate and 4 weeks post-embolization.

Assuming all aneurysms were ellipsoid, the calculated volume of each aneurysm was based on following formula: Volume = $(4\pi/3) \times (W/2)^2 \times (H/2)$, where W is width and H is height of aneurysms. Aneurysmal configurations on pre-procedural CT angiography were evaluated and quantified using 3D reconstruction software (Rapidia; Infinitt Co, Seoul, South Korea). Packing density was expressed as a percentage, dividing total coil volume by aneurysmal volume.

Conventional angiography was performed before, immediately after and 4 weeks following coil embolization. CT angiography was performed before and 4 weeks after embolization, using a 64-channel CT scanner (Discovery CT750 HD; GE Healthcare, Milwaukee, WI, USA). Scanning parameters were as follows: 64 x 0.625 mm detector collimation, 0.984:1 pitch value, 0.5 rotation time, 1.25-mm slice thickness, 1-mm reconstruction interval, 0.5 x 0.5 x 1 mm voxel size, x-ray tube voltage of 120 kVp, and noise index of 6.14 within 150-350 mAs. A total of 1.6 ml/kg body weight of nonionic contrast material (Ultravist-370; Schering, Berlin, Germany) was administered at a rate of 2.7 ml/sec by power injector (EnVision CT; Medrad Inc, Indianola, PA, USA), which was then flushed with 37.5 ml of normal saline at a rate of 2.5 ml/sec. CT angiography was initiated 5 sec after attenuation value in thoracic aorta (by bolus tracking technique) reached 100 Hounsfield units (HU).

Histologic response

Coiled renal segmental arteries and aneurysms were harvested on Day 1 (acute phase: segmental arteries, 6; aneurysms, 4) and at Week 4 (chronic phase: segmental arteries, 14; aneurysms, 4) post-embolization. All tissues were fixed in 10% buffered formalin phosphate. Aneurysms were sectioned transversely across the neck and across parent artery, and sectioning of segmental vessels was across main renal arteries. Routine hematoxylin-eosin (H&E) staining was done, as well as

immunostaining of macrophages (Clone MAC387, Thermo Fisher Scientific, Fremont, CA; dilution 1:200). (24)

Based on estimated white blood cell influx, inflammatory response was graded as follows: 0, absent; 1, few inflammatory cells; 2, scattered inflammatory cells; 3, diffuse infiltrates; 4, dense/intensive infiltrates. (25) Proportions of unorganized thrombus and fibrocellular tissue, relative to overall areas of embolization, were used to grade organizing thrombus as follows: 0, absent; 1, 1-25%; 2, 26-50%; 3, 51-75%; 4, 76-100%. (25, 26) Neointimal proliferation in areas of embolization was also graded as follows: 0, absent; 1, partial coverage; 2, complete coverage. (27)

Statistical analysis

All computations relied on commercially available software (MedCalc, v11.1.1.0, MedCalc Software, Mariakerke, Belgium). To determine if values were normally distributed, the Kolmogorov-Smirnov test was applied. The Mann-Whitney U test was used to compare acute and chronic phase histologic responses of renal segmental arteries and carotid sidewall aneurysms. A two-tailed p-value <0.05 was uniformly considered indicative of statistical significance.

RESULTS

In vitro studies

Swelling ratios decreased as concentration of cross-linking agent increased in distilled water at 37 ℃ and in dog blood at 37 ℃ **(Figure 2).** Bending diameters and coil volumes are presented in **Table 1**.

In vivo studies

Degree of occlusion

All normal renal segmental arteries showed complete occlusion (n=20) immediately and complete occlusion (n=14) at 4 weeks after the embolization procedures **(Figure 3).** Immediate post-procedural angiography of carotid aneurysms treated by PVA polymer coil showed either complete occlusion (n=5) or residual neck only (n=3) in aneurysms. Four weeks after embolization, two coiled aneurysms showed major recanalization with compaction of coil mass, despite complete occlusion on immediate post-procedural angiography. One aneurysm rated as complete occlusion earlier showed minor recanalization at 4 weeks, and another instance of residual neck was complete occlusion with mild coil protrusion at 4 weeks **(Figure 4).**

Average packing density of coiled aneurysms was 39.8% (range, 20-67%). In the two aneurysms demonstrating major recanalization, packing densities were 20% and 26%, respectively.

Histologic response

Mean grades of post-embolization inflammation in normal renal segmental arteries were 3.2 (range, 3-4) in acute phase and 3.5 (range, 2-4) in chronic phase. In the carotid aneurysms, mean grades were 3.8 (range, 3-4) in acute phase and 3.2 (range, 3-4) in chronic phase. Acute inflammatory cells predominated in acute phase, and chronic inflammatory cells predominated in chronic phase. Grades of inflammation did not differ significantly by phase (acute vs chronic) (p>0.05).

Mean grades of unorganized thrombus in renal segmental arteries were 4 (range, 4-4) in acute phase

and 1.4 (range, 1-2) in chronic phase. In carotid aneurysms, mean grades were 4 (range, 4-4) in acute phase and 1.2 (range, 1-2) in chronic phase.

Mean grades of fibrocellular tissue in renal segmental arteries were 0 (range, 0-0) in acute phase and 3.9 (range, 3-4) in chronic phase. In carotid aneurysms, mean grades were 0.5 (range, 0-1) in acute phase and 3.8 (range, 3-4) in chronic phase**.** The proportion of unorganized thrombus decreased with time, whereas fibrocellular tissue increased.

Mean grades of neointimal proliferation in carotid aneurysms were 0 (range, 0-0) in acute phase and 2 (range, 2-2) in chronic phase **(Figures 5, 6)**.

Grades of unorganized thrombus, fibrocellular tissue, and neointimal proliferation differed significantly by phase (acute vs chronic) (all $p<0.05$) **(Table 2)**.

Table 1. Mean bending diameter and volume in water and dog blood at 37 ℃

	37℃ water		37℃ dog blood	
Cross-Linking Agent (wt %)	**Bending diameter (mm)**	**Volume (mm^3)**	**Bending diameter (mm)**	**Volume (mm^3)**
0.5+1	1.21	5.61	1.35	5.08
0.5+2	0.93	4.94	1.26	4.15
0.5+3	0.90	4.80	1.22	3.73
0.5+6	0.86	4.46	0.94	3.51
1+2	2.62	5.04	2.69	3.89
1+3	2.03	4.66	2.29	3.52
1+6	1.37	4.00	1.56	3.42
2+3	6.25	4.53	6.38	3.47
2+6	1.41	3.96	1.68	3.37
3+6	2.93	3.77	3.51	2.84

[a] Data are the mean values

[b] ℃ means degree Celsius

[c] mm means millimeter

[d] mm^3 means cubic millimeter

Table 2. Histologic response

Grade	Normal renal segmental artery		P value [c]	Carotid sidewall aneurysm		P value [c]
	Acute	Chronic		Acute	Chronic	
Inflammation	3.2 (3-4)	3.5 (2-4)	0.091	3.8 (3-4)	3.2 (3-4)	1.000
Unorganized thrombus	4 (4-4)	1.4 (1-2)	0.001	4 (4-4)	1.2 (1-2)	0.029
Fibrocellular tissue	0 (0-0)	3.9 (3-4)	0.001	0.5 (0-1)	3.8 (3-4)	0.029
Neointima	N/A	N/A		0 (0-0)	2 (2-2)	0.029

[a] Data are the mean grade and data in parentheses indicate the range.

[b] N/A means not applicable

[c] Acute and chronic phase were compared.

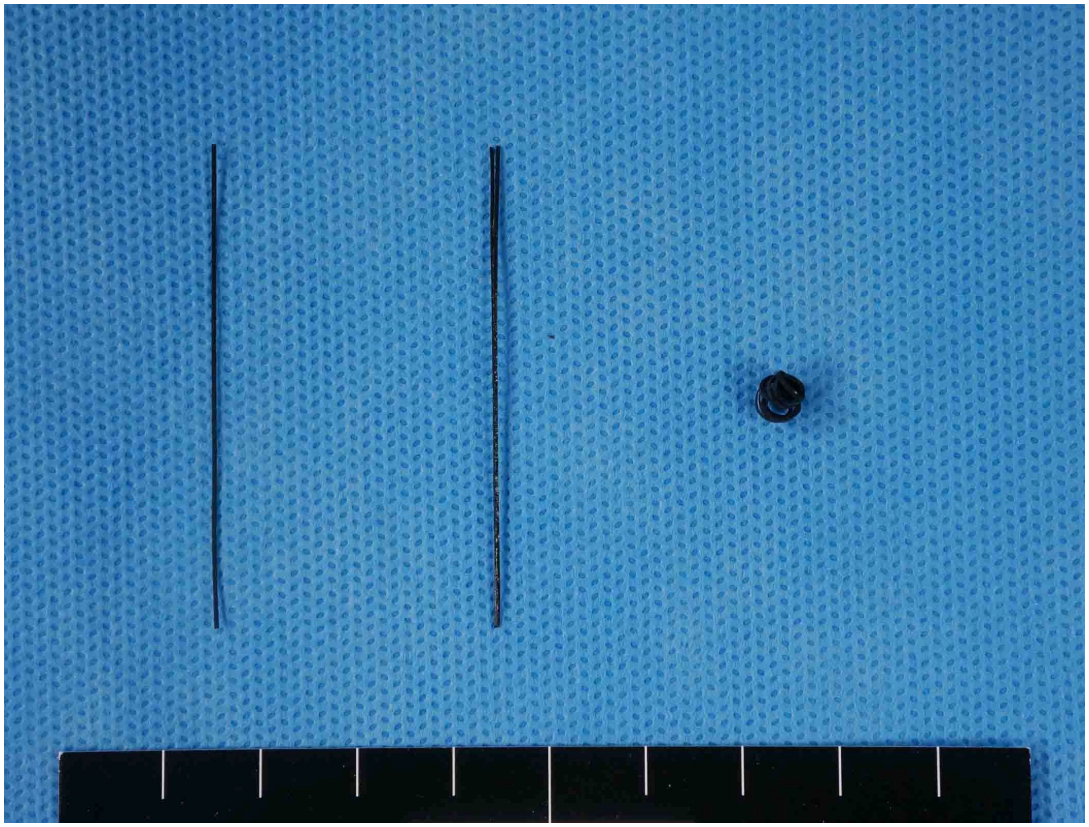

Figure 1. PVA polymer coil (left), PVA polymer bundle (center), and intertwined PVA polymer bundle (right).

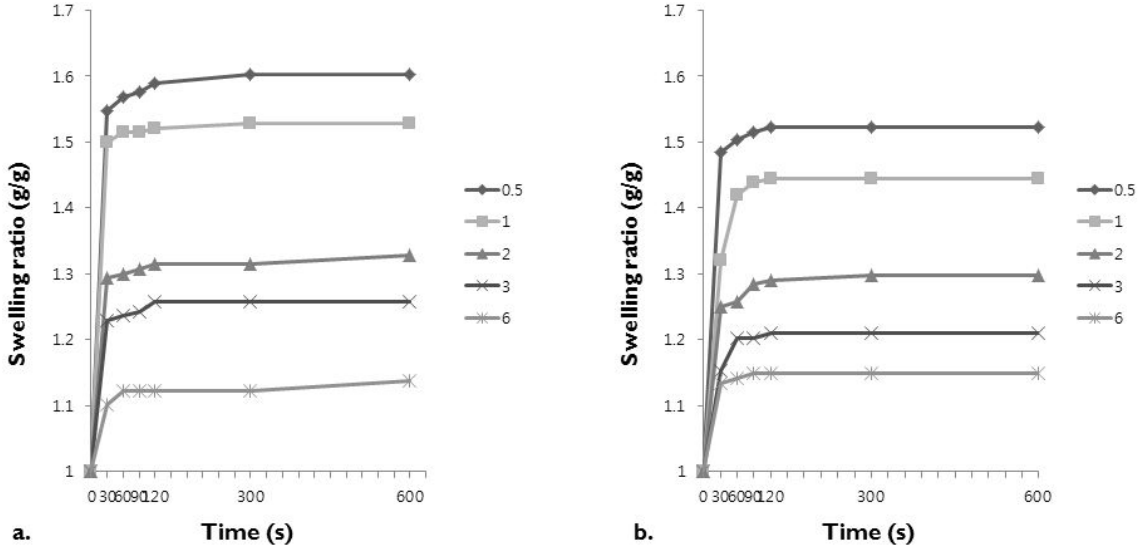

Figure 2. PVA hydrogel films swell to maximum extent within 2 min, achieving steady state thereafter in varying concentrations of cross-linking agent. Swelling ratio declined as levels of cross-linking agent rose in (a) distilled water and (b) dog blood, both at 37 ℃.

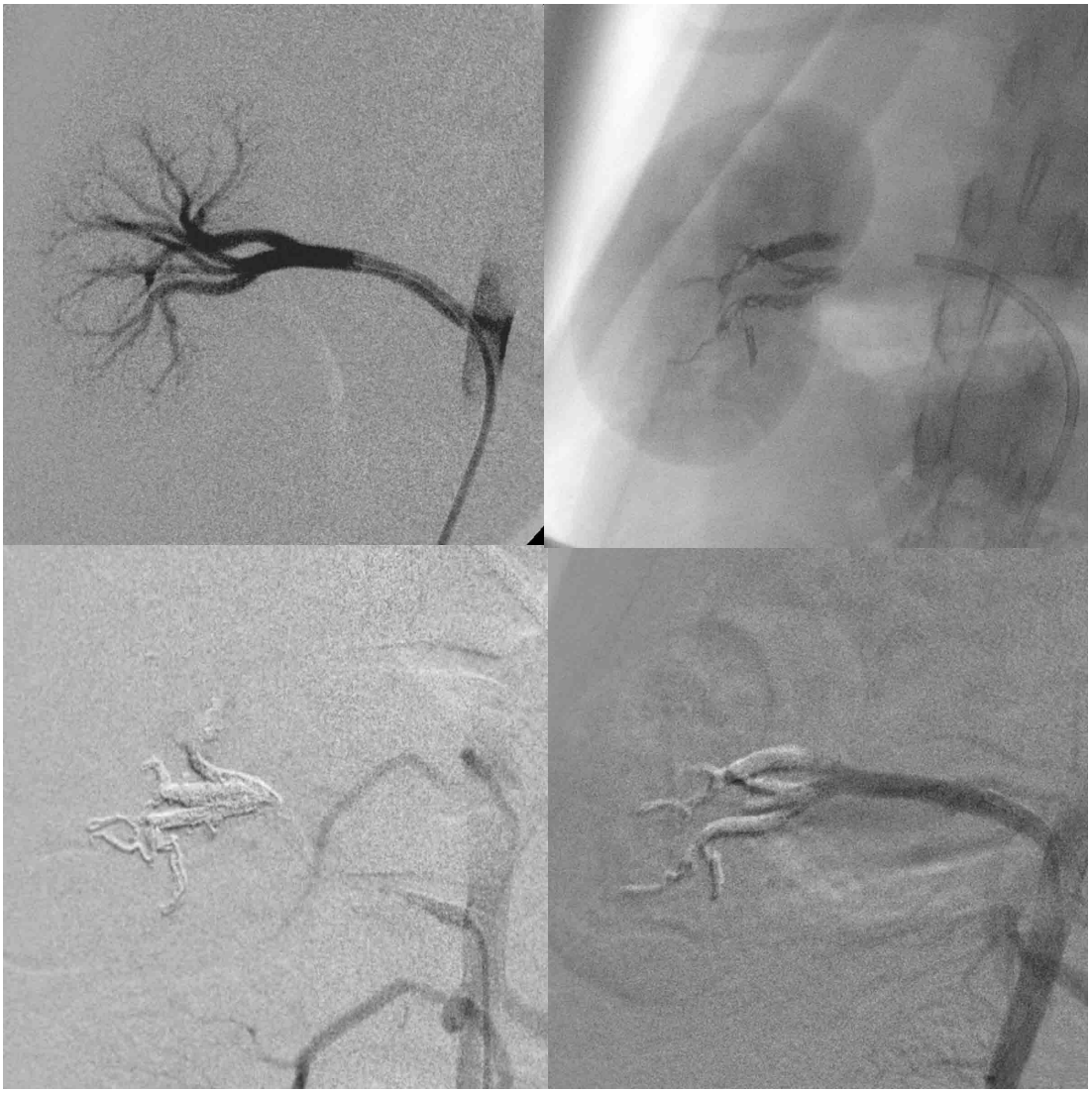

Figure 3. (a) Pre-procedural angiography of normal renal artery and its branches; (b) PVA polymer coil embolization performed; (c) Complete arterial occlusion documented by immediate post-procedural angiography; and (d) complete occlusion on follow-up angiography (Week 4).

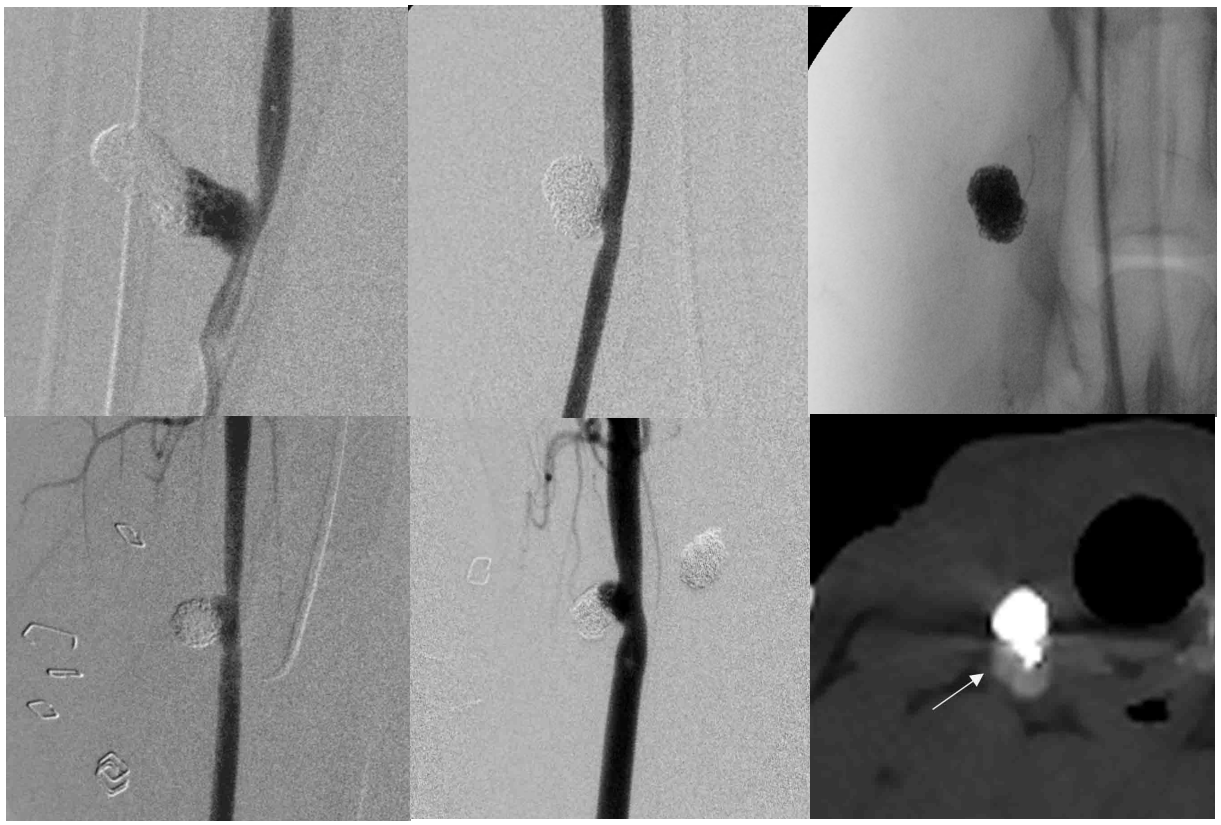

Figure 4. Endovascular embolization of two carotid sidewall aneurysms performed using PVA polymer coil: (a) Immediate post-procedural angiography showing residual neck only; (b) Complete occlusion on follow-up angiography (Week 4); (c) Fluoroscopic view of PVA polymer coil protrusion; (d) Complete occlusion documented by immediate post-procedural angiography; (e) Minor recanalization seen on follow-up angiography (Week 4); and (f) CT angiography demonstrating minor recanalization of aneurysmal neck (arrow).

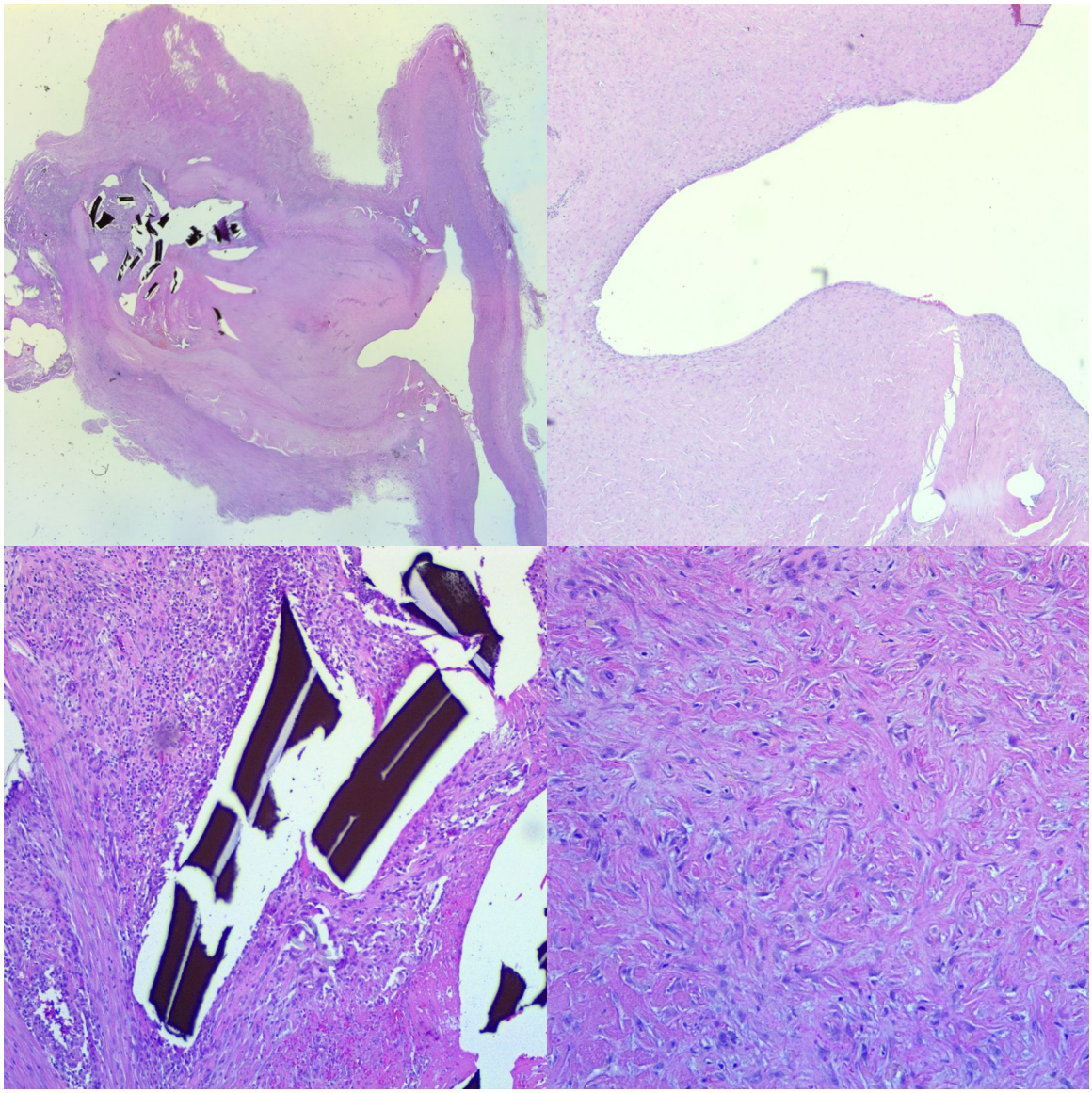

Figure 5. (a) Low-magnification light microscopic view of aneurysm treated by PVA polymer coil (H&E, X12.5); (b) High-magnification light microscopic view of coiled aneurysm, with complete neointimal coverage of aneurysmal neck (H&E, X50); (c) Chronic inflammatory cells (H&E, X100; and (d) Abundant fibrocellular tissue (H&E, X200).

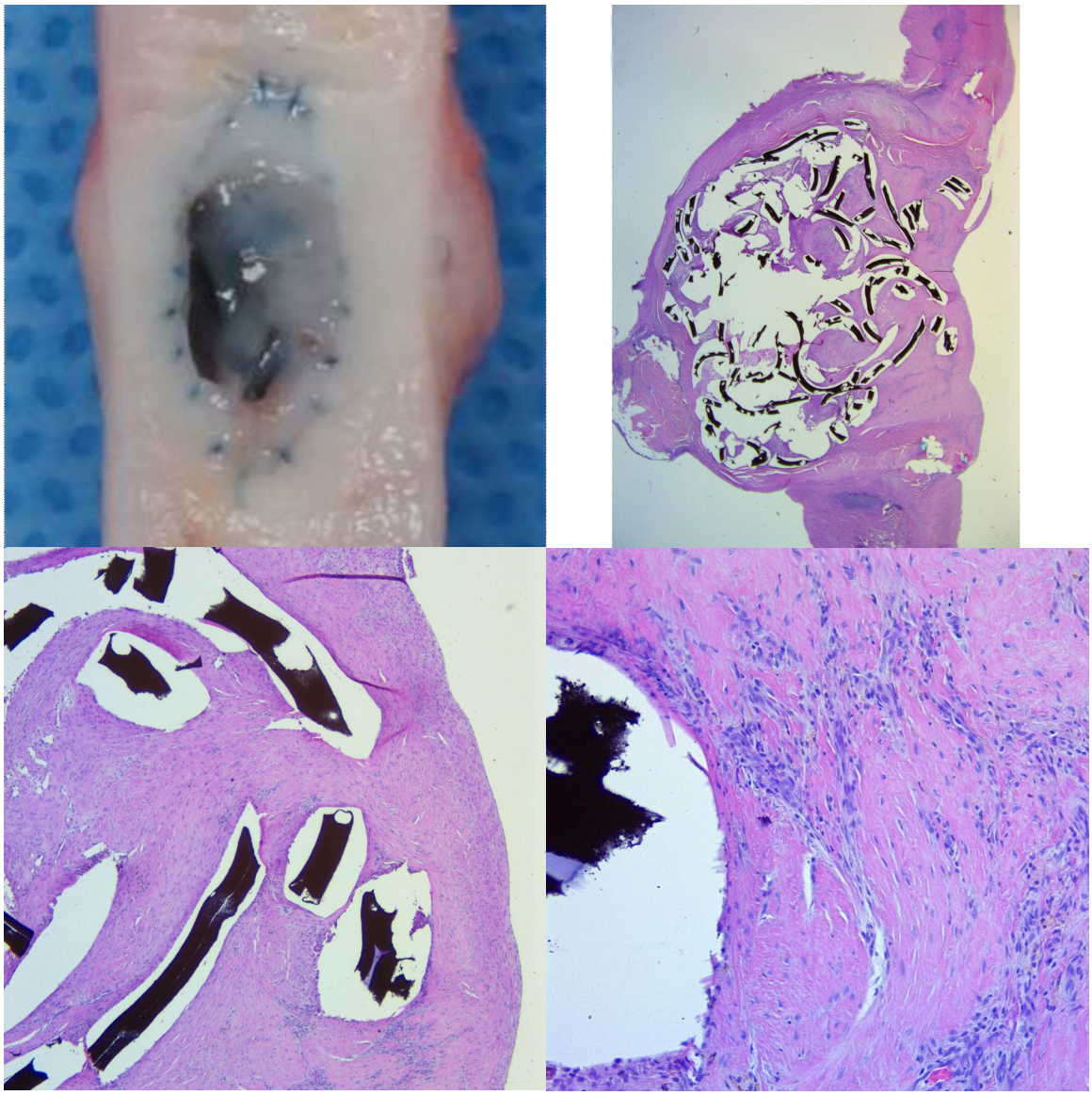

Figure 6. (a) Macroscopic view of coiled aneurysmal neck from arterial lumen showing complete neointimal coverage of aneurysmal neck; (b) Low-magnification light microscopic view of aneurysm treated by PVA polymer coil (H&E, X12.5); (c) High-magnification light microscopic view of coiled aneurysm, with complete neointimal coverage of aneurysmal neck (H&E, X50); and (d) Chronic inflammatory cells and fibrocellular tissue (H&E, X200).

DISCUSSION

The polymeric embolization coil of bilayer PVA strand with bending and swelling properties was fabricated by cross-linking PVA and tantalum particles for therapeutic vascular occlusion. PVA polymer coil produced superior occlusion of normal renal segmental arteries and feasible occlusion of surgically constructed carotid aneurysms (with packing density ≥30%) in our canine vascular model. Endovascular PVA coil embolization was clinically acceptable in the radiological feasibility via fluoroscopy and CT. In histologic response, chronic inflammatory cells predominated with time, organization of thrombus was progressive, and neointimal proliferation was ongoing on the coiled aneurysmal sac.

PVA polymer is widely used in medical devices due to its favorable properties, (2, 19, 20) especially its variable capacity to swell in the presence of chemical cross-linking agents and in water environments. Subsequently, a range of bending diameters is possible and may be beneficial in various vascular applications. The ease with which PVA polymer and other materials cross-link is also advantageous. (28) Of note, the use of PVA in drug delivery has been studied. (21)

The radio-opacity of PVA polymer coil is acquired by tantalum, which is used extensively to enhance the radio-opacity of other medical products, (embolic agents and stents). (29-31) In this study, PVA polymer coil displayed sufficient radio-opacity for performing endovascular embolization under fluoroscopy and for detecting masses of packed coil during clinical fluoroscopy and by CT. There were no distinct artifacts capable of clouding our assessments of occlusion and vascular flow. In fact, PVA polymer coil (like other polymer coils) displayed fewer artifacts on CT than metallic coil (eg, metal-induced beam hardening and streak artifacts). (22) Overall, PVA polymer coil can present predictable and controllable delivery with superior fluoroscopic radio-opacity and adequate CT imaging quality.

The fabricated coil and delivery system seemed inadequate for embolization of carotid sidewall aneurysms. For coil delivery, saline injection and push devices were employed, similar to those used for fibered coils. A better delivery system is clearly warranted to broaden the scope of use.

During embolization, the packing density of PVA polymer coil (average, 39.8%; range, 20-67%) was comparable to that of detachable metallic coils. (32-34) At lower packing density (<30%), compaction of coils was more prominent in the presence of recanalization, whereas higher packing density (≥30%) generally corresponded with acceptable occlusion over time. It may be that a critical packing density is required for durable PVA polymer coil embolization of aneurysms.

In instances of coil protrusion, parent arterial flow was preserved, with neointimal proliferation around protruded coil. Thus, mild coil protrusion may not necessarily result in occlusion of parent arteries, signifying another potential benefit of PVA polymer coil.

Use of PVA polymer coil was also more economical than other embolic agents, such as detachable metallic coil or Onyx. (17, 34) For carotid sidewall aneurysms, mean cost was $2.00 (<$0.09/coil using 0.08 coils/mm^3), with packing density ≥30%.

By design, the 4-week follow-up point was set as chronic phase, but longer-term tissue response rightly should be investigated. However, considering the changes that occurred between acute and chronic phases, the histologic response to PVA polymer coil over the course of time (including fibrocellular organization of thrombus and neointimal proliferation) may be acceptable. In chronic phase, the mass of packed coils within carotid aneurysms changed shape as fibrocellular ingrowth advanced. Post-procedural evolution of embolic occlusion, from immediate to 4-week angiography, is shown in **Figure 4**. Complete occlusion in chronic phase ultimately may depend on the nature of histologic response.

This study entailed a number of limitations. First, small number of animals in this study may not be enough to investigate PVA polymer coil completely. Second, its coagulation system is not as close to the human as other models such as the pig model although the canine model is an excellent model for aneurysms. Third, direct comparisons of PVA polymer coil with existing embolic agents, such as metallic coils or liquid agents, were not done at this time. Furthermore, present findings offer only preliminary insight. Long-term clinical study is mandatory to confirm the feasibility and utility of PVA polymer coil for vascular use.

In conclusion, use of PVA polymer coil embolization in a canine vascular model resulted in superior occlusion of normal renal segmental arteries and feasible occlusion (with packing density ≥30%) of surgically constructed carotid aneurysms. PVA polymer coil is thus acceptable for this purpose, in terms of radiologic feasibility and histologic response. A more sophisticated coil design and improved delivery system are warranted to broaden the range of practical clinical applications.

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국문 초록

연구 목적: 개 혈관 모델을 이용하여 새로운 색전 물질로서의 PVA 고분자 코일의 효용성과 조직학적 반응을 실험적으로 고찰하고자 한다. PVA 고분자 코일은 PVA 와 Tantalum 을 결합하여 개발되었으며 그 기본적 특성을 팽창률과 휨 지름을 통하여 체외실험에서 밝히고자 한다.

연구재료와 방법: 정상 신장 분지 동맥과 경동맥 동맥류를 개 혈관 모델을 통하여 구현하였다. PVA 고분자 코일 을 이용한 혈관내 색전술을 X 선 투시하에 개 (n=10) 정상 신장 분지 동맥 (n=20), 개 경동맥 동맥류 모델 (n=8)에서 시행하였다. 혈관 폐색 정도는 색전술 시행 직후와 4 주후에 혈관조영술 (DSA)와 컴퓨터 단층 촬영 (CT) 혈관 조영술을 통하여 평가하였다. 조직학적 반응은 색전술 후 급성기 (1 일후; 신장 분지 동맥, 6; 경동맥 동맥류, 4)와 만성기 (4 주후; 신장 분지 동맥, 14; 경동맥 동맥류, 4)로 나누어 염증세포 특성, 혈전 기질화 정도, 신내막 형성을 평가하였다.

결과: 코일의 팽창률은 결합 물질의 농도가 높아짐에 따라 감소하였고 평균 휨 지름은 37℃증류수에서 2.05 mm (0.86-6.25), 37℃개 혈액에서 2.29 mm(0.94-6.38)이었다. 신장 분지 동맥의 폐색 정도는 4 주후까지 잘 유지되었으나 (완전폐색, 20; 안정화 폐색 14), 경동맥 동맥류 모델에서의 혈관 폐색은 1 일후 (완전폐색, 5; 불완전 폐색, 3)에 비해 4 주후 (안정화 폐색, 1; 불안정화 폐색, 3)으로 잘 유지되지 않았다. 조직학적 반응은 만성기로 접어들면서 만성 염증 세포가 대부분을 차지하고 혈전 기질화가 진행하였고 경동맥 동맥류 모델에서는 신내막이 모두 형성되었다.

결론: PVA 고분자 코일을 이용한 혈관 색전은 신장 분지 동맥에서는 우수한 효용성을 보였으며 경동맥 동맥류 모델에서는 30%이상의 충전률을 보일때 안정적인 폐색을 유지하였다.

주요어: PVA (polyvinyl alcohol), 고분자 코일, 색전 물질, 혈관내 색전술

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