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Steven G. Imbesi, Kimberly Knox and Charles W. Kerber

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Aneurysmal Pressure Changes with Nondetachable Balloon Placement and Fluid Infusion: Rationale for Liquid Embolization

Steven G. Imbesi, Kimberly Knox, and Charles W. Kerber

BACKGROUND AND PURPOSE: To improve the safety and efficacy of liquid embolization, we evaluated changes in pressures in experimental aneurysms.

METHODS: We created three replicas of a lateral sidewall aneurysm and placed them in a physiologic flow circuit. A 3 × 10-mm nondetachable balloon was positioned in the parent vessel across the aneurysmal neck. Intra-aneurysmal pressures were measured at baseline and after balloon inflation. Fluid was infused into the sac via a 1.45F microcatheter during inflation, and maximal pressures were noted. Measurements were repeated eight times in each aneurysm.

RESULTS: After balloon inflation, average intra-aneurysmal pressures increased: 12 mm Hg (13%, $\sigma_n - 1 = 0.46$) for aneurysm 1 (baseline mean arterial pressure [MAP], 94 mm Hg), 15 mm Hg (58%, $\sigma_n - 1 = 0.88$) for aneurysm 2 (baseline MAP, 26 mm Hg), and 15 mm Hg (58%, $\sigma_n - 1 = 0.92$) for aneurysm 3 (baseline MAP, 26 mm Hg). During inflation and infusion, pressures increased slightly: 1.1 (0.94%, $\sigma_n - 1 = 0.64$), 1.6 (3.9%, $\sigma_n - 1 = 1.1$), and 1.9 (4.6%, $\sigma_n - 1 = 1.2$) mm Hg for aneurysms 1, 2, and 3, respectively. Despite complete balloon occlusion of the distal aneurysmal neck, a channel between the proximal aneurysmal neck and the parent-vessel lumen persisted along the microcatheter. Fluid exited the sac via this channel, preventing a concomitant, significant increase in pressure during infusion.

CONCLUSION: Intra-aneurysmal pressure modestly increased with inflation of a parent-vessel balloon across the neck. When liquid was infused into the sac during inflation, further increases were minimal.

The platinum detachable coil is currently approved by the Food and Drug Administration for the endovascular obliteration of an aneurysm; however, innovative investigators and clinicians have begun to experiment with liquid embolic agents for this purpose (1–4). Although platinum detachable coils have revolutionized the treatment of intracranial aneurysms, incomplete occlusion or recanalization of the aneurysm sac is occasionally noted with these devices (5–7). Noncompressible, more-permanent devices or novel embolization agents are needed for the neurointerventionalist's armamentarium.

Use of cyanoacrylate cement for the intravascular occlusion of vessels has been performed for many

years in the treatment of arteriovenous malformations. This agent is efficacious and provides permanent occlusion (8, 9). Therefore, the deposition of cyanoacrylate polymer in an aneurysm sac should offer more-permanent obliteration of the aneurysm. The main issue with the use of a liquid embolic agent is safety because once the agent is applied it cannot be removed (3, 4).

The balloon angioplasty technique has been used for the endovascular treatment of wide-necked aneurysms to help contain platinum detachable coils in an aneurysm sac during device deposition (10, 11). This procedure has led to the development of a similar technique to achieve a safer deposition of liquid embolic agents, namely, placement of a microcatheter in the aneurysmal sac to deliver the agent and concurrent placement of a nondetachable balloon across the aneurysmal neck to contain it inside the aneurysm (12). As a result, this technique helps prevent the untoward flow of liquid polymer into the lumen of adjacent, normal parent vessel. An ongoing concern with this method of aneurysmal obliteration is the possibility of increasing pressure in the aneurysm (and causing its theoretical iatrogenic rupture). The aneurysmal sac is thought to be a closed system after

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Address reprint requests to Steven G. Imbesi, MD, Associate Professor of Radiology and Neurosurgery, Department of Radiology, University of California, San Diego Medical Center, 200 West Arbor Drive, Mail Code 8756, San Diego, CA 92103.

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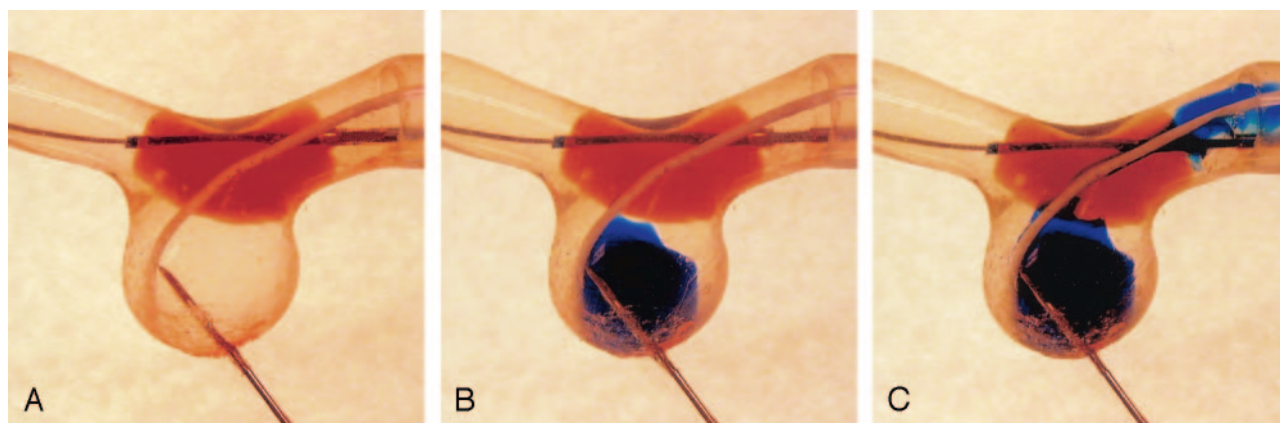


FIG 1. Clear, elastic, silicone replica of a lateral sidewall aneurysm.

A, A needle is inserted through the dome, with its tip in the sac to measure intra-aneurysmal pressure. A microcatheter is positioned with its tip in the lumen of the aneurysm. A nondetachable silicone balloon placed in the parent vessel across the aneurysmal neck is inflated, with the use of dyed fluid for visualization.

B, Infusion of dyed fluid into the aneurysm sac via the microcatheter during balloon inflation.

C, Infused fluid exits the aneurysmal sac along a channel created by the microcatheter between the nondetachable balloon and the wall of the parent vessel; fluid collects in the lumen of the proximal parent vessel.

complete balloon inflation across the neck is achieved. Therefore, the subsequent infusion of liquid into the closed space of the aneurysmal sac would increase the pressure in the sac.

Methods

We created three identical, clear, elastic, silicone replicas of a lateral side-wall aneurysm in the laboratory from a single vascular cast by using the lost wax technique. Details of this process were described previously (13, 14). The diameter of the aneurysmal sac measured 10 mm, and its neck was 5 mm wide. The replicas were placed in a circuit of pulsatile, clear, non-Newtonian fluid that mimicked the rheologic properties of blood (15, 16). A blood pump (model 1421; Harvard Apparatus Corp, Natick, MA) cycling at one pulse per second provided fluid flow. This flow was adjusted to replicate human physiologic flow profiles, velocities, and volumes. Using a flowmeter (square wave electromagnetic flowmeter; Carolina Medical Electronics, Inc., King, NC), we constructed flow profiles with 40% forward flow during diastole compared with flow during systole. Polyvinyl alcohol particles were placed in the flowing fluid, and their distance traveled over time was measured to calculate flow velocities. Fluid volume was measured in a graduated cylinder over time to determine the flow volume. We standardized the flow volumes at 280 mL/min (0.0047 L/s) and peak systolic velocities of 80 cm/s (0.80 m/s). These parameters were chosen to mimic those found in the normal human intracranial arteries in the anterior circulation (17).

A 25-gauge needle was inserted through the aneurysmal dome and attached to a pressure monitor (model 414, dual pressure Option 21; Tektronix, Beaverton, OR) by means of a fluid-electrical transducer. A 1.45F microcatheter was placed with its tip in the aneurysmal sac. A 3 × 10-mm nondetachable balloon was positioned in the adjacent parent vessel across the aneurysmal neck (Fig 1A). Because the nondetachable balloon was inflated to completely occlude the parent vessel, a bypass channel of fluid flow was incorporated into the system to prevent pressure from building up in the parent vessel after balloon inflation; this system was similar to normal collateral vascular anatomy. We opacified the fluid with isobaric dye to aid visualization and infused it into the aneurysm sac via the microcatheter, as also into the nondetachable balloon (Fig 1B). Changes in pressure were recorded by using the monitor, and

images were obtained by using a mini-DV digital video at shutter speeds of up to 1/30th of a second. Baseline intra-aneurysmal pressures were measured. The balloon was then inflated to occlude the parent vessel, and intra-aneurysmal pressures were again recorded. Last, fluid was infused into the aneurysm sac at a rate of 0.5 mL/minute while the balloon remained inflated; maximal pressures were identified. Of note, this fluid infusion rate was arbitrarily chosen to mimic the presumed general infusion rate of a liquid embolic agent during aneurysmal embolization. The rate was selected to be slow enough for excellent control of deposition of the agent yet allow for a relatively short total treatment time. That is, for an aneurysm 1 cm in diameter (luminal volume, 0.39 cm³) the total embolization time was approximately 1 minute. For aneurysm 1, baseline pressures were set at a mean arterial pressure (MAP) of 94 mm Hg to replicate the normal human physiologic condition. For aneurysm 2, baseline arterial pressures were lowered to a MAP of 26 mm Hg to maximize the sensitivity of the pressure monitor by reducing the scale so that any miniscule changes in pressure could be identified. To confirm the results at this lower level, the measurements were recorded in aneurysm 3, which had a baseline MAP of 26 mm Hg. All measurements were repeated eight times in each of the three aneurysms. Using the difference in MAPs between the baseline pressure and the pressure after inflation or after inflation with infusion, we calculated the average pressure increase and the standard deviation ($\sigma_n - 1$).

Results

Tables 1–3 list the pressure measurements obtained in each of the three aneurysms at baseline, after balloon inflation across the aneurysmal neck, and during fluid infusion into the aneurysm sac. In addition, they list the change in pressure before and after balloon inflation and before and after infusion during balloon inflation. After balloon inflation, intra-aneurysmal pressures increased. Values were as follows: for aneurysm 1, 12 mm Hg ($\sigma_n - 1 = 0.46$), a 13% increase; for aneurysm 2, 15 mm Hg ($\sigma_n - 1 = 0.88$), a 58% increase; and for aneurysm 3, 15 mm Hg ($\sigma_n - 1 = 0.92$), a 58% increase. During concurrent balloon inflation and infusion of fluid, the intra-an-

TABLE 1: Physiologic pressure measurements in aneurysm 1

Baseline	Balloon Inflation	Fluid Infusion	Change	
			Balloon Inflation – Baseline	Fluid Infusion – Balloon Inflation
94	106	107	12	1
94	107	107	13	0
93	106	107	13	1
94	106	107	12	1
94	106	108	12	2
94	106	108	12	2
95	107	108	12	1
94	106	107	12	1

Note.—Data are MAPs in units of millimeters of mercury

TABLE 2: Low pressure measurements in aneurysm 2

Baseline	Balloon Inflation	Fluid Infusion	Change	
			Balloon Inflation – Baseline	Fluid Infusion – Balloon Inflation
26	41	43	15	2
26	40	41	14	1
26	42	43	16	1
26	40	44	14	4
26	42	43	16	1
25	41	42	16	1
26	41	43	15	2
26	42	43	16	1

Note.—Data are MAPs in units of millimeters of mercury.

TABLE 3: Low pressure measurements in aneurysm 3

Baseline	Balloon Inflation	Fluid Infusion	Change	
			Balloon Inflation – Baseline	Fluid Infusion – Balloon Inflation
26	41	45	15	4
26	41	43	15	2
25	41	43	16	2
26	41	43	15	2
26	41	42	15	1
26	40	43	14	3
26	43	43	17	0
26	42	43	16	1

Note.—Data are MAPs in units of millimeters of mercury.

eurysmal pressures further increased, but only slightly. The average additional increase were as follows: for aneurysm 1, 1.1 mm Hg ($\sigma_{n-1} = 0.64$), a 0.94% increase; for aneurysm 2, 1.6 mm Hg ($\sigma_{n-1} = 1.1$), a 3.9% increase; and for aneurysm 3, 1.9 mm Hg ($\sigma_{n-1} = 1.2$), a 4.6% increase.

Although the inflated balloon completely occluded the distal neck of the aneurysm, a channel between the proximal aneurysmal neck and the lumen of parent vessel persisted along the course of the microcatheter between the inflated balloon and the wall of the parent vessel. During the infusion, fluid could exit the aneurysmal sac via this channel, and its egress prevented a concomitant, significant elevation in intra-aneurysmal pressure during the infusion (Fig 1C).

Discussion

At present, the endovascular treatment of intracranial aneurysms is somewhat limited. The only device currently approved in the United States is the platinum detachable coil. Incomplete occlusion or recanalization of the aneurysm is occasionally noted with this device, usually in aneurysms with a wide-neck or in those with a large lumen. Noncompressible, more-permanent devices or novel embolization agents are needed for the neurointerventionalist's armamentarium. In addition, because these liquid agents cannot be removed once applied, a safe method of deposition must be developed. Liquid embolic agents could be safely deposited into an aneurysm sac in conjunction with a device to protect the parent vessel and prevent unwanted dissemination of embolic material into the normal cerebral vasculature. Silicone nondetachable balloons have been used to protect the parent vessel when wide-necked aneurysms are occluded with platinum coils and when coil prolapse into the adjacent parent vessel is a concern. A similar technique should also enable the safe deposition of a liquid embolic agent; however, this method may be feasible only with placement of a balloon across the aneurysm neck, inflated to complete occlusion of the parent vessel. This is because of the Bernoulli effect produced when the balloon is only partially occlusive. With partial balloon inflation, the flow velocity in the patent but narrowed remaining vascular lumen must increase to maintain a stable flow rate (i.e., volume per unit time). The development of this increased flow velocity with only partial balloon inflation may increase the likelihood for polymer extravasation and thus be detrimental in terms of the safe deposition of a liquid embolic agent. Therefore, maximal safety is achieved when the balloon is inflated to the point of occluding the lumen of the parent vessel. However, with this configuration and a microcatheter simultaneously positioned with its tip in the aneurysmal sac, intra-aneurysmal pressure can potentially increase during the deposition of a liquid embolic agent if the sac becomes a closed system when the nondetachable balloon is inflated across the aneurysmal neck.

To mimic human physiologic parameters, the baseline intravascular MAP was initially set at approximately 94 mm Hg. When the nondetachable balloon placed across the neck was inflated to the point of complete parent-vessel occlusion, intra-aneurysmal pressures increased modestly. The average pressure increase was 12 mm Hg with a standard deviation of 0.46 (aneurysm 1). Inspection of the individual measurements, as well as this small standard deviation, confirmed the reproducibility of the measured values. Although this was not an expected finding, it showed that intra-aneurysmal pressure does modestly increase during the balloon angioplasty technique. As this technique is now routinely and safely performed during in vivo coil occlusion of wide-necked aneurysms, patients appear to tolerate this modest increase well (18). The infusion of fluid into the aneurysmal sac during balloon inflation only minimally

increased the intra-aneurysmal pressures. The average increase was 1.1 mm Hg with a standard deviation of 0.64. Inspection of the individual measurements and small standard deviation once again confirmed the reproducibility of the measured values. This, too, was an unexpected but welcome finding because this minimal pressure should also be well tolerated in vivo, and it further confirms the potential feasibility of the balloon angioplasty technique for the intra-aneurysmal deposition of a liquid embolic agent to achieve aneurysmal occlusion.

To be certain that small pressure changes were not being identified, given the large range of the pressure monitor at physiologic levels, the experiments were repeated at a lower pressure level. To maximize the sensitivity of the pressure monitor, the scale was reduced, which resulted in widening of the individual pressure values across the range of the apparatus. This set of measurements was also repeated in an additional aneurysm to confirm the validity and reproducibility of the results. For these measurements, the baseline intravascular MAP was set at approximately 26 mm Hg. When the balloon placed across the aneurysmal neck was inflated to completely occlude the parent vessel, intra-aneurysmal pressures modestly increased. The average increases were 15 mm Hg with a standard deviation of 0.88 for aneurysm 2 and 15 mm Hg with a standard deviation of 0.92 for aneurysm 3. The infusion of fluid into the sac during balloon inflation only minimally increased the intra-aneurysmal pressures, even at this more sensitive pressure level. The average increases were 1.6 mm Hg with a standard deviation of 1.1 for aneurysm 2 and 1.9 mm Hg with a standard deviation of 1.2 for aneurysm 3. Inspection of the individual measurements and these small standard deviations confirmed the reproducibility of the measured values, and the similar results between the two models further validated the experiments. Although this measurement was not physiologic, it was more sensitive to changes in intra-aneurysmal pressure during the infusion of fluid into the aneurysm sac with associated occlusion of the parent vessel, and it further confirmed the potential feasibility of the balloon angioplasty technique for occluding aneurysms by using a liquid embolic agent.

Of interest, the reason for the lack of pressure increase was that, with this occlusion technique, balloon inflation across the aneurysmal neck to the point of occluding the parent vessel does cause the aneurysmal sac to become a closed system. The infusion of opacified fluid through the microcatheter and subsequently into the aneurysmal sac allowed for detailed visualization of the course of events after infusion. The fluid that exited the aneurysm sac, traversed the adjacent nondetachable balloon, and collected in the lumen of the proximal parent vessel. The microcatheter interposed between the inflated nondetachable balloon and the adjacent wall of the parent vessel created a patent channel that passed along the path of the microcatheter from the aneurysmal sac, through the proximal aneurysm neck, and into the lumen of

the parent vessel. During the infusion, fluid was able to exit the sac via this channel, and that egress prevented a concomitant, significant elevation in intra-aneurysmal pressure during the infusion.

Although other types of balloons were not tested, only the nondetachable silicone balloons are currently used in vivo with the balloon angioplasty technique. Therefore, this observed phenomenon may have been due to the inherent low compliance of the silicone balloons.

This technique does have two potential complications with in vivo use. With the prescribed technique, the nondetachable balloon in the parent vessel is in direct contact with the deposited liquid embolic agent (presumably cyanoacrylate polymer), and it may become affixed to the embolic agent as it polymerizes. However, silicone should not adhere to cyanoacrylate polymer, and this has been our experience in the laboratory, although this could be a theoretical concern in vivo. In addition, as in all cerebral embolization procedures, diligent observation of the liquid agent is mandatory during infusion because after the aneurysm is filled, the liquid agent could pass along the channel created by the microcatheter between the wall of the parent vessel and the nondetachable balloon, resulting in unwanted extravasation and occlusion of the normal, proximal parent vessel. Last, pressures were measured at an infusion rate of only 0.5 mL/min. Although injections at substantially higher rates are not likely to be performed (as they would decrease control of the deposition of liquid embolic agent), a faster rate may overwhelm the capacity for fluid to egress from the aneurysmal sac and potentially result in increased intra-aneurysmal pressure.

Conclusion

Use of laboratory-created vascular models with precise physiologic flow parameters allows for the development of improved neuroendovascular treatment paradigms, specifically the design of safer and more-permanent aneurysm embolization techniques for this often-lethal disease. Intra-aneurysmal pressure modestly increased with parent-vessel balloon inflation across the aneurysm neck; however, clinical practice of this technique has not resulted in significant morbidity or mortality. Of note, further pressure elevation with concurrent intra-aneurysmal liquid infusion during balloon inflation across the aneurysm neck was minimal.

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