Long-term results in direct carotid–cavernous fistulas after treatment with detachable balloons

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Transarterial embolization of direct carotid–cavernous fistulas (CCFs) using detachable balloons is the best initial option for occlusion of the fistula and preservation of the internal carotid artery. However, the long-term safety and efficacy of this treatment is unknown. The authors reviewed the long-term outcome of 87 patients with 88 direct CCFs occluded by detachable balloons. Clinical follow up was obtained in 48 (83%) of 58 patients treated with latex balloons (mean follow-up period 10 years, range 5.9–15.5 years) and 28 (97%) of 29 patients treated with silicone balloons (mean follow-up period 4 years, range 1–6.6 years). Two patients were treated with both balloon types. There were no late recurrent symptoms of cranial bruit, proptosis, chemosis, or arterialized conjunctiva in patients treated with either latex or silicone balloons. Diplopia improved in all patients; however, five patients required shortening of the lateral rectus muscle. Delayed ischemia occurred in three patients: one patient had a transient ischemic episode 5 years after treatment with latex balloons and two patients (85 and 90 years old) who had ruptured spontaneous intracavernous aneurysms suffered cerebral infarctions 6 weeks and 4 months, respectively, after treatment with silicone balloons. There were five deaths in the series unrelated to balloon treatment. These results show that after transarterial embolization of direct CCFs using either silicone or latex detachable balloons, the long-term risks are low for fistula recurrence, symptomatic foreign body reaction, symptomatic pseudoaneurysm formation, and cerebral ischemia.

KEY WORDS • carotid–cavernous fistula • detachable balloon • embolization • long-term results

AFTER detachable balloons were introduced by Serbinenko in 1974, Debrun and coworkers popularized their use for the treatment of direct carotid–cavernous fistulas (CCFs).1-4 Latex balloons were used initially to occlude direct CCFs, but by 1987 silicone balloons were more readily available. Reports of several large series have shown that transarterial embolization of direct CCFs by detachable balloons is the best option for initial treatment.1,2,5,9,11,16-18,22-24 However, no controlled studies with long-term results have documented the safety and efficacy of detachable balloons. In the United States, they are not yet available commercially, but are only available with an investigational device exemption from the Food and Drug Administration (FDA).

In our experience with 100 consecutive CCFs treated by latex and silicone detachable balloons, 88 fistulas were successfully occluded using detachable balloons and the internal carotid artery (ICA) was preserved initially in 75% of cases.11 Early results showed a 3% rate of transient ischemic events and a 4% risk of a permanent neurological deficit, including one death. In addition to the long-term risk of cerebral ischemia, the rates of fistula recurrence and pseudoaneurysm formation are unknown. Pseudoaneurysms usually arise from early deflation of the detachable balloon and may enlarge, leading to mass effect.12 In our review of the literature, we found no reports of pseudoaneurysm rupture. The potential association between silicone breast implants and connective tissue disease,20 as well as allergic reactions caused by latex, call for a careful review regarding the use of silicone and latex for bioimplant devices.

In this long-term follow-up study of 87 patients with 88 fistulas that were successfully occluded with detachable balloons, we determined the rates of fistula recurrence, symptomatic foreign body reaction, symptomatic pseudoaneurysm formation, and cerebral ischemia. A comparison of the use of latex and silicone detachable balloons for the treatment of direct CCFs is discussed.

Clinical Material and Methods

From 1979 to 1993, 98 patients with 100 direct CCFs were admitted consecutively and treated with a detachable balloon in attempting occlusion of the CCF. Eighty-seven patients obtained successful occlusion. Debrun latex detachable balloons (Ingenor Medical Inc., Paris, France) were used in the first 58 of these patients; thereafter, sili-
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cone detachable balloons (ITC Detachable Balloon Occlusion System; Interventional Therapeutics Corp., Fremont, CA) were used in 27 patients. Two patients were treated using both balloon types. Ninety-four latex balloons were detached in 29 fistulas; 92 were inflated with hypertonic, water-soluble contrast material (meglumine iothalamate 300 mg%) and two were inflated with silicone fluid. Sixty-five silicone balloons were detached in 29 fistulas: 64 were filled with isosmotic, water-soluble contrast material (metrizamide 200 mg%) and one was filled with hydroxyethylmethacrylate (HEMA).

Clinical follow up included telephone contact with the patient, an immediate relative, the patient’s physician, or chart review. Any brain imaging examination performed subsequent to treatment was analyzed, and magnetic resonance (MR) angiography was offered to some patients. Nine patients underwent delayed posttreatment MR imaging or MR angiography for symptoms of the head and neck. Five patients were recalled to undergo MR imaging because they were at risk for developing pseudoaneurysms due to pretreatment with massive dilation of the cavernous sinus or the use of multiple or large balloons. No patient underwent posttreatment cerebral angiography for symptoms of the head and neck. The patients were queried for signs of fistula recurrence including orbital bruit, retroorbital pain, proptosis, chemosis, conjunctival injection, and cranial nerve palsy. The patient’s medical history was assessed, especially for new medical problems such as allergies or autoimmune disorders.

Results

Clinical information was maintained on 48 (83%) of 58 patients with direct CCFs occluded with detachable latex balloons; the mean follow-up period was 10 years (range 5.9–15.5 years). Long-term follow up was achieved in 28 (97%) of 29 patients treated by detachable silicone balloons; the mean follow-up period for that group was 4 years (range 1–6.6 years). Of 12 patients lost to follow-up study, five were treated with ICA occlusion and seven with fistula occlusion alone.

Fistula Recurrence

There was no long-term clinical or radiographic evidence of fistula recurrence in patients treated with latex or silicone detachable balloons. There were no late recurrent signs of cranial bruit, retroorbital pain, proptosis, chemosis, or arterialized conjunctiva. Visual acuity was unchanged or improved in 16 (94%) of 17 patients who had preoperative visual loss. Although diplopia improved in all patients, five patients required surgical procedures for its correction.

Cerebral Ischemia

Two patients had delayed permanent neurological deficits. In the first case, an 85-year-old woman suffered a nondisabling cerebral infarction of a left M1 branch 4 months after receiving successful treatment using a silicone detachable balloon for a ruptured intracavernous aneurysm. Computerized tomography scans showed a deflated balloon in the M1 middle cerebral artery with a small infarction. The patient recovered with minor speech and motor disability. In the second case, a 90-year-old woman suffered a disabling left hemisphere infarction 6 weeks after a silicone detachable balloon had prolapsed into the ICA, resulting in complete occlusion. Four patients with transient ischemic attacks were treated with heparin acutely, followed by long-term antiplatelet therapy.

Purposeful ICA occlusion was performed in 23 patients (mean age 42.6 years, range 12–77 years). No delayed ischemic events, hemorrhage, or de novo aneurysm formation occurred in this group after 1 to 14 years (mean 6.9 years). The incidence of de novo aneurysm formation was evaluated radiographically and clinically. Both MR imaging and MR angiography disclosed no de novo aneurysm formations. The remaining patients who did not have long-term posttreatment imaging studies were asymptomatic; in this group, the incidence of asymptomatic de novo aneurysm formation is unknown.

No allergies, autoimmune, or connective tissue diseases arose after treatment with detachable balloons. Five deaths occurred that were unrelated to treatment with detachable balloons. The causes of these deaths were gunshot wound, alcohol-related liver failure, cerebral arteritis that predated treatment of the CCF, preexisting malignant glioma, and senile dementia (Table 1).

Symptomatic and Asymptomatic Pseudoaneurysms

In seven patients known to have pseudoaneurysms after therapy, five were asymptomatic. One patient, who was initially symptomatic, improved with time after an unsuccessful attempt at pseudoaneurysm balloon occlusion (Fig. 1). Five years after treatment with a latex balloon, a 43-year-old nurse suffered a transient ischemic attack due to a 6-mm pseudoaneurysm of the ICA; she remains well 7 years later on antiplatelet therapy. Two patients with pseudoaneurysms were lost to follow up, including one who required ICA occlusion. Pseudoaneurysms were identified in three (23%) of these 12 patients; none was symptomatic (Fig. 2).

Discussion

Although several studies have shown that transarterial embolization using detachable balloons is the best initial treatment for direct CCFs, neither latex nor silicone
detachable balloons are approved by the FDA despite their nearly 20 years in use. These balloons held investigational device exemptions before 1993 but never received premarketing authority by the FDA because there were no controlled studies with long-term results. This is the first report that documents the long-term safety and efficacy of latex and silicone detachable balloons.

**Autoimmune and Allergic Reactions**

In this study, mean follow-up periods of 10 years for latex detachable balloons and 4 years for silicone detachable balloons showed that direct CCFs did not recur after 48 hours. Apparently, a thrombus forms around the balloon that prevents fistula recurrence even with balloon

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**Fig. 1.** A and B: Right (A) and left (B) internal carotid artery (ICA) angiograms displaying bilateral carotid–cavernous fistulas (CCFs). C: Angiogram showing the left CCF to be occluded with three detachable balloons (arrowhead) and patency of the left ICA preserved, restoration of blood flow to the right hemisphere after occlusion of the right CCF, and right ICA (arrow) with six detachable balloons. D: Left vertebral angiogram showing collateral flow to the anterior circulation through the posterior communicating arteries (arrow). E: Magnetic resonance angiogram obtained 10 years later showing basilar artery (arrow), left ICA (arrowhead), and occlusion of the right ICA. There is no evidence of fistula recurrence, pseudoaneurysm formation, ICA stenosis, or ectasia. Magnetic resonance angiography is a noninvasive alternative to cerebral angiography.

**Fig. 2.** Serial angiograms obtained during a 7-year period showing progressive shrinking of a pseudoaneurysm. A: Initial angiogram revealing the direct carotid–cavernous fistula. B: Successful occlusion with a latex detachable balloon. C: Six weeks later, an \(8 \times 7\) mm pseudoaneurysm is shown; the patient has recurrent retroorbital pain. D: Two years later, the pseudoaneurysm has decreased to \(8 \times 7\) mm. E: Seven years later, the patient remains asymptomatic and the pseudoaneurysm measures 3 mm in diameter.
deflation. There is no clinical evidence that latex or silic-one balloons in the cerebrovasculature cause inflammatory or autoimmune reactions. No allergies or unusual medical conditions developed and no unexplained or related deaths occurred. Miyachi, et al.,14 studied the histopathology of experimental aneurysms occluded by silicone and latex balloons using light and electron microscopy. They showed that endothelialization and thrombus formation occurred more readily with latex than with silicone balloons. In both types of balloons, there was no evidence of eosinophilia or infiltration by polymorphonucleocytes and macrophages into the cerebral vessels.14

Cerebral Ischemia

In this series, the incidence of delayed cerebral ischemia was low; one patient suffered transient ischemia and two had cerebral infarctions. It is notable that both cerebral infarctions occurred in elderly patients (ages 85 and 90 years) who had spontaneous direct CCFs. In these cases the ICA may have lost its elasticity from atherosclerosis and caused the silicone balloons to prolapse into the artery. Elderly patients with spontaneous CCFs caused by a ruptured aneurysm may be at higher risk for cerebral ischemic events after treatment. The best treatment for wide-necked aneurysms may not be detachable balloons filled with water-soluble, contrast-filled material; parent vessel occlusion with or without bypass graft may be necessary.

Of 23 patients who underwent ICA occlusion, none developed cerebral ischemia. Enlargement and development of new aneurysms may occur in patients who undergo ICA occlusion for giant unclippable aneurysms.21 However, limited follow-up imaging studies in this series have showed no evidence of accelerated atherosclerosis or de novo aneurysm formation.

Pseudoaneurysm Formation

Pseudoaneurysms are remnants of the wall defect of the ICA at the site of the previous fistula that form after the detachable balloon deflates. The pseudoaneurysm is located within the cavernous sinus and has the potential for the following: enlargement that causes mass effect on surrounding structures; rupture that leads to a recurrent CCF; or development of a thrombus that can embolize to the distal cerebrovasculature. Alternatively, the pseudoaneurysm may remain asymptomatic and decrease in size. Our results show a low incidence of clinically symptomatic pseudoaneurysms. Perhaps the pseudoaneurysm forms from a hard fibrotic shell that prevents further growth or rupture. We have elected to observe patients with asymptomatic pseudoaneurysms.

Debrun, et al.,4 reported that “venous pouches” or pseudoaneurysms developed at the balloon placement site after balloon deflation in approximately 44% of cases. In our series, three early pseudoaneurysms required occlusion of the parent artery for symptom relief and one became asymptomatic within 6 weeks. A major concern has been that these pseudoaneurysms could enlarge, thereby compressing and injuring cranial nerves or rupturing to cause a fistula recurrence or subarachnoid hemorrhage. Only one patient developed late symptoms (that is, transient ischemic attack) related to pseudoaneurysm formation; she has been asymptomatic for 7 years after initiating antiplatelet therapy. No late symptomatic pseudoaneurysms caused mass effect or ruptured. Although pseudoaneurysms may enlarge, we documented that two pseudoaneurysms became smaller (Figs. 1 and 3). We also witnessed one posttraumatic pseudoaneurysm develop into a CCF. Additionally, we have documented the appearance of one small pseudoaneurysm on 10-year follow-up MR imaging obtained in a case of “spontaneous” fistula occlusion that occurred after an unsuccessful attempt at fistula occlusion.
Carotid–cavernous aneurysms have a benign natural history; symptomatic ones usually have a large neck. Pseudoaneurysms may behave similarly to carotid–cavernous aneurysms; both are difficult to treat using endovascular techniques. When the diameter of the aneurysm neck approaches the diameter of the aneurysm itself, there is a higher risk of balloon prolapse into the ICA.

Silicone fluid or HEMA, a permanent polymerizing compound, has been recommended to fill balloons placed into aneurysms for permanent occlusion. However, HEMA is currently unavailable. Also, a relatively wide neck makes these aneurysms less suitable for treatment using the Guglielmi detachable coil.

Conclusions

In this study covering mean follow-up periods of 10 years for latex detachable balloons and 4 years for silicone detachable balloons, we found no recurrent fistulas, no hemorrhagic events, and a low risk for cerebral ischemia. Clinically, the latex and silicone balloons used in cerebral vessels are biologically inert. We conclude that transarterial embolization with detachable balloons remains the best initial treatment for direct CCFs. The results of this study may serve as a standard for comparison with future treatment alternatives, such as platinum coils and intravascular stents.

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