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Observational Study

Pseudoaneurysm formation following transarterial embolization of traumatic carotid-cavernous fistula with detachable balloon: An institutional cohort long-term study

Iampreechakul P *et al.* Pseudoaneurysm after balloon treatment in TCCF

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Abstract

BACKGROUND

The goal of therapy for traumatic carotid-cavernous fistula (TCCF) is the elimination of fistula while maintaining patency of the parent artery. The treatment for TCCF has evolved from surgery to endovascular management using detachable balloons, coils, liquid embolic agents, covered stents, or flow-diverter stent through arterial or venous approaches. Despite the withdrawal of detachable balloons from the market in the United States since 2004, transarterial embolization with detachable balloons has currently remained the best initial treatment for TCCF in several countries. However, the pseudoaneurysm formation following transarterial detachable balloon embolization has rarely been observed in long-term follow-up.

AIM

To determine the occurrence and long-term follow-up of pseudoaneurysm after transarterial detachable balloon for TCCF.

METHODS

Between January 2009 and December 2019, 79 patients diagnosed with TCCF were treated using detachable latex balloons (GOLDBAL2) of four sizes. Pseudoaneurysm sizes were stratified into five grades for analysis. Initial and follow-up assessments involved computed tomography angiography at 1 mo, 6 mo, 1 year, and longer intervals for significant cases. Clinical follow-ups occurred semi-annually for 2 years, then annually. Factors analyzed included sex, age, fistula size and location, and balloon size.

RESULTS

In our cohort of 79 patients treated for TCCF, pseudoaneurysms formed in 67.1%, with classifications ranging from grade 0 to grade 3; no grade 4 or giant pseudoaneurysms were observed. The majority of pseudoaneurysms did not progress in size, and some regressed spontaneously. Calcifications developed in most large pseudoaneurysms over 5-10 years. Parent artery occlusion occurred in 7.6% and recurrent fistulas in 16.5%. The primary risk factors for pseudoaneurysm formation were identified as the use of specific balloon sizes, with balloon SP and No. 6 significantly associated with its occurrence ($P = 0.005$ and $P = 0.002$, respectively), whereas sex, age, fistula size, location, and the number of balloons used were not significant predictors.

CONCLUSION

Pseudoaneurysm formation following detachable balloon embolization for TCCF is common, primarily influenced by the size of the balloon used. Despite this, all patients with pseudoaneurysms remained asymptomatic during long-term follow-up.

Key Words: Pseudoaneurysm formation; Traumatic carotid-cavernous fistula; Direct carotid-cavernous fistula; Transarterial embolization; Detachable balloon; Endovascular treatment; Computed tomography angiography; Long-term follow-up

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Core Tip: This study investigated the incidence and determinants of pseudoaneurysm formation following transarterial detachable balloon embolization in treating traumatic carotid-cavernous fistula over a decade. It highlighted balloon size as a significant risk factor, with larger balloons notably increasing pseudoaneurysm occurrence. Despite the high incidence of pseudoaneurysms, all affected patients remained asymptomatic through long-term follow-up, underscoring the procedure's overall safety. These findings emphasize the critical role of selecting appropriate balloon sizes to mitigate risk and optimize outcomes, offering valuable insights for clinicians in managing this complex condition effectively.

INTRODUCTION

Traumatic carotid-cavernous fistulas (TCCFs) are high-flow shunts directly communicated between the cavernous segment of the internal carotid artery (ICA) and the cavernous sinus, resulting from trauma[1]. TCCFs were categorized as Type A by the Barrow classification of CCFs[2]. Spontaneous resolution of TCCFs is extremely rare[3]. The typical clinical manifestations, which depend on the venous drainage of the cavernous sinus, include pulsatile proptosis, conjunctival chemosis, red eye, and/or audible bruit. Rarely, aggressive neurological symptoms, especially deterioration of consciousness, may develop due to cortical venous reflux, leading to cerebral ischemia and/or hemorrhage[4].

The management of TCCFs has evolved significantly, transitioning from surgical to endovascular methods, utilizing detachable balloons or coils through arterial or venous approaches[5]. The first case of endovascular occlusion of TCCF using a fixed balloon catheter was described by Prolo and Hanberry[6] in 1971. Later, Serbinenko[7], a

Russian neurosurgeon, pioneered the use of detachable balloons for TCCF treatment while preserving the ICA in 1974. This technique led to a new era for management of TCCF by the endovascular route. Subsequently, Debrun *et al*[8-10] developed another version of detachable balloon, and transarterial detachable balloon embolization became more popularized for treatment of TCCF in many countries for many years. However, there were some balloon-related complications including premature deflation, early detachment, and/or balloon migration resulting in recurrence of the fistula, ischemic stroke, or pseudoaneurysm formation[11-17]. In 2004, detachable balloons were withdrawn from the market in the United States, and detachable coils were used instead for occlusion of TCCF[18]. Nevertheless, detachable balloon embolization currently remains the preferred treatment option for TCCF in several countries including ours[5,19-21].

The pseudoaneurysm formation following endovascular treatment of TCCF with detachable balloon has rarely been observed, especially in long-term follow-up[12,22]. We conducted a retrospective cohort study to ascertain the occurrence and long-term follow-up of pseudoaneurysm after transarterial embolization of TCCF with detachable balloons. Risk factors for the occurrence of pseudoaneurysm were also investigated.

MATERIALS AND METHODS
Study population and data collection
This retrospective cohort study was conducted at a tertiary neurosurgical center, with ethics committee approval from our institute. From January 2009 to December 2019, 119 consecutive patients with TCCF were recruited. Inclusion criteria were patients with TCCF treated by transarterial embolization using detachable balloons. The exclusion criteria were patients with TCCF treated by other options, including coiling (n = 11), coiling and balloon (n = 9), and combined endovascular and surgical treatment (n = 4). In addition, 16 patients with incomplete data were excluded from enrollment. The final cohort of our study included 79 patients (56 males and 71 females). Their age ranged from 11 years to 68 years, with a mean age of 34.82 ± 13.01 years. The flow chart of our study is illustrated in Figure 1.

Diagnosis was based on symptoms, trauma history, medical examination, computed tomography (CT) scan, and cerebral angiography. Demographic data collected included age, sex, cause of injury, and clinical symptoms at presentation.

Study assessment and criteria

The fistula location was classified into five regions according to the cavernous ICA segmentation as described by Debrun *et al*[12]. These segments of ICA included C1 (anterior ascending segment), C2 (junction between the anterior ascending and horizontal segment), C3 (horizontal segment), C4 (junction between the horizontal and posterior ascending segment), and C5 (posterior ascending segment) (Figure 2).

Based on the study of Chi *et al*[23], we classified the size of the fistula as small, medium, and large. Small-sized fistulas had good antegrade ipsilateral ICA flow, represented by opacification of both the anterior cerebral artery (ACA) and middle cerebral artery (MCA). Medium-sized fistulas had fair antegrade flow, represented by opacification of either the ACA or MCA. Large-sized fistulas had poor antegrade flow, represented by opacification of neither the ACA nor MCA (Figure 3).

The size of pseudoaneurysms was stratified by five grades including: Grade 0, no pseudoaneurysm; grade 1, small pseudoaneurysm (< 5 mm); grade 2, medium (5–10 mm); grade 3, large (11–25 mm); and grade 4, giant (> 25 mm).

The detachable latex balloon (GOLDBAL; Balt Extrusion, Montmorency, France) with four different sizes, including balloon No. 4, No. 5, No 6., and SP, was used in our study (Table 1). SP is abbreviated from the name and surname of Professor Sirintara Pongpech, Thai neurointerventionist, who designed this balloon size. Balloon SP contains a maximum volume of 0.9 mL and expands to 12 mm × 13 mm.

Following transarterial balloon embolization, all patients underwent CT angiography (CTA) at 1 mo. If pseudoaneurysms occurred, CTA follow-up was performed at 6 mo and 1 year. For large-sized pseudoaneurysm (grade 3) or giant (grade 4) pseudoaneurysm, CTA follow-up was carried out every 1 year to 3 years. The clinical follow-up was conducted every 3 mo to 6 mo for 2 years after the procedure and annually

thereafter. Factors including sex, age, size and location of fistula, number of balloons, and the size of balloon, were statistically analyzed. All images were evaluated independently by the experienced neuroradiologist (SH) using Picture Archiving and Communication System (PACS; FUJIFILM, Stamford, CT, United States).

Neurointerventional techniques

All endovascular procedures were performed under general anesthesia in a specialized biplane neuroangiography suite. Using the transfemoral approach, a 9 F introducing catheter was positioned into the cervical ICA. Subsequently, cerebral angiography was performed to assess the location and size of fistula, presence of any collateral supply through the circle of Willis, and venous drainage pattern. Additionally, contralateral carotid angiography during compression of the ipsilateral carotid artery was carried out to evaluate function of the anterior communicating artery. The precise fistula site was delineated by vertebral artery injection with simultaneous ipsilateral carotid compression. Following systemic heparinization, the balloon mouthed delivery microcatheter (Baltacci; Balt, Montmorency, France) was cautiously navigated by flow guidance into the orifice of the fistula under fluoroscopic road-mapping (Figures 4 and 5). The balloon was gradually inflated with iodinated contrast media, ensuring it did not exceed the maximum volume specified by the manufacturer for each balloon size (Table 1). Following the obliteration of the fistula by confirmation through a contrast media injection *via* the guiding catheter, the balloon was detached by gently pulling the microcatheter. Immediate post-embolization angiography was then performed to verify complete closure of the fistula. Multiple detachable balloons might be required if a single balloon failed to completely occlude TCCF. Post-procedure, all patients were advised absolute bed rest for 72 h to prevent balloon migration.

Statistical analysis

Data analysis was performed using the SPSS 16.0 software package (SPSS Inc, Chicago, IL, United States). Continuous data were expressed as mean (standard deviation) or

median (interquartile range), and categorical variables were presented as numbers and corresponding percentages. Differences between groups were assessed using the Kruskal-Wallis test for continuous variables and Pearson Chi-square or Fisher's exact tests for categorical variables. A P value < 0.05 was considered statistically significant.

RESULTS

Study population and demographics

Patient and fistula characteristics are summarized in Table 2. The causes of injury were predominantly motor vehicle accidents (75 patients, 94.9%), followed by assault (2 patients, 2.5%), falling from height (1 patient, 1.27%), and gunshot injury (1 patient, 1.27%). Clinical manifestations included pulsating proptosis (61 patients, 77.2%), conjunctival chemosis (39 patients, 49.4%), red eye (49 patients, 62.0%), audible bruit (28 patients, 35.4%), cranial nerve palsy (8 patients, 10.1%), and hemiparesis (2 patients, 2.5%).

Fistula characteristics

The cohort consisted of 79 fistulas including 14 (17.7%) small, 31 (39.2%) medium, and 34 (43.1%) large fistulas. Fistula locations were right-sided in 40 cases (50.6%) and left-sided in 39 cases (49.4%). The orifice of the fistula was located at C1 in 1 patient (1.3%), C2 in 7 patients (8.9%), C3 in 26 patients (32.9%), C4 in 25 patients (31.6%), and C5 in 20 patients (25.3%).

Treatment outcomes

Treatment outcomes, detailed in Table 2, showed complete obliteration of the fistula in 78 patients (98.8%) and nearly complete obliteration in 1 patient (1.3%). One balloon was used in 54 patients (64.6%), two balloons in 20 patients (25.3%), and three balloons in 8 patients (10.1%). Recurrent fistulas occurred in 13 patients (16.5%) (Figures 5 and 6). Parent artery occlusion after treatment or during follow-up was observed in 6 patients (7.6%).

Pseudoaneurysm formation and regression

During a follow-up period of 2-10 years, grade 0 pseudoaneurysm were detected at final CTA follow-up in 24 patients (32.9%), grade 1 in 22 patients (30.1%), grade 2 in 18 patients (24.7%), and grade 3 in 9 patients (12.3%). There were no grade 4 or giant pseudoaneurysms in our study. Spontaneous regression of pseudoaneurysm size occurred in 10 patients (13.7%), with no progression in size observed. Most large pseudoaneurysms developed calcifications around the aneurysmal wall during follow-up at 5 years to 10 years (Figure 7). All patients harboring pseudoaneurysms were asymptomatic during long-term follow-up.

Risk factors for pseudoaneurysm formation

Univariate analysis indicated that sex, age, size, location of fistula, and number of balloons used were not related to the occurrence of pseudoaneurysm. The main factor for pseudoaneurysm formation was the size of the balloon including the use of balloon SP (P = 0.005) and balloon No. 6 (P = 0.002) (Table 3). The use of balloon SP was associated with higher rates of complete obliteration of fistula without pseudoaneurysm formation, whereas balloon No. 6 developed large-sized pseudoaneurysms compared with other sizes.

Complications related to balloon embolization

Other balloon-related complications were found in 4 patients. Early detachment and migration of the detachable balloon occurred in 1 patient, but the balloon fragment was successfully retrieved with a snare without further ischemic symptoms. Three patients developed transient ocular motor nerve palsy after balloon embolization.

DISCUSSION

The goal of treatment of TCCF using a detachable balloon is to occlude the fistula while maintaining the carotid flow by the balloon placed into the cavernous sinus (venous

side)[24,25]. In our study, we compared therapeutic outcomes of patients with TCCFs treated with transarterial detachable balloon embolization from different centers as shown in Table 4[12-14,19-23,26-32]. Two principal complications identified in balloon embolization for TCCF are the recurrence of the fistula and the formation of a pseudoaneurysm. Numerous studies have explored and identified risk factors contributing to the recurrence of TCCF following balloon embolization[21,29,32]. However, our study primarily concentrated on investigating the relevant factors associated with the occurrence of pseudoaneurysm, as this aspect has been less extensively covered in the existing literature.

Detachable latex and silicone balloon

Materials for the detachable balloons are made of either natural rubber (latex) or silicone rubber[31]. Under an electron microscope, the silicone detachable balloons display a smooth surface, whereas latex balloons exhibit an irregular surface with numerous large deep craters. These surface irregularities in latex balloons cause turbulent flow, promoting thrombosis and a more pronounced inflammatory response. Consequently, latex balloons are more thrombogenic than their silicone counterparts[30,33]. *In vivo*, if the tail of latex balloons protruded into the parent artery, it may increase thrombus formation around the balloons, more likely leading to parent artery occlusion as found in 7.6% of our patients[34]. Latex balloons are less expensive than silicone balloons and offer greater elasticity, allowing for larger inflation sizes. Detachable latex balloons can be more firmly attached to delivery catheters than silicone balloons and therefore should offer appreciably less risk of premature detachment. Latex balloons have a variety of sizes and shapes and require a hand ligation attachment, and they were reported as more prone to early deflation[27].

Silicone balloons are softer than latex and tend to conform to the shape of the vessel or aneurysm, reducing the risk of vessel rupture. Silicone balloons are also biocompatible, with their shell not degrading over time inside the vessel unlike latex[35]. Detachable silicone balloons are semipermeable and must be inflated with isotonic

solutions. To prevent early deflation of the balloon, detachable silicone balloons require filling with iso-osmolar iodinated contrast agent before detachment[36-38]. On the other hand, latex balloons are not semipermeable, so the osmotic gradient between the balloon contents and the surrounding plasma has no influence on the role of premature deflation[29,40].

Balloons can be inflated with polymerizing substances, such as hydroxyethyl methacrylate, silicone fluid, or iodinated contrast material. A balloon filled with a polymerizing substance will produce better anatomic results and reduce the occurrence of a pseudoaneurysm. But the polymerizing substance may result in poor or incomplete recovery from ocular motor nerve palsy due to the remaining permanently solid balloon. In contrast, an iodine-inflated balloon may progressively deflate, possibly causing a pseudoaneurysm. However, when ocular motor nerve palsy occurs, balloon deflation will usually result in complete recovery from the palsy[24,28,31]. Currently, detachable silicone balloons are not available, and detachable latex balloons have been used by inflating with iodinated contrast material.

Pseudoaneurysm formation following transarterial balloon embolization

Pseudoaneurysms are remnants of the wall defect of the cavernous ICA at the orifice of the fistula that form following early deflation or migration of the detachable balloon[41,26]. The balloons usually become progressively deflated in 3 wk or 4 wk[10]. It is crucial for the balloons to stay inflated or retain their size and shape for approximately 2 wk to ensure a secure fibrous attachment to the vascular wall[11]. Premature deflation of the balloon often leads to the recurrence of fistulas and the subsequent development of pseudoaneurysms[14]. Balloons that deflate too early tend to migrate forward, ending up retained in the cavernous sinus[29]. The early deflation of balloons is caused primarily by relaxation or insufficiency of the ligature[10,12,20].

According to our review (Table 4), the incidence of pseudoaneurysm formation ranges from 2.4% to 44.0%. To our knowledge, there has been no study focusing on the long-term follow-up of pseudoaneurysm post-transarterial balloon embolization in

TCCF. Our study found the highest incidence of pseudoaneurysm formation at 67.1%, including small-sized pseudoaneurysms in 30.1% of cases, medium-sized in 24.7%, and large-sized in 12.3%. The size of pseudoaneurysm spontaneously regressed in 13.7% during follow-up CTA, and there was no progression of pseudoaneurysms in our series. Interestingly, most large pseudoaneurysms developed rim calcification during follow-up at 5 years to 10 years.

Impact of detachable latex balloon size on pseudoaneurysm formation
Currently, GOLDBAL is the only detachable latex balloon available in our institute. Its deployment requires a single microcatheter, and the balloon is secured over a coaxial microcatheter using a latex thread. This thread then forms a self-sealing valve when the balloon is detached. Proper preparation and deployment of this system demands significant experience and skill[36,42].

In our study, univariate analysis showed that factors such as sex, age, fistula size and location, and the number of balloons used were not significant contributors in pseudoaneurysm development. Instead, the main contributing factor was the size of the balloon, specifically the use of balloon SP ($P = 0.005$) and balloon No. 6 ($P = 0.002$). The SP balloon was linked to higher rates of complete fistula obliteration without pseudoaneurysm formation, while the balloon No. 6 was associated with the development of large pseudoaneurysms.

Detachable balloon SP and No. 6 have different shapes and sizes. The balloon SP is spherical, holding a maximum volume of 0.9 mL, and expands to dimensions of 12 mm × 13 mm when fully inflated. In contrast, the balloon No. 6 is cylindrical, with a maximum volume of 3 mL, and expands to 15 mm × 25 mm. Detachable balloon No. 6 is the largest size and the most difficult to advance through a 9 F guiding catheter with some friction. We speculate that the ligature might relax, or the balloon may be damaged during prolonged manipulation, leading to early deflation and the formation of large pseudoaneurysms.

Recent advances in coil and flow divertor technologies have significantly impacted the treatment of intracranial aneurysms. In contrast, the development of detachable balloons, specifically latex detachable balloons, has not had similar progress. Although not approved by the Food and Drug Administration for use in the United States, these balloons are utilized in certain Southeast Asian countries, reflecting regional differences in medical practice and regulation. The market for detachable latex balloons is notably small, leading to a decrease in their manufacturing[36]. Despite this, detachable balloons maintain a role in treating TCCF and occluding vessels. It is anticipated that future developments in detachable balloon technology could potentially address current limitations, such as the risk of pseudoaneurysm formation, thereby enhancing the efficacy and safety of these devices in clinical practice.

Management of pseudoaneurysms occurring after detachable balloon embolization
Pseudoaneurysms, following the treatment of TCCF with detachable balloons, may either enlarge, causing a mass effect, or remain asymptomatic and decrease in size. The incidence of clinically symptomatic pseudoaneurysms is relatively low[13]. Small pseudoaneurysms typically remain asymptomatic and stable in size, while larger pseudoaneurysms can cause symptoms such as cranial nerve palsy and severe retroorbital pain[14,24,41]. Spontaneous regression of pseudoaneurysms after detachable balloon occlusion of TCCF has rarely been reported[43].

In most cases, pseudoaneurysms tend to be asymptomatic and do not necessitate further intervention[12]. However, some authors have suggested more aggressive treatment due to potential complications, which include mass effect on adjacent structures, recurrent TCCF from rupture of the pseudoaneurysm, and cerebral embolism resulting from thrombus formation[22].

For large symptomatic pseudoaneurysms, treatment options may include permanent occlusion of the carotid artery or the use of covered stents to preserve the integrity of the ICA[12,22,24]. In selected patients, pseudoaneurysms can be safely and effectively treated by embolization with detachable coils[44]. In our study, all patients with

pseudoaneurysms remained asymptomatic, and no additional therapy was required during the long-term follow-up.

CONCLUSION

Our study showed that pseudoaneurysm formation was a common complication of detachable balloon embolization for treatment of TCCF. The main risk factor influencing this outcome was identified as the size of the detachable balloon used in treatment. Specifically, the balloon SP was associated with a higher success rate in completely obliterating the fistula without leading to the formation of pseudoaneurysms. In contrast, the largest balloon, No. 6, was more prone to result in the development of large-sized pseudoaneurysms. We speculate that the ligature might relax or the balloon may be damaged during prolonged manipulation, leading to early deflation and the formation of large pseudoaneurysms.

Despite the high incidence of pseudoaneurysm formation, it is noteworthy that all patients with pseudoaneurysms remained asymptomatic throughout the long-term follow-up period. This observation underscores the complexity of managing TCCF and the need for careful consideration of the tools and techniques employed in treatment.

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