REVIEW

Treatment of posterior circulation non-saccular aneurysms with flow diversion versus stent-assisted coiling: a systematic review and meta-analysis

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ABSTRACT

Treatment of non-saccular aneurysms of the posterior circulation poses a great challenge with unpredictable outcomes due to the absence of a true aneurysm neck and the presence of perforating vessels. In this article, we aim to compare endovascular treatment of unruptured posterior circulation non-saccular aneurysms with stent-assisted coiling (SAC) and flow diversion (FD) in terms of occlusion rate and clinical outcomes. A systematic search of electronic databases from inception to August 2019 identified 484 articles for screening. After proper inclusion/exclusion criteria, 15 articles were included and data were extracted and analyzed using meta-analysis of proportions. The pooled cohort consisted of 430 aneurysms: 128 (29.7%) treated with SAC in 5 studies and 302 (70.3%) treated with FD in 11 studies. Complete/near-complete occlusion was achieved in 83% after FD (95% CI 0.75 to 0.90; I^2=45%) and 84% after SAC (95% CI 0.72 to 0.91; I^2=22%), with no significant difference between techniques (p=0.95). Periprocedural complications were observed in 18% after FD (95% CI 0.14 to 0.23; I^2=0%) and 6% after SAC (95% CI 0.02 to 0.13; I^2=0%); the subgroup analysis was statistically significant (p=0.008). Furthermore, no statistically significant difference was observed in favorable clinical outcomes between groups. These results suggest similar efficacy in occlusion rate and favorable clinical outcome for posterior circulation non-saccular aneurysms treated with SAC and FD. Stroke was the most common complication regardless of treatment modality, and a lower periprocedural complication rate was noted with SAC. Further studies are needed with the primary focus of reducing the risk of stroke with either modality.

INTRODUCTION

Non-saccular aneurysms of the posterior circulation are rare with reported incidence rates <1%.[1] Non-saccular aneurysms are defined according to their radiographic appearance as an arterial dilatation >1.5 times the normal diameter without any neck, and can be further stratified into risk groups as fusiform, dolichoectasia or transitional.[2] Their presentation is highly variable, ranging from incidental findings on imaging to headache, cranial nerve palsy, brainstem compression, obstructive hydrocephalus, ischemic stroke, and subarachnoid hemorrhage (SAH).[3] In general, symptomatic lesions have a devastating natural history with reported mortality rates up to 80% when untreated.[4]

Currently, there is no standard of care for treatment of posterior circulation non-saccular aneurysms due to the complexity of these lesions.[3] The high morbidity and mortality related to surgical interventions favored the utilization of endovascular approaches as the primary treatment modality.[2] Morphologically, the absence of a true neck makes coil embolization as a single strategy unsuitable. Thus, complex endovascular reconstruction of the involved vessel has been utilized with stent-assisted coiling (SAC) and more recently with the use of flow diversion (FD) devices.[5 6]

Although treatment of non-saccular aneurysms by either SAC or FD has been widely studied in the anterior circulation,[3] the results could not be reproduced in the posterior circulation due to critical perforating vessels arising from the aneurysm itself.[7] Therefore, treatment of posterior circulation non-saccular aneurysms remains controversial, with conflicting results regarding the obliteration rate and the benefits/risks of SAC versus FD techniques.[5 8 9] The current meta-analysis aims to compare systematically-identified procedure-related outcomes and complications associated with SAC and FD for the treatment of posterior circulation unruptured non-saccular aneurysms.

METHODS

Search strategy

Our search strategy utilized the Population, Intervention, Comparison, Outcome and Study type (PICOS) question format: Do patients with unruptured non-saccular aneurysms of the posterior circulation (Population), in whom endovascular intervention with SAC or FD was performed (Intervention), differ in terms of aneurysm occlusion and complication rates (Outcome), based on current studies. Our review was in compliance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines.[10] Electronic searches were performed using Ovid Embase, PubMed, SCOPUS, and the Cochrane Databases from their dates-of-inception to August 2019. Database searches were completed using the following keywords: "posterior circulation" ("fusiform aneurysm" OR "dissecting aneurysm" OR "non-saccular aneurysm" OR "nonsaccular aneurysm") ("Pipeline" OR "PED" OR "Flow diverter" OR "Flow Diversion" OR "Coil" OR "stent-assisted coiling" OR "SAC") (online supplementary table 1).

Study selection

All articles were independently screened by two authors (RD and CPV) in accordance with PRISMA guidelines using predetermined selection criteria. Discrepancies between authors were resolved by a third investigator (VL). All articles were evaluated using the following inclusion and exclusion criteria.

Inclusion criteria for all articles were: (1) unruptured non-saccular aneurysms of the posterior circulation; (2) in cohorts managed by SAC and/or FD; (3) with at least one reported outcome of interest; (4) in patients aged >18 years. Outcomes of interest were aneurysm occlusion rates, modified Rankin Scale (mRS), and complication rates.[11]

Exclusion criteria included: (1) saccular morphology; (2) aneurysms of the anterior circulation; (3) treated with neither SAC nor FD; (4) lack of reported occlusion rates or complications rates; (5) patients aged <18 years (unless reported separately). For duplicate studies with overlapping cohorts, only the most complete report was included in the analysis. Additionally, studies were only considered in the meta-analysis if published in English and in an original article. Review articles, abstract, presentations, and editorials were not included.

Data collection

All incidence rates (IRs) (occlusion rates, mRS scores, complication rates) were extracted from the texts, tables and figures of full-length articles. Effect size estimates were either extracted directly from the text or calculated using validated methods.[12] Studies reported occlusions as complete, near-complete or incomplete; given that Griessenauer *et al*[13] combined complete and near-complete occlusions as one category, data from other studies were combined accordingly (online supplementary table 2). For studies that provided breakdown of mRS scores, values were combined into mRS 0–2 and mRS 3–6.

Quality assessment

To assess the reliability of the pooled results, the Grading of Recommendation, Assessment, Development, and Evaluation (GRADE) approach was utilized. Additionally, to determine the overall quality of the study, each article was evaluated using the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) criteria to analyze the ability of the study to answer the PICOS question of interest.[14]

Bias assessment

Publication bias was evaluated via funnel plots of all outcomes. A trim-and-fill method was utilized for recalculation of pooled effect size if bias by asymmetry was suspected.[15]

Statistical analysis

Fifteen studies representing 16 unique cohorts were analyzed. Data from included cohorts were pooled by meta-analysis of proportions via a logit transformation to provide a summary statistic. Studies were divided into two groups depending on treatment type (SAC vs FD). I^2 was used to estimate heterogeneity across included studies and 50% was considered as high heterogeneity. A random effect model was recruited for the analysis. Subgroup analysis was conducted using methods outlined by Borenstein and Higgins in the random effects model.[16] Statistical tests were two-sided, significance was considered at $\alpha=0.05$, and all analyses were conducted using R (version 3.6.0).

RESULTS

Search strategy

An initial search identified 656 studies representing 484 unique studies (online supplementary figure 1). Application of selection criteria to title and abstract yielded 32 publications for full-text analysis. Finally, 15 retrospective observational studies were included for analysis (online supplementary table 3). One study contained both treatment types and was separated into two cohorts based on treatment type.

Study characteristics

The 15 included studies had a pooled cohort of 430 aneurysms (online supplementary table 3); 128 of them underwent SAC (29.7%) in five studies,[4 5 8 17 18] while 302 aneurysms were treated with FD (70.3%) in 11 studies.[1 5 7 13 19–25] Median ages ranged from 50 to 63.5 years and the proportion of males in each respective study ranged from 35.7% to 89.1%. Mean follow-up time ranged from 4.9 to 25.2 months. The evaluated aneurysms included fusiform, dissecting, fusiform-dissecting, dolichoectatic, and transitional types. The locations were vertebral, posterior inferior cerebellar, basilar, superior cerebellar, and posterior cerebral arteries. The mean aneurysm size in these studies ranged between 7 and 14.2 mm (online supplementary table 2). Most patients presented with signs and symptoms of headache, dizziness, and a focal neurological deficit; some of them were asymptomatic and three patients had a previous history of non-aneurysm related subarachnoid hemorrhage. Three studies[13 20 25] included patients previously treated with either stent, coiling or balloon-assisted coiling procedures. Furthermore, 21 patients had combined therapy with coils, Onyx, or contralateral vertebral artery occlusion (online supplementary table 4). Furthermore, in order to account for potential differences in aneurysm sizes, a subgroup analysis of aneurysm size between FD versus SAC was performed, with a mean aneurysm size of 11.04 mm (95% CI 0.49 to 12.58; I2=91.7%) and 10.37 mm (95% CI 6.85 to 13.89; I2=87.5%) for the FD and SAC groups, respectively; no statistically significant difference in size was found (p=0.73).

Risk of bias assessment

GRADE assessment indicated that the pooled outcomes of the 11 studies on FD were of moderate certainty, whereas the pooled outcomes of the five studies on SAC were low certainty (online supplementary table 6). In terms of publication bias, funnel plots were generated for all outcomes and no asymmetry was suspected. By MOOSE criteria, all included studies were considered good quality, with respect to their applicability to our PICOS question (online supplementary tables 6 and 7). Additionally, for occlusion, complications, stroke, and mRS, funnel plots were generated to assess asymmetry and no asymmetry was noted (online supplementary figure 2).

Occlusion rates

Complete/near complete occlusion was achieved in 83% overall (95% CI 0.77 to 0.88; $I^2=41\%$) (figure 1), with pooled IR after FD and SAC of 83% (95% CI 0.75 to 0.90; $I^2=45\%$) and 84% (95% CI 0.72 to 0.91; $I^2=22\%$), respectively, based on all included studies. The subgroup analysis was not statistically significant (p=0.95).

Periprocedural complications

Periprocedural complications were noted in 15% overall (95% CI 0.10 to 0.21; $I^2=45\%$; figure 2), with pooled IRs after FD and SAC of 18% (95% CI 0.14 to 0.23; $I^2=0\%$) and 6% (95% CI 0.02 to 0.13; $I^2=0\%$), respectively. The subgroup analysis was statistically significant (p=0.008). A total of 12 studies were included for analysis (nine FD and four SAC).[1 4 5 13 17–22 24 25]

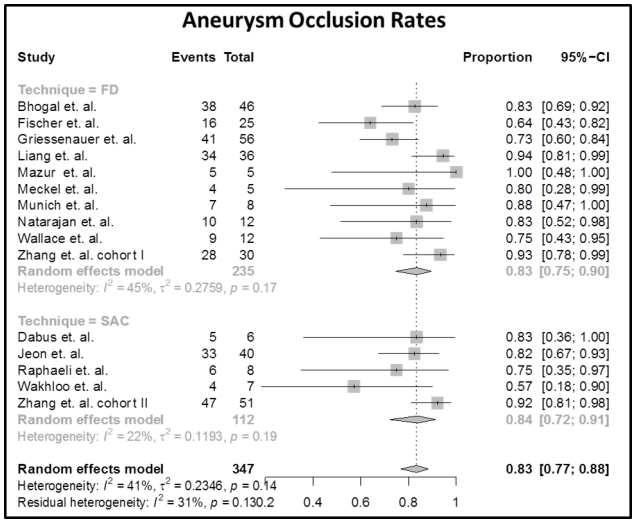

Figure 1 Forest plot of the incidence rates of occlusion for flow diversion (FD) and stent-assisted coiling (SAC) treatment groups. The proportions and 95% CI are represented by the middle of the square and the horizontal line.

Stroke IR was analyzed separately. One study did not report stroke rates by treatment type and was not included in analysis of stroke IR, yielding 11 studies that were included in this subgroup analysis (eight FD and four SAC).[1 4 5 17–22 24 25] Stroke occurred in 10% overall (95% CI 0.08 to 0.14; I^2=0%; figure 3) with pooled IRs after FD and SAC of 13% (95% CI 0.09 to 0.18; I^2=0%) and 5% (95% CI 0.02 to 0.11; I^2=0%), respectively. The subgroup analysis was statistically significant (p=0.04). A total of 11 studies were included for analysis (eight FD and four SAC).[1 4 5 17–22 24 25]

Complication details

A total of 56 complications in 430 cases were reported between the FD and SAC procedures, 51 (18%) and five (6%), respectively, all of them being related to vascular events (online supplementary table 5). In the SAC procedure group, four outcomes consisted of ischemic complications, and one death was assumed

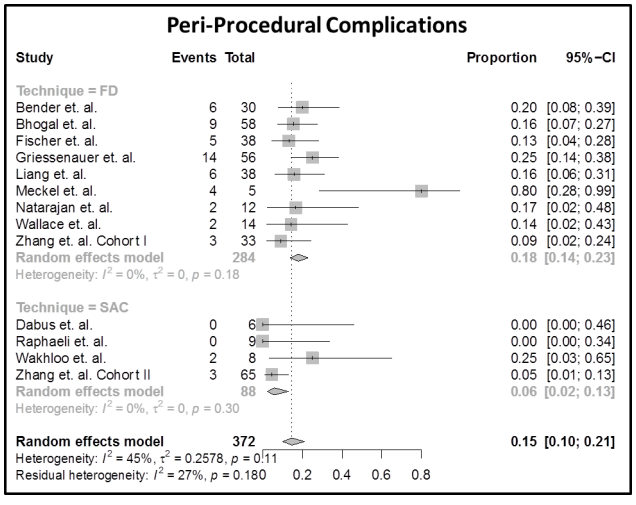

Figure 2 Forest plot of the incidence rates of periprocedural complications for flow diversion (FD) and stent-assisted coiling (SAC) treatment groups. The proportions and 95% CI are represented by the middle of the square and the horizontal line.

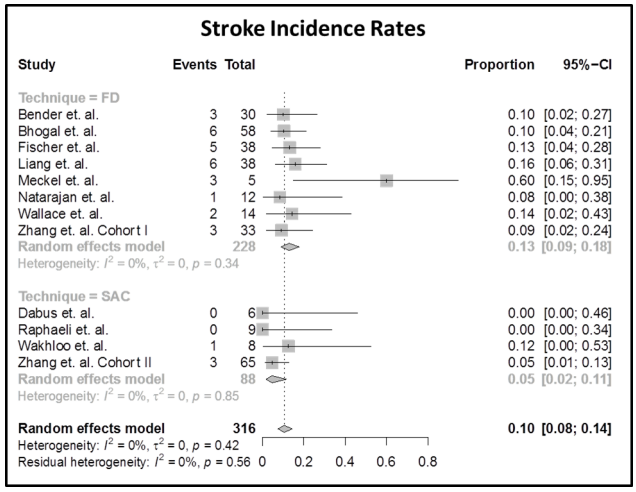

Figure 3 Forest plot of the incidence rates of strokes for flow diversion (FD) and stent-assisted coiling (SAC) treatment groups. The proportions and 95% CI are represented by the middle of the square and the horizontal line.

as a result of the treatment. FD-related complications followed the same pattern in terms of predominant ischemic events with 22 cases reported; hemorrhagic stroke, perianeurysmal edema, vasospasm, and cranial nerve deficit also occurred in this group. Remarkably, only two studies reported no complications,[17 18] both belonging to the SAC procedure group. Overall, 33 strokes could be differentiated from the total of 56 complications: 22 classified as ischemic (66%), three as hemorrhagic (9%) and eight were unclassified (online supplementary table 4).

Favorable clinical outcome

The mRS at last follow-up was extracted to evaluate clinical outcome (online supplementary table 5); mRS <3 was defined as favorable. A total of six studies were included for analysis (five FD and two SAC).[1 5 17 22–24] The mRS was found to be <3 in 90% overall (95% CI 0.67 to 0.98; I^2=84%; figure 4), with pooled incidence rates of mRS <3 after FD and SAC of 83% (95% CI 0.51 to 0.96; I^2=82.5%) and 97% (95% CI 0.89 to 0.99; I^2=0%), respectively. When analyzed as a whole and also among FD studies, a high degree of heterogeneity was present and the subgroup analysis was not statistically significant (p=0.07).

DISCUSSION

Treatment of fusiform aneurysms of the posterior circulation continues to pose a great challenge with unpredictable outcomes due to the absence of a true aneurysm neck and the presence of perforating vessels arising from the lesion and adjacent vessel walls.[2] Overall, these lesions have a poor natural history with no standard of care, and management options include antiplatelets, anticoagulation, SAC, FD, and microsurgery.[26] Complex morphology and larger size have been associated with increased morbidity and mortality when untreated and with increased risk of post-procedural complications following treatment. Therefore, the safety and efficacy of available treatment options are highly dependent on the patient's overall clinical condition and the particularities of the underlying lesion, as well as the specific treatment modality and the final clinical and radiographic outcomes. In this manuscript, we report the first meta-analysis comparing the two principal endovascular treatment modalities for unruptured non-saccular posterior circulation aneurysms: FD and SAC.

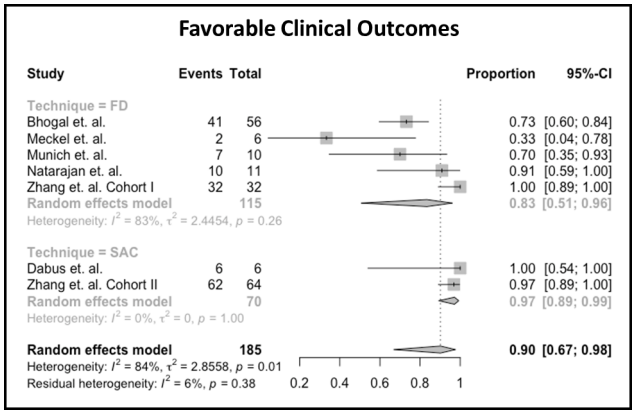

Figure 4 Forest plot of the incidence rates of favorable clinical outcomes (mRS 0–2) for flow diversion (FD) and stent-assisted coiling (SAC) treatment groups. The proportions and 95% CI are represented by the middle of the square and the horizontal line. mRS, modified Rankin score.

Stent-assisted coiling embolization

SAC embolization technique for treatment of wide-neck intracranial aneurysms was approved by the US Food and Drug Administration (FDA) in 2002. Since then, SAC has been used for treatment of non-saccular aneurysms to maintain the flow in the parent vessel while the coils are deployed within the aneurysmal dilatation to achieve obliteration.[3] We included four case series[4 8 17 18] and one retrospective comparative study[5] reporting on outcomes for treatment of unruptured non-saccular aneurysms of the posterior circulation, with SAC representing 29.7% of all aneurysms in this study. The efficacy of treatment with SAC was determined by the rate of aneurysm occlusion at last follow-up, with a complete/near-complete occlusion rate of 84% for aneurysms treated with this modality.

Endovascular remodeling with flow diversion devices

Endovascular remodeling with FD devices has emerged as an efficient treatment modality for complex aneurysms.[19] Since the approval of the pipeline embolization device (PED) by the FDA in 2011 for large and giant internal carotid artery aneurysms, the use of these devices has expanded to other applications outside the FDA approved indications, including fusiform aneurysms of the posterior circulation. Multiple trials studying the feasibility and safety of this procedure for treatment of complex aneurysms have been reported and robust data are available supporting its use for fusiform aneurysms of the anterior circulation.[27 28] However, for lesions in the posterior circulation, increased periprocedural complications have been reported and thus treatment with FD remains controversial within this location. In this study, we included 10 case series[1 7 13 19–25] and one retrospective comparative study[5] assessing the efficacy and safety of FD in the treatment of unruptured non-saccular aneurysms of the posterior circulation. The efficacy of treatment with FD was determined by the aneurysm occlusion rate at last follow-up, with a reported complete/near-complete occlusion rate of 83% for aneurysms treated with this modality. Recent meta-analyses looking at treatment of non-saccular posterior circulation aneurysms with FD reported mean complete/near-complete occlusion rates ranging from 52–85.2% and mean stroke rates ranging from 17–23%.[29 30] These findings are consistent with our results with an occlusion rate of 83% and a stroke rate of 18% following treatment with FD.

Occlusion rate

Multiple variables can be measured in order to assess treatment efficacy.[5] Both angiographic and clinical outcomes are commonly reported, including: immediate occlusion rate, occlusion rate at last follow-up, Kaplan-Meier occlusion time, Raymond classification, and mRS scores.[5] Out of all these parameters, occlusion rate at last follow-up was the only one that was measured consistently in all included cohorts. Classification was defined as complete, near-complete or incomplete occlusion with the exception of Zhang *et al*,[5] who utilized the Raymond score to classify the occlusion rate at last follow-up; for this study, complete occlusion was considered equal to Raymond type I, near-complete to Raymond type II, and incomplete as Raymond type III, according to its standardized interpretation. Griessenauer *et al*[13] reported complete and near complete occlusion indistinctively. Consequently, complete and near complete occlusion were pooled together for all the included studies. In terms of individual studies, Mazur *et al*[7] reported an occlusion rate of 100% at last follow-up for lesions treated with FD; however, three out of eight aneurysms were not included in their subgroup analysis as they were lost to follow-up. In contrast, the lowest complete occlusion rate reported was 58.69% by Bhogal *et al*.[1] In our study, no statistically significant difference in occlusion rates between SAC and FD was found in the subgroup analysis, suggesting equivalent efficacy between treatment modalities.

Periprocedural complications

The complex morphology of non-saccular aneurysms, added to the increased morbidity and mortality associated with lesions of the posterior circulation, contribute to the significant risk of periprocedural complications regardless of the treatment modality.[5] The reported periprocedural complications included cranial nerve deficit, stroke, transient ischemic attack, vasospasm, perianeurysmal edema, retained wire tip, SAH, embolus formation, parent artery occlusion, and in-stent thrombosis.[2 31]

Based on the results of this meta-analysis, complication rates were significantly lower in patients treated with SAC (6%) compared with FD (18%). Stroke was the most common complication with an incidence rate that was significantly different between FD and SAC groups at 15% and 5%, respectively. Although it is difficult to decipher important factors such as the severity of stroke and the role of perforators with antiplatelet regimen in these studies, the results can be summarized as follows: (1) for occlusion rates, the use of SAC and FD was statistically equivalent; (2) for periprocedural complications, a lower rate was associated with SAC in comparison to FD; (3) stroke was the most common complication and SAC was associated with lower rates than FD; and (4) SAC and FD were equivalent in terms of favorable clinical outcomes (defined by mRS).

Study strength, limitations, and applicability

This study has inherent strength and limitations. It was primarily designed to offer a comparative study between SAC and FD modalities and to investigate the safety, efficacy, and outcomes of these two endovascular techniques. The study's main strength lies in offering an up-to-date summary on outcomes of these modern treatment modalities of posterior circulation non-saccular aneurysms.

The main limitation lies in the retrospective nature of the included cohorts and the potential for inherent bias, since the majority of the studies assessed only one treatment modality and

only one study reported a direct comparison between SAC and FD. In addition, these lesions are heterogeneous with regards to location, size, and extent of the involved vessels. Detailed characterization of aneurysm morphology, location, and presence of thrombus or involvement of perforators was not feasible. Also, patients have a broad variation in the severity of clinical symptoms and neurological deficits. Other limitations are related to variations in treatment practices including anticoagulation regimen and duration, population-specific disparities, and combination treatment with SAC+FD. The inability to address the results of using FD devices with or without coils represents another limitation. Therefore, the applicability of these results to the management of non-saccular posterior circulation aneurysms is unclear. However, this analysis represents a status report of the available literature and several valid conclusions can be drawn along a fine line between applicability and generalization of the results.

The main risk with either technique is related to ischemic complications. Therefore, future risk reduction in endovascular treatment of non-saccular posterior circulation aneurysms should focus primarily on reducing the incidence of stroke regardless of the treatment modality. It should also be noted that FD is relatively new compared with SAC and the difference in treatment outcomes during the learning curve of newly applied endovascular techniques should not be underestimated.[32] Another important inference is related to the fact that there is currently no standard of care for posterior circulation non-saccular aneurysms. Therefore, future studies should focus primarily on developing management guidelines based on clinical presentation, aneurysm characteristics and location, as well as patient age and comorbidities. These variables play a crucial role in selecting the optimal procedure for each patient. Also, a registry is warranted for these lesions with a better classification system, taking into consideration the specific radiographic and clinical characteristics of the aneurysm, the patient, and the treatment modality.

CONCLUSION

Posterior circulation non-saccular aneurysms have a poor natural history with no standard of care, and management options include SAC and FD. In this meta-analysis, we present a status report of the current endovascular treatment with SAC versus FD in terms of occlusion rate and clinical outcomes. The results suggest equivalent efficacy regarding aneurysm occlusion rate. Stroke was the most common complication for both treatment modalities, and a lower periprocedural complication rate was noted with SAC. Given the complexity of these lesions and the intrinsic limitations of the existing literature, the results of this study have to be interpreted carefully. Additional variables need to be addressed when considering treatment of these lesions, and registries are needed to improve outcomes and further develop treatment modalities based on scientific data.

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Contributors All clinical investigators involved met the criteria for authorship. RAD: planning, conduct, reporting, conception and design, acquisition of data and interpretation of data. ST: planning, conduct, conception and design, analysis of the data and interpretation of the data. CP-V: conduct, conception, acquisition of data. TV-B: interpretation of data, conception, critical review. VML: analysis of the data and interpretation of the data, critical review. NDT: supervision, critical review. AQ-H: supervision, critical review. RGT: planning, conduct, reporting, conception and design, interpretation of data, supervision, critical review.

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