Stereotactic radiosurgery for intracranial dural arteriovenous fistulas: a systematic review

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OBJECT The goal of this study was to evaluate the obliteration rate of intracranial dural arteriovenous fistulas (DAVFs) in patients treated with stereotactic radiosurgery (SRS), and to compare obliteration rates between cavernous sinus (CS) and noncavernous sinus (NCS) DAVFs, and between DAVFs with and without cortical venous drainage (CVD).

METHODS A systematic literature review was performed using PubMed. The CS DAVFs and the NCS DAVFs were categorized using the Barrow and Borden classification systems, respectively. The DAVFs were also categorized by location and by the presence of CVD. Statistical analyses of pooled data were conducted to assess complete obliteration rates in CS and NCS DAVFs, and in DAVFs with and without CVD.

RESULTS Nineteen studies were included, comprising 729 patients harboring 743 DAVFs treated with SRS. The mean obliteration rate was 63% (95% CI 52.4%–73.6%). Complete obliteration for CS and NCS DAVFs was achieved in 73% and 58% of patients, respectively. No significant difference in obliteration rates between CS and NCS DAVFs was found (OR 1.72, 95% CI 0.66–4.46; $p = 0.27$). Complete obliteration in DAVFs with and without CVD was observed in 56% and 75% of patients, respectively. A significantly higher obliteration rate was observed in DAVFs without CVD compared with DAVFs with CVD (OR 2.37, 95% CI 1.07–5.28; $p = 0.03$).

CONCLUSIONS Treatment with SRS offers favorable rates of DAVF obliteration with low complication rates. Patients harboring DAVFs that are refractory or not amenable to endovascular or surgical therapy may be safely and effectively treated using SRS.

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KEY WORDS arteriovenous fistula; dural arteriovenous fistula; stereotactic radiosurgery; radiosurgery; review

CURRENT treatment strategies for intracranial dural arteriovenous fistulas (DAVFs) include microsurgical ligation, transarterial or transvenous embolization, stereotactic radiosurgery (SRS), and various combinations of these therapeutic options. Endovascular therapy, most commonly performed via transvenous routes, has become the preferred treatment approach for DAVFs.^{27,44,48} Due to the immediate obliteration that can be achieved with endovascular or surgical occlusion, SRS is typically reserved for lesions that cannot be obliterated with endovascular or surgical approaches, or for patients who pose a high surgical risk due to medical comorbidities. Therefore, published SRS series for DAVFs remain relatively few and comprise mostly retrospective, single-center studies.

In this systematic review, we evaluate the obliteration rate of DAVFs in patients treated with SRS. We also compare obliteration rates between cavernous sinus (CS) and noncavernous sinus (NCS) DAVFs, and between DAVFs with and without cortical venous drainage (CVD), by using available data in the literature.

Methods

Inclusion Criteria

In our attempt to balance between the largest possible patient population and a relatively homogeneous cohort, the following inclusion criteria for this systematic review were devised: 1) the study must contain at least 5 patients

ABBREVIATIONS AVM = arteriovenous malformation; CS = cavernous sinus; CVD = cortical venous drainage; DAVF = dural arteriovenous fistula; GKS = Gamma Knife surgery; LINAC = linear accelerator; NCS = noncavernous sinus; SRS = stereotactic radiosurgery; TSS = transverse and sigmoid sinus.

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who had intracranial DAVFs treated with SRS without concurrent arteriovenous malformations (AVMs) or arterial aneurysms; 2) the study must have included post-SRS outcome data regarding DAVF obliteration rates; and 3) the language of the study must be English. Patients who underwent prior or combined therapies other than SRS for their DAVFs and/or had prior hemorrhages were not excluded.

Literature Search

A systematic literature review was performed on March 3, 2014, using PubMed with the following search term: “dural arteriovenous fistula OR arteriovenous fistula AND radiosurgery.” Following the search, the articles were then screened by title and abstract. The remaining articles underwent further detailed review for relevance and usable data matching the inclusion criteria. Articles with insufficient post-SRS data and overlapping published data from the same institution in a more recent study were excluded. However, those with partially overlapping but supplementary treatment outcomes data from the same institutions were not excluded from the review.

Literature Review and Data Extraction

No registered review protocol was used in this study. This review follows the guidelines set forth by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement. Available demographic, radiosurgical, and clinical and radiological outcomes data were extracted from studies that met the inclusion criteria. Demographic data included number of patients, sex, and age. Radiosurgical data included the type of SRS device used (i.e., Gamma Knife, linear accelerator, proton beam) and radiosurgical parameters (mean margin dose, isodose line, and treatment volume). Outcomes data reviewed for each study included duration of follow-ups, complete obliteration rates as determined using modalities specified by the respective studies, hemorrhages following SRS, SRS-related new or worsened neurological deficits, and SRS-related deaths.

The DAVFs were categorized by location (CS, transverse and sigmoid sinus [TSS], and other locations) whenever possible. The NCS DAVFs included those located at the TSS and other locations. The CS DAVFs were classified using the Barrow classification system, whereas NCS DAVFs were classified using the Borden classification system.^{4,5} For studies that used the Cognard classification system, patients were reclassified using the Borden classification system as follows: Cognard Types I and IIa were categorized as Borden Type I; Cognard Types IIb and IIa + b were categorized as Borden Type II; and Cognard Types III, IV, and V were categorized as Borden Type III.⁸ To assess the association between treatment outcomes and CVD, patients were also classified into groups of DAVFs without CVD (Borden Type I or Cognard Types I and IIa) and with CVD (Borden Types II and III or Cognard Types IIb, IIa + b, III, IV, and V). Table 1 outlines the Borden, Cognard, and Barrow classification systems.^{4,5,8}

Statistical Analysis

Descriptive statistics for this review were determined

TABLE 1. Classification systems for DAVFs

Authors & Categories	Description
Cognard et al., 1995	
Type I	Drainage into dural venous sinus w/ normal antegrade flow
Type IIa	Drainage into dural venous sinus w/ retrograde flow
Type IIb	Drainage into dural venous sinus w/ normal antegrade flow & CVD
Type IIa & IIb	Drainage into dural venous sinus w/ retrograde flow & CVD
Type III	Direct drainage into cortical vein w/o venous ectasia
Type IV	Direct drainage into cortical vein w/ venous ectasia
Type V	Direct drainage into perimedullary veins
Borden et al., 1995	
Type I	Drainage into dural venous sinus or meningeal vein
Type II	Drainage into dural venous sinus & CVD
Type III	Direct drainage into cortical vein
Barrow et al., 1985	
Type A	Direct high-flow shunts btwn ICA & CS
Type B	Indirect low-flow shunts btwn meningeal branches of ICA & CS
Type C	Indirect low-flow shunts btwn meningeal branches of ECA & CS
Type D	Indirect low-flow shunts btwn meningeal branches of both ICA & ECA & CS

ECA = external carotid artery; ICA = internal carotid artery.

using SPSS version 20.0.0 (IBM Corp., 2011), whereas statistical analyses of pooled data comparing obliteration rates were performed using Review Manager version 5.2.8 (The Nordic Cochrane Centre; The Cochrane Collaboration, 2012). The DAVF obliteration rates following SRS were extracted for DAVFs with and without CVD, and for CS and NCS DAVFs. Studies with obliteration rates for DAVFs both with and without CVD were included in the meta-analysis comparing their respective obliteration rates. Similarly, studies with obliteration rates for both CS and NCS DAVFs were analyzed in the meta-analysis comparing their respective obliteration rates. Odds ratios for individual studies and the sum of the included studies were computed using the Mantel-Haenszel test.

Under the assumptions of possible clinical diversity and methodological differences among the included studies, the random effects model was implemented in the analyses for this review. Study heterogeneity was detected using the chi-square and I^2 test statistics. However, the power of the chi-square test was limited by the inclusion of a small number of studies in the analyses; hence significant heterogeneity was considered to be present when both the chi-square value was within the 10% level of significance ($p < 0.10$) and the I^2 value exceeded 50%. Potential contributions to variations across studies are discussed in the limitations section of this review. Unclear risks of bias

were assumed for retrospective studies. All statistical tests were 2-sided, and $p < 0.05$ was considered statistically significant.

Results

Study Selection

The search yielded 1379 articles published between 1972 and 2014. The initial screening process led to the selection of 31 articles. Subsequently, 12 studies were excluded for reasons including insufficient post-SRS outcome data and overlapping published patient data from the same institution in another study. Finally, 19 series comprising 729 patients harboring 743 DAVFs who underwent SRS were identified.^{3,6,7,12,14,16,19,20,22,23,31–34,37,39,41,42,51} Figure 1 demonstrates an outline of the systematic review process. Four studies with partially overlapping but supplementary treatment outcomes data from two institutions were included in the systematic review. However, no two studies from the same institution were included in the same part of the analyses. All studies included were retrospective in design, comprising mostly small cohorts. Unclear risks of bias were assigned to all studies.

Overall Demographic Data, DAVF and Treatment Characteristics, and Outcomes

There was a slight female predominance among the 19 included studies, with 312 of the 580 patients (53.8%) with available demographic information identified as female. The mean patient age for the 19 studies ranged between 50 years and 69 years. The SRS modalities used were Gamma Knife surgery (GKS) and linear accelerator (LINAC)-based radiosurgery in 15 and 3 studies, respectively; in 1 study the specific SRS modality used was not documented. Prior endovascular embolizations and microsurgeries were performed in 199 of 701 (28.4%) and 34 of 726 (4.7%) of DAVFs, respectively. The mean follow-up period after SRS ranged from 12 months to 50 months (overall mean 28.9 months).

Combining the results of the included studies, in 438 of 642 DAVFs (68.2%) with follow-up data, complete obliteration was achieved following SRS. The mean obliteration rate between individual studies was 63% (95% CI 52.4%–73.6%). Angiography was performed in 292 patients, and complete obliteration was observed in 255 (87.3%). Post-SRS hemorrhage, new or worsened neurological deficit, and death occurred in 9 of 730 DAVFs (1.2%), 9 of 715 patients (1.3%), and 2 of 715 patients (0.3%), respectively. A summary of included SRS series for DAVFs along with the respective radiosurgical parameters is found in Table 2.

Outcomes for CS DAVFs Versus NCS DAVFs

Of the 700 DAVFs categorized by location, 323 (46.1%) were located in the region of the CS and 377 (53.9%) were located in NCS regions. Complete obliteration was achieved in 172 of 236 CS DAVFs (72.9%) and in 143 of 247 NCS DAVFs (57.9%). Post-SRS hemorrhages were observed in 0 of 295 patients with CS DAVF and in 3 of 237 patients with NCS DAVF (1.3%). The NCS DAVFs comprised 192 TSS DAVFs (50.9%) and 185 DAVFs at other

FIG. 1. Flowchart outlining the systematic review process. The initial PubMed search yielded 1379 articles, and the subsequent screening process led to the selection of 31 articles to undergo further detailed review for relevance and usable data matching the inclusion criteria. Twelve studies were excluded for reasons including insufficient post-SRS outcome data and overlapping published patient data from the same institution in another study. Finally, 19 series comprising 729 patients harboring 743 DAVFs who underwent SRS were identified and included in the review.

locations (49.1%). Complete obliteration was observed in 52 of 87 TSS DAVFs (59.8%) and in 38 of 71 DAVFs at other NCS, non-TSS locations (53.5%). Post-SRS hemorrhages were reported in 2 of 142 patients with TSS DAVFs (1.4%) and in 1 of 95 patients with NCS, non-TSS DAVFs (1.1%). A summary of CS and NCS DAVF treatment outcomes following SRS is found in Table 3. Despite the difference in complete obliteration rates between CS and NCS DAVFs, analysis of pooled data based on the random effects model from 5 studies with DAVF obliteration data for both CS and NCS DAVFs demonstrated no significant difference in their complete obliteration rates (OR 1.72, 95% CI 0.66–4.46; $p = 0.27$). No significant heterogeneity among the included studies was found in this analysis ($\chi^2 = 5.71$; $p = 0.22$; $I^2 = 30\%$). Results of the analysis are summarized in Fig. 2.

Outcomes for DAVFs With CVD Versus DAVFs Without CVD

In studies that reported CS DAVFs using the Barrow classification system, 3 (1.2%), 31 (12.4%), 19 (7.6%), and

TABLE 2. Summary of the 19 SRS series for DAVFs included in this systematic review

Authors & Year	No. of Pts	No. Female	Mean Age (yrs)	Mean No. DAVFs	Mean Radio FU (mos)	Previous Embo, n/N	Previous Microsurgery, n/N	SRS Modality	Mean Margin Dose (Gy)	Isodose Line (%)	Tx Vol (cm ³)	Complete Oblit, n/N	Complete Oblit on Angio, n/N	No. w/ Post-SRS Hem	No. w/ Other Neuro Defs	No. Dead
Pan et al., 2013*	321	180	57.8	321	21 for CS, 28 for NCS†	41/321	13/321	GKS	17.2	68.5 for CS, 57.7 for NCS	4.7 for CS, 16.9 for NCS	173/264	NA	2	0	1
Piippo et al., 2013	16	NA	NA	17	NA	13/17	0/17	LINAC	18	NA	NA	9/17	NA	0	0	0
Söderman et al., 2013*	65	NA	NA	67	NA	10/67	3/67	GKS	20–25	40–60	NA	37/63	37/63	2	2	0
Gross et al., 2012 ¹⁴	8	3	56.8	9	35†	4/9	0/9	LINAC	17.7	NA	1	8/9	NA	0	0	0
Oh et al., 2012	43	NA	NA	43	NA	30/43	0/43	GKS	19	NA	6.9	32/43	32/43	1	1	0
Hanakita et al., 2012	22	8	57	22	27†	10/22	2/22	GKS	21	NA	1.5	12/22	9/18	0	0	0
Yang et al., 2010†	40	18	69	44	45†	19/44	0/44	GKS	20	50 in 42, 60 in 2	2	32/44	21/44	1	0	1
Cifarelli et al., 2010	55	18	50	55	36	36/55	11/55	GKS	21	NA	NA	30/46	30/46	3	1	0
Kida, 2009	13	4	54.3	13	24†	7/13	0/13	GKS	18.9	NA	NA	5/13	NA	0	0	0
Söderman et al., 2006*	49	NA	NA	52	NA	7/52	3/52	GKS	22	NA	NA	28/41	28/41	2	1	0
Koebbe et al., 2005	18	9	65	23	46	13/23	0/23	GKS	20	NA	2.16	15/18	8/8	0	1	0
Pan et al., 2002*	20	9	53	20	19†	NA	NA	GKS	16.5–19	50–70	1.7–40.7	11/19	9/9	0	0	0
O'Leary et al., 2002	16	10	56	17	24	NA	NA	GKS	25, except 1 w/ 20.83	50	NA	10/13	10/13	0	1	0

(continued)

TABLE 2. Summary of the 19 SRS series for DAVFs included in this systematic review (continued)

Authors & Year	No. of Pts	No. Female Pts	Mean Age (yrs)	No. DAVFs	Mean Radio FU (mos)		Previous Embo, n/N	Previous Microsurgery, n/N	SRS Modality	Mean Margin Dose (Gy)	Isodose Line (%)	Tx Vol (cm ³)	Complete Oblit, n/N	Complete Oblit on Angio, n/N	No. w/ Post-SRS Hem		No. w/ Other Neuro Defs		No. Dead
Chung et al., 2002	8	6	56.3	8	17†		3/8	1/8	GKS	20	70	NA	1/8	NA	0	0	1	1	0
Friedman et al., 2001†	23	18	57	23	21		2/23	0/23	GKS	18	NA	9.6	7/17	7/17	0	0	0	0	0
Pollock et al., 1999†	20	17	67	20	12		2/20	0/20	GKS	20	≥50	2.8	13/15	13/15	0	0	1	1	0
Link et al., 1996†	29	17	61	29	NA		2/29	1/29	GKS	19.2	50–60	3.3	13/18	13/18	0	0	0	0	0
Lewis et al., 1994†	7	4	61	7	24		7/7	0/7	LINAC	15.6	NA	NA	3/7	3/7	0	0	1	1	0
Barcia-Salorio et al., 1994	25	NA	NA	25	50†		NA	3/25	NA	30–40, except 1 w/ 20	NA	NA	21/25	NA	0	0	0	0	0
Total§	729	312/580 (53.8%)		743			199/701 (28.4%)¶	34/726 (4.7%)¶					438/642 (68.2%)¶	255/292 (87.3%)¶	9/730 (1.2%)¶	9/715 (1.3%)**	2/715 (0.3%)**		

Angio = angiography; embo = embolization; FU = follow-up; hem = hemorrhage; NA = not available; neuro defs = neurological deficits; oblit = obliteration; pts = patients; radio = radiological; Tx = treatment.

* Studies with partially overlapping but complementary treatment outcomes data from the same institution.

† Distinction between clinical and radiological follow-up unclear.

‡ Studies with patients treated with combined endovascular embolization and SRS.

§ Excludes earlier studies with partially overlapping but complementary treatment outcomes data from the same institutions.

¶ Based on the number of DAVFs in patients with follow-up.

** Based on the number of patients with follow-up.

TABLE 3. Summary of DAVF treatment outcomes following SRS in lesions characterized by location and type

Characteristic	No. DAVFs (%)	Complete Oblit, n/N (%)	Post-SRS Hem, n/N (%)
DAVF location			
CS	323 (46.1)	172/236 (72.9)	0/295 (0.0)
NCS	377 (53.9)	143/247 (57.9)	3/237 (1.3)
TSS	192 (50.9)	52/87 (59.8)	2/142 (1.4)
Others	185 (49.1)	38/71 (53.5)	1/95 (1.1)
CS DAVFs			
Barrow Type A	3 (1.2)	1/3 (33.3)	0/3 (0.0)
Barrow Type B	31 (12.4)	11/11 (100.0)	0/31 (0.0)
Barrow Type C	19 (7.6)	3/4 (75.0)	0/19 (0.0)
Barrow Type D	198 (78.9)	6/7 (85.7)	0/198 (0.0)
NCS DAVFs			
Borden Type I	105 (47.7)	52/79 (65.8)	0/85 (0.0)
Borden Type II	60 (27.3)	15/35 (42.9)	1/38 (2.6)
Borden Type III	55 (25.0)	12/24 (50.0)	1/27 (3.7)
CVD			
DAVFs w/o CVD	157 (48.8)	76/102 (74.5)	0/131 (0.0)
DAVFs w/ CVD	165 (51.2)	69/123 (56.1)	6/144 (4.2)

198 (78.9%) were categorized as Barrow Types A, B, C, and D DAVFs, respectively. Complete obliteration was observed in 1 of 3 Type A (33.3%), in 11 of 11 Type B (100%), in 3 of 4 Type C (75%), and 6 of 7 Type D (85.7%) CS DAVFs. No post-SRS hemorrhages were reported in any of the CS DAVFs. Among studies that reported NCS DAVFs using the Borden classification system, 105 (47.7%), 60 (27.3%), and 55 (25.0%) were categorized as Borden Types I, II, and III, respectively. Complete obliteration was observed in 52 of 79 Borden Type I (65.8%), 15 of 35 Type II (42.9%), and 12 of 24 Type III (50.0%) NCS DAVFs. Post-SRS hemorrhages were reported in 0 of 85 patients with Borden Type I, in 1 of 38 patients with Type II (2.6%), and in 1 of 27 patients with Type III (3.7%) DAVFs. A summary of SRS outcomes for CS and NCS

DAVFs categorized using the Barrow and Borden classification systems is found in Table 3.

Of the 322 DAVFs with known venous drainage patterns, 165 (51.2%) had associated CVD and 157 (48.8%) did not have CVD. Complete obliteration was observed in 69 of 123 DAVFs (56.1%) with CVD and in 76 of 102 DAVFs (74.5%) without CVD. Post-SRS hemorrhage was reported in 6 of 144 DAVFs with CVD (4.2%) and in 0 of 131 DAVFs without CVD (0.0%). A summary of SRS outcomes for DAVFs with and without CVD is found in Table 3. Analysis of pooled data based on the random effects model demonstrated that DAVFs without CVD were associated with a significantly higher rate of complete obliteration following SRS compared with DAVFs with CVD among 9 studies with obliteration data for DAVFs both with and without CVD (OR 2.37, 95% CI 1.07–5.28; $p = 0.03$). No significant heterogeneity among the included studies was found in this analysis ($\chi^2 = 8.93$; $p = 0.35$; $I^2 = 10\%$). Results of the analysis are summarized in Fig. 3.

Only a few studies investigated the potential factors associated with complete obliteration of DAVFs following SRS. Conflicting factors were found between these studies. Factors found by the included studies to be significantly associated with obliteration are as follows: CS DAVFs, Borden Type I DAVFs, DAVFs without CVD, hemorrhage at presentation, target volume < 1.5 ml, and Cognard Types III or IV DAVFs.^{7,16,51} Factors found to be nonsignificant are as follows: patient age and sex, prior treatments, DAVF location and size, DAVFs with multiple arteriovenous connections versus DAVFs with single arteriovenous connections, and minimal radiation dose delivered to DAVFs.^{7,16,42} Table 4 outlines these factors investigated by studies included in this systematic review.

Discussion

Stereotactic radiosurgery was initially used in the treatment of AVMs in 1970 and was subsequently used to treat DAVFs in the late 1970s. Barcia-Salorio and colleagues first reported the use of SRS for treating DAVFs in 1982, followed by an SRS case series for DAVFs composed of 25 cases of CS DAVFs in 1994.^{2,3} Since then, a

FIG. 2. Forest plot of the ORs of obliteration rates for CS and NCS DAVFs treated with SRS. The estimated OR and 95% CI for each included study are represented by the center of the squares and the horizontal line, respectively. The summary OR and 95% CI are shown in bold, and are represented by the diamond. Tests of heterogeneity and overall effect are given below the summary statistics. M-H = Mantel-Haenszel. Figure is available in color online only.

FIG. 3. Forest plot of the ORs of obliteration rates for DAVFs with and without CVD treated with SRS. The estimated OR and 95% CI of each included study are represented by the center of the squares and the horizontal line, respectively. The summary OR and 95% CI are shown in bold, and are represented by the diamond. Tests of heterogeneity and overall effect are given below the summary statistics. Figure is available in color online only.

number of other studies have investigated the use of SRS for treating DAVFs in other locations, with variable rates of success. This systematic review of the literature, comprising 19 studies, found a reasonable rate of complete DAVF obliteration (63%), with relatively low complication rates. Although the complete obliteration rate determined using angiography is higher (87.3%), this may be biased because invasive modalities such as angiography are often performed to confirm complete obliteration following obliteration observed using noninvasive imaging modalities. The associated rates of post-SRS hemorrhage, neurological deficit, and mortality were 1.2%, 1.3%, and 0.3%, respectively. However, variations in obliteration and complication rates, such as risks of hemorrhage, may be dependent on factors such as the location and angioarchitecture of DAVFs. Therefore, we also categorized SRS treatment outcomes for DAVFs by location and venous drainage pattern.

Comparison of CS DAVFs and NCS DAVFs

Cavernous sinus DAVFs represent a subset of lesions that are distinct from NCS DAVFs. In contrast to other intracranial dural venous sinuses, the CS is located extradurally, not between the periosteal and meningeal layers.^{17,18} Due to its many routes of venous drainage, the presenting symptoms and signs of a CS DAVF are often benign.⁴⁶ These symptoms include blurred vision, bruit, diplopia, exophthalmos, chemosis, and glaucoma. Given the benign features of low-flow CS DAVFs and possibility of spontaneous occlusion, some authors have advocated conservative treatments, including cervical carotid artery and jugular vein compressions, as first-line therapies for these lesions.^{15,40} However, some cases present with intractable intraocular hypertension or reduced ocular perfusion pressure, thereby warranting more rapid interventions to prevent progressive vision loss.^{36,40,49}

Due to their unique anatomy and symptomatology, CS DAVFs are often categorized using the Barrow classification system.⁴ Type A fistulas represent direct high-flow shunts between the internal carotid artery and the CS, comprising mostly traumatic fistulas formed as a result of a tear in the cavernous segment of the internal carotid artery. These fistulas do not typically resolve spontaneously, and therefore require rapid intervention for cases of progressive visual loss. Barrow Type A CS DAVFs are often adequately treated via endovascular approaches, which provide immediate results. Thus, the number of Type A CS DAVFs treated using SRS is low (1.2% of reported CS

TABLE 4. Factors associated with DAVF obliteration via SRS among included studies

Authors & Year	Associated w/ DAVF Oblit	Not Associated w/ DAVF Oblit
Yang et al., 2013	CS DAVFs	
Cifarelli et al., 2010	Borden Type I DAVFs No CVD	Sex Prior endovascular therapy for DAVF Prior craniotomy for DAVF Location of DAVF Size of DAVF Multi-hole vs single-hole DAVF
Hanakita et al., 2012	No CVD Hem at presentation Target vol <1.5 ml Cognard Types III or IV DAVF	Age Sex Location of DAVF Prior therapy
Söderman et al., 2006		Minimal radiation dose to DAVF

DAVFs).^{10,25,26,28} Because complete obliteration of DAVFs following SRS is delayed, with a typical latency period of 1–3 years, SRS may represent a more suitable treatment modality for indirect, low-flow CS DAVFs classified as Barrow Types B, C, and D. In the largest SRS series for CS DAVFs to date, Pan et al. observed a complete obliteration rate of 70% with no reported cases of post-SRS hemorrhage or neurological morbidity in 156 indirect low-flow CS DAVFs.³⁴ Based on the compiled data from studies included in this review, a complete obliteration rate of 73% was achieved in CS DAVFs treated with SRS. Therefore, the decision between conservative management and intervention should be individualized for each patient; consideration should be given to the severity of symptoms, DAVF angioarchitecture, and the efficacy and safety of treatments.

Noncavernous sinus DAVFs also comprise a heterogeneous cohort of lesions with variable presenting symptoms. Patients with DAVFs involving the TSS often present with pulsatile tinnitus and bruit, and those with superior sagittal sinus DAVFs can suffer from progressive dementia.²¹ Intracranial hemorrhage, the most devastating presentation of DAVFs, is more commonly seen in DAVFs involving the tentorium or anterior fossa.^{1,21} To better characterize DAVF hemorrhagic risk, the Borden and Cognard classification systems are used.^{5,8,9} Borden Types II and III and Cognard Types IIb–V DAVFs confer significantly higher risks of hemorrhage than Borden Type I and Cognard Types I and IIa DAVFs. Thus, these high-risk DAVFs usually warrant more immediate treatments in which modalities such as endovascular embolization and microsurgical ligation are used.⁹ As reflected in our results, fewer Borden Types II and III DAVFs were treated using SRS than Type I lesions. In the largest series of NCS DAVFs treated using SRS, Pan et al. observed a similar trend.³⁴ Compared with the post-SRS obliteration rate for CS DAVFs (73%), the rate for NCS DAVFs appears to be lower (60%). However, this difference was not statistically significant in the pooled data analysis ($p = 0.27$). Post-SRS hemorrhage was observed more frequently in NCS DAVFs (1.3%) than in CS DAVFs (0%). Further categorization of NCS DAVFs demonstrated comparable obliteration rates for TSS DAVFs (60%) and DAVFs in other non-TSS locations (54%). Therefore, the efficacy of SRS does not seem to be restricted by DAVF location. More emphasis should be placed on understanding the angioarchitecture of DAVFs when selecting patients for SRS treatment.

Comparison of DAVFs With CVD and DAVFs Without CVD

It is well recognized that DAVFs with CVD have a significantly greater risk of hemorrhage compared with those without CVD. Söderman et al. reported a 1.5% annual risk of hemorrhage in 53 patients with unruptured DAVFs with CVD.⁴³ In the same study, this risk increased to 7.4% per year for those with ruptured DAVFs. Strom et al. reported a similar annual hemorrhage rate of 1.4% in 17 patients harboring DAVFs with CVD without prior hemorrhage.⁴⁵ The risk increased to 7.6% in those with DAVFs with CVD who presented with hemorrhage or nonhemorrhagic neurological deficit. Detailed analyses by Gross and Du of published studies found 6% and 10% annual

hemorrhage rates for Borden Types II and III DAVFs, respectively, in contrast to an annual hemorrhage rate of 0% for Borden Type I DAVFs.¹³ Although an annual hemorrhage rate of 3% for unruptured DAVFs with CVD was found in their study, the rate increased to 46% per year for ruptured DAVFs with CVD. The recurrence of bleeding can occur within the first few weeks following the initial hemorrhage. Duffau et al. observed a rebleeding rate of 35% within the first 2 weeks after the initial hemorrhage.¹¹ Significant mortality rates of up to 10.4% annually have been associated with the persistence of CVD.⁴⁷

Given the high morbidity and mortality rates observed in untreated or partially treated DAVFs with CVD, urgent treatment using modalities that offer immediate obliteration should be recommended for these lesions. Due to the risk of hemorrhage during the latency period between treatment and obliteration, SRS should not be recommended as the sole and/or first-line treatment for DAVFs with CVD. In this systematic review, we observed a higher risk of post-SRS hemorrhage for DAVFs with CVD compared with those without CVD (4.2% vs 0%). In addition, we found a significantly lower obliteration rate for SRS-treated DAVFs with CVD compared with those without CVD ($p = 0.03$). Therefore, patients harboring DAVFs with CVD should undergo endovascular embolization, microsurgical resection, or a combination of the two as initial therapy to rapidly reduce or eliminate the risk of hemorrhage. Stereotactic radiosurgery can be offered as an adjunct or salvage therapy in cases refractory to embolization or surgery.²⁹ For patients harboring DAVFs without CVD, the decision to treat should be based on the severity of symptoms. Close observation should be recommended to patients with nondisabling symptoms, whereas SRS and/or endovascular embolization should be reserved for those with intractable symptoms.

In patients selected to undergo endovascular embolization, SRS may represent an effective complementary therapy.^{7,12,22,23,35,39,51} Although endovascular embolization may provide immediate symptomatic relief and reduction of hemorrhage risk, the treatment may not afford long-term cure in cases of subtotal obliteration or delayed recanalization.²⁴ Therefore, SRS serves as a complementary treatment by potentially increasing the likelihood of permanent DAVF occlusion.^{24,51} However, the timing of embolization and SRS remains controversial. Some authors argue that embolization prior to SRS can reduce target volume and blood flow, thus facilitating obliteration by SRS. In contrast, others contend that the target margin may be obscured when embolization is performed prior to SRS, resulting in inadequate target delineation and ineffective treatment.

Study Limitations

This systematic review is limited by the pooled data available from largely retrospective, single-center studies, with all of the limitations and weaknesses inherent to retrospective designs. In an attempt to reduce the nuances separating detailed classification systems, best efforts were made to classify DAVFs into broader categories. Not all studies were included in this systematic analysis; insufficient DAVF obliteration outcomes data led to the ex-

clusion of certain studies from analyses. Insufficient outcomes data from some studies also limit certain comparative statistical analyses. Despite no significant findings in the tests of heterogeneity, the variability in the methods of clinical evaluation and determination of complete DAVF obliteration among studies remains difficult to overcome.

Verification of complete obliteration varied depending on the study institution; MRI or MR angiography, digital subtraction angiography, or a combination of these imaging modalities may have been used in different studies. Ideally, obliteration would be confirmed with cerebral angiography. However, when this is not advisable or the patient refuses, MRI and MR angiography or CT and CT angiography have been shown to be reasonable surrogates for cerebral AVMs, and this approach has been extended to DAVFs in contemporary practice.^{30,38} In addition, baseline characteristics of patients may vary significantly. Stereotactic radiosurgery was not the primary or sole treatment for all patients in this review; some patients underwent prior microsurgical ligation and/or embolization of their DAVFs. Patients in this review may also have been selected for SRS due to poor candidacy for microsurgery and/or embolization, or due to patient preference. However, data from these studies were insufficient to make such a distinction. Also, we did not differentiate results based on the type of SRS device used (e.g., LINAC, GKS, and so on) and cannot be certain if the results here are generalizable to all SRS platforms. Thus, results of this review should be interpreted with caution, and they may not be generalizable to all patients.

Conclusions

Stereotactic radiosurgery affords favorable rates of complete DAVF obliteration with acceptably low complication rates. Obliteration rates do not differ significantly between CS DAVFs and NCS DAVFs. However, DAVFs without CVD are associated with significantly higher obliteration rates than DAVFs with CVD. Therefore, careful patient selection for SRS based on DAVF angioarchitecture and hemorrhage risk is recommended. For DAVFs with CVD, SRS should be used as an adjuvant or salvage therapy. However, for DAVFs without CVD, SRS may be considered as a first-line therapy for patients who are unable or unwilling to undergo endovascular or surgical intervention, or it may be used in combination with embolization.

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