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ORIGINAL ARTICLE

Treatment Outcomes of Cavernous Sinus Dural Arteriovenous Fistulas: Comparison of Radiosurgery and Endovascular Embolisation

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Abstract

Background and Purpose Endovascular treatment (EVT) and stereotaxic gamma-knife radiosurgery (GKRS) can both effectively treat cavernous sinus dural arteriovenous fistulas (CSDAVF). This study compared the prognostic factors and treatment effectiveness of GKRS and EVT for different CSDAVF types.

Methods The charts of 200 patients undergoing GKRS and 105 patients undergoing EVT were reviewed for data on symptoms (e.g. orbital, cavernous, ocular, and cerebral). The CSDAVFs were classified into proliferative, restrictive, and late restrictive types. The prognostic factors for complete obliteration (CO) were evaluated in both the GKRS and EVT groups and the latent period to CO was measured. For statistical analysis χ^2-tests were used to compare final CO rates for EVT and GKRS across the three CSDAVF types.

Results The EVT and cavernous symptoms were significant independent predictors of CO. The CO rate after EVT (97.9%) was significantly higher than that after GKRS (63.5%) for restrictive CSDAVFs ($P<0.001$) but not for proliferative or late restrictive types. In the GKRS group, cavernous symptoms (hazard ratio, HR: 0.557) and target volume (HR: 0.853) predicted CO, but only target volume remained significant in multivariate analysis. In the EVT group, the latent period to CO was shortest for restrictive CSDAVFs (3.2 ± 1.6 months, $P=0.05$).

Conclusion Angioarchitecture did not affect treatment outcomes. Cavernous symptoms were strongly associated with lower complete obliteration rates in the GKRS but not the EVT group. The EVT method remains the treatment of choice, especially for restrictive CSDAVFs; however, compared to EVT, GKRS had lower complication rates and similar therapeutic effects for proliferative type fistulas.

Keywords Angioarchitecture · Arteriovenous fistula · Cavernous sinus · Endovascular treatment · Gamma knife

Abbreviations

CSDAVF	Cavernous sinus dural arteriovenous fistula
CO	Complete obliteration
EVT	Endovascular treatment
GKRS	Gamma knife radiosurgery
VOS	Venous outflow score

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Introduction

Dural arteriovenous fistulas (DAVFs) make up 7–15% of all intracranial arteriovenous malformations [1]. Cavernous sinus dural arteriovenous fistulas (CSDAVFs) are the most common type of DAVF in Asian populations [2, 3]. Unlike DAVFs in other locations, CSDAVFs are relatively benign due to their location outside the dura and possession of multiple extracranial and intracranial venous outlets [4]. Like the Borden and Cognard classification, the Barrow classification of carotid cavernous fistulas has been adapted for the classification of CSDAVFs. To facilitate microsurgery, the Barrow system divides indirect CSDAVFs into types B, C, and D depending on whether the arterial blood supplier is the external carotid artery, internal carotid artery, or both. Among the endovascular treatment (EVT) options, the transvenous approach is considered to be the treatment of choice and is associated with a 73–90% cure rate and relatively low complication rate in studies of more than 100 patients [5, 6].

Using the relationship between symptoms and venous drainage routes in CSDAVFs as a basis for a classification system, Suh et al. divided CSDAVFs into proliferative, restrictive, and late restrictive types [7]. Proliferative CSDAVFs receive numerous arterial feeders and are drained by multiple venous outlets; therefore, they mostly cause cranial nerve deficits. Late restrictive CSDAVFs drain primarily into the superior ophthalmic veins, and patients tend to present with ocular symptoms such as increased orbital pressure. Restrictive CSDAVFs are transitional between proliferative and late restrictive CSDAVFs, and patients typically exhibit a combination of cranial nerve and ocular symptoms. If the inferior petrosal sinus (IPS) or superior petrosal sinus (SPS) is involved, tinnitus will develop; if the middle cerebral vein or perimesencephalic vein is involved, which is rare, the patient might have neurologic deficits such as altered memory function, ataxia, or intracranial hemorrhage [8].

Recently, Luo et al. showed a significantly lower cure rate for proliferative (50%) than for restrictive and late restrictive CSDAVFs (50% versus 73% and 86%, respectively) [9]. Due to the relatively benign clinical course of most CSDAVFs, and the absence of reported hemorrhage or cranial paralysis during the latent period of stereotaxic gamma-knife radiosurgery (GKRS), GKRS is also considered to be an effective treatment for CSDAVFs [10]. The overall obliteration rate of CSDAVFs treated by GKRS is 70–80%, which is comparable to the rate for EVT [5, 9, 11]; however, the obliteration rate for specific types of CSDAVF as well as the impact of the angioarchitecture of the CSDAVFs is a relatively unexplored area [10, 12, 13]. The use of GKRS produces radiation necrosis of the vascular walls in the shunting to obliterate DAVFs, and theoretically the results of GKRS are less affected by venous outlet patterns than EVT [14]. Certain angioarchitectural features of CSDAVFs may have equivalent therapeutic responses to GKRS and EVT. So far, no direct comparison of the therapeutic effects of GKRS and EVT in treating CSDAVFs has been attempted. The aim of this study was thus to 1) compare the treatment effectiveness of GKRS and EVT, and 2) explore whether clinical symptoms or angiographic factors can help predict the outcomes of CSDAVFs treated with EVT or GKRS.

Materials and Methods

Patient Selection and Evaluation of Symptoms

This study was approved by the local ethics committee, and the board waived the informed consent requirement. Retrospectively, CSDAVF patients from our GKRS logbook were consecutively included who had received GKRS between 2002 and 2016, and patients from the angio room logbook who had received EVT. Excluded were patients who did not have complete digital subtraction angiography (DSA) on the date of treatment recorded in the picture archive and communications system ($n=21$), patients with direct type DAVFs ($n=9$), patients who experienced spontaneous regression before treatment ($n=2$), patients who had received prior treatment outside of the hospital ($n=5$), and patients with known Klippel-Trenaunay-Weber syndrome ($n=1$) or fibromuscular dysplasia ($n=1$). Patients' symptoms were identified by chart review and classified into orbital symptoms (chemosis, exophthalmos, periorbital pain and eyelid swelling), cavernous symptoms (ptosis, diplopia, anisocoria and ophthalmoplegia), ocular symptoms (ocular pain, glaucoma and retinal hemorrhage) and cerebral symptoms (altered memory function, ataxia and intracranial hemorrhage) [7].

Gamma-Knife Radiosurgery

The boundaries of the CSDAVFs targeted for irradiation were delineated using stereotactic magnetic resonance (MRA) and stereotactic digital subtraction angiography (DSA). Targets were generally delimited by the involved sinus wall, with arterial feeders and venous outflow excluded. Subsequent dose planning was based on findings from the integrated images. The dose planning strategy was to deliver an adequate radiation dose to the delineated target, while sparing the adjacent critical structures. Cranial nerve paralysis and brain stem injury are rare complications of GKRS [10]. Multiple isocenters were used to improve the dose conformity of the treatment volume (the median number of isocenters was 4) [15]. The average radiation volume was 6.97 ± 6.46 ml, the average target volume was 3.36 ± 4.96 ml, the average peripheral dose was 16.70 ± 3.08 Gy, and the average maximum dose was 23.22 ± 6.84 Gy. The abovementioned radiation parameters were used only in the subgroup analysis of the complete obliteration (CO) rate (see *treatment outcome evaluation*) for the GKRS group.

Endovascular Treatment

Detachable coils were available for use at the beginning of this study period. Intravenous access was preferred because it is relatively safe and associated with a low complication rate [6, 16]. A simple trans-inferior petrosal sinus (IPS) approach achieved successful embolization in 100 (95.2%) cases. If the occluded IPS could not be recanalized, which is common in late restrictive type CSDAVFs, attempts were made to navigate through the facial vein ($n=5$, 0.9%), through direct puncture ($n=3$, 2.8%), or by using an intra-arterial approach ($n=6$, 5.6%) [17, 18]. In the next step one or two microcatheters were placed in the fistula compartment of the cavernous sinus and the fistula was filled with detachable coils until the shunt disappeared; if there was residual flow in the fistula Onyx (Covidien Vascular Therapies, Irvine, CA, USA) was used to obliterate the fistula ($n=15$, 14.2%), or the procedure was terminated in cases in which using Onyx was considered too risky based on an assessment of the angiographic architecture ($n=19$, 18.1%). Progressive thrombosis in nearly obliterated CSDAVFs is anticipated [19]. The average coil length used was 260.2 ± 179.3 cm. The average amount of Onyx used was 1.4 ± 0.74 ml in 15 patients (14.2%). The length of coil used and the amount of Onyx used in the subgroup analysis were included to determine the rate of complete obliteration (CO, see *treatment outcome evaluation*) for the EVT group.

Angioarchitecture Analysis

The DSA performed on the same day as either GKRS or EVT was used for the angioarchitecture analysis. Barrow and Suh classifications were applied (Fig. 1) and patterns of arterial feeders and drainage veins were classified by 2 interventionists with 27 and 12 years of experience, respectively, working independently. Discrepancies were discussed by the two interventionists until agreement was reached. The label "fluffy" was applied to designate the presence of innumerable arterial feeders, especially from

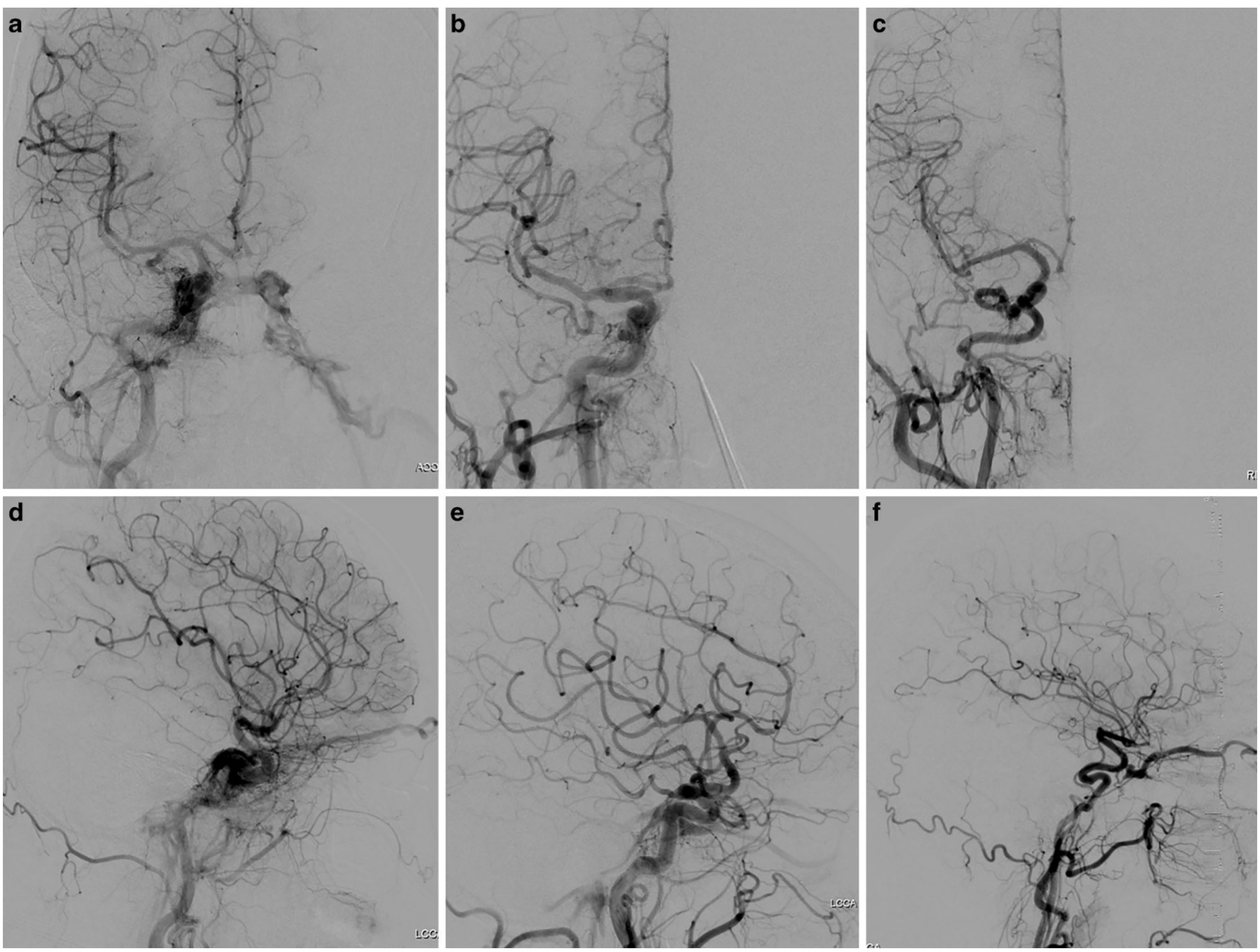

Fig. 1 Suh's classification of CSDAVFs into three different types: **a, d** The proliferative type CSDAVF. Note that the cavernous sinus has poorly delineated contours, innumerable arterial feeders, and multiple venous outlets. **b, e** The restrictive type CSDAVF. This type has fewer arterial feeders and venous outlets. **c, f** The late restrictive type CSDAVF shows drainage into a solitary venous outlet, usually the superior ophthalmic vein

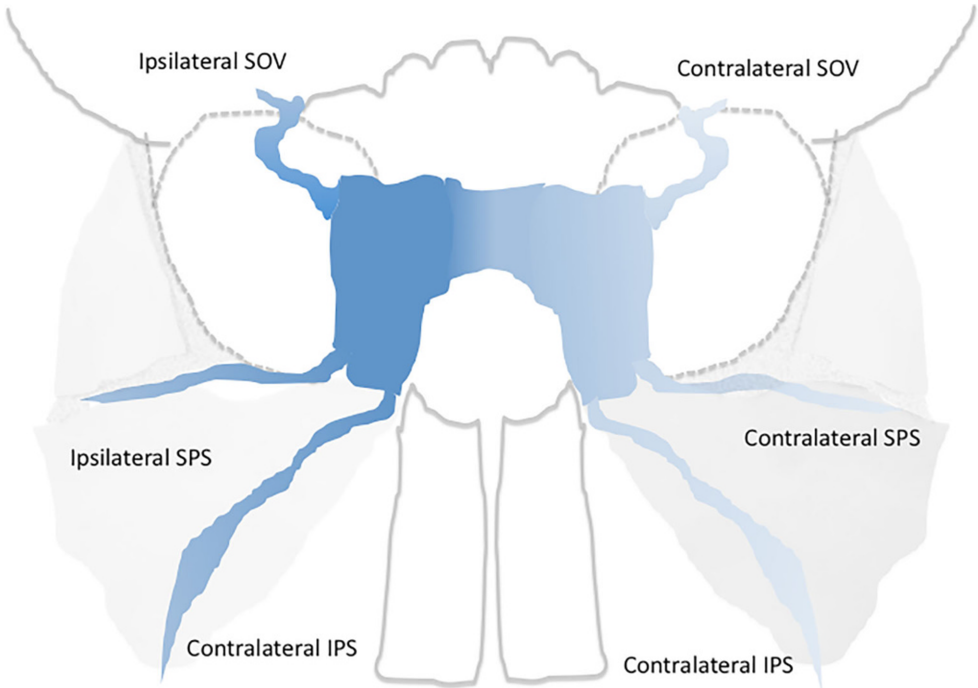

Fig. 2 Illustration of six major venous outflows of a cavernous sinus dural arteriovenous fistula. *SOV* superior ophthalmic vein; *SPS* superior petrous sinus; *IPS* inferior petrous sinus

the internal maxillary artery and ophthalmic arteries. There were six venous outlets: the ipsilateral superior ophthalmic vein, ipsilateral superior petrosal sinus, ipsilateral inferior petrosal sinus (IPS), contralateral superior ophthalmic vein, contralateral superior petrosal sinus, and contralateral IPS. The venous outlet score (VOS) was defined as the number of venous outlets ranging from 0 (no venous outlets) to 6 (all 6 of the abovementioned venous outlets; Fig. 2). Cortical venous drainage (CVD) was defined as venous reflux into any of the following vessels: the superior middle cerebral vein, the perimesencephalic vein, and the cerebellar vein.

Treatment Outcome Evaluation

Initial treatment outcome was only evaluated in the EVT group. Immediate CO was defined as complete disappearance of abnormal fistula flow in immediate control angiography following EVT. All patients with immediate CO were followed up with control DSA 1 year later. All patients in the GKRS group and those with incomplete obliteration in the EVT group received follow-up treatment on an outpatient basis as needed, with MRA every 6 months until the MRA showed CO, and then a final control digital subtraction angiography to confirm CO. Final CO was defined for both groups as complete disappearance of abnormal fistula flow on follow-up MRA or DSA. The negative predictive value of post-GKRS MRA is high [20]. If symptoms persisted or worsened, then timely imaging was arranged. If there was any residual fistula in the last follow-up DSA or MRA, the treatment outcome was not categorized as CO. The primary endpoint was defined as either CO or receiving continued treatment. Complications were defined as any newly developed post-treatment ischemic or intracranial hemorrhage, confirmed by brain CT or MRI. A T2-weighted hyperintensity in the perilesional white matter on MRI was considered indicative of acute radiation effects. Transient cranial paresis was defined as worsening of cranial nerve function after initial treatment. Recurrence was defined as reappearance of a CSDAVF after CO.

Statistical Analysis

Statistical analyses were conducted using SPSS for Windows (version 20; IBM-SPSS, Chicago, IL, USA). The results are presented as medians (ranges) and numbers (percentages) for categorical and continuous variables, respectively. The χ^2-test was used to analyze the effects of gender, different symptoms, innumerable feeders, CVD, and immediate and final treatment outcomes. Kendall's tau was used to analyze Barrow and Suh's classifications. Mann-Whitney U-tests were used to evaluate VOS, and independent *t*-tests to compare the ages of patients in the GKRS and EVT groups. We also used Cox regression was also used as needed to determine the CO rate with respect to treatment options, symptoms, Suh's classification, presence or absence of innumerable feeders, VOS, CVD, embolization agent and radiation profile, after adjustment for gender and age. Only those variables with *P*-values less than 0.10 in univariate analyses were subsequently included in multivariate analyses. The latent periods before CO among different angiographic types in the GKRS and EVT groups

Table 1 Characteristics of patients with CSDAVFs treated by either GKRS or EVT

	GK radiosurgery ($n=200$)	Endovascular treatment ($n=105$)	*P*
M/F (%)	61/139 (30.5%)	31/74 (29.5%)	0.511
Age (years)	63.2 ± 13.5	64.6 + 13.8	0.496
Orbital symptoms	125 (62.5%)	75 (71.4%)	0.444
Cavernous symptoms	102 (51%)	56 (53.3%)	0.412
Ocular symptoms	75 (37.7%)	46 (42.9%)	0.180
Cerebral symptoms	45 (22.5%)	30 (28.6%)	0.157
Tinnitus	33 (17.5%)	20 (19.0%)	0.349
Barrow classification (B/C/D)	40/77/83	6/4/94	0.007*
Suh's classification (P/R/L)	49/92/59	33/58/14	0.01*
Numerous feeders (%)	86 (43.0%)	44 (41.9%)	0.476
VOS	1 (1–2)	2 (1–3)	0.001*
CVD	66 (33.0%)	31 (29.5%)	0.313

P/R/L proliferative/restrictive/late restrictive, *VOS* venous outflow score, *CVD* cerebral venous reflux
*statistically significant

Table 2 Cox regression analysis of CSDAVF treatment outcomes[a]

Complete obliteration Variable	*n*	Univariate HR (95% CI)	*P*-value	Multivariate HR (95% CI)	*P*-value
Treatment	237	–	0.001[b]	–	0.000[b]
GKRS	154	Ref		Ref	–
EVT	83	3.125 (2.16–4.50)		3.828 (2.723–5.383)	–
Symptoms					
Orbital symptoms	206	1.157 (0.807–1.659)	0.427	–	–
Cavernous symptoms	206	0.640 (0.451–0.907)	0.012[b]	0.584 (0.410–0.832)	0.003[b]
Ocular symptoms	206	0.903 (0.649–1.257)	0.547	–	–
Cerebral symptoms	206	0.907 (0.626–1.307)	0.600	–	–
Tinnitus	206	0.996 (0.687–1.487)	0.983	–	–
Angiographic findings					
Suh's classification	258	–		–	–
Proliferative type	63	Ref		–	–
Restrictive type	121	0.974 (0.604–1.572)	0.916	–	–
Late restrictive type	53	1.298 (0.846–1.911)	0.233	–	–
VOS	237	0.998 (0.861–1.157)	0.979	–	–
Innumerable feeders	103	0.574 (0.015–1.115)	0.188	–	–
Cerebral venous reflux	74	1.094 (0.915–1.309)	0.324	–	–

VOS venous outflow score, *CI* confidence interval, *HR* hazard ratio, *GKRS* gamma knife radiosurgery, *EVT* endovascular treatment, *CSDAVF* cavernous sinus dural arteriovenous fistula
[a]with adjustment for age and sex
[b]statistically significant

were determined using the Kaplan-Meier method and compared using the Breslow test. Final CO rates were compared with a χ^2-test. Statistical significance was set at $P < 0.05$.

Results

Patient Demographics

There were no significant between-group differences in any of the clinical symptoms. There were significantly more Barrow type D CSDAVFs, and fewer late restrictive type CSDAVFs in the EVT group than in the GKRS group. The imbalance of patients with late restrictive morphology be-

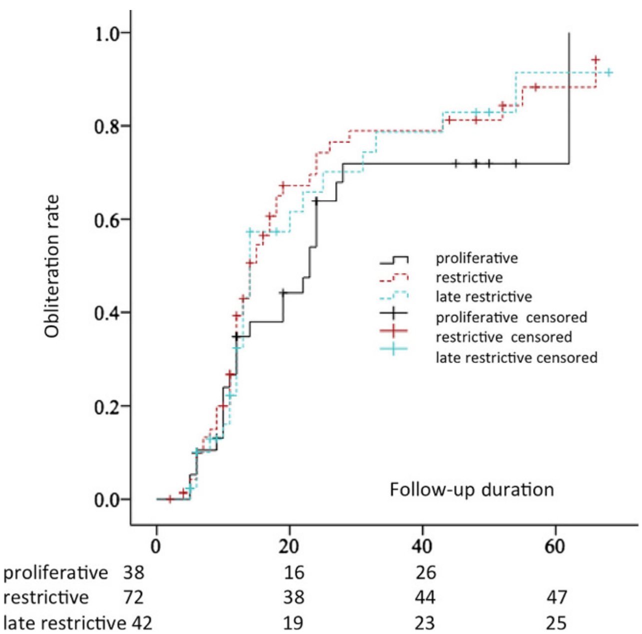

Fig. 3 Rate of complete obliteration 5 years after GKRS in CSDAVFs by Suh's classification type. The x-axis represents the number of patients achieving complete obliteration

tween the two groups was largely a result of the belief during the first 11 years included in the database (2002–2012) that transvenous embolization was unlikely to be successful due to occlusion of the IPS; during this period patients with late restrictive morphology were predominantly referred for GKRS. The VOS scores were significantly lower in the GKRS group than in the EVT group (Table 1).

Associations between Angiographic Factors and Complete Obliteration

After adjusting for age and sex, Cox regression showed that treatment option was an independent predictor of CO. The use of EVT was more highly associated with CO (hazard ratio, HR: 3.828, 95% confidence interval, CI: 2.723–5.383; $P<0.001$) than GKRS. Having cavernous symptoms was also an independent predictor of CO (HR: 0.584, 95% CI: 0.410–0.832; $P=0.003$). Neither Suh's classification, VOS, CVD, nor multiple feeders were associated with the likelihood of CO (Table 2). In the EVT group, the initial CO rate was highest for restrictive CSDAVFs (74.1%), followed by late restrictive CSDAVFs (57.1%), and proliferative CSDAVFs (27.3%). The effect of EVT was greater than that of GKRS for all three types of CSDAVF; however, the final CO rate was significantly higher only for restrictive type CSDAVFs for the EVT group (97.9%) than for the GKRS group (63.5%; $P<0.001$).

Treatment Response in the GKRS Group

The overall CO rate was 63.5%, and the median duration to CO was 15 months (interquartile range, IQR 11–31 months, $n=98$) in the GKRS group. The median duration to CO was longer for proliferative CSDAVFs (23 months, IQR 11–62 months, $n=26$) than for restrictive CSDAVFs (14 months, IQR 11–26 months, $n=47$) and late restrictive CSDAVFs (14 months, IQR 12–33 months, $n=25$), but the differences were not significant ($P=0.532$; Fig. 3). Independent negative predictors of CO included having cavernous symptoms (HR: 0.557, 95%, CI: 0.363–0.854; $P=0.007$) and target volume (HR: 0.853, 95% CI: 0.739–985; $P=0.031$). No association was found between radiation volume, peripheral dose, maximum dose, symptoms, or angiographic parameters and CO (Table 3). Of the patients two (1%) developed a post-procedural 6th nerve palsy, but no occurrences of acute radiation effects or intracranial hemorrhage, and no recurrence.

Treatment Responses in the EVT Group

The overall initial CO rate was 57.1% in the EVT group. The Suh et al. classification was the only predictor of immediate CO for CSDAVFs: the initial CO rate was significantly higher for restrictive CSDAVFs (74.1%) than for late restrictive (57.1%) and proliferative CSDAVFs (27.3%, $P<0.001$). The overall final CO rate was 92.6% in the EVT group. There were significant differences in the CO rate between the Suh et al. classification types (Fig. 4). The duration of CO was significantly shorter for restrictive type CSDAVFs (3.3 ± 1.6 months) than late restrictive (8.4 ± 1.5 months) and proliferative type CSDAVFs (9.1 ± 2.7 months, $P=0.05$). No associations were found between VOS, CVD, innumerable feeder arteries, coil length, or onyx amount used and CO (Table 4). There were 3 (2.8%) minor thromboembolic events without major neurologic deficits or mortality, 35 (33.3%) cases had periprocedural transient cranial 6th ($n=28$) and/or 3rd nerve (7) paresis, all resolving spontaneously within 2 months, no cases of intracranial hemorrhage and 1 case of a restrictive type that recurred 2 months after EVT treatment but subsequently spontaneously occluded.

Discussion

Angioarchitecture of CSDAVF

The vigorous blood flow in proliferative type CSDAVFs causes swelling of the cavernous sinus and therefore leads mainly to cavernous symptoms, followed by orbital symptoms [7]. The fact that outcomes are worse in proliferative

Table 3 Cox regression analysis of GKRS outcomes[a]

Complete obliteration Variable	*n*	Univariate HR (95% CI)	*P*-value	Multivariate HR (95% CI)	*P*-value
Symptoms					
Orbital symptoms	128	0.876 (0.555–1.383)	0.570	–	–
Cavernous symptoms	102	0.557 (0.363–0.854)	0.007[b]	0.643 (0.369–1.112)	0.119
Ocular symptoms	75	0.953 (0.635–1.430)	0.817	–	–
Cerebral symptoms	44	0.918 (0.579–1.456)	0.717	–	–
Tinnitus	33	1.072 (0.649–1.771)	0.785	–	–
Angiographic findings					
Suh et al. classification	200	–		–	–
Proliferative type	49	Ref		–	–
Restrictive type	92	0.788 (0.449–1.382)	0.406	–	–
Late restrictive type	59	1.027 (0.627–1.681)	0.916	–	–
VOS	200	0.881 (0.726–1.069)	0.198	–	–
Innumerable feeders	200	0.784 (0.0523–1.176)	0.239	–	–
Cerebral venous reflux	74	1.189 (0.950–1.448)	0.131	–	–
Radiation profile					
Target volume (ml)	102	0.853 (0.739–0.985)	0.031[b]	0.863 (0.746–0.998)	0.046[b]
Radiation volume (ml)	102	0.932 (0.855–1.015)	0.103	–	–
Maximum dose (Gy)	102	0.968 (0.961–1.089)	0.590	–	–
Peripheral dose (Gy)	102	1.209 (0.957–1.927)	0.112	–	–
Percentage (%)	102	1.025 (0.985–1.067)	0.231	–	–

VOS venous outflow score, *HR* hazard ratio
[a]With adjustment for age and sex
[b]statistically significant

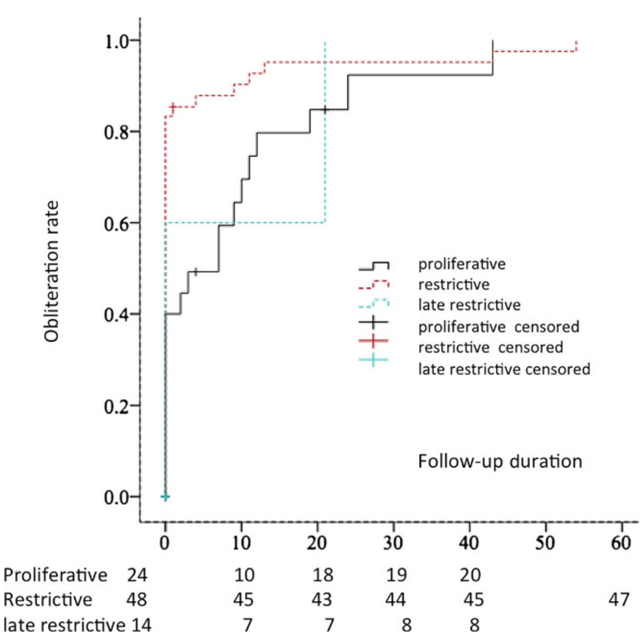

Fig. 4 The rate of complete obliteration 5 years after EVT in CSDAVFs by Suh et al. classification type. The x-axis represents the number of patients achieving complete obliteration

type CSDAVFs than in the other two types, regardless of treatment, suggests that cavernous symptoms are predictors of incomplete obliteration. Certain restrictive and all proliferative type CSDAVFs were also found to shared the feature of innumerable arterial feeders. Conversion from restrictive to late restrictive type with less venous outlets is part of the natural history or post-treatment response of the CSDAVF [21–23]. The study confirmed that the natural course of CSDAVF evolution is from proliferative to restrictive type and subsequently to late restrictive type but the duration of the evolution varies from one individual to another. It appears that timely diagnosis can affect the therapeutic outcome given that the CO rate is highest for restrictive type CSDAVFs.

Venous Outflow

The characteristic multiple channels of the cavernous sinus (CS) represent a two-edged sword for embolization: unlike DAVFs in other locations, CSDAVFs cured by occluding the CS rarely cause neurologic sequelae because the sinus has multiple potential venous drainage outlets [24]. On the

Table 4 Cox regression analysis of EVT outcomes[a]

Complete obliteration					
Variable	*n*	Univariate		Multivariate	
		HR (95% CI)	*P*	HR (95% CI)	*P*
Symptoms					
Orbital symptoms	33	0.690 (0.370–1.285)	0.242	–	–
Cavernous symptoms	27	0.708 (0.374–1.138)	0.287	0.669 (0.349–1.282)	0.225
Ocular symptoms	26	1.64 (0.582–1.927)	0.840	–	–
Cerebral symptoms	19	0.996 (0.531–1.877)	0.996	–	–
Tinnitus	20	1.072 (0.649–1.771)	0.785	–	–
Angiographic findings					
Suh et al. classification	–	–		–	–
Proliferative type	19	Ref		Ref	–
Restrictive type	29	0.841 (0.287–2.462)	0.752	1.570 (0.558–4.415)	0.861
Late restrictive type	6	1.418 (0.515–3.902)	0.499	0.669 (0.349–1.282)	0.393
VOS	54	0.935 (0.729–1.199)	0.596	–	–
Innumerable feeders	54	1.390 (0.762–2.537)	0.283	–	–
Cerebral venous reflux	54	1.010 (0.738–1.382)	0.950	–	–
Device profile					
Coil length (cm)	54	0.762 (0.998–1.002)	0.779	–	–
Onyx (ml)	15	0.701 (0.367–1.339)	0.282	–	–

VOS venous outflow score, *HR* hazard ratio
[a]With adjustment for age and sex

other hand, it is also technically demanding to obliterate all venous outflow. Although the risk of diverting flow from a posterior collateral to the pontomesencephalic vein via a bridging vein is low, a few cases have been reported of worsening symptoms or brain stem edema due to alteration of the flow direction following embolization [25]. Recurrence or redirection of flow should be taken into account if the symptoms change during the latent period of treatment. Satomi et al. observed that the possibility of developing CVD was low after partial treatment because the posterior drainage routes of CSDAVFs tend to close before the anterior drainage routes [26, 27]. It is necessary to ensure that there is no CVD at the end of embolization. In contrast to much of the existing literature, Liu et al. reported that venous outflow score (VOS) was not predictive of treatment outcome since the treatment of late restrictive type CSDAVFs (with a solitary venous outlet) had a lower success rate [28]. Compartmentalization of the cavernous sinus was associated with less venous outflow and fewer cases of CO in the EVT group. Compartmentalization is of less concern with GKRS because the cranial III, IV and VI nerves have a high tolerance for radiation [29].

EVT Treatment

The immediate CO rate for restrictive CSDAVFs is higher than that for proliferative and late restrictive CSDAVFs because the chronicity of the late restrictive type is longer than that of the restrictive type. Therefore, the risk of chronically occluded IPS recanalization is lower [23–26]. Closing the extensive shunting zone of the proliferative type is equivalent to obliteration of almost the whole cavernous sinus. Additionally, interventionists need to close all venous outlets before embolization to achieve CO. These dual challenging tasks explain the lower initial CO rate for proliferative CSDAVFs. Onyx has the potential to improve the immediate CO rate but it carries the potential risks of trigeminocardiac reflex-induced bradycardia or damage to the cranial III, IV and V nerves [30, 31]. Using detachable coils alone can also achieve a satisfactory final CO rate but might result in transient cranial paresis due to a mass effect [21–32]. In the only case of CSDAVF recurrence in the EVT group, no residual shunt was detected in the immediate control angiography. Previously reported cases of recurrence after morphologic resolution of the CSDAVF were associated with overlooked residual shunting hidden by the embolization agent in immediate control angiography or arising de novo from an adjacent region [33, 34]. Progressive sinus thrombosis, angiogenesis after manipulation, or regrowth of a pre-existing second angiographic occult DAVF have been hypothesized [35].

GKRS Treatment

The incidence (33%) of cortical venous drainage (CVD) from CSDAVFs in the GKRS group was similar to that from DAVFs in other locations [10, 36]. The CVD was more often associated with venous outflow restriction and more aggressive behavior of the DAVF in other locations [3, 36] and was associated with a lower likelihood of CO following GKRS in an earlier pooled analysis [10] but not in the present study. The explanation is that venous outflow from multiple sites in the cavernous sinus decreased the severity of the CVD. No patients experienced worsening of neurologic deficits or intracranial hemorrhage in the GKRS group during the latent period, confirming the safety of GKRS as an alternative treatment for CSDAVF, even in the presence of CVD. The use of GKRS induces a wide spectrum of radiobiological responses in small-size vessel walls such as perivascular or subendothelial edema, fissuring of the wall, intraluminal hemorrhage, thrombus formation, necrosis of endothelial cells, increased interstitial colloids, and increased fibroblastic activity, subsequently leading to therapeutic effects on arteriovenous malformations as well as fistulas [14, 37]. These arterial feeders are located on the sinus wall and should be the target of irradiation. In the current study, no significant differences were found in final CO rates for the three types of CSDAVF or for the presence of innumerable feeders. This suggests that the therapeutic effect of GKRS is due primarily to the radiation profile rather than the angioarchitecture. In patients with a similar disease, cerebral arteriovenous malformation, Taeshineetanakul et al. found an association between the obliteration rate and higher flow through feeding arteries but not with venous morphology [38].

Limitations

There were several limitations to this study. First of all, this was a retrospective study covering a long period of time. A prospective randomized trial is warranted to confirm the results. Secondly, liquid embolic agents such as Onyx became treatment options part way through this period; however, the treatment strategy consistently involved the use of detachable coils as the initial strategy and therefore the study population was relatively homogeneous. Although Onyx used as the first-line embolization agent for proliferative CSDAVFs might potentially increase the immediate CO rate, it also increases the risk of complications. Further evaluation of long-term outcomes is needed. Thirdly, a higher percentage of patients in the GKRS group than in the EVT group experienced symptom relief and did not return for follow-up, possibly leading to an underestimation of the therapeutic effects of GKRS. Fourthly, the complication rates for both groups were too low to analyze the contribution of CSDAVF types. To the best of our knowledge, this is the first study to compare the effects of EVT and GKRS based on symptomology and angioarchitecture. Finally, the relatively small sample size of late restrictive type CSDAVFs ($n = 14$) in the EVT group may have resulted in a type II error and it is difficult to draw any conclusions on the comparative efficacy of the two treatments for this particular morphology. This could be assessed further in a prospective cohort study.

Conclusion

Cavernous symptoms were found to be a useful clinical predictor of a low complete obliteration rate. The EVT remains the treatment of choice to resolve CSDAVF, especially for restrictive type CSDAVFs; however, in this study, GKRS had a lower complication rate and had a relatively homogeneous therapeutic effect on all types of CSDAVFs. The use of GKRS had therapeutic effects on proliferative type CSDAVFs that were similar to those of EVT.

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Conflict of interest H.-C. Yang, C.-J. Lin, C.-B. Luo, C.-C. Lee, H.-M. Wu, W.-Y. Guo, W.-Y. Chung and K.-D. Liu declare that they have no competing interests.

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