Complication risk of endovascular embolization for cerebral arteriovenous malformation

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ABSTRACT

Objective: The embolic agents currently used for the treatment of AVMs are n-butyl cyanoacrylate (NBCA) and ethylene-vinyl alcohol copolymer (ONYX). The purpose of this study was to examine the overall NBCA and ONYX embolization-related complication rate.

Methods: We retrospectively reviewed 147 consecutive patients with cerebral AVMs treated mainly with endovascular NBCA and ONYX embolization. Demographics, including age, sex, presenting symptoms, and angiographic factors including AVM size, deep venous drainage, and involvement of eloquent cortex were recorded. Number of pedicles embolized, the obliteration rate, and any complications were recorded. Complications were classified as the following: bleeding and ischemic complications. The ischemic complications were also classified as transient neurologic deficit, and permanent deficits. Modified Rankin Scale (mRS) scores were collected pre- and postembolization on all patients. Univariate regression analysis of determinants of complications was performed.

Results: We reviewed 147 patients with BAVM (58.5% male; mean age ± SD at treatment: 27.5 ± 11.1 years) treated with endovascular embolization. Two hundred twenty embolization, 144 NBCA and 76 ONYX embolizations were performed. Complete obliteration of BAVMs were achieved in 29 patients (19.7%). Additional gamma-knife radiosurgery were performed for 32 (21.8%) patients. There were 5 Spetzler–Martin grade I (3.4%), 20 grade II (13.6%), 54 grade III (36.7%), 44 grade IV (30%), and 24 grade V (16.3%) AVMs. There were a total of 7 (4.8% per patient, 3.2% per procedure) complications. There were bleeding complications in 2 patients (1.4% per patient, 0.9% per procedure), transient neurologic deficits in 4 (2.7% per patient, 1.8% per procedure) and 1 permanent deficit (0.7% per patient, 0.5% per procedure). Of the 147 patients, 141 (95.9%) were mRS 0–2, 6 (4.1%) were mRS = 3 at discharge. Univariate analysis of risk factors for embolic agent showed that ONYX was not significantly associated with complications ($X^2 = 0.3, P > 0.5$).

Conclusions: Embolization of brain AVMs is safe, 95.9% of patients had excellent or good outcomes at discharge after AVM embolization using liquid embolic agents, with a complication rate of 4.8%. ONYX embolization was not associated a higher rate of complications comparing with NBCA embolization.

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rhages and any prior treatment and angiographic features including maximal size, location, presence of deep venous drainage, and involvement of eloquent cortex. These factors were used to arrive at a Spetzler–Martin grade for each AVM. For each embolization session, the number of pedicles embolized, the agents used, and the overall percentage of volume reduction was recorded as well as any complications that occurred during the procedure. Complications were categorized as the following: bleeding and ischemic complications. The ischemic complications were also classified as transient neurologic deficits (defined as new neurologic deficits that resolved completely within 7 days), and permanent deficits.

2. Management of AVM

Endovascular embolization procedures were performed intraarterially via a transfemoral route with the patients under general endotracheal anesthesia. Standard transfemoral angiographic technique was used to obtain global angiographic images of the internal carotid arteries and vertebral arteries as appropriate. Systemic heparinization was initiated before microcatheter navigation, to achieve an activated clotting time (ACT) 2–3 times the normal clotting time. Superselective catheterization was performed by using flow-directed microcatheters of the arterial pedicles supplying the nidus. Following careful analysis of the superselective angiogram, embolization was performed by using either NBCA or ONYX (Onyx18). Detachable coils have also been used in the obliteration of AV fistulae and to decrease flow in AVMs in preparation for NBCA in 15 patients. If necessary, multiple pedicles were embolized at 1 session, with the goal to typically embolize no more than 30–40% of the nidus in any 1 setting. Postprocedure, heparin therapy was not routinely reversed with the administration of protamine. All patients were observed closely and strict blood pressure control after embolization. The mean arterial pressure was kept typically between 65 and 75 mm Hg for 24–48 h postembolization. Subsequent embolizations were performed typically at 3- to 6-month intervals. Additional gamma-knife radiosurgery were performed for 32 patients at 1 month after embolization.

3. Statistical analysis

We analyzed patient age, sex, history of seizures, associated aneurysms, periprocedural hemorrhage, AVM size, deep venous drainage, deep location (basal ganglia/infratentorial), the eloquence of the adjacent brain, Spetzler–Martin grade, number of stages, and primary treatment modality to determine whether these factors were predictive of complications and unfavorable outcomes after embolization. Univariate tests (X² test) and a multivariate logistic regression model were used to describe the effect of these factors on embolization complications. mRS scores were collected on patients before embolization and post-final embolization on all patients. Adjusted odds ratios with 95% confidence intervals are presented. P ≤ 0.05 was considered to be statistically significant.

4. Results

In our series, 147 patients underwent 220 embolization sessions, with a total of 396 pedicles embolized. There were 86 male (58.5%) and 61 female (41.5%) patients, with a mean age of 55.3 ± 10.1 years. Presenting symptoms were hemorrhage in 69 (46.9%), seizure in 43 (29.3%), headache in 21 (14.3%), focal neurologic deficit in 11 (7.5%), and no symptom in 3 (2.0%). There were 5 (3.4%) grade I, 20 (13.6%) grade II, 54 (36.7%) grade III, 44 (30%) grade IV, and 24 (16.3%) grade V patients, separated by Spetzler–Martin grade. The majority (71.4%) of the AVMs were medium-sized AVMs (3–6 cm) with the mean AVM size of 4.0 cm (range 1–8 cm). Deep venous drainage was found in 52 (35.4%) patients, and superficial venous drainage was noted in 95 (64.6%) patients. AVM location was eloquent adjacent brain tissue in 113 (76.9%) patients. Twelve (8.2%) BAVMs were located infratentorial location and 135 (91.8%) were supratentorial. Seven (4.8%) patients had 9 associated aneurysms rising from feeding artery (Fig. 1).

Patients underwent a total of 220 embolization sessions, with 91 (61.9%) having 1 session, 42 (28.5%) having 2 sessions, 12 (8.2%) having 3 sessions, and 2 patients (1.4%) having 4 or more sessions of embolization. There were 98 sessions (44.5%) performed within 1–2 months in patients who had ruptured AVM. NBCA was used in 144 embolizations (63.5%), ONYX (Onyx18; M.T.I-ev3, Irvine, CA) in 76 embolizations (34.5%), and coils were used adjunct to NBCA in 15 embolizations. Mean volume reduction was 33% (range, 5–95%) in NBCA embolization and 63% (range, 10–100%) in ONYX embolization on immediate postembolization angiograms. Additional radiosurgery was performed in 32 patients (21.8%) at 1–2 months following embolization.

There were a total of 7 complications (4.8% of patients, 3.2% of procedures) in this series, of which 2 (1.4% of patients, 0.9% of procedures) were hemorrhagic, and 5 (3.4% of patients, 2.3% of procedures) were ischemic. One hemorrhagic complication was caused by technical microperforation. Of the 5 ischemic complications, transient neurologic deficits in 4 (2.7% per patient, 1.8% per procedure) and 1 permanent deficit (0.7% per patient, 0.5% per procedure) (Table 1).

In a univariate analysis, none of the clinical symptoms, AVM characteristics, or embolization results that were examined was found to be statistically significant (Table 2). Multivariate analysis was not performed because none of the factors met statistical significance in the univariate analysis. There were 141 patients (95.9%) who were mRS 0–2 and 6 were mRS = 3 at discharge.

| Table 1 Complications caused by NBCA and ONYX embolizations. |
|------------------|------------------|------------------|
|                  | NBCA             | ONYX             | Total             |
| Bleeding         | 1                | 1                | 2                |
| Ischemic         | 2                | 3                | 5                |
| Transient neurologic deficit | 1 | 2 | 3 |
| Hemiparesis      | 1                | 2                | 3                |
| Ataxia           | 1                | 0                | 1                |
| Permanent deficits | 0              | 1                | 1                |
| Visual field deficit | 0             | 1                | 1                |

| Table 2 Factors predictive for complications. |
|------------------|------------------|------------------|------------------|
| Factor            | OR (95%CI)        | X²               | P value          |
| Patient age (>30 years) | 2.1 (0.5–9.7)   | 0.9              | >0.25            |
| Sex (female)      | 3.8 (0.8–18.9)   | 2.7              | >0.05            |
| Unrupture         | 2.3 (0.4–11.8)   | 1.0              | >0.25            |
| Associated aneurysms | 3.7 (0.5–30.4)  | 1.5              | >0.10            |
| Spetzler–Martin grade II | 2.7 (0.8–8.7)  | 1.4              | >0.10            |
|            III | 1.3 (0.3–6.5) | 0.1            | >0.50            |
| IV            | 0.9 (0.05–16.5) | 0.005           | >0.9             |
| Embolization sessions | 1                 | 0.6 (0.3–9.1) | 0.3              | >0.5 |
| | 2                 | 0.4 (0.05–3.3)  | 0.7              | >0.25            |
| | 3                 | 2.0 (0.2–18.5)  | 0.4              | >0.25            |
| Embolization materials | Onyx18             | 1.5 (0.4–6.4) | 0.3              | >0.05 |
| Volume reduction (%) | >60               | 0.8 (0.2–2.6) | 0.1              | >0.5 |

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5. Discussion

In this series, there were 7 permanent complications (4.8%) with 0.7% permanent complications and 2.7% transient complications. Five of these were ischemic (3.4% of patients, 2.3% of procedures) and 2 hemorrhagic (1.4% of patients, 0.9% of procedures). There was no mortality in this study. The rate of permanent disabling complications or death in this series is somewhat less than those of many of the more recent series. The reasons for this can be multifactorial and can include patient selection, embolic materials, procedural technique, and postprocedure management. Safer, more permanent embolic agents such as NBCA and ONYX have led to more successful AVM embolization and improved treatment outcomes. Despite improvements in endovascular techniques and embolic agents \[8,14,15,18,19\], the complication profile of brain AVM embolization is of concern and the risks of embolization must be weighed against the potential benefit. There have been several recent large series describing morbidity and mortal-

Fig. 1. A 48-year-old patient with a ruptured parieto-occipital AVM. (A) CT scanning at onset. (B) Right internal carotid artery (ICA) angiogram in lateral projection. (C) Left vertebral artery (VA) angiogram in lateral projection. Demonstrating a parieto-occipital AVM with multiple feeders and cortical veins draining to the superior sagittal sinus (pre-embolization). There was an aneurysm on the feeding artery (arrow). (D) The aneurysm was embolized with ONYX before AVM embolization (arrow head). During AVM embolization, the leakage of contrast medium was found at the inferior part of AVM nidus (arrow), which was fed by the right posterior cerebral artery. This residual nidus was embolized using another Marathon microcatheter. (E and F) Lateral projections of right ICA and left VA angiograms done after embolization. The AVM showed a complete occlusion. (G) Axial CT, performed 1 day later, showed a small combined intraparenchymatous and intraventricular hematoma. This patient was treated with lumbar puncture and recovered completely within 3 weeks.
ity with current embolization technique [5,7,16,20,21]. Hartmann et al. found that 14% patients showed treatment-related neurologic deficits, 2% showed permanent disabling deficits with 1% treatment-related mortality (1%), which is higher than the rate in our series [5]. They also showed that increasing patient age, number of embolizations, and absence of a pretreatment neurologic deficit were associated with new neurologic deficits. They did not test the Spetzler–Martin grade or any specific morphologic features to be predictive of risk for permanent deficit. Ledezma et al. found a total of 16.1% complications in their series, of which 6.5% were clinically significant and 9.5% were technical complications in 168 patients. Their treatment-related mortality was 1.2%, with 2 deaths directly related to embolization. They found that periprocedural hemorrhage and a Spetzler–Martin grade of III through IV were predictive of embolization complications in their multivariate analysis. Hauck et al. reported on preoperative embolization with ONYX in 41 patients undergoing 82 embolization sessions and found an overall 12.2% per-patient rate of permanent deficit [6]. Their rate of permanent deficits is higher than that in our series and those of the other aforementioned recent series and more aggressive rapid volume reduction (75%) may have contributed to the higher rate of permanent deficits in their series. In another recent report, Jayaraman et al. had 8 (4.2%) permanent deficits, 5 (2.6%) ischemic and 3 hemorrhagic (1.6%), and found that basal ganglia location, though not statistically significant, was associated with a higher risk of a new deficit. However, in our univariate analysis, Spetzler–Martin grade was not associated with a higher risk of permanent deficit. In addition, neither the number of pedicles embolized per session nor the total number of embolization sessions was associated with a higher rate of complication in our series. Periprocedural hemorrhage is thought to be caused by microperforation or hemodynamic changes after embolization, mainly by alterations in feeder pressures [21], as demonstrated by our 2 cases. Factors that have been found to predispose to hemorrhage include significant venous embolization, certain angio-architectural features, and persistent venous stagnation within the nidus [4,10,13,14]. In our series, hemorrhagic complications were seen in 2 patients (1.4%). Weber et al. reported ONYX embolization in 93 patients with 80% volume reduction, hemorrhagic complications occurred in 2 patients. Similar to spontaneous intracranial hemorrhage, hemorrhage may present with no symptoms (an incidental finding on routine postprocedure computed tomography), headaches, or more aggressive manifestations such as dense hemiparesis, focal neurologic deficits, coma, and death [1,2,9]. Not all hemorrhages lead to neurologic deterioration, in cases of neurologic deterioration, emergent hematoma evacuation, simultaneous AVM resection, and aggressive perioperative intracranial pressure control can lead to good to excellent outcomes [12].

6. Conclusions

NBCA and ONYX AVM embolization is a safer and more efficacious for AVM embolization. The permanent neurologic deficits rate was low. In a multivariate analysis, and ONYX embolization with a higher volume reduction was not a predictive factor for complications after AVM embolization.

Conflict of interest

We had declared that there was no conflict of interest.

References
