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Efficacy of Endovascular Treatment of Meningiomas: Evaluation with Matched Samples

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PURPOSE: To evaluate the clinical efficacy, cost-effectiveness, and safety of presurgical devascularization of meningiomas. **METHODS:** Matched samples of embolized and nonembolized groups of meningiomas were compared. The study variables for clinical efficacy were estimated blood loss, number of transfusions, surgical resection time, and length of hospitalization. The cost-effectiveness was evaluated by adjusting all hospital costs to 1991 dollar amounts, and adding additional embolization costs and fees to the hospital cost totals for the embolized group. A qualitative comparison of complications was made. **RESULTS:** All dependent variables evaluating the clinical efficacy of the procedure (estimate blood loss, 533 cc versus 836 cc; number of transfusions, 0.39 units versus 1.56 units; surgical resection time, 305.8 minutes versus 337.5 minutes; and length of hospitalization, 10.6 days versus 15.0 days) displayed trends of higher means in the nonembolized group; however, only the estimated blood loss and number of transfusions variables were significant. The cost-effectiveness of the procedure was not statistically significant. The mean cost was $29,605 for the embolized group and $38,449 for the nonembolized group. There were three major and nine minor complications in the nonembolized group and zero major and six minor complications in the embolized group. There were four additional minor complications caused by the embolization procedure. **CONCLUSION:** Endovascular devascularization of meningiomas is beneficial for large meningiomas because it diminishes the necessity of intraoperative transfusions and decreases blood loss. The additional day of hospitalization, embolization costs, and costs of complications do not conversely increase treatment costs. There were no major complications or adverse long-term effects caused by the embolization procedure.

Index terms: Meninges, neoplasms; Interventional neuroradiology; Economics; Efficacy studies

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The term *meningioma* was first suggested by Harvey Cushing in 1922 to describe a benign meningeal tumor (1, 2). Because their clinical course is relatively quiescent, they can grow to large sizes before detection; this has caused a fascination with meningiomas by anatomists, surgeons, and pathologists for centuries. They are common tumors comprising 10% to 15% of intracranial masses. They frequently are vascular lesions which, combined with their large size at presentation, may result in difficulties controlling intraoperative bleeding.

Embolizations of meningiomas preoperatively for control of hemorrhage are relatively recent procedures (3–10) with the advent of suitable embolic materials (11–15) and endovascular techniques (16, 17). Despite the large number of embolizations performed, there have been few studies to support their efficacy (18, 19). The procedure has the potential to lengthen the hospitalization, to cause additional risk to the patient, and to add additional costs to the health care system.

The purpose of this study was threefold: (*a*) to analyze the clinical efficacy of embolization, (*b*) to evaluate its cost-effectiveness, and (*c*) to survey the additional risks of embolization.

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Matched samples (size, location, and angioblastic versus nonangioblastic meningioma subtype) of embolized versus nonembolized meningiomas were statistically compared for the 36 patients included in this investigation.

Materials and Methods

Patient Selection

This study was a retrospective comparison of embolized versus nonembolized matched groups. All of the selected tumors, both embolized and nonembolized, were candidates for embolic devascularization and potentially embolizable by microcatheter techniques. If there were more than one nonembolized matching case for an embolized case, the pair was selected randomly. The groups were first matched by *size* of meningiomas (±½ cm) which, ostensibly, adversely impacts the resection and influences all of the study variables.

Location was the second selective criterion for matching of subjects, because it alters the ease of resection. The meningiomas were compared at two different locations. *Convexity* and *falx* meningiomas can be easily devascularized in the initial stages of the surgical procedure by occlusion of the supplying middle meningeal artery, anterior falx artery, or occasionally the superficial temporal artery. *Subfrontal*, *sphenoid wing*, and *temporal* meningiomas frequently acquire a portion of their blood supply from a location opposite the initial surgical exposure and therefore it is more difficult to gain access to the vascular pedicles supplying blood to the tumor.

The meningiomas under investigation were also partially matched for tumor subtypes. *Angioblastic* meningiomas were matched on a case-by-case basis. All other tumor subtypes (ie, transitional, meningothelial, syncytial) were freely matched, because there is little evidence to differentiate these tumors clearly on the basis of vascularity.

An effort was made to limit the time span of the study (a 5-year period) to ensure that surgical techniques were uniform for all cases. All meningiomas were resected by 5 of 27 neurosurgeons at our institution. The time-span limitation also allowed for more accurate comparison of hospital and procedural costs and length of hospitalization. All hospital costs were adjusted for inflation to 1991 dollar values. The additional costs caused by complications related to the embolization procedure were also included in the total costs.

Variables Studied

Clinical efficacy of the procedure was evaluated by analyzing four dependent variables: (*a*) estimated blood loss during surgery, (*b*) number of transfusions, (*c*) length of the surgical procedure, and (*d*) length of hospitalization. Cost-effectiveness was analyzed by comparing total hospital charges for the two groups; this total was adjusted for inflation. The additional costs incurred for embolization were included for the embolized sample. A qualitative assessment was made of the complications found in the two comparative groups (surgical versus surgical plus embolization).

Embolization Method

All tumors in the embolized group were partially or completely devascularized by a superselective coaxially placed Tracker 18 catheter. Either gelfoam powder (Upjohn) or polyvinyl alcohol particles (Biodyne and ITC) were used in each case. No embolizations were performed from the internal maxillary or external carotid trunks. Larger particle sizes were used when catheter positions were limited to the main middle meningeal artery proximal to the petrous and ophthalmic collaterals. All embolizations were performed by one of three interventionalists with special expertise in neurointerventional procedures.

Statistical Analyses

To test the hypotheses that estimated blood loss during surgery, number of transfusions, length of the surgical procedure, length of hospitalization, and cost-effectiveness are equivalent in patients with embolized and nonembolized meningiomas, Wilcoxon's signed rank tests were applied. This nonparametric test was necessary, because the data did not meet the assumptions for parametric tests. Two-tailed alternative hypotheses that the variables differ between the two groups were used for length of hospitalization and cost-effectiveness. However, for estimated blood loss during surgery, number of transfusions and length of surgical procedure one-tailed alternative hypotheses that estimated blood loss, number of transfusions and length of surgical procedure were reduced for patients with embolized meningiomas were used, because it was felt that increases in these variables could not be attributable to embolization.

Results

There were 226 patients in the 5-year interval who were operated on for resection of a meningioma; 33 embolized and 193 nonembolized patients. There were 18 matches for size, location, and tumor subtypes. The average size of the meningiomas was 5.7 cm for both groups.

The data are presented in Table 1 for estimated blood loss, number of transfusions, length of surgical procedure and hospitalization, and cost-effectiveness. All variables indicated the hypothesized trend of higher values for the nonembolized group. However, only the estimated blood loss and number of transfusions could be considered to be statistically significant ($P = .048$ and $P = .041$, respectively). The

TABLE 1: Variables studied in 18 matched pairs of meningiomas

Patient	EBL, ccs	T, units	S, min	H, d	C, dollars
1E	400	0	480	15	38 549
1N	350	3	320	3	19 508
2E	500	0	195	14	23 698
2N	1 000	1	355	11	25 220
3E	700	0	270	12	30 596
3N	200	0	250	8	43 138
4E	350	0	190	12	21 036
4N	200	0	260	10	25 575
5E	900	0	425	5	26 375
5N	600	0	385	8	22 492
6E	400	0	250	14	32 714
6N	900	0	335	8	23 505
7E	300	3	715	9	31 328
7N	600	2	325	10	24 161
8E	1 500	2	235	8	31 782
8N	300	0	220	22	47 704
9E	500	0	305	10	34 146
9N	800	0	390	16	69 182
10E	350	0	350	6	23 420
10N	500	2	345	15	24 629
11E	400	0	360	7	26 776
11N	600	0	265	33	45 174
12E	1 200	2	210	11	40 214
12N	1 500	7	615	45	95 662
13E	200	0	180	13	24 767
13N	800	1	295	17	47 470
14E	150	0	155	6	16 042
14N	500	0	200	7	20 627
15E	600	0	395	11	32 664
15N	2 000	2	265	9	22 962
16E	600	0	300	11	26 143
16N	600	0	480	9	19 603
17E	350	0	195	21	42 358
17N	3 500	8	435	30	98 379
18E	200	0	240	6	30 296
18N	100	0	335	9	17 082
E average	**533**	**.39**	**305.8**	**10.6**	**29 605**
N average	**836**	**1.56**	**337.5**	**15.0**	**38 449**
P value	.048	.041	.171	.192	.246

Note.—E indicates embolized; N, nonembolized; EBL, estimated blood loss; T, transfusions; S, surgical procedure length; H, length of hospitalization, and C, hospital cost.

remaining dependent variables failed to reach the significance level: for length of surgical procedure, $P = .171$; for length of hospitalization, $P = .192$; and for cost-effectiveness, $P = .246$.

Complications are presented in Table 2 for the surgical procedures of each group along with complications associated with embolization. Three patients developed major complications and nine patients developed minor complications in the nonembolized group. However, for the embolized group, there were no major and six minor surgical complications. In addition, there were a total of four minor complications in three patients attributed to the embolizations.

Discussion

The presurgical management of meningiomas frequently includes an endovascular embolization for devascularization. It is essential to analyze the clinical efficacy, cost-benefit relationship, and complications of the procedure. This retrospective record review was initiated to address these specific issues. Matched groups

TABLE 2: Surgical and embolization complications in 18 matched pairs of meningiomas

Patient	Surgical Complications (Direct or Indirect) Major	Minor	Endovascular Complications	Material
1E	. . .	Cerebrospinal fluid leak Transient expressive aphasia	. . .	Gelfoam
1N	. . .	. . .	. . .	. . .
2E	. . .	. . .	. . .	PVA + Gelfoam
2N	. . .	. . .	. . .	. . .
3E	. . .	Transient L facial droop	. . .	PVA
3N	. . .	. . .	. . .	. . .
4E	. . .	. . .	. . .	Gelfoam
4N	. . .	. . .	. . .	. . .
5E	. . .	. . .	. . .	PVA
5N	. . .	. . .	. . .	. . .
6E	. . .	Postoperative focal seizure	. . .	Gelfoam
6N	. . .	Cerebrospinal fluid leak	. . .	. . .
7E	. . .	Cerebrospinal fluid leak Tear of superior sagittal sinus	. . .	Gelfoam
7N	. . .	. . .	. . .	. . .
8E	. . .	. . .	. . .	Gelfoam
8N	. . .	Postoperative focal seizure	. . .	. . .
9E	. . .	. . .	. . .	PVA
9N	Death, pneumonia	. . .	. . .	. . .
10E	. . .	. . .	. . .	Gelfoam
10N	. . .	Transient L side weakness	. . .	. . .
11E	. . .	. . .	. . .	PVA
11N	. . .	Transient hemiparesis Subdural hematoma Postoperative seizures	. . .	. . .
12E	. . .	. . .	Transient L hand weakness	PVA
12N	L temporal hematoma aphasia	Seizures	. . .	. . .
13E	. . .	. . .	Tumor contrast extravasation 10-cm groin hematoma	PVA
13N	. . .	Transient L hemiplegia	. . .	. . .
14E	. . .	. . .	. . .	PVA
14N	. . .	. . .	. . .	. . .
15E	. . .	Brain edema	. . .	PVA
15N	. . .	Postoperative seizures	. . .	. . .
16E	. . .	. . .	8-cm groin hematoma	Gelfoam
16N	. . .	. . .	. . .	. . .
17E	. . .	Transient hemiparesis	. . .	Gelfoam
17N	Air embolism R hemiplegia, aphasia Acute myocardial infarction	. . .	. . .	. . .
18E	. . .	. . .	. . .	PVA
18N	. . .	Transient R hemiparesis	. . .	. . .

Note.—E indicates embolized; N, nonembolized; and PVA, polyvinyl alcohol particles.

of embolized and nonembolized patients presenting with meningiomas were analyzed.

Clinical Efficacy

The efficacy of the procedure was confirmed by the significant reductions in the estimated blood loss and number of required transfusions. Although a trend of shortened surgical procedures and reduced convalescent periods (reductions of length of surgical procedure and hospitalization) were noted, they failed to reach a level of significance with our data group to validate these particular observations. However, the additional hospital day added to the total as a consequence of the embolization did not significantly extend the hospital interval. Extrapolation of these results to all meningiomas is not valid because the tumors in our series were large (mean, 5.7 cm). This size is larger than the average meningioma at presentation, and smaller meningiomas may not demonstrate similar significant benefits after embolization to warrant the additional risks and costs associated with the procedure.

There was variability, in particular, with the estimated blood loss and transfusions. Some of this is related to statistical variation. Part of the variability, in addition, is probably related to inaccuracy of the estimations of blood loss. There were three citations of the blood loss in each chart (surgeon's, nurse's, and anesthesiologist's). We chose the estimate of the anesthesiologists because they might be less biased. A prospective study would probably be superior with greater attention being paid to estimating blood loss accurately.

There is always a possibility of bias in selection of patients in a retrospective study. However, it would appear that the prospective decision for embolization versus nonembolization of a meningioma would depend on the surgeon's assessment of the ease of resection of the mass. Under those conditions the assumption could be made that the embolized sample would be a more difficult group to resect in general; in other words, biased negatively for each variable. This is negated, somewhat, by matching of pairs in each group.

Difference in surgical techniques for each case is a valid concern. There is a natural bias for some surgeons to consider preoperative devascularization more frequently than others. This is an obvious bias of the study. However, to generate a sample size of this magnitude from a single surgeon's experience from one institution from a 5-year period would have been difficult.

Cost-effectiveness

Procedural and equipment costs and professional fees incurred from the embolization procedure have the potential to escalate the cost of health management. In most cases, the procedure was completed on the day before surgery which added an extra day to the length of hospitalization. However, as the practice of medicine moves toward cost containment and managed care, these data support the reimbursement for embolization of *large* meningiomas despite the added cost of the procedure. This point, however, should be tempered by regional variations in fees assessed for the procedure. In our institution, embolization did not increase costs. In fact, the average total costs for patient care was less in the embolized group (29 606 versus 38 451). However, with the sample size it could not be considered statistically significant. Furthermore, as stated previously, the cost-effectiveness of the procedure for small meningiomas has not been addressed in this investigation.

Complications

With the advent of microcatheter techniques, superselective embolizations may be performed using a variety of embolic materials. The authors' initial material of choice for embolization was gelfoam powder. This was later modified to the smaller sizes of polyvinyl alcohol particles (150 to 250 and 250 to 350 μm sizes). Adherence to proper techniques during embolization procedures should result in a low number of complications with the majority of these being minor. The complications attributed to embolization in our series of 18 presented cases were limited to two groin hematomas, one intratumoral contrast extravasation, and one transient episode of mild hand weakness. An elderly patient developed transient, mild hand weakness which may have been related to atherosclerotic disease at the carotid bifurcation. There were, however, no long-term significant complications caused by the embolization procedure.

Significant complications related to embolization of the middle meningeal branches are low in general (2% to 3%). They include orbital complications from small collaterals through the superior orbital foramen or the canal of Hyrtl (sphenoid bone canal) (20). In some cases the entire ophthalmic supply may originate from the middle meningeal artery. The authors' protocol includes a digital subtraction exam with the orbit included in the field of view at a catheter position where the embolization will be performed.

In addition to orbital involvement, injury to the seventh cranial nerve when proximal to the petrous branch of the middle meningeal artery is a consideration. Larger particulate emboli may be used (250 to 350 or 350 to 500 μm) to lessen this risk. A provocative test with 20 mg of lidocaine may also be used.

Worsening of mass effects after embolization in patients with significant edema can be blunted by pretreatment with steroids. The risk of intratumoral hemorrhage (21, 22) may be decreased by embolization with larger particles (less tumor necrosis with particles versus gelfoam powder); however, this is at the expense of extent of tumor devascularization. Overinjection of contrast or saline into a middle meningeal artery branch with spasm in a more proximal location around the catheter may play a role in contrast extravasation or hemorrhage from the tumor. This study has addressed embolization of superselected external carotid branches. Risks versus benefits for nonselective embolization of the external carotid or internal maxillary trunks (23, 24), or for internal carotid branches, have not been evaluated in this study (25, 26).

This is a retrospective study with a limited number of cases and the potential of inherent biases of a retrospective study; however, a retrospective study may also be used to validate observations or note trends in addition. The mean cost, length of surgery, and length of hospitalization were lower in the embolized group but were not significant. With the emphasis on efficacy and cost containment, this study may be used to lay the groundwork for a larger, more comprehensive, prospective, randomized, multicenter trial.

In conclusion, the efficacy of embolization of *large* meningiomas has been shown to reduce significantly surgical blood loss and the need for transfusions. In contrast, there was not a significant increase in the total costs for the patients and second party payers. There were no major complications attributed to the embolization procedure. All minor complications associated with the embolization were short term. Although the efficacy and safety of embolization for preoperative devascularization of meningiomas are verified by this study, its cost-effectiveness remains unsubstantiated.

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