Cost-effectiveness of Endovascular Therapy in the Surgical Management of Cerebral Arteriovenous Malformations

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PURPOSE: To determine the economic effect of endovascular therapy in conjunction with surgery for cerebral arteriovenous malformations. **METHODS:** Twenty-five patients with arteriovenous malformations treated with embolization and surgical excision or embolization alone were compared with reported results in 475 patients who underwent surgery only. Respective mean morbidity and mortality rates were calculated and a cost-effectiveness analysis was performed in terms of costs of hospitalization, professional fees, and other direct procedural and indirect costs. Quality-adjusted life-years saved were also calculated. **RESULTS:** The net effective treatment cost per cure was \$71 366 (in 1992 dollars) for embolization and surgery compared with \$78 506 for surgery alone. This resulted in a 9% average savings per treated patient. Cost per quality-adjusted life-year calculations resulted in a cost of \$6734 for embolization and surgery and \$9814 for surgical treatment alone, with savings as high as 34% when endovascular therapy was used. **CONCLUSION:** Endovascular therapy in conjunction with surgery resulted in significant economic benefits for treatment of cerebral arteriovenous malformations.

Index terms: Arteriovenous malformations, cerebral; Arteriovenous malformations, embolization; Economics

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Patients with untreated arteriovenous malformations (AVMs) have a significant risk of hemorrhage, permanent neurologic deficit, and uncontrolled seizures (1–5). Surgical excision of cerebral AVMs is considered a definitive therapy. Endovascular therapy has become established as a useful and valuable adjunct for the surgical management of cerebral AVMs (6–9). It is currently accepted that endovascular therapy also renders AVMs of higher grades (lesions greater than 5 cm) more acceptable for surgical excision (6, 10, 11). These lesions are often difficult to resect, particularly very large lesions or lesions in eloquent areas of the brain. Therefore, as the sole method of treatment, an un-

staged surgical approach carries considerable risk (6, 7, 12–16). Endovascular therapy is still relatively new and is not readily available in many institutions. In addition, endovascular therapy carries with it considerable cost, which is usually added to an already costly surgical procedure (17).

The effect on health care costs of endovascular therapy used in conjunction with surgery is unclear (17). This study was developed to provide a framework for the assessment of endovascular therapy as a new technology, as well as to evaluate the economic and therapeutic impact of this treatment as an adjunct to conventional surgical management of cerebral AVMs.

Materials and Methods

We reviewed the hospital records of 61 patients with intraparenchymal cerebral AVMs treated with endovascular therapy. These patients were seen at our institution over a 2-year period between 1989 and 1991. However, only patients completely cured by embolization or who had complete surgical excision after embolization were considered for this analysis. The number of such patients

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TABLE 1: Reports of morbidity and mortality in the surgical treatment of cerebral arteriovenous malformations

Study	Year	No. of Patients	Mortality, %	Morbidity, %*
Wilson et al (20)	1979	65	5	28
Amarcher et al (19)	1952–1970	187	5	11
Pool (21)	1961	15	20	20
Pool (literature review) (21)	1961	187	11	15
Heros (18)	1978-1988	153	1	24

^{*} Early morbidity (less than 1 year follow-up).

was 25. Of these, two patients were treated with embolization alone. Patients who received radiation therapy were excluded regardless of whether they had received embolization. In addition, patients with any prior embolic or surgical treatment were also excluded from this group in order to avoid confounding factors. However, patients undergoing multistaged embolization and/or surgery at our institution were included. All patients included in the study were considered cured, as defined by a complete absence of the nidus on postsurgical angiograms. The study group included 11 men and 14 women, with a mean age of 34 years.

In all cases vascular access was obtained by means of transfemoral catheterization. A 5F to 6F guiding catheter was placed in the proximal cerebrovascular circulation. The microcatheter was then introduced into the central nervous system circulation through the guiding catheter. A flow-directed catheter was generally used (2.1, Balt, Montmorency, France). Once the microcatheter was positioned as close to the arteriovenous shunt as possible, an angiogram was obtained through the microcatheter to outline the vascular tree and evaluate the volume of AVM filling and the flow across the arteriovenous communication. The angiogram was also evaluated to ensure that arteries supplying normal brain were not embolized. In many cases amobarbital (30 to 50 mg intraarterial push via microcatheter) was administered to evaluate neurologic function. When neurologic deficit was seen, embolization was not performed in the pedicle. In general N-butyl cyanoacrylate (NBCA) (TriPoint Medical, Raleigh, NC) was used to perform the embolizations. NBCA was mixed with iophendylate in mixtures that varied from 2:1 to 1:5 (NBCA:iophendylate). The decision about the relative volumes of NBCA and iophendylate was based on the angiographic data and catheter position. The rate of injection was controlled by the appearance of embolic material as it crossed the arteriovenous communication. The goal of embolization was to thrombose the arteriovenous communication with the embolic material. After embolization, the catheter was immediately removed to prevent gluing of the catheter in place. Generally, one to five pedicles were embolized during each staged embolization. A control angiogram was obtained after embolization to evaluate the results of the procedure.

The literature was also reviewed to assess the morbidity and mortality rates of patients treated with surgical man-

agement only (Table 1). Studies that used multitreatment therapy, including embolization or radiosurgery in addition to conventional surgery, were not used so that the sampling would be similar to our own group. We found 475 surgical patients in the studies reported in the literature who had demographic characteristics similar to those in our group, including having complete angiographic cure (18–21).

We believed it justifiable and reasonable to use patients who showed complete angiographic cures since that is the goal of therapy. Moreover, it would have been unduly complex to consider patients who had partial cures, some of whom may be continuing with ongoing therapy, and it would have been difficult to compare our group with the cases reported in the literature, since the major studies tended to include patients in whom an angiographic cure was achieved. Although this approach could result in lower cost estimates for embolization, it would be more than offset by an underestimation of the true benefits (see "Discussion") and resultant cost savings of embolization as a surgical adjunct. Mean morbidity and mortality rates were calculated for our group of patients and for the literaturebased group. For our group, these rates were calculated by summing the total number of persisting neurologic deficits and deaths, respectively, and dividing by the total sample size. The rates for the literature-based group were calculated by using proportional weighted averages of the reported rates (Table 1), such that studies with the largest number of patients also had the greatest contribution to the overall mean morbidity and mortality. Note that morbidity was not weighted because of our small number of patients with persisting neurologic deficits and because of the lack of normalization across the literature studies for this factor. However, some variance was allowed for in assessing the impact on the results of milder or resolving deficits as part of the sensitivity analysis (see "Results").

Cost-effectiveness Ratio

A mathematical derivation was used to compare the costs and efficacy of the two groups taking into account direct and indirect costs associated with treatment. Direct costs included the costs of hospitalization, professional fees, and morbidity costs resulting from stroke or hemorrhage. Indirect costs included productivity losses associated with morbidity and mortality. The following formula

was derived:

$$\frac{\sum\limits_{i \, = \, 1}^{n} H_{i} + \sum\limits_{i \, = \, 1}^{n} S_{i} - \sum\limits_{i \, = \, 1}^{n} \delta\left(Rx_{Si} - Rx_{Ei}\right) + \sum\limits_{i \, = \, 1}^{n} Mi_{strokes}}{n} + \frac{\frac{(Prod)}{2} \sum\limits_{i \, = \, 1}^{n} Mi}{(1 + r)^{a}} + \frac{(Prod)}{(1 + r)^{a}} \sum\limits_{i \, = \, 1}^{n} D_{i}}{(1 + r)^{a}}$$

Angiographic Cure

where Hi indicates the cost of hospitalization; Si, professional surgical fees; δ , indicator function (ie, $\delta = 1$ if embolization resulted in a cure without the need for surgery and 0 if surgery was required*); Rx_{Si} and Rx_{Ei}, surgical and embolization treatment costs; Mi, morbidity costs†; Di, mortality costs†; Prod, productivity earnings; n, the total number of patients in a given series (eg, total from the literature or total from our institution); and r, the discount rate. † This ratio indicates the total cost to society associated with an angiographic cure. Both direct and indirect costs are considered. Direct costs include estimates based on hospital and physician charges as well as procedure complications (neurologic deficits or strokes). The indirect costs include the morbidity and mortality experience and the impact these have on a person's productivity or lifetime earnings capacity. A summary of charges and cost estimates for hospitalization, professional fees, and mortality appears in the Appendix.

Cost per Year of Life Calculations

Cost per year of life saved were also calculated for both groups using direct and indirect costs; morbidity and mortality rates; and life-table data. Quality-adjusted life-year calculations were performed, taking into account the decreased quality of life that might result from an associated morbidity. Inherent in such calculations is the assumption that a decreased quality-of-life year saved is equivalent to a fraction of a life-year saved in which there is no morbidity. This is termed a *fractional benefit* and was chosen to be 50% in our study, a figure similar to that used in previous studies (22).

Cost of Hospitalization

These costs were estimated from our institutional average of prevailing total charges for patients undergoing hospitalization for surgical excision of cerebral AVMs.

These costs were averaged with diagnostic-related group (DRG) allowable charges published by the federal government (personal communication, Stanford University Hospital Billing Office) (23).

Professional Fees

Professional fees were estimated on the basis of average fees at our institution, as well as from the DRG of average allowable surgical or professional fees associated with endovascular therapy. Professional costs for endovascular therapy included the professional component for diagnostic angiography (supervision and interpretation) performed in conjunction with the endovascular technique (personal communication, Stanford University Hospital Cath/Angio Labs).

Costs Associated with Productivity Losses

These costs were calculated by taking the average age for both series (about 34 years) and subtracting this from an assumed retirement age of 65 years. The average nonfarm industrial wage in the United States was used to calculate the average lifetime earnings of an individual. The average annual income for persons in the United States in 1991 was \$21 258 (24, 25). This was discounted using 4%, 5%, and 6% discount rates. These calculations were performed for productivity losses associated with mortality. Morbidity losses were taken as a percentage of mortality losses based on morbidity and mortality ratios (26). The morbidity and mortality ratio for this analysis was estimated to be 0.5. This ratio was calculated with respect to cerebral vascular diseases (26).

Costs of Complications

The cost of complications included primarily the cost for the treatment of stroke. The total costs of hospitalization associated with the treatment of stroke were estimates on the basis of our average institutional charges and DRG charges (personal communication, Stanford University Hospital Billing Office) (23). A professional component was not added here, since it was assumed that the attending surgeon or radiologist would have been reimbursed under the allowable professional charges for the procedure.

^{*} The indicator function is set to indicate additional savings that accrue when endovascular therapy is used alone to achieve a complete angiographic cure.

[†] Both Mi and Di are calculated with morbidity and mortality rates, respectively, and also factor in the sample size (n).

[†] The discount rate is essentially a method of time valuing of money. For example, a dollar saved in the year 2000 will not equal the value of a dollar saved today, primarily because of inflationary pressures that erode the value of money with time. The rate here was initially 5% per year. This figure varied, however, as part of a sensitivity analysis.

TABLE 2: Net effective treatment cost per angiographic cure at differing discount rates*

Discount Rate, %	Embolization and Surgery, \$	Surgery Alone, \$
4	77 254	86 161
5	71 366	78 506
6	66 984	72 809

^{*} In 1992 dollars. Cost is less in present value dollars if higher inflation in the future.

Results

The relative morbidity and mortality rates for endovascular therapy combined with surgery were 8% and 8%, respectively. These rates correspond to two patients in each category (2 of 25 patients). The mean morbidity calculated for surgical therapy alone (based on the literature experience) was 18.5% (88 of 475). The mean mortality calculated was 6% (30 of 475). The net effective treatment cost per angiographic cure was \$71 366 (1992 dollars) for embolization and surgery, in contrast to \$78 506 for surgical treatment alone. These results were calculated using a 5% discount rate. The results indicate a 9% average savings per treated patient. The discount rate chosen, however, does cause the cost-effective ratios to vary (Table 2). At a 4% discount rate, a savings of \$8907 was calculated, indicating a 10% reduction in costs when embolization was part of the treatment regimen. At a 6% discount rate, a savings of \$5825, or an 8% reduction in costs with the use of endovascular therapy, was realized.

Quality-Adjusted Life-Years

Given the morbidity and mortality experience at our institution and an average US life expectancy of 77 years, a total of 254 years of life were saved as a result of treatment. The literature experience yielded a total of 3467 years of life saved. (Both these figures were normalized according to the size of the patient population.) Using a 5% discount rate, embolization and surgery yielded a cost per year of quality-adjusted life-year saved per patient of \$6734 (1992 dollars). The surgical treatment alone had a cost of \$9814. This resulted in a savings of \$3080 per year of life saved, or a 31% reduction in costs when endovascular therapy was used (Table 3). Using a 4% discount rate, a savings of \$2892 was obtained, or a 31% reduction in the cost of a year of life saved when endovascular therapy

TABLE 3: Cost per-quality-adjusted life-year saved at differing discount rates*

Discount Rate, %	Embolization and Surgery, \$	Surgery Alone, \$
4	6 917	10 550
5	6 734	9 814
6	6 374	9 266

^{*} In 1992 dollars.

was part of the treatment regimen. Table 3 also indicates the results using a 6% discount rate.

Sensitivity Analysis

The morbidity-to-mortality ratio was decreased during sensitivity analysis because it can be argued that as many as 50% of neurologic deficits may improve with time (10,18). When the morbidity-to-mortality ratio was decreased to 0.25, the savings were less pronounced (Table 4). Embolization combined with surgery resulted in a treatment cost per angiographic cure of \$68 415, and \$71 645 for the surgery alone, using a 5% discount rate. This resulted in a \$3230 savings per treated patient, or a 4.5% reduction in cost. With a 4% discount rate, the savings calculated were \$3696, or 5% reduction in cost when embolization was used. With a 6% discount rate, the savings were \$2883, or a 4% overall cost reduction per angiographic cure. The results of such variations are also shown graphically in Figure 1.

Using the quality-adjusted life-year calculations, costs per discounted quality-adjusted year-of-life saved were also taken into account to show how savings might vary if life-years saved in the future are discounted. This approach suggests that a year of life enjoyed in the year 2000 may not be worth a year of life enjoyed today. For the primary analysis in this study we have chosen to value all years of life equally, since it is beyond the scope and intent of this study to examine the ethical and philo-

TABLE 4: Net effective treatment cost per angiographic cure with reduced morbidity-mortality ratio assumption*

Surgery, \$	\$
73 322	77 018
68 415	71 645
64 763	67 646
	68 415

^{*} In 1992 dollars.

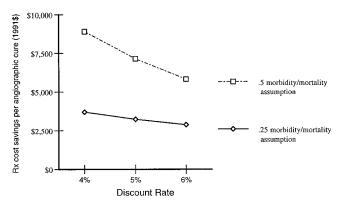


Fig 1. Treatment cost savings per angiographic cure varying with different discount rates and morbidity/mortality ratio assumptions.

sophical nuances resulting from such differing approaches. However, when such calculations were performed, no significant change in net savings was realized, although the overall costs per life-years saved increased. For example, using a 4% discount rate, the cost per discounted quality-adjusted year of life saved using the combined approaches was \$32 733 (1992 dollars). The same cost for a surgical approach alone was \$48 136. This resulted in a 32% net savings using the combined approach, which does not significantly differ from the 34% savings calculated when all life-years were valued equally.

Discussion

Endovascular therapy has proved to be a useful adjunct in the surgical management of cerebral AVMs, but as with any new technology, particularly costly technologies, there is a need to determine its cost-effectiveness if society is to invest in its availability and diffusion (27–30). Our results indicate that embolization in conjunction with surgical treatment for cerebral AVMs has the ability to decrease morbidity and costs significantly. The savings are most marked when quality-adjusted life-years saved are calculated.

Many policymakers prefer the use of qualityadjusted life-year calculations because they take into account costs associated with decreased quality of life, such as might occur when patients suffer stroke or hemorrhage related to AVM treatment. Moreover, such calculations tend to minimize the impact of disparate productivity earnings that may exist on a gender or racial basis. We attempted to minimize these differences by taking into account an average nonfarm labor wage rate for the entire US population. Accordingly, our cost savings are considered conservative.

Quality-adjusted life-year calculations also tend to offset the benefits that might accrue from the treatment of younger persons with higher expected productivity earnings versus older patients who may no longer be in the work force. The inherent assumption in such calculations is that nonmorbid life-years saved are equal in older and younger patients. Some may take issue with this assumption, but we are unaware of any data that would justify doing otherwise.

The quality-adjusted life-year calculations show the highest savings for all discount rates chosen. Discount rates of 4% to 6% were chosen as fair rates of return and as the opportunity cost or alternative investment cost for society's dollars. Tables 2 through 4 indicate how sensitive the results are to varying the discount rates. Note that with lower discount rates the potential savings are greater than with higher discount rates. If a higher discount rate is chosen, a greater value is placed on savings in the present than if a lower discount rate is chosen. This means that a higher discount rate will give preference to those treatments that are more likely to produce results earlier rather than later (31). In other words, if the savings are more likely to be accrued in the future, then the overall benefits will appear less attractive, particularly in times of higher inflation.

The morbidity was varied in the sensitivity analysis to decrease compared with the initial analysis because many patients with neurologic deficits improve with time (10, 18, 32). Unfortunately, we have not had long-term follow-up in our series, and natural history assessment of neurologic deficits is therefore limited; hence, the sensitivity analysis was performed. Both series, however, were evaluated equally in terms of the cost expected per angiographic cure, indicating that the results reflected the immediate morbidity and mortality experience. This may somewhat overestimate costs saved with embolization and surgery, although there is no evidence and we have no reason to believe that there would be a significant difference between the two series as to the expected resolution of neurologic deficits. Even with decreasing morbidity taken into account, significant savings were indicated in this analysis.

This study has not taken into account surgical grading of lesions and surgical selection bias that may cause differences between the two groups of patients. Larger lesions in eloquent areas of the brain would be expected to increase relative morbidity and mortality rates, as well as overall costs. However, since our results are presented in the aggregate, grading the samples was not expected to significantly alter the orders of magnitude between the two series with respect to the accrued benefits of embolization. Current referral patterns at our institution and at other institutions in the United States usually lead to surgical treatment for smaller AVMs and those AVMs that are in less eloquent areas of the brain. Larger AVMs or AVMs in eloquent areas of the brain are often referred for embolization before surgery. (In some cases, radiation therapy may also be useful.) Results with embolization suggest that an angiographic cure can be achieved with smaller AVMs that have fewer arterial feeding pedicles. For example, a recently published series by Vinuela (10) shows that only 29 (9%) of 307 AVMs referred for embolization were small. In this series, a cure was achieved in 22 (7%) of 307 patients with embolization alone. However, all the 22 cured AVMs were small so that the authors were able to achieve a cure in 22 (76%) of 29 small AVMs treated with embolization alone. Although our mortality experience was slightly higher than that in the literature, the morbidity was significantly lower when embolization was done. Further study will be required to assess the relative morbidity and mortality ratios, taking into account surgical grading. In addition, there would be significant benefit in establishing a larger controlled trial to evaluate embolization versus surgical resection for those smaller lesions that may be cured without surgical intervention.

Nelson et al (17) showed that embolization adds a 30% to 40% cost to a surgical procedure for the treatment of cerebral AVMs. Moreover, their work indicated that embolization alone would require multiple treatments and would therefore result in the most costly form of therapy. We did not find that to be the case in our experience, although we only had two patients who were treated with embolization alone. In fact, the patients treated with embolization alone, even with multiple treatments, were found to have overall total costs per angiographic cure of 50% of that achieved with sur-

gical and endovascular therapy combined. Nelson and colleagues also included patients who underwent radiosurgery and took into account severity grading. The costs used in their study were considerably lower than those in our study, but health care costs are higher in the United States than in Great Britain, where their study was conducted. Other factors, such as diagnostic costs, were not taken into account. Moreover, they did not account for costs associated with complications, both direct and indirect.

It could be argued that much of our savings in the presence of embolization resulted from the two patients treated with embolization alone. This is an important point, since the additional costs of hospitalization and surgery are avoided. We did not think it necessary, however, to remove the two patients treated with embolization alone from the analysis because the focus of our study was on endovascular therapy and its role in the surgical management of patients with cerebral AVMs. It is fortunate, in our opinion, that in some cases surgery can be avoided by using endovascular techniques. If costs can also be reduced, then this is all the better, but whether savings result from embolization alone or in conjunction with surgery, embolization's role was considered in the aggregate during this study, because we were interested in its impact on cost.

As this study was designed to assess the cost and efficacy of embolization in the treatment of cerebral AVMs, we chose to exclude patients who had radiation therapy as part of their treatment. It was believed that removal of radiation therapy as a confounding factor could help to assess more accurately the impact of embolization on cost and treatment. There will be a need, however, to evaluate the role radiation therapy has on cost and treatment as well, since it appears to aid in the management of patients with AVMs (33–35). There is a need to examine the interplay between radiation therapy, endovascular therapy, and surgical excision on the cost and outcome of treated patients.

We considered both direct and indirect costs in order to capture the entire societal economic cost of illness associated with this procedure. Direct costs are those associated with the procedure itself, whereas indirect costs are those long-term costs resulting from morbidity and mortality. To include only the direct costs of the procedure would be to ignore a very significant portion of the overall economic costs to society.

If society is to have a realistic appraisal of the cost-efficacy of a procedure or any new technology, it is critical to capture the entire or total cost that can be expected.

In conclusion, our results suggest that endovascular therapy used in conjunction with surgery results in significant economic benefits in the treatment of cerebral AVMs. Our experience also shows a decrease in morbidity, although the mortality experience is not significantly different. This latter effect is thought to be due in part to the relatively small sample size in our series compared with the large literature-based experience. The cost savings are conservative and the true savings are likely to be greater, particularly when surgical selection bias and AVM severity are taken into account. Additional savings are likely to be greater if an angiographic cure is achieved with embolization only. In the absence of surgery, we have found a roughly 50% decrease in costs associated with an endovascular cure. Further experience will be required to determine whether endovascular therapy should be encouraged as the sole method of treatment when possible.

APPENDIX: Summary of Charges and Cost Estimates for Hospitalization, Professional Fees, Morbidity, and Mortality for Treatment of Cerebral Arteriovenous Malformations (in 1992 dollars)

Direct Costs	
Hospitalization (surgical)	44 000
Hospitalization (embolization)	24 500
Hospitalization and follow-up	
care (neurologic deficit)	8 000
Professional fees (surgical)	10 000
Professional fees (embolization)	5 000
Direct treatment cost (surgical)	54 000
Direct treatment cost (embolization)	29 500
Indirect Costs	
Productivity estimates	
Undiscounted	637 728
Discounted (present value)	
4%	196 623
5%	147 555
6%	111 034

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