Cost-effectiveness of angiography performed during surgery for ruptured intracranial aneurysms.

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Cost-effectiveness of Angiography Performed during Surgery for Ruptured Intracranial Aneurysms

David F. Kallmes and Michelle H. Kallmes

PURPOSE: To calculate the incremental cost-utility ratio for routine angiography performed during surgery for ruptured cerebral aneurysms. **METHODS:** Decision-tree and Markov analyses based on a cohort simulation were used to determine the incremental cost-utility ratio of routine intraoperative angiography versus no angiography. Input data from the literature were estimated for the following variables: frequency of unexpected aneurysmal rests and branch artery occlusions; annual rate of rehemorrhage of partially clipped aneurysms; prevalence of clinically relevant infarction resulting from branch artery occlusion; efficacy of clip repositioning; morbidity associated with intraoperative angiography; morbidity and mortality associated with aneurysmal rehemorrhage; sensitivity of intraoperative angiography for aneurysmal rests; and costs of intraoperative angiography, added duration of surgery, ischemic cerebral infarction, aneurysmal rehemorrhage, and rehabilitation. Sensitivity analyses were performed for all relevant input variables. A societal perspective was used, and cost-utility ratios less than $50 000/quality-adjusted life years (QALY) gained were considered acceptable. **RESULTS:** Baseline input variables resulted in an acceptable cost-utility ratio for routine intraoperative angiography ($19 000/QALY). The input variables with greatest influence on the cost-utility ratio were frequency of branch artery occlusions, angiographic morbidity, and cost of angiography. However, the cost-utility ratio remained acceptable even over wide ranges of these input variables. Frequency of unexpected partially clipped aneurysms, efficacy of clip repositioning, and costs of stroke, rehemorrhage, and rehabilitation had relatively little impact on the analysis. **CONCLUSION:** Routine intraoperative angiography is cost-effective if performed in a manner consistent with low morbidity in a patient cohort harboring at least some unexpected branch artery occlusions that, if uncorrected, would result in clinically relevant cerebral infarctions.

Index terms: Aneurysm, cerebral; Cerebral angiography; Economics

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Intraoperative angiography is gaining acceptance as a routine technique in the management of cerebral aneurysms and arteriovenous malformations (1–3). Recent studies have shown not only that intraoperative angiography may uncover unexpected findings in a high percentage of cases but also that the test can be done with minimal added morbidity (1–4). Many centers routinely perform intraoperative angiography, and the cost-effectiveness of the technique has received limited attention (3).

Decision-tree analysis is a robust tool that has been used to study the cost-effectiveness of many interventions, including those used in a variety of neurovascular disorders (5–9). Cohort simulation can be applied to a Markov model of the decision tree to quantitate the impact over a lifetime of a given intervention, using either years of life gained or quality-adjusted life years (QALYs) gained as indexes of effectiveness (10, 11). We applied such a model to determine the incremental cost-utility ratio of routine intraoperative angiography performed during surgery for ruptured intracranial aneurysms.

Materials and Methods

Decision-Tree Algorithm (Fig 1).—Two algorithms were compared in this analysis, one in which all patients undergo routine intraoperative angiography (Fig 1A) and the

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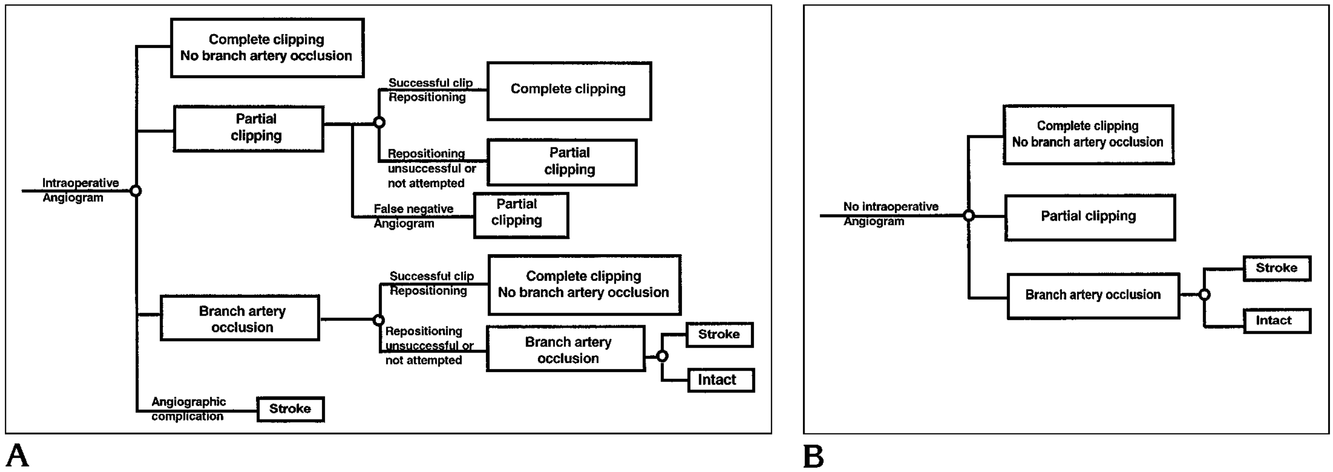

Fig 1. *A*, Algorithm for patients undergoing routine intraoperative angiography. *B*, Algorithm for patients who do not undergo routine angiography.

other in which no intraoperative angiography is performed (Fig 1B). In routine intraoperative angiography (Fig 1A), the angiogram shows either complete clipping, partial clipping, or branch artery occlusion, or an angiographic complication occurs. Suboptimal clip placement may or may not prompt repositioning, and attempted repositioning may or may not result in optimal placement. Uncorrected branch artery occlusions may or may not result in clinically relevant cerebral infarctions. In the absence of intraoperative angiography (Fig 1B), suboptimal clip placements remain uncorrected.

Partially clipped aneurysms and branch artery occlusions were considered independent variables; a patient may harbor either a partially clipped aneurysm or a branch artery occlusion, but both conditions are not present in a single patient. This assumption was employed not only because it markedly simplifies the decision-tree analysis but also because we are unaware of data that address the presence of both partially clipped aneurysms and branch artery occlusions in the same patient. We acknowledge as a limitation of our analysis that difficult aneurysms can result in both conditions' coexisting in the same patient.

Patients can harbor known or unknown fixed neurologic deficits from initial aneurysmal rupture before surgery. These preexisting neurologic deficits diminish the potential benefit from angiography, since correction of suboptimal clip placement cannot yield an intact patient. We modeled this latter portion of the cohort separately, in that patients with preexisting fixed neurologic deficits are presumed to gain no incremental benefit from angiography. This assumption was applied because it allows partial simplification of a relatively complex algorithm. As a result of this simplifying assumption, the benefit of angiography is slightly systematically underestimated when a portion of the cohort has fixed neurologic deficits at entry to the algorithm.

Excluded from this analysis are patients in whom intraoperative angiography is performed because of a high suspicion of an inadequate surgical result. In these cases, the use of intraoperative angiography is not considered "routine," and input data regarding suboptimal clip placement would be different from that for the algorithm for routine intraoperative angiography.

Markov Model (Fig 2).—The decision process can be modeled as a four-state discrete-time Markov chain with annual transitions in state occurring at the 6-month point in the cycle. We defined four Markov states (Fig 2): 1) complete clipping; these patients are considered cured, without risk of subsequent subarachnoid hemorrhage (SAH); 2) partial clipping; these patients are considered at risk for future SAH; 3) stroke; and 4) death. Markov state 1 can transition only to state 4, according to age-related death rates from standard life tables (12), without correction for comorbid disease. State 2 can transition to state 3, because of SAH-related morbidity, and to state 4, from SAH-related mortality as well as age-adjusted death rates. State 3 can transition to state 4 according to age-adjusted death rates. The self-loops noted in Figure 2 account for the times when no transition in state is made in a given year.

Cohort Simulation.—The cohort simulation was used to define visit ratios for each state and to calculate discounted costs and weighted, discounted utilities. Utility was quantified by using quality factors assigned to each state (11). A quality factor of 1.0 was assigned to Markov states 1 and 2. State 3 was assigned a quality factor of 0.76, and state 4 a quality factor of 0.0. QALY was calculated on the basis of these quality factors and on the duration spent in each state. In the baseline analysis, all future costs and utilities were discounted at 5% per year (13). A societal perspective was used for all costs and utilities. Microsoft Excel 5.0 was used to calculate all the cohort simulations and subsequent output.

Incremental Cost-Utility Ratios.—At issue is the added cost expended versus the added utility gained from implementing routine intraoperative angiography. As such, we calculated the incremental cost-utility ratio as the ratio of the incremental costs versus the incremental utility be-

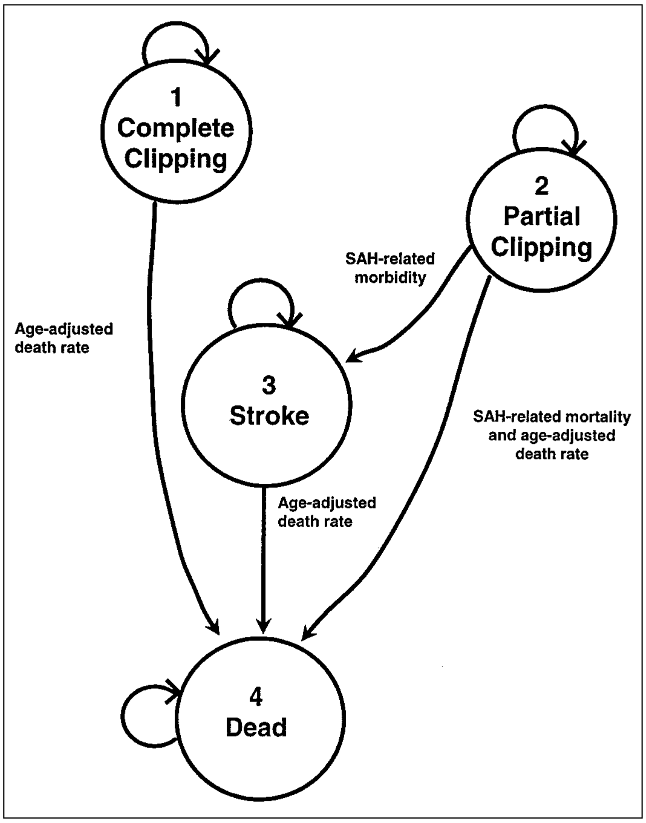

Fig 2. Markov transition diagram, showing the four states (state 1, complete clipping; state 2, partial clipping; state 3, stroke; state 4, death). *Arrows* denote transitions, and descriptors indicate transition probabilities. See text for details.

tween the two algorithms. Use of incremental ratios allowed us to disregard all costs and utilities common to both algorithms. All calculated incremental cost-utility ratios were rounded to the nearest $1000/QALY.

Input Data

The following input data were used to calculate the initial state probabilities and the state transition probabilities for the Markov chain used in the cohort simulation. See the Appendix for details regarding the formulas used to determine initial state probabilities.

Frequency of Unexpected Partially Clipped Aneurysms.—Multiple studies have reported frequencies of unexpected residual aneurysmal rests noted during intraoperative angiography (1–4, 14). Recent data suggest that the frequency approaches 5% to 8% (2, 3); the baseline value for our analysis is 7%. However, residual aneurysmal filling does not always compel the surgeon to change clip position (3), and attempted clip repositioning does not always result in aneurysmal occlusion (14). Thus, we applied a baseline efficacy of clip repositioning of 80% (2, 14), such that 20% of partial aneurysmal occlusions discovered by intraoperative angiography are still present at the end of the operative intervention.

Frequency of Unexpected Branch Artery Occlusions.—Unexpected branch artery occlusions resulting from aneurysmal clipping have been noted by several investigators, with both intraoperative (2, 3, 14, 15) and postoperative angiography (16–20). Although series from the 1960s noted unexpected branch arteries in up to 24% of cases, literature in the era of microsurgical techniques suggests that the frequency is on the order of 5% to 10%. A baseline value of 6% frequency of unexpected branch artery occlusions is used for our analysis. We applied an efficacy rate of 80% for the restoration by clip repositioning of normal flow in a branch artery previously occluded inadvertently by an aneurysmal clip.

Accuracy of Intraoperative Angiography.—Several authors have noted false-negative findings on intraoperative angiograms, in that postoperative examinations showed residual aneurysmal necks not noted on the intraoperative study (3, 4, 14, 15). Some of these cases resulted from "slipped clips," in which the position of the aneurysmal clip changed between surgery and postoperative angiography. Since our algorithm addresses the incremental benefit between routine intraoperative angiography and no angiography, such cases of slipped clips are equivalent between the two algorithms. However, other cases of false-negative findings on intraoperative angiograms result from limited views, poor exposure, or overlapping structures; these are actual "false-negative" findings (3, 4, 14, 15) (Fig 1A). Consequently, we applied a baseline sensitivity of intraoperative angiography of 80%. False-positive results on intraoperative angiograms for residual aneurysm have not been reported, so the specificity of intraoperative angiography for aneurysmal rests was presumed to be 100%. The accuracy of intraoperative angiography for branch artery occlusions was assigned a value of 100%, since false-negative and false-positive intraoperative angiographic findings have not been reported for branch artery occlusions.

Outcome after Branch Artery Occlusion.—Branch artery occlusions do not necessarily result in clinically evident cerebral infarctions. The reported prevalence of such infarctions after inadvertent branch artery occlusion ranges from 50% to 66% (17, 18). We applied a baseline value of 60% for the prevalence of clinically relevant cerebral infarction in the setting of uncorrected branch artery occlusions.

Outcome after Partial Aneurysmal Occlusion.—The natural history of aneurysmal rests is not well defined. Multiple studies in the literature report regrowth and rerupture of postoperative aneurysmal rests (20–24). Most of these studies represent case series, from which it is impossible to calculate annual rates of aneurysmal rehemorrhage. However, one report estimated an annual rate of 0.5% (23). Unfortunately, this value was based on a single ruptured aneurysm. The series by Lin et al (21) detailed 14 cases of rehemorrhage, which, these authors noted, represented about 1% of their total number of cases of aneurysmal clipping. If one assumes that the partially clipped aneurysms that did not rehemorrhage were followed up for as long as those that did rehemorrhage (mean, 9 years),

Baseline values and boundary values for sensitivity analyses for various input variables

	Baseline	Input Data Sensitivity Analysis		Incremental Cost-Utility Ratio ($/QALY)	
		Lower limit	Upper limit	Lower limit, $	Upper limit, $
Age, y	40	30	70	16 000	37 000
Partially clipped aneurysms, %	7	0	15	24 000	13 000
Efficacy of clip repositioning in partially clipped aneurysms, %	80	60	100	19 000	17 000
Branch artery occlusions, %	6	1	8	120 000	11 000
Efficacy of clip repositioning in branch artery occlusions, %	80	60	100	26 000	13 000
Branch artery occlusions that result in stroke, %	60	40	80	30 000	11 000
Sensitivity of angiography, %	80	60	100	19 000	16 000
Morbidity of angiography, %	0.5	0	3	14 000	136 000
No. of patients who are intact at entry	80	40	100	44 000	12 000
Quality factor, living with neurologic deficit	0.76	0.5	0.9	9000	34 000
Annual discount rate, %	5	0	10	7000	33 000
Annual rate of rehemorrhage in partially clipped aneurysms, %	0.75	0.5	3	19 000	10 000
Cost of angiography, $	1500	500	2500	7000	28 000
Cost of stroke, $	20 000	5000	35 000	21 000	15 000
Cost of treating subarachnoid hemorrhage from aneurysm rehemorrhage, $	30 000	10 000	50 000	19 000	17 000
Cost of rehabilitation, $	15 000	5000	25 000	20 000	16 000

Note.—Results are provided for boundary values of sensitivity analyses. Lower limit indicates the input value or output value for the lower limit of the sensitivity analysis, and upper limit indicates the corresponding upper limit. QALY indicates quality-adjusted life year.

the estimated rate of rehemorrhage would have been 1.5% per year. On the basis of these two series, we chose a baseline value of 0.75% per year for rehemorrhage rates of partially clipped aneurysms.

Outcome after Rehemorrhage.—We applied baseline values of 30% each for morbidity and mortality associated with aneurysmal rehemorrhage (25, 26).

Costs.—Angiographic costs were estimated on the basis of physicians' current procedural terminology (CPT) codes from the American Medical Association for 1996. CPT codes for a single second-order-vessel cerebral arteriogram are 36217 (catheterization) and 75665 (interpretation). The professional charges for these codes are $1002 and $188, respectively. We added technical charges for these CPT codes, based on institutional data, for a baseline total cost of $1500. Added operating room and anesthesiology costs were estimated from institutional data. The mean added duration of surgery from the use of intraoperative angiography has been reported to be 30 minutes (3). Operating room expenses are approximately $16 per minute in our institution. As such, combined with anesthesiology expenses, we applied a baseline value of $1000 in additional costs associated with prolonged surgical duration resulting from routine intraoperative angiography.

A recent report details costs associated with specific cerebrovascular events at academic medical centers (27). From this data we estimated the cost of SAH from rehemorrhage of a partially clipped aneurysm to be $30 000. We estimated the added acute-care cost of a clinically relevant cerebral infarction to be $20 000 (27), based not only on the cost of ischemic cerebral infarction but also on the added costs associated with prolonged hospital stay in the cohort of patients with SAH. Rehabilitation costs are carried for 1 year after admission for surgery, and were estimated to be $15 000 (28).

Acceptable Cost-Utility Ratios.—Incremental cost-utility ratios below $50 000/QALY are considered acceptable on the basis of comparisons with ratios reported for other medical interventions (29–31). The absolute value of a cost-utility ratio is of limited importance in a given analysis (32). However, reference to an acceptable limit not only allows a basis for comparison between our data and that of prior published reports but also defines a general ceiling for acceptable ratios as a given input variable is changed within a sensitivity analysis.

Input values for the baseline analysis and boundary values used in the sensitivity analyses are listed in the Table.

Results

Baseline Result.—Applying baseline values for all input data resulted in an incremental cost-utility ratio of $19 000/QALY.

Sensitivity Analyses.—Results of the sensitivity analyses are listed in the Table, while selected sensitivity analyses are shown graphically in Figures 3 through 7.

Partially Clipped Aneurysms.—Figure 3 represents a two-way sensitivity analysis in which both the frequency of unexpected partially clipped aneurysms and the annual rate of rehemorrhage of such aneurysms are varied. The solid line represents an annual rate of rehemorrhage less than that of our baseline value. The

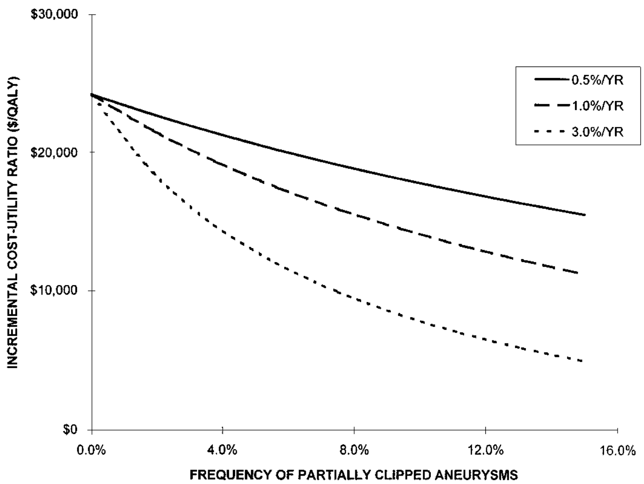

Fig 3. Sensitivity analysis for the effects on the cost-utility ratio of the frequency of unexpected partially clipped aneurysms. Separate curves are presented for various annual rates of rehemorrhage of partially clipped aneurysms (0.5% per year, *solid line*; 1% per year, *dashed line*; 3% per year, *dotted line*). See text for details.

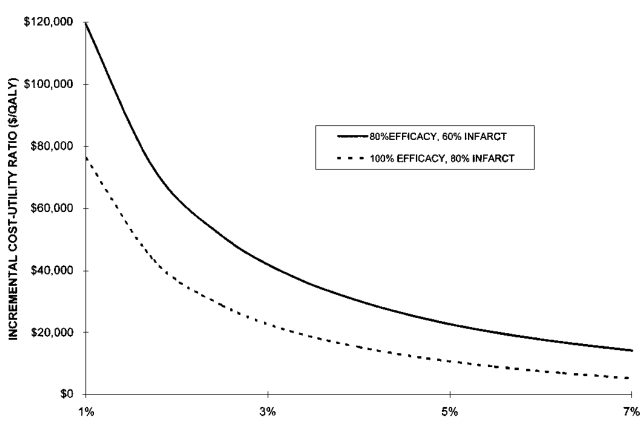

Fig 4. Sensitivity analysis for the effects on the cost-utility ratio of the frequency of unexpected branch artery occlusions. Separate curves are presented for a scenario in which the effect of clip repositioning is minimized (80% efficacy of restoring flow, 60% prevalence of clinically evident cerebral infarction with uncorrected branch artery occlusion) and for one in which the effect is maximized (100% efficacy of restoring flow, 60% prevalence of clinically evident cerebral infarction with uncorrected branch artery occlusion). See text for details.

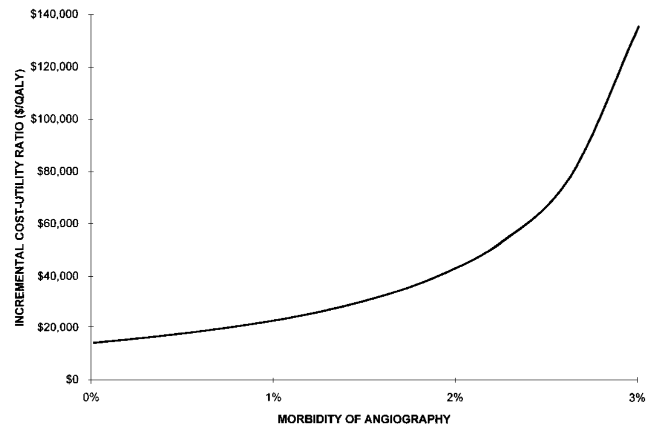

Fig 5. Sensitivity analysis for the effects on the cost-utility ratio of angiographic morbidity rate. See text for details.

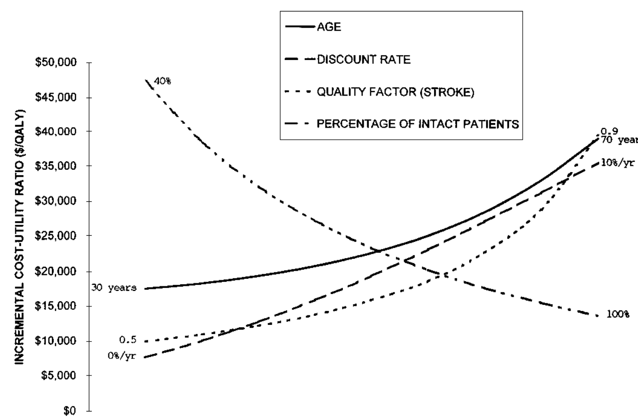

Fig 6. Sensitivity analysis for the effects on the cost-utility ratio of age, discount rate, quality factor assigned to living with neurologic deficit, and percentage of patients neurologically intact at the time of entry into the algorithm. The ranges of these input variables are listed in the Table, and include age (30 to 70 years), discount rate (0% to 10% per year), quality factor (0.5 to 0.9), and percentage of intact patients (40% to 100%).

dashed line represents an intermediate value, while the dotted line represents the upper limit of annual rate of rehemorrhage (3% per year).

Across broad ranges of input values for the frequency of partially clipped aneurysms, the cost-utility ratios remain far below the $50 000/QALY limit defined as acceptable in our analysis, regardless of annual rate of rehemorrhage. Changes in the annual rate of rehemorrhage result in marked alterations in the ratio for high frequencies of partially clipped aneurysms, while in the vicinity of our baseline frequency of 7% the effect of changing rupture rate was less marked. As expected, the curves converge for a frequency of partially clipped aneurysms of 0%, since the annual rate of rehemorrhage is irrelevant if such aneurysms do not exist in the analysis.

Branch Artery Occlusions.—Figure 4 represents a two-way sensitivity analysis that varies both the frequency of unexpected branch artery occlusion and the effects of such occlusions. The solid line represents a scenario in which the impact of routine intraoperative angiography is minimized, since clip repositioning does not necessarily restore flow to the artery and uncorrected branch occlusion results in cerebral in-

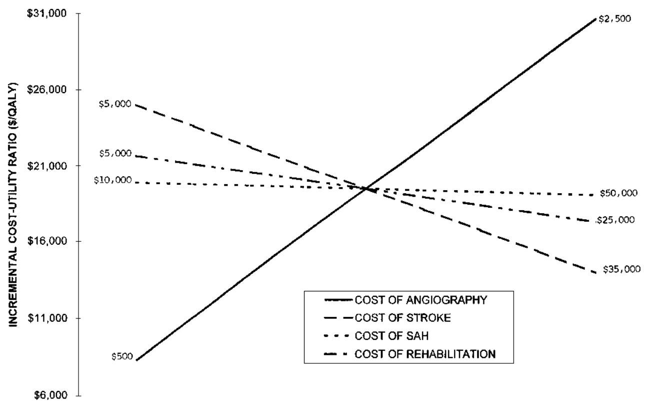

Fig 7. Sensitivity analysis for the effects on the cost-utility ratio of various costs. The ranges of these costs are listed in the Table, and include angiographic costs ($500 to $2500), added cost of stroke from branch artery occlusion ($5000 to $35 000), cost of rehemorrhage ($10 000 to $50 000), and annual cost of rehabilitation after stroke ($5 000 to $25 000).

farction in only 60% of cases. The dotted line represents a scenario in which the impact of angiography is maximized, since clip repositioning always results in restored flow and clinically relevant cerebral infarction results from uncorrected branch artery occlusions in 80% of cases.

This sensitivity analysis shows that the frequency of unexpected branch artery occlusions has a marked effect on the analysis, in that decreasing such frequencies below 2% results in steep increases in the cost-utility ratio. This relationship is maintained with both scenarios (solid and dotted lines, respectively, in Figure 4). Note, however, that our baseline value of unexpected branch artery occlusion of 6% results in cost-utility ratios far below our threshold for acceptable ratios, even when the impact of angiography is minimized (solid line in Figure 4).

Angiographic Morbidity.—Figure 5 shows the impact of angiographic morbidity on the cost-utility ratio. For morbidity rates below 1%, relatively little change in the ratio as a function of angiographic morbidity occurs. However, increasing the morbidity rate above 1.5% results in a steep increase in the incremental cost-utility ratio.

Discount Rate, Quality Factor, Percentage of Intact Patients, and Patients' Ages.—The impact of varying discount rates, the quality factor associated with living with a neurologic deficit, the percentage of patients entering the algorithm who are neurologically intact, and patients' ages are shown in Figure 6. The incremental cost-utility ratio remains at acceptable levels for the wide range of variables considered.

Costs.—The effects of varying each of the relevant costs are shown in Figure 7. The cost of angiography has a more marked influence on the analysis than do other cost considerations.

Discussion

This study represents an attempt to quantify the incremental cost-utility ratios associated with the routine use of angiography during surgery for ruptured aneurysms. The decision tree and Markov analyses applied in our algorithm allow assessment of the complex interchange among the myriad of relevant sequelae that result from the routine application of intraoperative angiography during aneurysmal clipping. For example, the correction of an unexpected branch artery occlusion has far-reaching impact in that not only is the patient's quality of life markedly changed but the short-term and delayed economic impact on society is altered. Limiting the cost analysis only to the added cost of angiography and operating room expenses would miss entirely the beneficial financial effect on society of diminished acute care and rehospitalization costs resulting from clip repositioning. Decision-tree and Markov analyses allow proper inclusion of the latter cost considerations.

Our data strongly suggest that routine use of intraoperative angiography during surgery for ruptured aneurysms is cost-effective. Our confidence is increased further when noting that favorable cost-utility ratios are maintained over wide ranges of many input variables. Furthermore, as noted in the description of our decision-tree analysis, our algorithm yields minor systematic underestimation of incremental benefit when the percentage of intact patients at entry is less than 100%. Inclusion of this benefit would only serve to improve the cost-effectiveness of intraoperative angiography.

Further study of the sensitivity analyses allows identification of those variables with the greatest impact on the analysis, such that subsequent research can be focused on these factors. These variables include frequency of branch artery occlusions, angiographic morbidity, and the fraction of the patient cohort that is neurologically intact at the time of entry into the algorithm.

Mild alterations in the frequency of unexpected branch artery occlusions have a striking effect on the analysis. However, favorable cost-utility ratios are maintained even when applying relatively low rates of successful clip repositioning and of clinically relevant cerebral infarctions resulting from branch occlusions. Unacceptable cost-utility ratios occur only when the frequency of unexpected branch artery occlusions is brought below 2%, at which point the increases in the cost-utility ratio are striking. However, most series have reported frequencies of unexpected branch artery occlusions far greater than 2% (2–4), suggesting that routine intraoperative angiography for identification and correction of these branch artery lesions is cost-effective.

The impact of angiographic morbidity is marked, in that increasing such morbidity from 1% to 2% results in a steep increase in the cost-utility ratio. Because most of the benefit derived from routine use of intraoperative angiography results from diminished stroke rates after correcting branch artery occlusions, morbidity related to angiographic complications carries great importance. As such, we emphasize that acceptable cost-utility ratios can only be achieved when angiography is performed safely. The actual complication rate associated with intraoperative angiography is not well defined, but reports suggest that such rates are on the order of 0.5% to 1.0% (4, 15). One might expect that intraoperative angiography would carry a higher risk than that of angiography performed in the angiography suite. Complication rates for the latter have been established by large prospective trials as approximately 0.3% to 0.5% (33, 34). However, most of the morbidity in these prospective trials has been limited to patients being treated for transient ischemic attacks associated with atherosclerotic disease rather than to those undergoing treatment for ruptured aneurysms (34). Thus, while intraoperative angiography might be of higher risk than standard angiography in a given patient, the population addressed in our study carries a lower baseline angiographic risk. As such, complication rates on the order of 0.5% for intraoperative angiography probably are valid.

Variation in the frequency of unexpected partially clipped aneurysms has relatively little effect on the analysis. Indeed, varying the frequency of partially clipped aneurysms from 0% to 15% results in only mild changes in the cost-utility ratio. The relevance of partially clipped aneurysms is not well documented in the literature, as discussed above. Annual rates of rehemorrhage are difficult to determine, since most of the data regarding rehemorrhage in partially clipped aneurysms are in the form of case series. However, the effects of partially clipped aneurysms remain relatively mild even when varying expected rehemorrhage rates from 0.5% to 3.0% per year. It is unlikely that the annual rate of rehemorrhage of partially clipped aneurysms is as high as 3%, since even completely unclipped ruptured aneurysms have delayed rehemorrhage rates of 3% per year or less (25, 26).

Our algorithm allows assessment of the relative impact of various costs on the cost-utility ratios, an important feature given the difficulty in determining societal costs associated with various interventions. For instance, the precise societal costs of acute stroke, SAH, and rehabilitation are difficult to ascertain. However, our sensitivity analyses showed that the impact of wide variation in these various costs had only mild impact on the cost-utility ratios. The most striking changes in the cost-utility ratio occur with changes in the cost of intraoperative angiography, and these costs are reasonably well defined. Granted, we applied charge rather than reimbursement data for the cost of angiography, and use of charge data typically results in higher values than use of corresponding reimbursement data. However, even when assigning angiographic costs as high as $2500, the overall cost-utility ratio remains well below $50 000/QALY. Furthermore, recent reimbursement data from states different from our own have estimated the cost of cerebral angiography to be as high as $2360 (35), which is markedly higher than our baseline. Given the unavoidable interstate differences in reimbursement, we offer what we consider to be representative data for angiographic costs, and provide a cost-sensitivity analysis so that individual practitioners can apply their own regional reimbursement data.

The impact of changing most other input variables is mild. Increasing patients' ages results in increased cost-utility ratios, since incremental differences in QALY decrease with diminishing life expectancy at the time of entry into the algorithm. Increased discount rates also cause increases in the cost-utility ratio, since delayed benefit from avoiding aneurysmal rehemorrhage becomes less valuable with higher discount rates. Changing the quality factor assigned to patients living with a neurologic deficit has minimal effect on the cost-utility ratios as long as the factor remains below 0.85.

Our explicit goal was to assess the cost-effectiveness of routine intraoperative angiography for ruptured aneurysms. However, our algorithm also can be applied to patients with unruptured aneurysms, providing appropriate input data can be determined. Most of the input data would be relatively equivalent between patient cohorts with ruptured aneurysms and those with unruptured aneurysms. These input data would include costs, patients' ages, discount rate, sensitivity and morbidity associated with angiography, efficacy of clip repositioning, and frequency of clinically relevant cerebral infarction resulting from branch artery occlusions. Other data, such as frequency of imperfect aneurysmal clip placement, can be different between the two groups, although the most recent series detailing intraoperative angiography shows no difference in the frequencies of imperfect aneurysmal clip placement between ruptured and unruptured aneurysms (2).

The variables most likely to differ between patients with ruptured versus unruptured aneurysms would include the percentage of patients neurologically intact at entry into the algorithm and the annual rate of delayed hemorrhage after partial aneurysmal clipping. The effects of both these variables can be determined by using the sensitivity analyses. Figure 6 shows that high percentages of intact patients, as would be present in patient cohorts with unruptured aneurysms, result in improved cost-utility ratios. Conversely, Figure 3 shows that lower rates of rehemorrhage, as would be expected in cases of unruptured aneurysm, result in higher cost-utility ratios. However, the effect of increased rates of delayed rehemorrhage is relatively mild across the range of frequencies of partially clipped aneurysms included in our analysis.

We did not vary the operative morbidity between the two algorithms in our study. The possibility exists that clip repositioning as well as prolonged anesthesia might increase the operative morbidity, but the literature contains only minimal data regarding the correlation between postoperative neurologic deficit and duration of surgery (36). The increased morbidity associated with clip repositioning and prolonged anesthesia would be easily modeled with our current algorithm, since incremental increases in operative morbidity are interchangeable with angiographic morbidity. Such analysis suggests that favorable cost-utility ratios can only be maintained if added operative and anesthesia-related morbidity resulting from the routine use of intraoperative angiography remains low.

We used age-adjusted death rates for the Markov analysis, without accounting for comorbid disease. Since most patients who suffer an SAH from ruptured aneurysms are otherwise healthy, this approximation probably is valid.

Unexpected, completely unclipped aneurysms have been reported in up to 4% of cases in series of postoperative angiography (18), yet our analysis excludes such cases while focusing only on partially clipped aneurysms. The natural history of completely unclipped aneurysms is likely to be different from that of partially clipped aneurysms, in that the former type rehemorrhage more frequently than do the latter. However, completely unclipped aneurysms have not been reported in the literature detailing intraoperative angiography, suggesting that the rare occurrence of a completely unclipped aneurysm noted at postoperative angiography probably results from a slipped clip, which would not have been identified at intraoperative angiography (3, 4, 14, 15). Since an incremental change in the frequency of unclipped aneurysms with the application of intraoperative angiography is not expected, this variable is excluded from our analysis.

We applied the same input data for all aneurysms, regardless of size or location. However, the natural course of some aneurysmal rests, such as those at the basilar bifurcation, may be less favorable than that of aneurysms located elsewhere (21). Furthermore, the frequency of unexpected findings may vary with the location (17, 18) and size (2) of the aneurysm.

We do not include lost wages as part of our analysis, even though we use the societal perspective, because of the unresolved debate in recent literature regarding the most appropriate manner in which lost wages should be addressed. Some authorities suggest that the true indirect costs should be limited to the costs associated with replacing or retraining workers (37). Also, including lost wages in addition to assigning lower quality factors may lead to "double jeopardy," since the societal impact is at least partially taken into account by the quality of life issues (38). Furthermore, at least some of the hypothetical patient cohort in our analysis do not represent wage earners, given the patients' ages as well as the predominance of female subjects. Last, even without including lost wages, intraoperative angiography results in acceptable cost-utility ratios. Inclusion of lost wages would only improve these ratios.

We apply rehabilitation costs for only 1 year, and one might argue that rehabilitation costs are accrued longer than this in many cases. Limited data exist regarding rehabilitation costs beyond the first year. Furthermore, as noted above, cost-utility ratios are acceptable even with our baseline assumptions, and inclusion of rehabilitation costs beyond the first year would only improve these ratios.

We performed a separate cost-utility analysis for routine postoperative rather than intraoperative angiography for surgery on ruptured aneurysms (39). In that analysis we conclude that relatively high rates of unexpected unclipped aneurysms are necessary for postoperative angiography to be cost-effective, and that in most scenarios the routine use of postoperative angiography does not yield acceptable cost-utility ratios. The differences between that analysis and the analysis presented here are numerous. Postoperative angiography offers the relative advantage over intraoperative angiography of detecting slipped clips (3, 4, 14, 15). However, postoperative angiography cannot be used to correct branch artery occlusions in a timely fashion, since such occlusions most likely would already have resulted in cerebral infarction at the time of the postoperative study. Furthermore, incremental increases in morbidity and costs related to a second craniotomy are not present in the case of intraoperative angiography, but are of great importance in the postoperative angiographic analysis. Some observers might suggest that a direct comparison between intraoperative and postoperative angiography might be relevant. However, using a cost-ineffective technique (ie, postoperative angiography) as a baseline to assess intraoperative angiography would falsely improve the apparent cost-effectiveness of intraoperative angiography. This latter consideration is the primary reason we chose not to conduct a direct comparison between intraoperative and postoperative angiography.

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Appendix

The formulas used to determine the proportion of patients in the various Markov states at entry into the model are provided below for the portion of the patient cohort that is neurologically intact at entry. None of the patient cohort begins the simulation in state 4 (dead).

Routine Intraoperative Angiography: Initial State Probabilities

Completely clipped aneurysm: $(1-CX_{ANG})[C+(P)(S_{ANG})(EFF_P)+(B)(EFF_B)+(B)(1-EFF_B)(1-INF)]$

Partially clipped aneurysm: $(1-CX_{ANG})[(P)(1-S_{ANG})+(P)(S_{ANG})(1-EFF_P)]$

Stroke: $(1-CX_{ANG})[(B)(INF)(1-EFF_B)]+CX_{ANG}$

No Routine Angiography: Initial State Probabilities

Completely clipped aneurysm: $C+(B)(1-INF)$

Partially clipped aneurysm: P

Stroke: $(B)(INF)$

where

C = frequency of completely clipped aneurysms before angiography

P = frequency of partially clipped aneurysms before angiography

B = frequency of branch artery occlusions before angiography

EFF_B = efficacy of clip repositioning in branch artery occlusion

EFF_P = efficacy of clip repositioning in partially clipped aneurysms

S_{ANG} = sensitivity of angiography

INF = prevalence of cerebral infarction in uncorrected branch occlusions

CX_{ANG} = morbidity rate of angiography

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