Endovascular and Surgical Management of Multiple Intradural Aneurysms

Review of 122 Patients Managed between 1993 and 1999

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Summary

Patients with multiple intradural aneurysms present unique clinical challenges, particularly when presenting with subarachnoid haemorrhage. This study was undertaken to retrospectively review the management of such patients treated at a single institution. Consecutive patients with multiple intradural aneurysms managed at our institution between 1993 and 1999 were studied. The 122 patients had a total of 305 aneurysms. In most patients presenting with subarachnoid haemorrhage, the aneurysm responsible for the bleed could be identified with a fair degree of certainty, as confirmed by subsequent surgical and autopsy findings. Irregularity of the aneurysm (false sac or polylobulation) was the most useful criterion for making this determination. Failure to recognize all aneurysms on the original angiogram remained an uncommon but clinically important problem. Posterior inferior cerebellar and anterior communicating artery aneurysm locations were disproportionately more likely, and para-ophthalmic less likely, to be responsible for the subarachnoid haemorrhage. There was a trend for patients with uncertainty regarding the site of bleeding to have all aneurysms treated, and for cure to be obtained in a shorter time. Surgical and endovascular complication rates and patient outcomes were not dissimilar from what one would expect for single aneurysm patients. During follow-up, we observed a haemorrhage rate from unruptured aneurysms of 1.1% per patient-year of observation, and a de novo aneurysm formation rate of 0.76% of patients per year.

In conclusion, we feel that although patients with multiple intradural aneurysms have more complex management issues than those with single aneurysms, good outcomes can be achieved with appropriate use of endovascular and/or surgical therapy. The goal in the acute setting following subarachnoid haemorrhage is recognition of all aneurysms and urgent treatment of the one responsible for the haemorrhage. When there is uncertainty, more than one aneurysm may need to be treated. Decisions on subsequent treatment of remaining unruptured aneurysms must be individualized.

Introduction

The discovery of multiple intradural aneurysms (MIAs) in a single patient raises a number of difficult management issues, particularly in the acute setting following subarachnoid haemorrhage (SAH). The major decisions to be made include the determination of which aneurysm is responsible for the haemorrhage, the choice of proper treatment modality depending on the characteristics of the aneurysm and the degree of certainty about the origin of the haemorrhage, and then subsequent management of unruptured aneurysms.

Previous publications have focused on criteria for identification of the ruptured lesion pri-

or to treatment,[1-4] outcome following treatment by a single technique such as surgery,[5] coiling,[6] or largely conservative treatment,[7] subsequent risk of bleeding from previously unruptured aneurysms,[8,9] or the development of new aneurysms over time[10-14]. Many papers discuss all intracranial aneurysms together, without making a clear distinction between cavernous and intradural locations[5,6,15,16]. However, the very different clinical manifestations and therapeutic indications make differentiation between these groups important.

The aim of this report is to delineate the demographics of a population of patients with multiple intradural aneurysms, examine the accuracy of prediction criteria for choosing which aneurysm bled (based on verification by intraoperative findings and clinical follow-up results) and assess the complication rate and outcomes following surgical or endovascular management. Clinical and angiographic follow-up after treatment of the aneurysm that ruptured, or in patients presenting without a history of SAH, is used to provide information on the haemorrhage rate from previously unruptured aneurysms and the de novo formation of aneurysms in this patient population.

Clinical Material and Methods

Patient Population

Consecutive patients with intracranial aneurysms presenting between 1993 and 1999 were identified from a database in which information has been gathered prospectively. Patients with giant, dissecting, inflammatory, or AVM-associated aneurysms were excluded. Infundibula and ectasias were not counted as aneurysms. During the study period, there were a total of 147 patients with multiple intracranial saccular aneurysms managed by the team at Bicêtre from among 557 consecutive aneurysm cases (26.4% multiplicity). Our focus is on patients with multiple aneurysms at risk of causing SAH (i.e. intradural aneurysms). Thus, the 15 patients among these 147 with a cavernous aneurysm or aneurysms and only a single intradural aneurysm were not included. There were ten patients with insufficient clinical or angiographic information. Of the remaining 122 patients, 84 (68.8%) were managed acutely by our team following SAH (hereafter referred to as the "hemorrhagic" group), 15 (12.3%) were managed elsewhere acutely after SAH and subsequently referred for treatment of the remaining aneurysm(s) (the "post-hemorrhagic" group), and 23 (18.9%) were discovered for other reasons and had no history of SAH (the "other" group). Thus, the hemorrhagic and post-hemorrhagic groups collectively comprise patients with a history of subarachnoid haemorrhage. Patients in the "other" group were identified for the following reasons: incidental, 15; mass effect, two; TIA/stroke, two; and screening, four (two for polycystic kidney disease, two for positive family history).

All patients presenting acutely after SAH were graded clinically according to the Hunt & Hess classification[17] and were studied immediately with four-vessel angiography on a General Electric unit. The following criteria were systematically considered to help determine which aneurysm had bled among the hemorrhagic group: computerized tomography (CT) findings, aneurysm irregularity (false sac or polylobulation), body and neck size (which were estimated at the time of this study based on comparison to the size of the proximal internal carotid artery) and proximity along the parent vessel. In addition, other clinical and angiographic findings (such as a third cranial nerve palsy, focal vasospasm on angiography, etc.) were taken into account when relevant. The certainty of determining which aneurysm had bled was classified as "obvious", "probable", or "unknown", based on the above findings. This classification was performed independently by two authors (PJP and MM), and was based on an overall impression using all of the above information, rather than a formal score calculated with these criteria. The designation "obvious" was only used when the aneurysm had a false sac (defined as irregular lobulation with stagnation of contrast), or when the combination of aneurysm locations and CT / angiographic findings was unequivocal (e.g. mirror middle cerebral artery aneurysms with focal intraparenchymal haemorrhage ipsilateral to a large aneurysm, and a small, regular-shaped contralateral aneurysm). The aneurysm responsible for the haemorrhage was verified whenever possible by intraoperative or autopsy information. The post-hemorrhagic group was not included in the above analysis because the initial decision as to which aneurysm had bled was made elsewhere, and at times there was insuffi-

cient information to allow proper assessment of the criteria at the time of this study (e.g. no pre-treatment CT or angiogram was available for review). The most appropriate treatment (endovascular, surgical, or combination therapy) was determined by the interventional neuroradiology and neurosurgical teams involved. The approach to this decision-making evolved over time as experience with endovascular therapy increased. Thus no uniform policy can be described for the duration of this study period. However, we can say that by the end of the study endovascular therapy was used as the primary modality of choice whenever it was considered feasible for the aneurysm thought to be the source of the bleeding. The goal acutely was always the prevention of rebleeding by treatment of the ruptured aneurysm as quickly as possible.

All endovascular therapy consisted of coiling using Guglielmi detachable coils (GDC) (Target Therapeutics, Fremont, California), with or without technical adjuncts such as balloon remodelling. Patients were followed clinically and angiographically after treatment. Outcome was classified at six months using the Glasgow Outcome Scale (GOS)[18]. In cases of endovascular therapy, follow-up angiography was routinely performed at three months, one year and three years after the initial procedure, with intermediate controls at six and 18 months in cases of partial occlusion or if recanalization or regrowth was demonstrated. Angiography following surgically treated cases was performed as deemed necessary by the treating surgeon.

Data Analysis

Data were collected prospectively in a database. Chart reabstraction was used for verification of data correctness and completeness. All data records were checked for missing values and logical inconsistencies. Statistical analyses were performed using unpaired t tests, chi square and Wilcoxon rank-sum tests, were appropriate. Statistical significance was set at a probability value less than 0.05.

Results

Demographics

There were 84 females (68.9%) and 38 males (31.1%). The mean age at presentation was 46.4 years (range 12-77 years). The sex distribution was not significantly different between patients with and without a history of subarachnoid haemorrhage (67/99 (67.7%) patients with

Table 1 **Location of Ruptured and Unruptured Aneurysms**

Location	Ruptured aneurysms	Unruptured aneurysms	Total # aneurysms at this location	Percent of all aneurysms^ for SAH&	Percent responsible
paraophthalmic	7	33	40	13.1	17.5+
posterior communicating	22	28	50	16.4	44.0
anterior choroidal	0	6	6	2.0	0
carotid termination	2	15	17	5.6	11.8
middle cerebral	32	80	112	36.7	28.6
anterior communicating	17	17	34	11.1	50.0*
pericallosal	2	10	12	3.9	16.7
posterior inferior cerebellar	8	2	10	3.3	80.0*
anterior inferior cerebellar	0	1	1	0.3	0
superior cerebellar	2	3	5	1.6	40.0
basilar termination	7	9	16	5.2	43.8
posterior cerebral	0	2	2	0.7	0
Total	99	206	305	99.9	32.5@

^number of aneurysms at this location divided by total number of aneurysms
&number of ruptured aneurysms divided by total number of aneurysms (ruptured&unruptured) at this location
@average percentage of aneurysms responsible for SAH (total ruptured divided by total unruptured)
+significantly less frequently responsible for SAH (p value < 0.05)
**significantly more frequently responsible for SAH (p value < 0.05)*

subarachnoid haemorrhage were female compared to 17/23 (73.9%) among patients without a history of SAH, p=0.55). Medical history included hypertension in 21 patients (17%), polycystic kidney disease in seven, Ehlers-Danlos in one, and fibromuscular dysplasia in one. Information on smoking and family history was not collected prospectively with sufficient consistency to allow comment. Among the 84 patients presenting acutely after SAH, the Hunt and Hess grade was as follows: Grade I, n=10; Grade II, n=39; Grade III, n=19; Grade IV, n=13; and Grade V, n=3. Thus, 49/84 (58.3%) patients were good clinical grade (I or II) and 35/84 (41.7%) were poor grade.

Details of the Aneurysms

There were a total of 305 intradural aneurysms in 122 patients (mean 2.5 per patient, range 2-6). There were 78 patients with two aneurysms (63.9%), 31 with three, ten with four, two with five aneurysms, and one with six. The number of aneurysms was not significantly different between patients with a history of SAH (249 aneurysms in 99 patients, mean 2.5 per patient) and those without a history of SAH (56 aneurysms in 23 patients, mean 2.4 per patient) (p value 0.69) nor between males and females (mean 2.6 and 2.5, respectively; p value 0.80). In addition to the intradural aneurysms, there were 13 patients with extradural aneurysms (11 cavernous, 2 cervical).

The average maximal diameter of the aneurysms was 5.4 mm (range 2-20 mm). This was significantly larger for aneurysms that had bled (mean 7.0 mm) than for unruptured aneurysms (mean 4.7 mm) (p value <0.001). However, the maximal size was less than 1 cm for 64 of the 84 aneurysms (76.2%) responsible for the bleed in the hemorrhagic group. The average neck size, 2.7 mm, was also larger for ruptured aneurysms (mean 3.1 mm) than for unruptured aneurysms (mean 2.5 mm) (p value 0.001). The number of ruptured and unruptured aneurysms at each location is given in Table 1. There were a total of 271 anterior circulation (88.9%) and 34 posterior circulation (11.1%) aneurysms. The most frequent location, the middle cerebral artery (MCA), was more than twice as common as the next most frequent site, the posterior communicating artery (Pcomm) origin. Aneurysms at certain locations had a greater tendency to be the source of haemorrhage. Specifically, aneurysms of the posterior inferior cerebellar artery (PICA) and anterior communicating artery (Acomm) were significantly more likely than other sites to be responsible for SAH (p value 0.001 and 0.02, respectively), while para-ophthalmic lesions had a lesser propensity to account for the SAH (p value 0.03). Forty-four of the 122 patients had aneurysms located in mirror positions, more than half of which (23/44, 52.3%) were on the MCA.

Determination of which Aneurysm Bled

The following results are based on the 84 haemorrhagic patients managed by our team in the acute phase after SAH. The certainty with which the aneurysm that had caused the haemorrhage could be identified was classified as obvious in 46 cases (54.7%), probable in 26 cases (31.0%), and unknown for 12 patients (14.3%). Forty-two (91.3%) of the obvious cases had irregularity of the aneurysm, either a false sac (37 cases, 80.4%) or polylobulation (5 cases, 10.9%). For probable and unknown cases, none of the aneurysms had a false sac, and only nine (34.6%) and four (33.3%) cases had polylobulation, respectively. With regard to size, in 72 of the cases (85.7%) the aneurysm that was thought to be ruptured was the largest aneurysm, and in 68 cases (81.0%) it was the aneurysm with the greatest neck width. In only 49 cases (58.3%) was it the aneurysm located most proximal along the vasculature. The CT scan added useful information in 58 cases (69.0%). Often it was only suggestive of the side of the ruptured aneurysm, and angiographic criteria were required in addition to make the final determination among several aneurysms on that side. The CT scan was most often useful in patients with ruptured anterior communicating, middle cerebral artery, and posterior inferior cerebellar artery aneurysms, in which the haemorrhage pattern was more likely to be localizing.

There were 49 patients among the 84 in whom the aneurysm responsible for rupture could potentially be definitively verified by surgical (n=48) or autopsy (n=1) findings (Table 2). Among those, there were five cases in which operative findings were not definitive in determining the site. For 39 patients in whom the site responsible for SAH was considered obvious or probable, surgery confirmed that the initial

impression was correct in all cases. In five cases classified initially as unknown, the site could be determined either by operative (4) or autopsy (1) findings. In three of these cases there were only two aneurysms, but both were small and regular with diffuse, non-localizing SAH on CT. The fourth patient had six aneurysms distributed bilaterally, a slight predominance of SAH on the left, but a small, regular left MCA aneurysm and a larger, polylobulated anterior communicating artery aneurysm. The latter aneurysm was coiled, and then the patient was quickly operated on due to the uncertainty. Operative findings revealed that the left MCA aneurysm had bled. In the final case, there were four aneurysms distributed bilaterally with symmetric SAH and no clear angiographic criteria. The patient died without treatment ten days after the initial SAH due to the effects of the original bleed, and autopsy revealed that a right MCA aneurysm had bled.

Treatment of the Aneurysms

Among the 84 hemorrhagic cases, the aneurysm that was felt to be ruptured was treated surgically in 48 patients and by endovascular means in 33 cases. In the remaining three patients, two died due to poor initial grade without the ruptured aneurysm being treated, and one had attempted but unsuccessful coiling of the ruptured aneurysm. During the follow-up period, at total of 156 of the 210 aneurysms (74.3%) in the haemorrhagic patients were treated, 105 surgically and 51 by coiling. When the post-haemorrhagic and other cases were included, there were a total of 228 out of 305 aneurysms treated (74.8%), 89 by coiling (88 by our team, 1 prior to referral) and 139 by surgery (122 by our team, 17 prior to referral). Thus, 55 unruptured aneurysms were treated here by coiling and 74 by surgery. A total of 51 patients had surgery as the only treatment modality for their aneurysms, 38 were treated exclusively by coiling, and 30 by combined coiling and surgical therapy.

Among the haemorrhagic group, cure of all intradural aneurysms was achieved for 48 patients (57.1%), including 24 of 46 cases (52.2%) classified as obvious, 15 of 26 cases (57.7%) classified as probable, and nine of 12 cases (75.0%) categorized as unknown source of haemorrhage. Although not statistically significant, this demonstrates a trend toward definitive cure of all aneurysms when there is less certainty about which aneurysm bled. For the three cases in which the site of bleeding was unknown but cure was not achieved, the reasons were as follows: one patient with four aneurysms was treated by coiling of two aneurysms and sent back to the referring hospital for immediate surgery on the others, but died due to poor grade prior to surgery; one pa-

Table 2: **Verification of Aneurysm Rupture**

Verification / Certainty	Surgery confirms	Surgery / autopsy contradicts	Surgery / autopsy identifies site	No definitive answer
Obvious	24	-	-	2
Probable	15	-	-	1
Unknown	-	-	5	2
Total	39	-	5	5

Table 3 **Method of Treatment and Certainty of Hemorrhage**

Certainty / Treatment	Obvious - number (%)	Probable - number (%)	Unknown - number (%)	Total - number (%)
Surgery	26 (57.8)	16 (64.0)	6 (54.5)	48 (59.3)
Endovascular	19 (42.2)	9 (36.0)	5 (45.5)	33 (40.7)
Total	45	25	11	81*

**3/84 patients did not have treatment – see text.*

tient with bilateral posterior communicating artery aneurysms in whom the larger one was clipped and post-operative angiography showed a slight decrease in size of the other, which has not been treated; one patient with an anterior communicating artery aneurysm and a superior cerebellar aneurysm in which only the former has been treated. The average time to achieve cure was 2.9 months (range 1 day to 2.1 years). This time period was shorter, on average, for cases in which the site of rupture was unknown (mean 1.9 months) compared to those classified as probable (mean 3.6 months) or obvious (mean 3.2 months), although not significantly so. Retrospective assessment at the time of this study estimated that among the 84 hemorrhagic cases, all aneurysms could have been treated with a single craniotomy in 39 cases (46.4%), while requiring more than one surgical approach in the remaining 45 cases (53.6%). There was no statistical evidence for a particular treatment (either surgery or coiling) of the ruptured aneurysm to be undertaken based on the certainty of haemorrhage (p value 0.96) (Table 3). There were eight instances in which endovascular therapy was attempted but could not be successfully achieved. Seven of these occurred during the treatment of unruptured aneurysms. The reasons for failure were wide neck in five (two of which were subsequently treated successfully with balloon remodelling), difficult access due to tortuous vessels in one, concern about adjacent branch occlusion in one, and clot in the parent vessel prior to complete delivery of the first coil in one.

Treatment Complications and Aneurysm Regrowth

Among the 210 aneurysms treated here there were a total of 13 treatment-related complications, five occurring in ruptured and eight in unruptured aneurysms. Five permanent operative complications occurred among the 122 surgically treated aneurysms. These consisted of two new deficits in ruptured aneurysms (hemiplegia and moderate upper extremity weakness), and three deficits in unruptured cases (two cases of moderate hemiparesis, and one large infarction leading to death). There were eight complications related to coiling of 88 aneurysms, three in ruptured aneurysms and five in unruptured aneurysms. All three complications in patients with ruptured aneurysms were thromboembolic; two were immediate and were treated by thrombolysis, with no permanent sequelae in one patient but a massive infarct and death in the other; the third occurred in a patient with a fractured coil in the adjacent internal carotid artery. The patient was sedated and paralyzed post-coiling for intracranial pressure control, and at some point in the following days developed a large infarct. Delayed follow-up angiography demonstrated a major MCA branch occlusion. This patient has a permanent major deficit. The five complications occurring in unruptured aneurysms included three thromboembolic problems, two of which were treated by thrombolysis. In these cases, one has a mild persistent upper extremity deficit, the other a persistent hemiplegia. In the third case, clot in the internal carotid during coiling led to abandonment of the procedure, with no sequelae. The other two complications included transient post-coiling hemiparesis for 15 minutes, of unknown etiology (possible vasospasm or emboli), which resolved completely without treatment, and one case of rupture during coiling leading to transient worsening and immediate surgery, with no permanent sequelae. The rates of permanent complications for aneurysms treated by surgery and coiling are given in Table 4. The overall permanent procedural morbidity and mortality rate was 4.3% (4.9% for ruptured aneurysms (1.2%

Table 4: **Rates of Permanent Treatment Complications**

	Ruptured Aneurysms - number (%)	**Unruptured Aneurysms - number (%)**	**Overall - number (%)**
Surgical	2/48 (4.2)*	3/74 (4.1)+	5/122 (4.1)
Endovascular	2/33 (6.1)^	2/55 (3.6)*	4/88 (4.5)
Overall	4/81 (4.9)	5/129 (3.9)	9/210 (4.3)

**all morbidity, no mortality +one death (1.4%), two permanent morbidities (2.7%)*
^one death (3.0%), one permanent morbidity (3.0%)

mortality and 3.7% morbidity) and 3.9% for unruptured aneurysms (0.8% mortality and 3.1% morbidity).

During the angiographic follow-up period, there were six cases in which aneurysms regrew. Five of these occurred following endovascular therapy (two due to coil compaction, two related to coil migration, and one due to recanalization) and one case was due to expansion of a surgical neck remnant. None of these presented with repeat SAH. The surgical regrowth has been subsequently coiled a total of three times, and now has a small stable remnant. One aneurysm had a failed attempt at recoiling and is being considered for surgical therapy. Another with recanalization has been successfully recoiled. The other three remnants are stable and are undergoing serial clinical and angiographic observation.

Follow-up and Risk of Haemorrhage

There were a total of 170.0 patient-years of prospective clinical follow-up (average 1.4 yrs). During this time, there was no rebleeding among patients in the haemorrhagic group. There was one case of SAH in a patient who initially had two incidental right-sided unruptured aneurysms clipped, and bled from one of two previously unrecognized left-sided aneurysms four years later. In retrospect, although initial images were poor, the aneurysm that bled was likely present on the initial study, and the other "new" aneurysm likely was as well. The total time at risk of haemorrhage from unruptured aneurysms is calculated by taking total follow-up (date of presentation until final follow-up date) in those patients for whom all aneurysms are not cured, or pre-cure follow-up (date of presentation until date of cure of all aneurysms) for patients in which cure is achieved. This time can be used to comment on haemorrhage rates from unruptured aneurysms. There were a total of 87.7 patient-years of clinical follow-up time at risk of haemorrhage from previously unruptured aneurysms. The occurrence of a single bleed over this time equates to a risk of 1.1% per patient-year of observation.

De Novo Aneurysm Formation

The average prospective angiographic follow-up for all cases was 1.1 yrs, yielding at total of 131.1 patient-years of information. During this time, one case of probable de novo aneurysm formation was documented in a 35-year-old woman with Ehlers-Danlos syndrome. This patient was treated elsewhere in 1990 for a ruptured posterior inferior cerebellar artery aneurysm. Four-vessel angiography at the time was reported to be otherwise normal. Five years later she suffered another SAH, this time due to a ruptured anterior communicating artery aneurysm. Three additional unruptured aneurysms were also present (superior cerebellar, posterior communicating, and pericallosal locations). Unfortunately the original films were not available for us to review retrospectively to verify the absence of these aneurysms on the original study. This equates to a de novo aneurysm formation rate of 0.76% of patients per year, or, if one counts the four new aneurysms in this one patient, a rate of 3.1% per year. In addition, two previously unrecognized aneurysms were noted during review of angiograms for this study (one superior cerebellar and one mirror MCA), and two previously unrecognized aneurysms were seen when a patient with no history of SAH but two treated aneurysms returned with a SAH from a carotid termination aneurysm contralateral to the previously treated one, and also had a mirror MCA aneurysm.

Clinical Outcomes

The Glasgow outcome score (GOS) at six months for the hemorrhagic group of patients is given in Table 5. Good outcome (GOS 1 & 2) was achieved in 76.1% of haemorrhagic patients overall, including 92.5% of good grade (Hunt and Hess I & II) patients and 51.9% of poor grade (Hunt and Hess III to V) patients. Among the patients treated for unruptured aneurysms, 92.9% had a good outcome (22 patients with GOS of 1, four GOS of 2, one GOS of 3, zero GOS of 4, and one GOS of 5, ten patients without follow-up to six months).

Discussion

The management of patients with multiple intradural aneurysms provides several unique challenges, including determination of which aneurysm is responsible for the haemorrhage, how many can and should be treated in the acute setting, and by what means, and the appropriateness of subsequent treatment of unruptured aneurysms. When managing a patient with SAH, one must always bear in mind the

high incidence of aneurysm multiplicity and scrutinize the original angiogram, particularly mirror locations, for potential multiplicity. Our patient population had rate of intradural aneurysm multiplicity (26.4%) within the range of previous studies, which have reported between 7.7 and 44.9% [15,19-22]. Although the mean age of our patients (46.4 years) was similar to the recent Finnish report on multiple intracranial aneurysms, [22] we had a clear female preponderance (68.9%) which was not seen there (53% female) but has been noted previously [23].

In our series, certain aneurysm locations appear under- (anterior communicating and posterior communicating arteries) or over-represented (MCA, para-ophthalmic) relative to the distribution reported for aneurysms overall [21,23-25]. Other reports on multiple aneurysms have found similar distributions to what we observed [5,6,26]. This of course raises the question as to whether patients with multiple aneurysms are a fundamentally different population, with various genetic or environmental factors predisposing to multiplicity.

The propensity of an aneurysm at a given site to be responsible for haemorrhage is potentially useful information in cases of uncertainty regarding which aneurysm has bled. Previous information implicated anterior communicating, posterior inferior cerebellar and basilar locations to have a high probability of rupture, and MCA a low risk [4]. In our study we found that posterior inferior cerebellar and anterior communicating locations were significantly more frequently responsible for SAH, while para-ophthalmic aneurysms were less frequently responsible (Table 1). One must be cautious, of course, examining multiple subgroups with small sample sizes in this way. In addition, there is no one site which is overwhelmingly more or less likely to bleed, and thus the above information is of limited clinical usefulness. Clearly, other criteria are required for determination of which among several aneurysms visualized was the source of bleeding, and this decision is ultimately one based on the collective weight of evidence. In the past, a large number of criteria have been used to make this judgement, including clinical signs (e.g. focal neurological findings), electroencephalography, a localized pattern of bleeding on CT or MRI, and angiographic criteria including focal mass effect or vasospasm, intraaneurysmal clot, proximity along a vessel, and aneurysm size or irregularity (lobulation, false sac) [1,2,4,27-29]. Nehls et al [4] summarized their experience into an algorithm that remains useful today. We agree that many of the criteria used previously continue to add useful information, but in isolation are often not definitive. For example, the CT scan added useful information in the majority of cases (69%) in our study, yet Lee et al [30] alert us to the risk of false localization. This is particularly a risk in patients who may have arachnoid scarring from previous haemorrhage or surgery, which could make the spread of subarachnoid blood atypical. More than three decades ago Wood reported the tendency for the largest aneurysm to be responsible for the bleed [28]. This was the case in 85.7% of patients in our study. Greatest neck width was almost equally correlated, since the aneurysm with the largest neck had bled 81% of the time. However, these size parameters alone cannot be used as reliable criteria to determine which aneurysm has bled. We found proximity along the vessel, which has previously been promoted as predictive [31], to be less use-

Table 5: **Outcome of Patients at Six Months after SAH***

GOS / Hunt&Hess Grade	1	2	3	4	5	Total
H&H I-II	31 (77.5%)	6 (15.0%)	2 (5.0%)	0 (0%)	1 (2.5%)	40
H&H III-V	10 (37.0%)	4 (14.8%)	5 (18.5%)	0 (0%)	8 (29.6%)	27
Total	41 (61.2%)	10 (14.9%)	7 (10.4%)	0 (0%)	9 (13.4%)	67

**There were 17 patients who did not have 6 month follow-up evaluation available*

ful. In only slightly more than half of our cases the most proximal aneurysm was responsible for the haemorrhage. Aneurysm irregularity, and in particular the presence of a false sac, remained the most important and definitive piece of information for determining which aneurysm had bled. Of course the term "false sac", as used here, is a radiological one, and should not be confused with the traditional pathologically defined "false aneurysm". The two terms may or may not refer to the same entity, and thus in the absence of radiological-pathological correlation they should be considered separate. Using all of the above criteria, we felt the choice of a culprit aneurysm was obvious in more than half of the cases (54.7%). This is clearly a conservative number, since our bias is always towards ensuring that the aneurysm responsible for the haemorrhage is not missed. Even assuming that all cases classified as "probable" were correct, there were still 14.3% of patients for whom there was significant uncertainty about which aneurysm had ruptured. Older studies have reported numbers as low as 48% [32] and 77% [1] for determining the causal lesion, while more recent reports site the ability to identify the aneurysm that bled in 95% [3] and 97.5% [4] of cases.

Regardless of the precise percentage, in most cases we can be fairly confident of which aneurysm bled, but our bias has to be to ensure that we are never misjudging, and as a result failing to treat, a ruptured aneurysm. When there is remaining uncertainty, all possible aneurysms should be treated acutely to protect the patient from rebleeding. The impetus for treatment at this stage is to ensure treatment of the ruptured aneurysm, not to prevent bleeding from previously intact aneurysms, the risk of which is low [3,8,16,24,33]. The degree of uncertainty may have implications for the type of therapy used for a given patient. Surgery has often been recommended in the past because of the ability to treat many aneurysms via the same surgical exposure. In fact, it has previously been estimated that as high as 63% [5] and 74% [34] of multiple aneurysm patients could have all aneurysms treated with a single craniotomy. In our study, this estimate was only 46.4%, similar to that reported by Hiro et al [3] (53%). We did not, in fact, observe a greater tendency to use surgical treatment as the degree of certainty about the site of haemorrhage increased, which was a somewhat surprising finding. Endovascular therapy alone may at times be a very good option, for example if multiple craniotomies would be required for treatment, but only if all aneurysms which are potentially responsible for the haemorrhage have appropriate morphology to be treated in this manner. When this is not the case, the direct surgical approach (if they are all in one territory) or combined surgery and coiling is preferable. Although coiling of several aneurysms (up to five) has been performed in a single session [35,36], we have concerns that working for a prolonged time in one vessel, or putting multiple vascular territories at risk of thromboembolic complications simultaneously, is potentially dangerous.

There was no statistically significant tendency to use a certain type of treatment, depending on the degree of uncertainty about which aneurysm was responsible for the haemorrhage. Rather, as mentioned above, the driving force in the decision was the clinicians' certainty that all aneurysms of concern could be managed acutely, by whatever means. There was a trend for patients with increased uncertainty to be more likely to have all intradural aneurysms treated (75% of "unknown" cases versus 52% of "obvious"), and to achieve cure more quickly (average 1.9 months for "unknown" versus 3.2 months for "obvious"), as one would expect. Regardless of the criteria used to judge which aneurysm has bled, their accuracy remains speculative unless they are validated by objective evidence. Only autopsy or surgical findings can unequivocally confirm which aneurysm has ruptured, although even with direct inspection the determination is not always possible [3]. Previous authors have been able to definitively verify the source of haemorrhage in 64% [4] and 82% [3] of cases. Because many of our cases were treated exclusively by endovascular means, our verification rate was lower than this (44/84, 52%). However, among the cases with surgical or autopsy information, the determination could be made in 90% (44/49). There were no cases in which surgical or autopsy findings refuted our initial impressions, whether that impression was classified as "obvious" or "probable".

One may also indirectly validate the criteria used for choosing which aneurysm has bled by clinical follow-up, demonstrating the absence of rebleeding. If one assumes that the wrong aneurysm was selected for treatment, then the observed rebleed rate should follow the natur-

al history of a ruptured, untreated aneurysm. This is initially very high (4% in the first 24 hours), reaches a cumulative value of 50% at six months, and thereafter is approximately 3% per year [24,37]. Taking the total patient follow-up time among hemorrhagic patients, from the time of treatment of the first aneurysm until death or the treatment of other aneurysms, and using the above figures, we would have expected to see 26 rebleeds if the wrong aneurysm was consistently being treated. Thus, the absence of any rebleed observed in these patients following SAH also argues that the criteria used for determining which aneurysm has bled are reliable, although we could still be wrong some of the time and be fortunate enough to not have the patient suffer a rebleed during our observation period. Thus obviously this method is not a sensitive way to detect errors.

Our relatively short follow-up, limited largely by treatment of some of the unruptured aneurysms, limits comment on the rate of bleeding from previously unruptured aneurysms. We observed one haemorrhage in 87.7 patient-years of follow-up for unprotected, previously unruptured aneurysms (1.1% annual risk per patient). Using a range of estimates for the natural history of unruptured aneurysms of 0.05% - 1.4% per year [8,16,24,38,39], which includes one estimate specifically from patients with multiple aneurysms [7], one would expect to see zero or one bleed during this amount of follow-up time. Thus, our follow-up on these patients is not sufficiently long to make any significant statement regarding the rates previously quoted, other than saying that observation of a single bleed from a previously unruptured aneurysm is consistent with the range of estimates currently used. With relatively short follow-up and only one outcome event of interest, we cannot comment on differential natural histories of various subgroups (e.g. based on presence or absence of previous subarachnoid haemorrhage, size of the aneurysm, etc.), as has been previously done. The above analyses are based on the assumption that each patient has only one remaining unruptured aneurysm. Multiple aneurysms remaining would presumably increase the risk, but there are no good data on the amount by which this is increased (e.g. is a patient with three unruptured aneurysms at three times the annual risk of bleeding as someone with one, or at the same risk, or somewhere in between?). Thus, the numbers provided for estimates of haemorrhage may overestimate the risk per aneurysm.

Failure to recognize all aneurysms on the initial study still remains a significant source of error, despite the now routine visualization of the vertebrobasilar system and the improved quality of imaging. The only bleeding during follow-up in our series occurred in a patient with two unruptured aneurysms that had been surgically treated. She presented four years later with SAH from one of two previously unrecognized contralateral aneurysms. There were two other patients in whom an aneurysm was newly recognized during review of angiograms for this study. Clearly, the implications of missing an aneurysm in the acute phase after SAH are even greater, since it may represent the source of bleeding and thus missing it would place the patient at risk of recurrent haemorrhage. Other authors have reported similar problems in the past [3,5,9]. Yasui et al. report that 7/25 patients presenting with haemorrhage from previously unruptured aneurysms had the aneurysms missed on original studies. Hino et al found that among patients with multiple aneurysms presenting with SAH, in five of six cases where the aneurysm responsible for the bleed was not correctly diagnosed pre-operatively it was due to the aneurysm being missed on the original angiogram. Autopsy data has confirmed "angiographic misses", with 12% of patients thought to have a single aneurysm actually harbouring more than one, and 8% of patients with recognized multiple aneurysms on angiography having more than expected [32]. The use of rotational angiography (with or without three-dimensional reconstruction) and close scrutiny of the angiogram by one or more individuals may help to reduce these numbers. Thus, a major problem in patients with multiple aneurysms is recognizing all the aneurysms, not simply choosing the correct one responsible for the haemorrhage.

Given the above comments, one must always be cautious when referring to a newly seen aneurysm as "de novo", as opposed to one that is just recognized at subsequent angiography. Of the eight newly recognized aneurysms in our study, four were felt to be truly de novo and the other four simply previously unrecognized. Prior studies have estimated rates of de

novo formation to be approximately 2% per year, with a suggestion that the risk may be increased in patients with multiple aneurysms [11,40]. Our data is within that range (0.76% of patients per year, with that patient having developed four new aneurysms). Sakaki et al comment on the role of hypertension in promoting new aneurysm formation [13]. Our patient had a clear underlying predisposition, Ehlers-Danlos syndrome. Since publication of the findings of the International study on unruptured aneurysms [16], there has been renewed interest in the relationship of aneurysm size to the risk of rupture. Categorization of aneurysms according to variable cut-off points (such as 10 mm) has led to much controversy because of the observation that many ruptured aneurysms seen are well below this size. In our patients, the aneurysms that had ruptured were statistically significantly larger than the unruptured aneurysms on average, but remained below 10 mm in 76.2% of cases. Thus, we believe that although size and the risk of rupture are clearly related, assessment of this risk is much more complex than simply placing an aneurysm into an arbitrary size category.

The complication rates associated with treatment are presented in Table 4. The rates in our series compare favourably with the other reports which have addressed surgica [15,26] and endovascular6 [36]; treatment of patients with multiple intracranial aneurysms. The technical failure rate of coiling for ruptured aneurysms was low (1/34 patients, 2.9%). Although aneurysm regrowth is not infrequent following surgical or endovascular treatment (6/210 cases, 2.9%), none of these patients have suffered recurrent SAH during follow-up. Nonetheless, close clinical and angiographic follow-up is recommended. The remnant not infrequently remains stable over time (3/6) and, if necessary, further treatment is generally feasible. Several authors have previously reported a significantly poorer outcome for patients with multiple aneurysms than for those with a single aneurysm [5,41]. Although we did not directly compare to the outcome in a contemporaneous cohort of patients with single aneurysms, our overall rate of good outcomes, and management mortality in patients presenting with SAH, are consistent with figures reported in general following SAH (most of which mix patients with single and multiple aneurysms) (Table 5).

Conclusion

We have presented our experience in managing patients with multiple intradural aneurysms by surgical and endovascular means. Using widely accepted criteria described previously by other authors, we found that the aneurysm responsible for the bleed could usually be identified with a fair degree of certainty, as confirmed by subsequent surgical and autopsy findings.

Aneurysm irregularity (false sac or polylobulation) was the most definitive criterion for making this determination, while other factors such as CT findings and size were often helpful but less conclusive. Failure to recognize all aneurysms on the original angiogram remains a significant problem, and continued demand for and careful scrutiny of high-quality angiography is required to minimize this problem. Particular aneurysm locations were significantly disproportionately more (posterior inferior cerebellar and anterior communicating artery) or less (para-ophthalmic) likely to be responsible for the subarachnoid haemorrhage. As one would expect, there was a trend for patients with uncertainty regarding the site of bleeding to have all aneurysms treated, and for cure to be obtained in a shorter time. The observed rates of haemorrhage from unruptured aneurysms (1.1% per patient-year of observation) and de novo aneurysm formation (0.76% of patients per year) are consistent with previous reports in the literature for patients with single or multiple aneurysms. Although some studies have suggested poorer outcomes in patients with multiple aneurysms, our surgical and endovascular complication rates and patient outcomes were not dissimilar from what one would expect for single aneurysm patients. Thus we feel that although patients with multiple intradural aneurysms have more complex management issues than those with single aneurysms, good outcomes can be achieved with appropriate use of endovascular and/or surgical therapy.

The goal in the acute setting following subarachnoid haemorrhage is recognition of all aneurysms and urgent treatment of the one responsible for the haemorrhage. When there is uncertainty, more than one aneurysm may need to be treated. Decisions on subsequent treatment of unruptured aneurysms must be individualized.

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