Surgery for Unruptured Intracranial Aneurysms in the ISAT and ISUIA Era

Laurent Thines, Philippe Bourgeois, Jean-Paul Lejeune

ABSTRACT: Background: The ISAT and ISUIA studies, along with the improvement of endovascular treatment (EVT) have strongly influenced the management of intracranial aneurysms (IA). We present our experience in the microsurgical treatment of unruptured IA in this context. Methods: We retrospectively reviewed a consecutive series of non-giant UIAs selected for surgery during a five-year period. Patients and aneurysms characteristics, surgical results and outcome assessed by the Glasgow Outcome Scale (GOS) at three month follow-up were studied. Results: Eighty-five patients underwent 93 surgical procedures to obliterate 113 UIAs. Those were incidental in 89% of the cases and mainly located on the middle cerebral artery (65%). Patients were assigned to surgery according to their medical history (young, previous subarachnoid haemorrhage), aneurysm characteristics (wide neck, branch at the neck, “small” size, associated “surgical” aneurysm) or failure of EVT (5%). Operatively, 48% of UIAs had thin wall or blebs and 71% were occluded with one titanium clip. Thrombectomy or temporary clipping were necessary in 4% and 11% of the cases, three aneurysms peroperatively ruptured, four were deemed unclippable, three paraclinoid UIAs had an intracavernous residue and 16% were wrapped because of a small neck remnant (class 2). The mortality rate was 0% and 4% of the patients experienced a definitive major neurological deterioration. Final GOS was unchanged in 96% of the patients. Conclusions: Despite reduction in operative cases and in appropriately selected patients ineligible to EVT, microsurgical clipping of non-giant anterior circulation UIAs can still achieve good outcome with very low mortality and neurological morbidity.

RÉSUMÉ: La chirurgie des anévrismes intracraniens non rompus à l’ère d’ISAT et d’ISUIA. Contexte : Les études ISAT et ISUIA ainsi que l’amélioration du traitement endovasculaire (TEV) ont fortement influencé le traitement des anévrismes intracraniens (AI). Nous présentons notre expérience du traitement microchirurgical des AI non rompus (AINR) dans ce contexte. Méthode : Nous avons revu rétrospectivement une série consécutive d’AINR non géants pris en charge chirurgicalement sur une période de 5 ans. Les caractéristiques des patients et des anévrismes, les résultats chirurgicaux et l’évolution clinique évaluée au moyen de l’échelle de Glasgow à trois mois ont été examinés. Résultats : Quatre-vingt-cinq patients ont subi 93 interventions chirurgicales pour exclure 113 AINR. Ces anévrismes avaient été découverts fortuitement chez 89% des patients et étaient localisés préférentiellement au niveau de l’artère cérébrale moyenne (65%). Les patients étaient orientés vers la chirurgie selon leur histoire médicale (patient jeune, antécédent d’hémorragie sous-arachnoïdienne), les caractéristiques de l’anévrisme (collet large, branche artérielle au collet, petite taille, autre anévrisme « chirurgical » associé) ou échec du TEV (5%). Au moment de la chirurgie, on a constaté que 48% des AINR avaient une paroi mince ou des phlyctènes en surface et 71% ont été exclus au moyen d’un seul clip en titane. Nous avons dû faire une thrombectomie et réaliser un clippage temporaire respectivement chez 4% et 11% des patients. Trois anévrismes se sont rompus pendant la chirurgie. Quatre anévrismes ont été considérés comme non-clippable ; 3 AINR paraclinoidiens gardaient une portion intracranae résiduelle et nous avons dû procéder à l’enrobage d’un petit collet résiduel (classe 2) chez 16% des patients. Le taux de mortalité a été de 0%. Quatre pour cent des patients ont présenté une détérioration neurolgique permanente majeure. Le score final selon l’échelle de Glasgow était inchangé chez 96% des patients. Conclusions : Malgré une diminution du nombre de cas traités chirurgicalement et chez des patients bien sélectionnés qui ne sont pas éligibles au TEV, le clippage microchirurgical des AINR non géants de la circulation antérieure peut offrir de bons résultats fonctionnels et comporte un très faible taux de mortalité et de morbidité neurologique.

CLINICAL MATERIAL AND METHODS

Study population
In our institution, we currently treat approximately 250 ruptured and unruptured intracranial aneurysms per year. In recent years, EVT was the favoured treatment for 60% of aneurysms and the remaining 40% were referred to MST. Cases of patients with UIAs are discussed during weekly cerebrovascular meetings and managed by a multidisciplinary neurovascular team, with close collaboration between neurologists, interventional neuroradiologists and neurosurgeons.

Patients are prospectively recorded in the neurovascular database, from which we performed a retrospective analysis of a consecutive series of UIAs selected for surgery during a five-year period (January 2000 to December 2005). Patients carrying giant aneurysms (>25 mm) were excluded from the study.

Surgical procedure
One of the experienced neurovascular surgeons of our department conducted the surgical procedure in 87% of the cases, through a classical fronto-pterional approach (except for pericallosal or PICA aneurysms). MST was classically performed using titanium Yasargil clips (Braun Aesculap, Tuttlingen, Germany). When necessary, a temporary clipping under mild hypothermia, controlled hypertension and burst suppression was performed to secure the final clipping. If the aneurysm couldn’t be completely excluded without compromising the patency of collateral arterial branches at the aneurysm base, a neck remnant was preserved and wrapped with periosteum. When the aneurismal neck was perfectly exposed and clipped, the sac was then punctured to ensure complete exclusion and a postoperative angiography was not routinely scheduled. When difficulties were encountered during the exposition or the clipping, or if the surgeon had any doubt about the quality of the treatment, a postoperative DSA was performed (16% in this series).

Studied parameters
Patients’ characteristics were recorded: age at assessment, sex, vascular risk factors (high blood pressure -HBP, smoking) and history of subarachnoid haemorrhage (SAH). Aneurysm characteristics were studied: mode of diagnosis (context, imaging technique), location, size, number, surgical aspects (thickness of the wall, presence of blebs) and reasons for referral to surgery. Surgical procedures were analysed: time to surgery, main technique (number of clips, complications), additional technique (temporary clipping, wrapping) and anatomical result according to Raymond’s classification.6,7 Postoperative clinical complications were all monitored. Initial and final outcomes were assessed with the Glasgow Outcome Scale (GOS) (1 = dead, 2 = vegetative state, 3 = severe disability, 4 = moderate disability, 5 = good recovery) at discharge and at three month follow-up.

Statistical analysis
Statistical analysis used Chi-square tests to assess relationship between vascular risk factors and aneurysm wall aspects; age or prior history of SAH and aneurysm size in treated patients; aneurysm wall thickness and temporary clipping, number of clips applied or presence of aneurysmal remnants; and decrease in the GOS score at discharge and age, aneurysm wall thickness or location, presence of multiple aneurysms or the use of temporary clipping. When subgroups were too small (<5), the Fisher exact test was applied. Statistical significance was assigned for P values < 0.05.

RESULTS

General data
Eighty-five patients (27 Male (M), 58 Female (F), mean age 45 years) underwent definitive MST of at least one UIA during the study period. Patient and aneurysm characteristics are summarized in Table 1. Vascular risk factors, namely HBP and/or smoking were found in 56% of the cases. Ninety-three procedures were performed to obliterate 113 UIAs (46% of the patients carrying multiple aneurysms). UIAs were in their vast majority incidental and the diagnosis was done on brain MRI, cerebral angiography and computed tomogram (CT) scan respectively in 55%, 32% and 13% of the cases. The location was the middle cerebral artery and the anterior circulation respectively in 65% and 86% of the aneurysms.

Management decision-making process
Patients were assigned to surgery after a multidisciplinary meeting and according to their medical history (young age, previous subarachnoid haemorrhage), aneurysm characteristics contraindicating EVT (wide neck, branch at the neck, very small size, associated “surgical” aneurysm) or failure of a previous EVT attempt. Patients were younger than 50-years-of-age in 66% of the cases or had suffered from a previous SAH in 27% of the cases. Those two parameters influenced the decision in favour of treatment respectively in 46% and 16% of the cases. Patients over 50 and patients without prior SAH had significantly larger aneurysms: respectively >10 mm (P = 0.002) and >7 mm (P = 0.002). The main argument for referring patients to surgery was (per aneurysm): wide neck 57%, association with an other’surgical” aneurysm 17%, collateral branch arising from the neck or sac 12%, EVT failure 5%, very small size 5%, optic nerve compression 1% and others, including patient’s preference, 3%. Mean time to surgery was five months and during that latency period none of the aneurysms had ruptured.

Operative findings
Operatively, 48% of UIAs had a thin wall with translucent areas or blebs. On the contrary, 30% of the aneurysms had a thick or rigid wall due to atherosclerosis, calcifications or thrombosis. Atherosclerotic presentation was significantly associated with HBP (P = 0.03), smoking (P = 0.01) or both (P = 0.002). In most of the cases, the procedure was relatively straightforward and the aneurysm was obliterated with the application of just one (71%) or two (20%) titanium clip(s). Remodelling of the aneurysm with three or more clips was necessary in 4%. Additional techniques, like intra-aneurismal thrombectomy or temporary clipping, were necessary.
respectively in 4% and 11% of the cases. The use of several clips or temporary clipping was closely correlated with the aneurysm wall thickness (respectively P = 0.004 and P = 0.04). Three aneurysms peroperatively ruptured, four aneurysms (4%) were deemed unclippable (one transitional carotido-cavernous, one thrombosed and calcified postero-carotid, two very small (1mm) middle cerebral and postero-carotid aneurysms), three paraclinoid transitional UIAs were left with an intracavernous residue (3%) and 18 (16%) were wrapped because of a small neck remnant. Overall complete (class 1) or near complete occlusion (class 2) was achieved in 93% of the cases. Atherosclerosis or calcifications were frequently associated with aneurismal remnants (47%) but this did not reach statistical significance (P > 0.05).

**Clinical outcome**

The postoperative course of patients after 93 microsurgical procedures is summarized in Table 2. Minor immediate postoperative complications occurred in 18% of the cases and major complications (aphasia, motor deficit or memory loss) in 9% of the cases but both led to a definitive neurological deficit in 4% of the cases. The mortality rate was 0%. Initial GOS was 5 in 97% of the cases because some patients had suffered previous SAH or stroke. Immediate postoperative outcome was stable in 92% of the patients and decreased in seven patients (GOS 5 to 4 in five, GOS 5 to 3 in one and GOS 4 to 3 in one). Clinical worsening at initial discharge was independent of age, aneurysm wall thickness, use of temporary clipping and treatment of multiple aneurysms in the same procedure (P > 0.05) but significantly correlated (P = 0.007) to aneurysm location on the anterior communicating artery or the posterior circulation (postero-carotid, PICA). Final GOS at three months was unchanged compared with the preoperative GOS in 96% of patients (recovery of three previously deteriorated patients). Four patients remained definitively disabled (GOS 5 to 4 in three, GOS 4 to 3 in one). Outcome was comparable between patients having single or multiple UIAs (P > 0.05). Overall no statistical difference was found between preoperative, discharge and three month follow-up GOS scores (P > 0.05).

**DISCUSSION**

As it has been shown recently, the improvement of management strategies has reduced case-fatality rates of
aneurismal SAH by 17% over the last three decades. However, aneurysm rupture remains a devastating disease and despite progress in microsurgical, endovascular and neurocritical care treatments, it is still associated with mortality rates as high as 30-45% and morbidity in survivors of 30-50%. If there are few debates about the need to treat a ruptured aneurysm regarding the poor prognosis in case of re-rupture, there are no uniform guidelines about treatment indications for UIAs. To solve this problem, continuing efforts have been employed in recent years to better understand the natural history of UIAs and particularly their risk of haemorrhage. Several factors have been linked to a higher risk of rupture: size, prior SAH, posterior circulation location, HBP, smoking or family history of intracranial aneurysm or SAH. In the recent literature, a certain consensus arose to support treatment for definite subgroups of UIAs, like those above > 7-10 mm, occurring in young patients (< 50-year-old) particularly if located on the posterior circulation or associated with an other previously ruptured aneurysm. Our results showed that our decision making process conformed to those general recommendations. When a neurovascular team is considering an UIA for treatment, it is also of paramount importance to accurately determine the individualized balance of risks and benefits of treatment versus natural history. Physicians have to take into account the outcomes provided by the literature, but more importantly, have to evaluate their own mortality / morbidity rates and the factors influencing them. In previous studies, conflicting results about MST have been presented with mortality varying from 0 to 3.8% and morbidity from 1.5 to 12%. In their meta-analysis in 1994, King et al found a mortality rate of 1% and a morbidity rate of 4.1%. A few years later, Raaymakers et al estimated that the mortality and morbidity rates for non-giant unruptured aneurysms were respectively 0.8% and 1.9% for anterior circulation aneurysms, and 3.0% and 12.9% for posterior circulation aneurysms. We showed in our study that obtaining a mortality rate of 0% was feasible, which is of paramount importance when comparing MST with EVT series that usually report a mortality rate > 1%. Our major morbidity rate was below 5% (96% of patients with stable GOS score), which is the usual outcome achieved with MST of UIAs in appropriately selected patients by experienced neurovascular teams in high-volume centres. It is interesting to note that despite the strong reduction in operated cases in France and in our institution, we managed to maintain the quality of surgical results compared with older series, probably because of the improvement of surgical techniques and monitoring, peroperative and postoperative care.

However, we have to acknowledge that the present results are mainly relevant for anterior circulation aneurysms since few posterior circulation aneurysms were treated. Nevertheless, in this selected series of UIAs, MST seems competitive with EVT in terms of clinical outcome and also of anatomical results. For comparison, recent interventional neuroradiological studies reported the following mortality and morbidity: 0 to 3.4%, 0.27 to 7.7%, and 7.7%. Aneurysm recurrence occurs in 20 to 30% of the cases at delayed follow-up in most of the studies, necessitating retreatment in about 3 to 10% of the cases. As proposed by other authors, and because of the uncertainty about the

### Table 2: Postoperative complications after 93 microsurgical procedures

<table>
<thead>
<tr>
<th>Feature</th>
<th>Immediate postoperative course</th>
<th>Definitive deficit</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Nb</td>
<td>%</td>
</tr>
<tr>
<td><strong>Minor complications</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Seizure</td>
<td>7</td>
<td>8%</td>
</tr>
<tr>
<td>Anosmia</td>
<td>3</td>
<td>3%</td>
</tr>
<tr>
<td>IIIrd nerve palsy</td>
<td>1</td>
<td>1%</td>
</tr>
<tr>
<td>Swallowing disturbance (X)</td>
<td>1</td>
<td>1%</td>
</tr>
<tr>
<td>Meningitis</td>
<td>1</td>
<td>1%</td>
</tr>
<tr>
<td>Non surgical CSH</td>
<td>1</td>
<td>1%</td>
</tr>
<tr>
<td>Silent frontal ischemia or contusion on CT</td>
<td>2</td>
<td>2%</td>
</tr>
<tr>
<td>Silent remote cerebellar haemorrhage on CT</td>
<td>1</td>
<td>1%</td>
</tr>
<tr>
<td><strong>TOTAL -</strong></td>
<td>17</td>
<td>18%</td>
</tr>
<tr>
<td><strong>Major complications</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aphasia and/or motor deficit</td>
<td>6</td>
<td>6%</td>
</tr>
<tr>
<td>Memory disturbance</td>
<td>3</td>
<td>3%</td>
</tr>
<tr>
<td>Death</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td><strong>TOTAL -</strong></td>
<td>9</td>
<td>9%</td>
</tr>
</tbody>
</table>

X: vagus nerve, CT: computerized tomography, CSH: chronic subdural hematoma
durability of coiling, MST could be proposed as the first therapeutic option for anterior circulation UIAs (essentially middle cerebral artery, carotid termination or pericallosal aneurysms) above 7 mm in young patients (< 40 years-of-age) particularly if associated with prior SAH. Future results from randomized studies, such as the CURES Trial 2 conducted by our Canadian colleagues\(^{35}\), will be very helpful in determining which treatment modality would be more beneficial for patients carrying UIAs.

The main limitation of this study is the low level of evidence provided (case series without control) and its retrospective aspect. Furthermore, interpretation of the clinical results should be moderated because it especially applies to non-giant anterior circulation UIAs. Indeed, this series was collected in the era of the ISAT and the ISUIA studies when the consensus was to propose MST for UIAs unsuitable for coiling and mainly located on the anterior circulation. Giant aneurysms were also excluded from the study because they had a very different behaviour and postoperative prognosis. Furthermore, the accuracy of outcome results might be questionable in so far as it was only measured with the GOS score: no complimentary neurocognitive or quality of life scales were used\(^{36,37}\) and the clinical follow-up was not performed by an independent neurologist but by the operating surgeon. Finally, postoperative angiographies were not available for a majority of patients. However, when accessible, these exams confirmed the surgical findings, in terms of aneurysm remnants, in 79% of the cases, and underestimated remnants compared with operative inspection in 21% of the cases. This was probably due to the lack of three-dimensional reconstructions at the time of patients management.

**CONCLUSION**

The management decision-making with respect to non-giant UIAs is not always simple because of their relatively benign natural history in the short term and the relative lack of reliable evidence. If a specific treatment is required, its occlusion rate has to be high (> 90%) and its morbidity-mortality rates have to be maintained very low (close to 0%). In appropriately selected patients, MST of UIAs can offer favourable outcome in 96% of cases. However, when accessible, these exams confirmed the surgical findings, in terms of aneurysm remnants, in 79% of the cases, and underestimated remnants compared with operative inspection in 21% of the cases. This was probably due to the lack of three-dimensional reconstructions at the time of patients management.

**REFERENCES**