Validation of effectiveness of keyhole clipping in nonfrail elderly patients with unruptured intracranial aneurysms

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OBJECTIVE Advanced age is known to be associated with a poor prognosis after surgical clipping of unruptured intracranial aneurysms (UIAs). Keyhole clipping techniques have been introduced for less invasive treatment of UIAs. In this study, the authors compared the complications and clinical and radiological outcomes after keyhole clipping between nonfrail elderly patients (≥ 70 years) and nonelderly patients.

METHODS Keyhole clipping (either supraorbital or pterional) was performed to treat 260 cases of relatively small (≤ 10 mm) anterior circulation UIAs. There were 62 cases in the nonfrail elderly group (mean age 72.9 ± 2.6 years [± SD]) and 198 cases in the nonelderly group (mean age 59.5 ± 7.6 years). The authors evaluated mortality and morbidity (modified Rankin Scale score > 2 or Mini–Mental State Examination [MMSE] score < 24) at 3 months and 1 year after the operation, the general cognitive function by MMSE at 3 months and 1 year, anxiety and depression by the Beck Depression Inventory (BDI) and Hamilton Rating Scale for Depression (HAM-D) at 3 months, and radiological abnormalities and recurrence at 1 year.

RESULTS Basic characteristics including comorbidities, frailty, and BDI and HAM-D scores were not significantly different between the 2 groups, whereas the MMSE score was slightly but significantly lower in the elderly group. Aneurysm location, largest diameter, type of keyhole surgery, neck clipping rate, and hospitalization period were not significantly different between the 2 groups. The incidence of chronic subdural hematoma was not significantly higher in the elderly group than in the nonelderly group (8.1% vs 4.5%, p = 0.332); rates of other complications including stroke and epilepsy were not significantly different. Lacunar infarction occurred in 3.2% of the elderly group and 3.0% of the nonelderly group. No patient in the elderly group required re-treatment or demonstrated recurrence of clipped aneurysms. The MMSE score at 3 months significantly improved in the nonelderly group but did not change in the elderly group. The BDI and HAM-D scores at 3 months were significantly improved in both groups. No patient died in either group. The morbidity at 3 months and 1 year in the elderly group (1.6% and 4.8%, respectively) was not significantly different from that in the nonelderly group (2.0% and 1.5%, respectively).

CONCLUSIONS Keyhole clipping for nonfrail elderly patients with relatively small anterior circulation UIAs did not significantly increase the complication, mortality, or morbidity rate; hospitalization period; or aneurysm recurrence compared with nonelderly patients, and it was associated with improvement in anxiety and depression. Keyhole clipping to treat UIAs in the nonfrail elderly is an effective and long-lasting treatment.

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KEY WORDS unruptured cerebral aneurysm; keyhole clipping; elderly; frailty; outcome; vascular disorders
Treatment of unruptured intracranial aneurysms (UIAs) has increased over the last 10 years because of the greater frequency of detection, mainly because of less invasive and high-quality imaging techniques.24 UIAs are often found in patients older than 70 years in the Japanese cohort (27% of cases) because of the long life expectancy.17,22,35,36 The absolute number of elderly patients with UIAs treated by clipping or coiling has also increased.24 UIAs occurring in patients older than 65 years account for 20%–25% of treated UIAs.5,6 However, advanced age as well as aneurysm size and location are strong predictors of poor outcome after both surgical clipping and endovascular coiling.6,53 Higher mortality and morbidity rates are associated with increasing age after treating UIAs and are more prominent with surgical clipping.6 Such a high morbidity rate in elderly patients with UIAs treated by clipping suggests the need for a less invasive clipping technique. Several keyhole approaches with and without endoscopic assistance have been advocated.41,46,55 Nevertheless, the efficacy of keyhole clipping for elderly patients with UIAs has not been evaluated. We have performed 260 cases of keyhole clipping for UIAs over the last 10 years at our institutions to achieve less invasive but long-lasting treatment. The present study was intended to determine whether the mortality and morbidity of elderly patients with UIAs treated using keyhole clipping were higher than those of nonelderly patients. We retrospectively compared the functional state, including cognition and depression as well as neurological function, of nonfrail elderly patients (≥70 years) with nonelderly patients after keyhole clipping of anterior circulation UIAs. We demonstrate that keyhole clipping techniques result in similar morbidity in nonfrail elderly patients and nonelderly patients and improve anxiety and depressive mood.

Methods

Patients

This retrospective study examined the medical records of all patients with surgically clipped UIAs at our institutions. The institutional ethics committees of the National Defense Medical College and Juntendo University Shizuoka Hospital approved this study, and written informed consent was obtained from all patients.

Between July 2005 and March 2015, 528 UIA cases were treated by surgical clipping at the National Defense Medical College and Juntendo University Shizuoka Hospital. Of the 528 cases, 260 were treated by microscopic keyhole clipping surgery for relatively small (<10 mm) anterior circulation UIAs during the time period studied. We defined elderly patients as those older than 70 years (70–79 years) at the time of treatment. The 260 cases included 62 UIAs in 61 elderly patients and 198 UIAs in 190 nonelderly patients. Patients dependent in daily life because of neurological deficits and those with severe comorbidities were excluded from our indication for keyhole clipping. Prior studies in neurosurgical patients have used functional status (Karnofsky Performance Status [KPS] < 70) or age (≥85 years) to define frailty.31,49 In the present study, all patients had a KPS of 100 except for 2 patients younger than 80 years with a KPS of 90. Frailty was quantified using the Canadian Study of Health and Aging Modified Frailty Index (mFI).10,51 The 11 variables (changes in everyday activity, history of diabetes mellitus, lung problems, congestive heart failure, myocardial infarction, cardiac problems, arterial hypertension, clouding or delirium, cerebrovascular problems, history of stroke, and decreased peripheral pulses) were used to calculate the mFI score (the number of presenting items). No elderly patient had an mFI score of more than 3 points. Therefore, all elderly patients in this study were considered to be nonfrail elderly patients.

Surgery

Three-dimensional CT angiography was mainly used for preoperative diagnosis and surgical planning. Clipping procedures were performed through either the supraorbital keyhole approach via an eyebrow skin incision for internal carotid artery aneurysms and anterior communicating artery aneurysms or the pterional keyhole approach via a lateral canthal skin incision for middle cerebral artery aneurysms. The endoscope was used to observe perforating arteries and confirm the completeness of the clipping but not during the clipping procedure. The details of the operative techniques are described elsewhere.30,33,34,42,43,46–48 All keyhole clipping surgeries were performed by a senior author (K.M.).

Neuropsychological and Radiological Examinations

The National Institutes of Health Stroke Scale (NIHSS) and modified Rankin Scale (mRS) score were evaluated a few days before the operation and at 3 months and 1 year after the operation. To assess the general cognitive functions, the mini–mental state examination (MMSE)18 and Hasegawa’s dementia scale—revised (HDS-R)16 were administered a few days before the operation and at 3 months and 1 year after the operation. Morbidity was defined as an mRS score greater than 2 or MMSE score less than 24 according to the International Study of Unruptured Intracranial Aneurysms (ISUIA).55 To assess the anxiety and depression states, the Beck Depression Inventory (BDI)2 and Hamilton Rating Scale for Depression (HAM-D)16 were evaluated a few days before the operation and at 3 months after the operation.

On the day after the operation, CT, 3D CT angiography, and diffusion-weighted MRI were performed to determine the completeness of the clipping and to identify any ischemic and hemorrhagic complications. Follow-up imaging was performed using 3D CT angiography (or MR angiography) at 1 year.

Statistical Analysis

Statistical analysis was performed using commercially available software (version 22.0, SPSS, IBM). Data are expressed as the mean ± SD. Univariate comparison of continuous variables with a normal distribution was performed using the Student t-test. All categorical data were assessed using the chi-square test, Mann-Whitney U-test, or Fisher’s exact probability test. Preoperative and postoperative NIHSS, mRS, MMSE, HDS-R, BDI, and HAM-D scores were compared using the Wilcoxon signed-rank
Results

Patient Characteristics and Keyhole Clipping Surgeries

Table 1 shows the basic characteristics of the patients in the elderly and nonelderly groups. The mean age was 72.9 ± 2.6 years in the elderly group and 59.5 ± 7.6 years in the nonelderly group. The elderly group comprised significantly more females than the nonelderly group. The number of comorbidities was not significantly different between the 2 groups. Screening imaging was mainly performed for nonrelated symptoms, such as headache or vertigo, and other complaints, or the UIAs were discovered on Brain Dock (medical checkup with MR angiography); the reasons for UIA discovery were not significantly different between the groups. The preoperative NIHSS and mRS scores were not significantly different between the 2 groups. The MMSE and HDS-R scores of the elderly patients were slightly but significantly lower than those of the nonelderly patients. Two patients in the elderly group had preoperative MMSE scores of less than 24 points (both 23 points). The BDI and HAM-D scores were higher in the elderly group than in the nonelderly group, but the difference was not statistically significant. The preoperative KPS and mFI scores were not significantly different between the 2 groups.

Table 2 shows the characteristics of the treated UIAs and the keyhole clipping surgeries. The aneurysm locations, mean largest diameter, and multiplicity were not significantly different between the 2 groups. The types of keyhole surgery, size of the mini-craniotomy, neck clipping rate, and mean operation time were also not significantly different between the 2 groups. Fifty-seven nonelderly patients (28.8%) and 10 elderly patients (16.1%) were discharged the day after the operation. The rate of next-day discharge was significantly higher (p < 0.05) in the nonelderly patients. However, the mean hospitalization period after the operation was 2.2 ± 0.8 days in the elderly group and 2.7 ± 4.7 days in the nonelderly group, with no significant difference.

Postoperative Complications, Neuropsychological State, and Radiological Findings

Postoperative complications after the keyhole clipping surgery in elderly and nonelderly patients are shown in Table 3. In the elderly group, 1 patient suffered transient dementia due to subdural effusion but no patient had symptomatic cerebral infarction or epilepsy. The occurrence rate of chronic subdural hematoma (CSDH) was higher in the elderly patients (8.1%) than in the nonelderly patients (4.5%) but was not significantly different (p = 0.332). Postoperative diffusion-weighted imaging showed lacunar infarcts in 3.2% of the elderly patients and 3.0% of the nonelderly patients. No patient showed any brain contusion. No elderly patient required re-treatment of the clipped aneurysms. At 1 year after the operation, 1 patient in the nonelderly group and no patient in the elderly group exhibited recurrence of the clipped aneurysm.

The postoperative neuropsychological status after keyhole clipping in elderly and nonelderly patients at 3 months and 1 year is shown in Table 4. The HDS-R, MMSE, BDI, and HAM-D scores were slightly but significantly better in the nonelderly group than in the elderly group.

A comparison of the postoperative neuropsychological states with the preoperative states is shown in Table 5. In the nonelderly group, the HDS-R and MMSE scores at 3 months and 1 year after the operation, and both BDI and HAM-D scores at 3 months were significantly improved.
TABLE 2. Characteristics of the aneurysms and keyhole surgeries

<table>
<thead>
<tr>
<th>Variable</th>
<th>Nonelderly Group (n = 198)</th>
<th>Elderly Group (n = 62)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACoA</td>
<td>48</td>
<td>15</td>
<td>NS*</td>
</tr>
<tr>
<td>ICA</td>
<td>37</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>MCA</td>
<td>113</td>
<td>37</td>
<td></td>
</tr>
<tr>
<td>Mean largest diameter, mm</td>
<td>6.3 ± 1.8</td>
<td>6.4 ± 1.9</td>
<td>NS‡</td>
</tr>
<tr>
<td>Multiplicity, %</td>
<td>15</td>
<td>16</td>
<td>NS*</td>
</tr>
<tr>
<td>Type of keyhole, no.</td>
<td></td>
<td></td>
<td>NS*</td>
</tr>
<tr>
<td>Supraorbital</td>
<td>85</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>Pterional</td>
<td>113</td>
<td>37</td>
<td></td>
</tr>
<tr>
<td>Mean size of keyhole, mm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maximum diameter</td>
<td>26.8 ± 3.5</td>
<td>26.3 ± 2.7</td>
<td>NS‡</td>
</tr>
<tr>
<td>Minimum diameter</td>
<td>23.2 ± 2.3</td>
<td>22.7 ± 2.3</td>
<td>NS‡</td>
</tr>
<tr>
<td>Neck clipping, %</td>
<td>96</td>
<td>98</td>
<td>NS†</td>
</tr>
<tr>
<td>Mean op time, mins</td>
<td>177 ± 39</td>
<td>171 ± 36</td>
<td>NS‡</td>
</tr>
<tr>
<td>Mean postop hospitalization</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>period, days</td>
<td>2.7 ± 4.7</td>
<td>2.2 ± 0.8</td>
<td>NS‡</td>
</tr>
</tbody>
</table>

ACoA = anterior communicating artery; ICA = internal carotid artery; MCA = middle cerebral artery; NS = not significant.
* Chi-square test.
† Fisher’s exact probability test.
‡ Mann-Whitney U-test.

In the elderly group, the HDS-R and MMSE at 3 months were not significantly different from the preoperative scores, but the HDS-R at 1 year had improved significantly. In addition, the BDI and HAM-D scores at 3 months after the operation had significantly improved.

The mortality and morbidity rates after the keyhole clipping surgery are listed in Table 6. Mortality at 3 months and 1 year was 0% in both the elderly and nonelderly groups. Morbidity at 3 months and 1 year was 1.6% and 4.8%, respectively, in the elderly group and 2.0% and 1.5%, respectively, in the nonelderly group, with no significant difference in the 2 groups. In the elderly group, the reason for the diagnosis of morbidity was MMSE score less than 24 points in all cases. One patient had an MMSE of 23 points at 3 months and 3 patients had an MMSE of 21, 22, and 23 points at 1 year after the operation, but all of these patients were completely independent in daily life.

Discussion

Advanced age is the strong predictor of poor outcome in both surgical clipping and endovascular coiling of UIAs and is more prominent in clipping. The present study demonstrated that surgical outcomes in the nonfrail elderly patients with relatively small anterior circulation UIAs treated by keyhole clipping, including perioperative complications, radiological abnormalities, hospitalization, and mortality and morbidity, were not significantly different from those in the nonelderly patients. Furthermore, the depression scores of the elderly patients, as well as for the nonelderly patients, significantly improved after keyhole clipping.

The keyhole concept of clipping is not intended to reduce the size of craniotomy to the size of a real keyhole, but rather to minimize the craniotomy required to access the aneurysms. Adequate bony drilling of either the frontal skull base in the case of the supraorbital approach or the sphenoid ridge in the case of the pterional keyhole approach is mandatory for successful keyhole clipping. Furthermore, reducing brain tension by aspirating CSF is useful to expand the space for the subdural approach and reduce brain retraction. Preexisting brain atrophy in addition to excessive CSF removal might be a cause of postoperative CSDH. Although the incidence of CSDH in the elderly group was relatively higher than that in the nonelderly group, the wider subdural space was still beneficial to access the aneurysms without excessive brain retraction in the elderly.

The ISUIA study clearly demonstrated that neuropsychological impairments as well as functional disability are major contributors to morbidity after treatment of UIAs, so the examination of cognitive function is mandatory to assess the true postoperative state. Moreover, anxiety and depression also reflect on quality of life. Therefore, this study used depression evaluations (BDI and HAM-D) as well as cognitive tests (MMSE and HDS-R) to elucidate the true state of the elderly patients after keyhole clipping. Change in general cognitive function after UIA treatment is controversial; some authors do not think that UIA treatment changes a patient’s cognitive function after surgery. The functional outcome of patients with UIAs treated using surgical clipping was reported to have progressively improved at the high-volume centers in the late 2000s to 2010s. Furthermore, clipping surgery performed by experienced neurosurgeons with meticulous procedures results in preservation of cognitive functions as well as memory after the operation. Subtle brain damage detected by T2-weighted MRI due to mi-
Keyhole clipping in the elderly

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Recently, the incidence of CSDH formation in patients with anterior circulation UIAs treated using keyhole clipping was reported as 9.3%, and the incidence of CSDH requiring bur hole drainage as 4.7%, with male sex and advanced age (>60 years) as significant risk factors. A traumatic arachnoid tear with CSF entering the subdural space, especially in elderly males with brain atrophy, is a known causative factor for the formation of CSDH after head injury. Although our study showed that CSDH did not affect the morbidity rate, additional surgical intervention should be minimized in elderly patients after clipping surgery. Therefore, we have introduced arachnoidplasty of the opened sylvian fissure and carotid cistern using a collagen sheet soaked in fibrin glue after clipping to reduce the risk of CSDH formation.

Clipping of UIAs in elderly patients is controversial because of their short life expectancy and high postoperative mortality and morbidity associated with UIAs treated by standard clipping in elderly patients have been reported to be 0%–5.2% and 5.6%–26.8%, respectively. The 1-year mortality and morbidity rates associated with UIAs treated by keyhole clipping in patients older than 70 years were 0% and 4.8%, respectively. Although the present study included only relatively small UIAs of the anterior circulation, the surgical results attained through keyhole clipping are considered to be better than those achieved by standard clipping.

Anxiety and depression in patients with UIAs result from fear of aneurysm rupture and the risk of treatment complications. The preoperative scores of the anxiety and depression scales are known to improve after either clipping or coiling treatment. In the present study, the elderly patients had relatively higher depression scores than the nonelderly patients, but the depression scores were significantly improved after the keyhole clipping in both groups. Anxiety and depression in elderly patients with UIAs are regarded as important reasons to choose surgical intervention. Our present study showed that keyhole clipping surgery may improve the depressive mood of patients harboring an UIA, even in elderly patients.

The present study showed a relatively high incidence of CSDH (8.1%) requiring bur hole irrigation in elderly patients with UIAs treated by keyhole clipping. Several studies showed older age as a risk factor for CSDH in patients with UIA treated by conventional clipping surgery. Recent advances in minimally invasive keyhole clipping surgery may improve the depressive mood of patients harboring an UIA, even in elderly patients.

The surgical mortality and morbidity associated with UIAs treated by standard clipping in elderly patients have been reported to be 0%–5.2% and 5.6%–26.8%, respectively. The 1-year mortality and morbidity rates associated with UIAs treated by keyhole clipping in patients older than 70 years were 0% and 4.8%, respectively. Although the present study included only relatively small UIAs of the anterior circulation, the surgical results attained through keyhole clipping are considered to be better than those achieved by standard clipping.

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### Table 4. Comparisons of postoperative neuropsychological status after keyhole clipping in elderly and nonelderly patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>Nonelderly Group (n = 198)</th>
<th>Elderly Group (n = 62)</th>
<th>p Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>At 3 mos postop</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NIHSS score</td>
<td>0.0 ± 0.3</td>
<td>0.0 ± 0.3</td>
<td>NS</td>
</tr>
<tr>
<td>mRS score</td>
<td>0.0 ± 0.3</td>
<td>0.0 ± 0.2</td>
<td>NS</td>
</tr>
<tr>
<td>HDS-R score</td>
<td>29.1 ± 1.2</td>
<td>27.8 ± 2.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MMSE score</td>
<td>29.4 ± 1.3</td>
<td>28.3 ± 1.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BDI score</td>
<td>2.1 ± 3.2</td>
<td>4.0 ± 4.1</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>HAM-D score</td>
<td>1.5 ± 2.0</td>
<td>2.3 ± 2.0</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

At 1 yr postop

<table>
<thead>
<tr>
<th>Variable</th>
<th>Nonelderly Group (n = 198)</th>
<th>Elderly Group (n = 62)</th>
<th>p Value*</th>
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<tbody>
<tr>
<td>NIHSS score</td>
<td>0.0 ± 0.2</td>
<td>0.0 ± 0.1</td>
<td>NS</td>
</tr>
<tr>
<td>mRS score</td>
<td>0.0 ± 0.3</td>
<td>0.0 ± 0.1</td>
<td>NS</td>
</tr>
<tr>
<td>HDS-R score</td>
<td>29.2 ± 1.3</td>
<td>28.1 ± 2.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MMSE score</td>
<td>29.2 ± 1.5</td>
<td>28.3 ± 2.3</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Non–p values are presented as the mean ± SD.

* Mann-Whitney U-test.

### Table 5. Comparisons of postoperative neuropsychological status before and after keyhole clipping surgeries in elderly and nonelderly patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>Preop</th>
<th>At 3 Mos Postop</th>
<th>At 1 Yr Postop</th>
<th>p Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>NIHSS score</td>
<td>0.0 ± 0.1</td>
<td>0.0 ± 0.3</td>
<td>0.0 ± 0.2</td>
<td>NS</td>
</tr>
<tr>
<td>mRS score</td>
<td>0.0 ± 0.1</td>
<td>0.0 ± 0.3</td>
<td>0.0 ± 0.3</td>
<td>NS</td>
</tr>
<tr>
<td>HDS-R score</td>
<td>28.7 ± 1.8</td>
<td>29.1 ± 1.2</td>
<td>29.2 ± 1.3</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>MMSE score</td>
<td>29.0 ± 1.7</td>
<td>29.4 ± 1.3</td>
<td>29.2 ± 1.5</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>BDI score</td>
<td>6.8 ± 5.9</td>
<td>2.1 ± 3.2</td>
<td>&lt;0.005</td>
<td></td>
</tr>
<tr>
<td>HAM-D score</td>
<td>3.7 ± 3.5</td>
<td>1.5 ± 2.0</td>
<td>&lt;0.005</td>
<td></td>
</tr>
</tbody>
</table>

At 1 yr postop

<table>
<thead>
<tr>
<th>Variable</th>
<th>Nonelderly Group (n = 198)</th>
<th>Elderly Group (n = 62)</th>
<th>p Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>NIHSS score</td>
<td>0.0 ± 0.1</td>
<td>0.0 ± 0.3</td>
<td>0.0 ± 0.1</td>
</tr>
<tr>
<td>mRS score</td>
<td>0.0 ± 0.1</td>
<td>0.0 ± 0.2</td>
<td>0.0 ± 0.1</td>
</tr>
<tr>
<td>HDS-R score</td>
<td>27.2 ± 2.6</td>
<td>27.8 ± 2.1</td>
<td>28.1 ± 2.2</td>
</tr>
<tr>
<td>MMSE score</td>
<td>28.0 ± 2.4</td>
<td>28.3 ± 1.8</td>
<td>28.3 ± 2.3</td>
</tr>
<tr>
<td>BDI score</td>
<td>7.7 ± 6.1</td>
<td>4.0 ± 4.1</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>HAM-D score</td>
<td>4.3 ± 4.1</td>
<td>2.3 ± 2.0</td>
<td>&lt;0.005</td>
</tr>
</tbody>
</table>

Non–p values are presented as the mean ± SD.

† Wilcoxon signed-rank test.

### Table 6. Mortality and morbidity after keyhole clipping surgeries in elderly and nonelderly patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>Nonelderly Group (n = 198)</th>
<th>Elderly Group (n = 62)</th>
<th>p Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 mos postop</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mortality</td>
<td>0</td>
<td>0</td>
<td>NS</td>
</tr>
<tr>
<td>Morbidity†</td>
<td>4/198 (2.0%)</td>
<td>1/62 (1.6%)</td>
<td>NS</td>
</tr>
<tr>
<td>1 yr postop</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mortality</td>
<td>0</td>
<td>0</td>
<td>NS</td>
</tr>
<tr>
<td>Morbidity†</td>
<td>3/198 (1.5%)</td>
<td>3/62 (4.8%)</td>
<td>NS</td>
</tr>
</tbody>
</table>

Non–p values are presented as the mean ± SD.

* Fisher’s exact probability test.

† As defined in the ISUIA study (mRS score > 2 or MMSE score < 24).
mortality and morbidity. However, elderly people form a heterogeneous population with respect to surgical intervention because frailty is common in the elderly. Distinct from medical comorbidity and disability, medical frailty in elderly patients is associated with a significantly increased risk of postoperative complications and is significantly related to mortality, hospitalization, and institutionalization in various surgical settings, including cardiac, pulmonary, orthopedic, and urological surgery, but it has not been discussed much in neurosurgery.\textsuperscript{1,5,28,45,54} The present study excluded the indication of keyhole clipping in elderly patients with neurological deficits associated with frailty and severe comorbidities. Quantification of frailty using the mFI showed that our patients in the elderly group were not included in the frailest quintile (mFI score ≥ 3 points).\textsuperscript{10,51} Our series showed that surgical mortality and morbidity and hospitalization within 3 days for these nonfrail elderly patients treated by keyhole clipping were not significantly different from those for the nonelderly patients. Furthermore, the anxiety and depression in the elderly patients were significantly improved after keyhole clipping surgery. Nonfrail elderly as defined in our study will sooner or later become frail. Anxiety and depression are known to reduce the quality of life in the elderly and are important in the development of frailty. Frail elderly patients with psychosocial factors have more adverse outcomes than nonfrail patients with various types of disorders.\textsuperscript{12,52} Therefore, given that the knowledge of having UIAs can cause increased levels of anxiety and depression, keyhole clipping surgery without inducing neurological deficits might be beneficial in delaying the onset of frailty in these patients.

Limitations

Several studies have shown the superiority of endovascular treatment of UIAs over surgical clipping, especially in elderly patients.\textsuperscript{6,21,15,55,56} Recent data published after 2010 showed the mortality and morbidity rates after endovascular treatment of UIAs, including posterior circulation aneurysms in elderly patients (≥ 65 years), ranged from 1.1% to 8.7%.\textsuperscript{6,27,38,50} In this study, we limited the location and size of the UIAs to the anterior circulation and relatively small aneurysms. Comparison of our data for keyhole clipping in the elderly with that of endovascular treatment is beyond the scope of the study. However, our results of a surgical morbidity rate of 1.6% at 3 months and 4.8% at 1 year after surgery without aneurysm recurrence and re-treatment suggest that keyhole surgery is not inferior to endovascular treatment.

Conclusions

Keyhole strategies for clipping surgery in nonfrail elderly patients with relatively small anterior circulation UIAs did not significantly increase the perioperative complications, hospitalization, radiological abnormalities, mortality and morbidity at 3 months and 1 year after the operation, and 1-year recurrence rate; outcomes were comparable to those of the nonelderly patients. General cognitive functions did not decrease significantly, and anxiety and depression significantly improved after surgery in the elderly patients. These findings suggest that keyhole clipping to treat UIAs in the nonfrail elderly is an effective and long-lasting treatment.

References

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**Disclosures**

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

**Author Contributions**

Conception and design: Mori, Tomura. Acquisition of data: Mori, Wada, Otani, Tomiyama, Toyooka, Fujii, Kumagai, Takeuchi, Yamamoto, Nakao. Analysis and interpretation of data: Mori, Arai. Drafting the article: Mori, Arai. Critically revising the article: Mori. Reviewed submitted version of manuscript: Mori. Approved the final version of the manuscript on behalf of all authors: Mori. Statistical analysis: Fujii, Tomura. Administrative/technical/material support: Mori. Study supervision: Mori, Arai.

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