Simultaneous Craniotomies for Multiple Intracranial Aneurysm Clippings – One-stage Surgery with Multiple Craniotomies

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Research Article

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Abstract

The treatment of multiple intracranial aneurysms (MIAs) involves various modalities and sometimes requires staged operations. This study aimed to prove the efficacy and safety of one-stage multiple craniotomies (OSMC) for multiple cerebral aneurysms. We retrospectively reviewed the medical records of the patients who underwent surgical clipping of an intracranial aneurysm at Seoul National University Bundang Hospital between 2003 and April 2020. The surgical results, complications, and lengths of hospital stay were compared between the patients who underwent OSMC and those who underwent multi-stage multiple craniotomies (MSMC). The demographic characteristics of the OSMC and MSMC groups (n = 82 and 43, respectively) were similar. There were no statistically significant differences between the two groups when the amount of blood transfused, complications, and surgical results were compared ($p = 0.925$, $p = 0.528$, and $p = 0.898$, respectively); however, the operation time and hospitalization period (353.9 min vs. 490.3 min and 12.3 days vs. 21.8 days, respectively; $p < 0.0001$ for both) were shorter in the OSMC group. The treatment cost (17,000 USD vs. 22,000 USD, $p < 0.0001$) was lower in the OSMC group. OSMC for aneurysm clipping in patients with MIAs is a relatively safe and economical method. Furthermore, it has good clinical outcomes. This new surgical method is well worthwhile in that it can be applied to patients who are afraid to undergo multiple surgeries, and it is considered an option that can be tried for neurosurgeon who are contemplating how to treat mUIA patients.

Introduction

Multiple intracranial aneurysms (MIAs) account for 7–35% of diagnosed intracranial aneurysms [15, 23, 26], and have a higher risk of rupture than single intracranial aneurysms [13, 31]. Therefore, multiple unruptured intracranial aneurysms (mUIAs) require active treatment. Currently, there are no widely accepted treatment guidelines for multiple intracranial aneurysms, and there is no specific surgical approach that has been optimized for each situation [1, 7, 15, 23]. Studies have reported good mUIAs treatment results with endovascular treatment alone, and some have reported good results with combined and staged clipping, and endovascular treatment [18, 29]. However, multiple craniotomies are required when the intracranial aneurysm location results in difficulties with endovascular treatment. Generally, a unilateral approach is used when performing microscopic clipping of mUIAs in the anterior circulation [25]. If all of the mUIAs cannot be treated with one approach, staged operations should be considered [30, 34]. Although it is uncommon, there have been cases in which two or more craniotomy procedures were performed using one incision [5, 11, 31]. There few studies on bilateral craniotomy, most of which are case reports [6, 7, 12, 20, 28]. In these cases, little has been reported on the preferred method when one-stage multiple craniotomies (OSMC) and multi-stage craniotomies (MSMC) were compared. To provide evidence in support of OSMC as a novel treatment for mUIA, we retrospectively analyzed the OSMC and MSMC results for mUIA clipping.

Materials And Methods

Study Design and Inclusion Criteria

Our hospital’s institutional review board approved this retrospective study. The requirement to obtain informed consent from the patients was waived. A review of the electronic medical records database of the patients who underwent IA clipping from May 2003 to April 2020 at our neurovascular center identified 3,128 surgeries. Among them, 1,212 surgeries were performed on patients with MIAs, and 1,130 patients underwent elective surgery for mUIAs. Seven hundred cases were excluded because all of the aneurysms that were located unilaterally could be treated with a single craniotomy. In addition, 200 cases were excluded because all of the lesions were treated with a combination of microsurgical clipping and coil embolization. Once these cases were excluded, 230 of 1,130 mUIA surgeries were included in this study.

There were 90 and 140 patients in the OSMC and MSMC groups, respectively. Several cases were excluded from the MSMC group, such as those with insufficient surgical data because the first craniotomy was performed at another hospital. In both groups, patients who underwent less than 6 months of follow-up (8 in OSMC and 10 in MSMC groups) were excluded. Finally, 82 and 86 surgeries that were performed on 82 and 43 patients were included in the OSMC and MSMC groups, respectively (Fig. 1).

Demographic and clinical data

Demographic and radiological data were obtained, including the patient's age, sex, medical history, and aneurysm characteristics such as the size, number, and location. The type and combination of craniotomies performed for each patient were investigated, and the estimated blood loss (EBL, mL), amount of blood transfused (units), operation time (min), and anesthesia time (min) were obtained. In the MSMC group, the aforementioned variables were combined and analyzed for two surgeries. The postoperative digital subtraction angiography (DSA) and brain computed tomography angiography (CTA) images were used to evaluate the surgical results. The medical records were used to determine the postoperative complications, including infection, hemorrhage, symptomatic infarction, cranial nerve injury, and length of postoperative hospital stay. Clinical outcomes were compared using the pre- and postoperative modified Rankin Scale (mRS) scores. Considering the recovery period required after surgery, the study was only conducted for patients who could be followed up for more than 6 months. In the case of the MSMC group, the period between the two surgeries was also investigated.

Surgical technique

One-stage multiple craniotomies (OSMC)

In the patients with multiple aneurysms, the number of craniotomies required was determined based on the number and location of the aneurysms. The order of the craniotomies was determined by considering the aneurysm profile. Bilateral pterional craniotomy was performed most often, and the interhemispheric or far lateral approach was used when necessary, depending on the aneurysms’ locations. Among the pterional craniotomy cases, also depending on the aneurysms' locations, a key-hole craniotomy with minimal skin incision was performed. Two methods were used to perform bilateral pterional craniotomy. The first method involved performing head fixation that was appropriate to each surgical position for every two craniotomies. A new surgical drape was also performed for each craniotomy. The second method involved fixing the table once in the neutral position and then tilting the table alternately to both sides. In some cases, the bilateral pterional and interhemispheric approaches were performed simultaneously. In these cases, the surgical position was adjusted by tilting the operating table. After the bicoronal incision, the interhemispheric approach was performed first; thereafter, the operating table was rotated to obtain the surgical position for the pterional approach.

Multi-stage multiple craniotomies (MSMC)

Patients in the MSMC group underwent two independent surgical sessions, and only one type of craniotomy was performed at each surgery. After the first operation, the patient recovered and was discharged with normal postoperative management. The second operation was performed while considering the patient's clinical situation, with at least a 1 month interval between the two operations.

Treatment cost

In terms of the surgery cost, we investigated the total medical expenses incurred during the hospitalization for the surgery and the patient copayment. In Korea, there is a medical insurance system available that allows for almost the entire population (98%) to be eligible for mandatory subscription. Through the application of a reimbursement system for some of the treatment activities that are classified as mandatory items, patients who undergo surgical clipping only pay 5% of the expenses incurred. The total treatment cost paid by the patient consists of 5% of the items covered by the reimbursement system and the sum of the remaining items that are not covered. In the MSMC group, the total treatment costs for the two surgeries were combined because the treatment costs per person were compared. All of the costs are expressed in Korean won converted into United States dollars based on the international exchange rate of ₩1100=$1.

Statistical analysis

Statistical analyses were performed using SPSS for Windows version 25 (IBM Corp., Armonk, NY, United States). Continuous and categorical variables are presented as the mean (range) and number (percentage), respectively. The Mann–Whitney U test was used to analyze continuous variables, because the variables were not normally distributed. Categorical variables were analyzed using either the Chi-square or Fisher's exact tests according to the expected cell frequencies. The linear-by-linear association test and chi-square test were used to compare the procedure characteristics. Statistical significance was set at an alpha level of $p = 0.05$.

Results

Demographic and clinical characteristics

The total number of patients in the OSMC group was 82, consisting of 64 women and 17 men, with a mean age of 57.8 years (range, 37–74 years). The MSMC group consisted of 43 patients, 38 women and 5 men, with a mean age of 57.3 years (range, 36–74 years). There were no statistically significant differences in the sex, age, and medical history. The patient's demographic information is summarized in Table 1.

Table 1
Demographic and clinical characteristics

Characteristic	OSMC	MSMC	p-value[a]
Patient number	82	43	
Mean age, years (range)	57.8 (37–74)	57.3 (36–74)	0.704[b]
Sex, female (%)	64 (78.0)	38 (88.4)	0.204
Medical history, number (%)			
Hypertension	44 (53.7)	22 (51.2)	0.692
Diabetes	6 (7.3)	4 (9.3)	0.471[c]
Dyslipidemia	19 (23.2)	5 (11.6)	0.120
Smoking	23 (28.0)	7 (16.3)	0.142

[a] Chi-square test

[b] Mann–Whitney *U* test

[c] Fisher's exact test

Abbreviations: OSMC, one-stage multiple craniotomies; MSMC, multi-stage multiple craniotomies.

Radiological and procedure characteristics

The number and location of the aneurysms treated with craniotomy are summarized in Table 2. The number of aneurysms in the patients in the OSMC and MSMC groups were 2.8 and 2.6, respectively, and there was no significant difference between the two groups (p = 0.95). Moreover, no significant difference was noted when the size of the largest aneurysm in each patient was compared (5.19 mm vs. 6.42 mm, p = 0.06). Table 3 summarizes the information on the surgical approach used in each group and the combination of surgical approaches used during the surgery. In the OSMC group, 82 surgeries were performed. Of these surgeries, 80.5% and 15.9% (66 and 13 craniotomies, respectively) were bilateral pterional craniotomies, and a combination of the interhemispheric (IH) approach and pterional craniotomy, respectively. There were two surgeries in which bilateral pterional craniotomies and the IH approach were used simultaneously, i.e., three types of surgical approaches were used in one operation. In addition, there was one surgery in which a far lateral approach and pterional craniotomy were performed simultaneously. In the MSMC group, 86 surgeries were performed. Of these surgeries, 88.4% and 7.0% (38 and 3 cases, respectively) were bilateral pterional craniotomies, and a combination of the IH approach and pterional craniotomy, respectively. One surgery combined pterional craniotomy and an orbito-zygomatic approach, and another combined pterional craniotomy and a retromastoid suboccipital approach.

Table 2
Radiological characteristics

Characteristic	OSMC	MSMC	p-value
Location of the aneurysms, number (%)	247	122	
Paraclinoid ICA	51 (20.6)	14 (11.5)	
ICA bifurcation	4 (1.6)	7 (5.7)	
MCA	132 (53.4)	76 (62.3)	
ACoA	15 (6.1)	6 (4.9)	
distal ACA	18 (7.3)	3 (2.5)	
PCA or SCA	7 (2.8)	3 (2.5)	
BA	2 (0.8)	1 (0.8)	
PICA	1 (0.4)	1 (0.8)	
Untreated or coil embolization	17 (6.9)	11 (9.0)	
Number of aneurysms (range)	2.8 (2–7)	2.6 (2–5)	0.095[a]
Average maximum size, mm (range)	5.19 (12.7–2.0)	6.42 (15.6–2.4)	0.060[b]

[a] Chi-square test

[b] Mann–Whitney U test

Abbreviations: OSMC, one-stage multiple craniotomies; MSMC, multi-stage multiple craniotomies; ICA, internal carotid artery; MCA, middle cerebral artery; ACoA, anterior communicating artery; ACA, anterior cerebral artery; PCA, posterior cerebral artery; SCA, superior cerebellar artery; BA, basilar artery; PICA, posterior inferior cerebellar artery.

Table 3
Procedure characteristics

Characteristic	OSMC	MSMC	p-value
Combination craniotomies, number (%)	82	43	0.461[a]
Bilateral pterional	66 (80.5)	38 (88.4)	0.263[b]
Pterional and IH	13 (15.9)	3 (7.0)	0.158[b]
Etc.[c]	3 (3.6)	2 (4.7)	
Craniotomy type, number (%)	166	86	
Rt. pterional	74 (44.6)	41 (47.7)	
IH	15 (9.0)	3 (3.5)	
Lt. pterional	76 (45.8)	40 (46.5)	
Etc.[d]	1 (0.6)	2 (2.3)	

[a] Linear-by-linear association test

[b] Chi-square test

[c] List of the other craniotomy combinations: One-stage — bilateral pterional craniotomies and IH, 2 cases; one-stage — Lt. pterional craniotomy and Lt. far lateral approach, 1 case; multi-stage — Lt. pterional craniotomy and Rt. orbito-zygomatic approach, 1 case; multi-stage — Rt. pterional craniotomy and Lt. RMSOC, 1 case.

[d] List of the other craniotomy types: One-stage — far lateral approach to Lt. PICA aneurysm; multi-stage — Rt. orbito-zygomatic approach to SCA, BA, and AChA aneurysms; multi-stage – Lt. RMSOC for Lt. PICA aneurysm

Abbreviations: OSMC, one-stage multiple craniotomies; MSMC, multi-stage multiple craniotomies; IH, interhemispheric; Rt., right; Lt., left; PICA, posterior inferior cerebellar artery; SCA, superior cerebellar artery; BA, basilar artery; AChA, anterior choroidal artery; RMSOC, retromastoid suboccipital craniotomy.

Surgical outcomes, clinical outcomes, and cost

To determine the amount of blood loss, the number of units transfused intra- or postoperatively was also investigated (Table 4). The average number of red blood cell (RBC) units transfused was 2.0 units. The mean operation and average anesthesia times were 353.9 min and 423.8 min, respectively, and the average length of postoperative hospital stay was 12.3 days. For the MSMC group, the same variables for the two surgeries were examined. They were then combined and these values were used in the comparison. The average EBL and number of RBC units transfused were 1050.9 mL and 2.1 units, respectively. The mean operation and anesthesia times were 490.3 min and 621.0 min, respectively. The average postoperative hospitalization period was 21.8 days. When comparing the OSMC and MSMC groups, there were no statistically significant differences in the EBL and volume of blood transfused ($p = 0.106$ and $p = 0.925$, respectively); however, there were significant differences in the operation and anesthesia times, and length of hospital stay ($p < 0.0001$ for all).

Table 4
Surgical outcomes

Characteristic	OSMC	MSMC	p-value[a]
Mean estimated blood loss, mL (range)	889.5 (200–2500)	1050.9 (350–2600)	0.106
Mean RBC transfusions, unit (range)	2.0 (0–9)	2.1 (11–0)	0.925
Mean FFP transfusions, unit (range)	0.7 (0–6)	1.0 (13–0)	0.279
Mean operation time, minutes (range)	353.9 (215–615)	490.3 (285–805)	< 0.0001*
Mean anesthesia time, minutes (range)	423.8 (215–770)	621.0 (405–945)	< 0.0001*
Mean length of hospitalization, days (range)	12.3 (8–51)	21.8 (17–47)	< 0.0001*
Number of operations, number	82	86	
Complete obliteration, number (%)	60 (73.2)	31 (72.1)	0.898[b]
Remnant or stenosis, number (%)	22 (26.8)	12 (27.9)	
Remnant	19 (23.2)	11 (25.6)	
Stenosis	3 (3.7)	1 (2.3)	

[a] Mann–Whitney U test

[b] Chi-square test

Abbreviations: OSMC, one-stage multiple craniotomies; MSMC, multi-stage multiple craniotomies; RBC, red blood cell; FFP, fresh frozen plasma.

An asterisk (*) indicates a p-value < 0.05.

After the surgery, the results were evaluated using DSA or brain CTA (Table 4). There was no significant difference in complete obliteration between the OSMC and MSMC groups (73.2% vs. 72.1%, $p = 0.898$). In the OSMC group, residual aneurysms and arterial stenosis were found in 19 and 3 cases, respectively (23.2% and 3.7%, respectively). In the MSMC group, residual aneurysms and arterial stenosis occurred in 11 and 1 cases, respectively (25.6% and 2.3%, respectively). Among the stenosis cases, one patient in both the OSMC and MSMC groups had postoperative infarction complications, and revision surgery was performed.

There were 6 and 4 cases (7.3% and 4.7%, respectively) with postoperative complications (Table 5) in the OSMC and MSMC groups, respectively, with a p-value of 0.528. This indicated that this difference was not statistically significant. The complications that occurred in the OSMC group were as follows: 2 infections, 1 infarction, and 1 hemorrhage (2.4%, 1.2%, and 1.2%, respectively), and revision surgeries were performed for each patient. There was also one cranial neuropathy case (oculomotor nerve palsy) that occurred after surgery for a superior cerebellar artery aneurysm and one visual field defect due to optic nerve compression, which was confirmed after surgery for an ophthalmic artery aneurysm. In the MSMC group, the following complications occurred: 1 postoperative infarction and 3 postoperative hemorrhages (1.2% and 3.5%, respectively). The average period until the last follow-up visit was 28.5 months and 28.9 months in the OSMC and MSMC groups, respectively. The clinical outcomes that were evaluated using the mRS showed good results in both groups (0.4 vs. 0.3, $p = 0.698$). Among the patients with postoperative complication, few patients showed persistent neurological disability. Lastly, as confirmed at the outpatient clinic, all but one patient (1.2%) showing visual field defects in the OSMC group recovered. All patients in the MSMC group with complications recovered and confirmed no neurological symptoms.

Table 5
Clinical outcomes

Characteristic	OSMC	MSMC	p-value[a]
Number of operations, number	82	86	
Complications, number (%)	6 (7.3)	4 (4.7)	0.528[b]
Postoperative infection	2 (2.4)	0	
Postoperative infarction	1 (1.2)	1 (1.2)	
Postoperative hemorrhage	1 (1.2)	3 (3.5)	
Etc.[c]	2 (2.4)	0	
Mean final follow-up visit, months (range)	28.5 (6–92)	28.9 (6–170)	0.494
Mean preoperative mRS score (range)	0.1 (0–2)	0.2 (0–2)	
Mean postoperative mRS score (range)	0.4 (0–2)	0.3 (0–1)	
Permanent neurological disability (%)	1(1.2)[d]	0	0.304

[a] Mann–Whitney U test

[b] Fisher's exact test

[c] List of the other complications: Third nerve palsy after Lt. SCA aneurysm clipping and visual field defect due to optic nerve compression after Lt. OphA aneurysm clipping.

[d] Visual field defect due to optic nerve compression after Lt. OphA aneurysm clipping

Abbreviations: OSMC, one-stage multiple craniotomies; MSMC, multi-stage multiple craniotomies; mRS, modified Rankin Scale; Lt., left; SCA, superior cerebellar artery; OphA, ophthalmic artery.

Finally, we compared the surgery costs between the two groups (Table 6). Regarding the total treatment cost, the average values for the OSMC and MSMC groups were \$17,749 and \$22,563, respectively. This difference was statistically significant ($p < 0.001$). In Korea, medical insurance covers a large part of aneurysm surgery; thus, the actual amounts paid by the patients were compared. In terms of the mean co-payment, there was also a statistically significant difference between the OSMC and MSMC groups (\$4,845 vs. \$5,764; $p = 0.045$).

Table 6
Treatment costs

Characteristic	OSMC	MSMC	p-value[a]
Mean total expenditure, USD	$17,749.25	$22,563.16	< 0.0001*
Maximum	$35,925.21	$51,095.61	
Minimum	$8,037.76	$14,999.05	
Mean co-payment, USD	$4,845.00	$5,764.58	0.049*
Maximum	$13,835.76	$10,455.02	
Minimum	$1,409.01	$2,310.48	

[a] Mann–Whitney U test

Abbreviations: OSMC, one-stage multiple craniotomies; MSMC, multi-stage multiple craniotomies.

An asterisk (*) indicates a p-value < 0.05.

Discussion

In cases of MIA, the risk of rupture is relatively high, all aneurysms in need of treatment should be treated as soon as possible; however, as mentioned above, there are no specific guidelines for this process [7, 16, 25]. If possible, all of the aneurysms should be treated endovascularly [3, 21]. However, there is no reason to avoid one stage operation if multiple lesions can be operated simultaneously [25]. Even in cases of lesions in multiple areas, single craniotomies may be attempted [1, 22]. In other cases, multimodality treatment [2] or staged operations are attempted [24, 27]. Staged operations may be performed in cases where the lesion is at a location that requires different craniotomies, such as in bilateral middle cerebral artery aneurysms. In patients with aneurysms that require multiple craniotomies, there should be a time interval between the two operations. With OSMC, we attempted an extremely shortened form of this time interval.

OSMC are an attempt to eliminate the 'time' between the surgeries by performing multiple approaches concurrently; thus, this may be considered a worthwhile method. Based on the experience of various methods of minimal invasive surgery attempts and the accumulation of knowledge accumulated by previous researchers, multiple approaches could be attempted at once. Regarding MSMC, it is difficult to keep the vital signs stable when considering the continued possibility of aneurysm rupture during the first postoperative management process [7, 19, 32]. Even if the patient recovers well without any complications in the acute postoperative phase, the second operation should be carried out within 1 to 2 months [14]. This is because the patient needs time to physically or psychologically recover after the surgery. One study found that patients with unruptured aneurysms experienced a poor quality of life preoperatively; this concept also applies to patients who are between surgeries [4].

In the OSMC group, the operation and anesthesia times, and hospitalization period were short, and the economic burden (total treatment cost and co-payment amount) was lessened; however, these results may reflect the omission of the overlapping elements in each surgical procedure. Simply put, time was saved and the economic burden was lessened with the OSMC group because the induction, extubation, and recovery processes were omitted once for each patient, compared to the MSMC group. Contrastingly, there was no substantial difference in the amount of blood loss, surgical results, and complications, which may be considered variables that are only related to surgery, regardless of whether the two operations were performed separately or consecutively. In other words, we propose that two craniotomies with one type of anesthesia do not result in increased blood loss or an increased incidence of complications. Moreover, prolongation of the anesthesia time and CSF overdrainage could be factors that induce complications; however, the incidence of complications relating to these two factors did not increase.

In this study, the remnant ratio (OSMC and MSMC groups: 23.2% and 25.6%, respectively) was higher than the remnant incidence rate (13.3–18%) reported in other studies [9, 17]. DSA or brain CTA were used to determine whether there was complete obliteration after surgery and DSA can be considered a more accurate test than brain CTA [8]. We performed a study in which the surgery results were strictly determined using DSA rather than brain CTA. In fact, in the patients for whom DSA was used to determine the presence of remnants, most of the remnants were not identified on the brain CTA that was performed at the postoperative follow-up visit, and no additional surgeries were performed due to an increase in the remnant aneurysm size.

Our study had several limitations. Since this was a retrospective study, selection bias should be considered. This study only targeted mUIAs; therefore, caution should be exercised when OSMC are applied to aneurysmal subarachnoid hemorrhage (aSAH) patients with MIAs. Although some studies have reported OSMC in patients with multiple aneurysms and aSAH who underwent emergency surgery [20, 28, 31], we propose that the use of OSMC should be considered carefully because brain relaxation is difficult. This study is the result of an analysis of the surgeries performed in a single, large-scale, neurovascular center in Korea. Therefore, we propose that the results reflect the factors that apply to OSMC performed in a well-equipped hospital with skilled neurovascular surgeons and anesthesiologists, and that OSMC is recommended under similar conditions. Finally, among the various treatment methods for multiple aneurysms, we only compared between microsurgeries, not endovascular surgery. However, most of the cases in our study could be considered significant because craniotomy is the preferred treatment method for aneurysms when compared to endovascular surgery. With the aim of studying the overall strategy for the treatment of multiple aneurysms, a follow-up study that compares and analyzes the treatment outcomes, including those for endovascular surgery, should be performed.

In conclusion, there were no significant differences in the occlusion and complication rates when OSMC was compared to MSMC. Moreover, OSMC showed favorable results in terms of the operation time, hospitalization period, blood loss, and hospital expenses. Therefore OSMC could be considered for its beneficial effect on the patient time and economic burden.

Declarations

Funding

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Compliance with Ethical Standards

Conflicts of interest/competing interests

The authors declare that they have no conflicts of interest or competing interests.

Research involving Human Participants and/or Animals (Ethical approval)

This study was approved by the local ethics committee and institutional review board (B-2007/622-106). This retrospective observational study involving human participants was in accordance with the ethical standards of the local ethics committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent

The Seoul National University Bundang Hospital Ethical Committee approved the study protocol and waived the requirement for individual patient consent to be provided for the study.

Availability of data and material

Not applicable.

Code availability

Not applicable.

Authors' contributions

All the authors contributed to the study conception and design. Dongwook Seo and Hyunjun Jo performed the material preparation, and data collection and analysis. The first manuscript draft was written by Dongwook Seo. All the authors commented on previous versions of the manuscript. All the authors read and approved the final manuscript.

Consent to participate

The Seoul National University Bundang Hospital Ethical Committee waived the requirement for individual patient consent to be provided for the study.

Consent for publication

The Seoul National University Bundang Hospital Ethical Committee waived the requirement for individual patient consent to be provided for the study.

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Figures

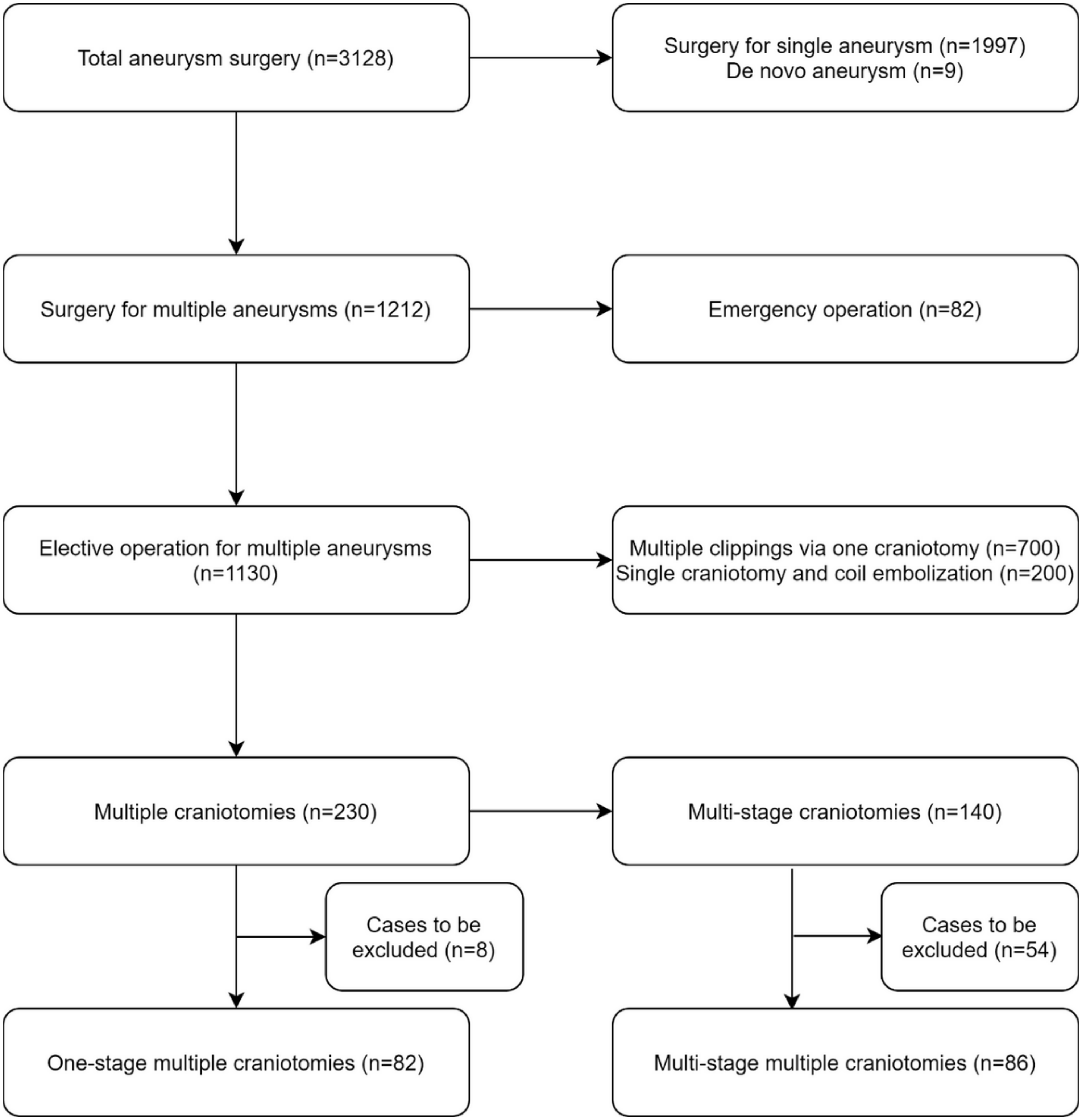

Figure 1

Flow chart to demonstrate the study’s inclusion/exclusion criteria and subgroups