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Minimally invasive thumb-sized pterional craniotomy for surgical clip ligation of unruptured anterior circulation aneurysms

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Abstract:	Less invasive surgical approaches for intracranial aneurysm clipping may reduce length of hospital stay, surgical morbidity, treatment cost, and improve patient outcomes. We present our experience with a minimally invasive pterional approach for anterior circulation aneurysms performed in a major tertiary cerebrovascular center and compare the results with an aged matched dataset from the Nationwide Inpatient Sample (NIS). From August 2008 to December 2012, 22 elective aneurysm clippings on patient's ≤55 years of age were performed by the same dual fellowship-trained cerebrovascular/endovascular neurosurgeon. One patient (4.5%) experienced transient post-operative complications. 18 of 22 patients returned for follow-up imaging and there were no recurrences through an average duration of 22 months. A search in the NIS database from 2008 to 2010, also for patients aged ≤55 years of age, yielded 1,341 hospitalizations for surgical clip ligation of unruptured cerebral aneurysms. Inpatient length of stay and hospital charges at our institution using the minimally invasive thumb-sized pterional technique were nearly half that of NIS (length of stay: 3.2 vs 5.7 days; hospital charges: $52,779 vs $101,882). The minimally invasive thumb-sized pterional craniotomy allows good exposure of unruptured small and medium-sized supraclinoid anterior circulation aneurysms. Cerebrospinal fluid drainage from key subarachnoid cisterns and constant bimanual microsurgical techniques avoid the need for retractors which can cause contusions, localized venous infarctions, and post-operative cerebral edema at the retractor sites. Utilizing this set of techniques has afforded our patients with a shorter hospital stay at a lower cost compared to the national average.
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February 20, 2013

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Elizabeth Sheeley
Associate Editor, *Journal of Visualized Experiments*

Dear Ms Sheeley:

Thank you for allowing us to submit a revision of the manuscript entitled, "**Minimally invasive thumb-sized pterional craniotomy for surgical clip ligation of unruptured anterior circulation aneurysms"**, to the *Journal of Visualized Experiments*. We have responded to the reviewers comments and provided a detailed summary of responses.

This study was performed with ethical adherence. All authors have read and approved the submitted manuscript; the manuscript has not been submitted elsewhere nor published elsewhere in whole or in part. I would like to disclose that I am a physician consultant for ev3/Covidien, Integra, and MicroVention. We thank you in advance for your time reviewing this manuscript.

Sincerely,

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Title: Minimally invasive thumb-sized pterional craniotomy for surgical clip ligation of unruptured anterior circulation aneurysms.

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KEYWORDS:
craniotomy, cerebral aneurysm, clip ligation, health care costs, length of stay, minimally invasive, retractorless, surgery.

SHORT ABSTRACT:
Minimally invasive thumb-sized pterional craniotomy for aneurysm clipping has afforded our patients with a shorter hospital stay at a lower cost compared to the national average.

LONG ABSTRACT:
Less invasive surgical approaches for intracranial aneurysm clipping may reduce length of hospital stay, surgical morbidity, treatment cost, and improve patient outcomes. We present our experience with a minimally invasive pterional approach for anterior circulation aneurysms performed in a major tertiary cerebrovascular center and compare the results with an aged matched dataset from the Nationwide Inpatient Sample (NIS). From August 2008 to December 2012, 22 elective aneurysm clippings on patient's ≤55 years of age were performed by the same dual fellowship-trained cerebrovascular/endovascular neurosurgeon. One patient (4.5%) experienced transient post-operative complications. 18 of 22 patients returned for follow-up imaging and there were no recurrences through an average duration of 22 months. A search in the NIS database from 2008 to 2010, also for patients aged ≤55 years of age, yielded 1,341 hospitalizations for surgical clip ligation of unruptured cerebral aneurysms. Inpatient length of stay and hospital charges at our institution using the minimally invasive thumb-sized pterional technique were nearly half that of NIS (length of stay: 3.2 vs 5.7 days; hospital charges: $52,779 vs $101,882). The minimally invasive thumb-sized pterional craniotomy allows good exposure of unruptured small and medium-sized supraclinoid anterior circulation aneurysms. Cerebrospinal fluid drainage from key subarachnoid cisterns and constant bimanual microsurgical techniques avoid the need for retractors which can cause contusions, localized venous infarctions, and post-operative cerebral edema at the retractor sites. Utilizing this set of techniques has afforded our patients with a shorter hospital stay at a lower cost compared to the national average.

INTRODUCTION:
Surgical clip ligation had been the mainstay of treatment for intracranial aneurysms but has been recently supplanted mostly by less invasive endovascular techniques.[1,2] Clinical trials including the *International Study of Unruptured Intracranial Aneurysms (ISUIA-1 and ISUIA-2)*, and the *International Subarachnoid Aneurysm Trial (ISAT*) have demonstrated lower morbidity and mortality, reduced length of hospital stay, and lower overall expense, with endovascular treatment compared to surgical clip ligation.[3–5] However, the higher aneurysm recurrence rate after endovascular therapy has led to the examination of the cumulative risk to the patients compared to surgical clip ligation.[3,4] Surgical treatment remains an important modality for aneurysm therapy, particularly for anterior circulation aneurysms that have morphologies that may be difficult to treat with endovascular means.

Unlike advancements in endovascular devices, few advances in surgical techniques have been made recently. Techniques to make surgical treatment less invasive have included the supraorbital craniotomy combined with the eyebrow incision for anterior circulation aneurysms and "retractorless surgery" to minimize surgical trauma to the brain during aneurysm clipping.[6–8] These less invasive surgical approaches may reduce length of hospital stay, surgical morbidity, treatment cost, and improve patient outcomes.[9]

Here, we present our experience with a minimally invasive approach to surgical clip ligation of unruptured intracranial aneurysms using a pterional approach for anterior circulation aneurysms performed in a major tertiary cerebrovascular center and compare the results with an age matched dataset from the Nationwide Inpatient Sample (NIS). The surgical technique will be reviewed, including patient preparation, brain relaxation, sylvian fissure dissection, and closure. Post-operative care and discharge requirements will also be outlined.

PROTOCOL:

Prior to performing this procedure, obtain all required institutional approval and patient consent.

1. Surgical Technique

1.1) Induce patient with general anesthesia.

1.2) Place radial arterial line for blood pressure monitoring.

1.3) Place patient in the supine position on the operating room table.

1.4) After the head is clamped into the Mayfield Head holder using standard techniques for a pterional craniotomy, position the head 30-45 degrees with the ipsilateral side up towards the ceiling, except for anterior-communicating artery aneurysms in which the head is placed at 60 degrees to allow for better visualization across the interhemispheric fissure.

1.5) Position the neck midline and translate anteriorly to maximize jugular venous drainage to prevent cerebral edema and then extend the head to position the ipsilateral zygoma at the highest point—this allows for frontal lobe relaxation and elevation from the orbital roof during dissection without the use of retractors.

1.6) Clip the hair in preparation for standard pterional scalp incision; use about a one to two inch strip behind the hairline.

1.7) Sterilely prep the skin and drape the surgical area according to standard of care.

1.8) Perform a standard curved scalp incision for a pterional approach extending from the midline of the scalp behind the hairline with a gentle curve posteriorly and inferiorly towards the tragus ending it about three millimeters anterior to the tragus and at the level of the superior edge of the zygoma. Perform this incision down to the skull above the superior temporal line and to the muscle fascia at the level of the temporalis muscle.

1.9) Use electrocautery for scalp hemostasis with the bipolar device .

1.10) Cut the temporalis muscle down to the skull using the bovie monopolar electrocautery device.

1.11) Raise a myocutaneous flap keeping the temporalis muscle attached to the undersurface of the scalp for now. Fish-hooks are used to evert the flap after the temporalis muscle is elevated from the skull using a combination of monopolar electrocautery and a periosteal elevator.

1.12) Perform an inverse subfascial dissection in the avascular plane from the undersurface of the myocutaneous flap using Metzenbaum scissors, keeping the fascia and subfacsial fat pad with the scalp to avoid injury to the facial nerve.

1.13) Secure the temporalis muscle posteriorly and inferiorly to expose the pterional region with "star" fishhooks.

1.14) Keep all components of the myocutaneous flap moist with wetted gauze.

1.15) Drill a single temporal 5mm burr-hole at the posterior-most aspect of the planned craniotomy with a 2mm cutting burr so that the foot plate of the side-cutting drill can be inserted into this hole and then use a side-cutting drill with a foot plate to remove the thumb-sized (approximately 3x4cm) kidney-shaped craniotomy centered anteriorly around the pterion.

1.16) Using a No. 1 Penfield, separate the dura on all sides of the pterion and have an assistant gently retract the dura away from the bone surface that is being drilled to minimize risk of penetrating the dura and causing cortical injury.

1.17) Remove the pterion with a drill: anteriorly, until the superior and lateral aspects of the orbital roof are smooth and flattened down to the outer cortical table of bone, without entering the orbit, to maximize subfrontal exposure; medially, drill until the superior orbital fissure dura is exposed and remove any small pieces of bone that would interfere with medial exposure using either a drill bit or hand-held Lempert bone cutting device. Ensure that excellent hemostasis of all soft-tissue and bone surfaces has been obtained to avoid blood dripping into the intradural space during brain dissection and aneurysm exposure, using electrocaurtery and bone wax as needed, before opening the dura.

1.18) Gently elevate the dura and use a No. 11 scalpel to penetrate the dura and then use dural scissors to create a "C-shaped" opening in the dura with the base at the pterion. Secure the dura flat against the outer cortical bone of the orbit without having redundant dural leaflets that would otherwise obscure visualization of the proximal Sylvian Fissure and subfrontal region. This can be performed by using 4-0 Surgilons sutures to tack the dura to the scalp.

2. Brain Relaxation

2.1) Give 25-50grams of Mannitol at the time of bone flap removal to relax the brain if anesthesia agrees that the blood pressure will tolerate diuresis. Note: This will allow time for the diuresis to occur and ultimately will relax the brain to help maximize gravity dependent brain retraction during dissection.

2.2) Keep End-Tidal pCO2 between 30-35mm Hg to achieve slight hypercapnea. Note: This will safely allow for brain relaxation and maximize gravity dependent brain retraction during dissection.

2.3) Evacuate cerebrospinal fluid (CSF) to promote brain relaxation by opening the arachnoid cisterns in the interoptic, carotid-optic, and carotid-oculomotor cisterns and patiently suction CSF until the desired brain relaxation has been achieved. Note: This typically takes about one minute; no lumbar drain is needed with this technique and it dramatically opens the surgical corridors.

3. Sylvian Fissure Dissection

3.1) Bring the intra-operative microscope with the mouthpiece into the field using sterile techniques. Also bring surgical chairs with arm support into the field sterilely to maximize bimanual dexterity and to prevent surgeon arm and hand fatigue. Note: The mouthpiece should be adjusted before draping so that the surgeon can move the microscope with the mouth while simultaneously looking through the ocular pieces.

3.2) Perform dissection
Note: For anterior communicating artery aneurysms, no Sylvian Fissure dissection is required and minimal (2-3mm in extreme cases only, but this is a rare occurrence) to no gyrus rectus resection is needed using only subfrontal dissection; all other supraclinoid anterior circulation aneurysm locations (including posterior communicating artery) require < 1cm proximal Sylivan Fissure dissection to expose the supraclinoid internal carotid artery, its branches (posterior communicating and anterior choroidal arteries), the internal carotid artery terminus, the A1 and M1 origins, and the proximal A2 and M2 segments distal to their respective bifurcations. Total Sylvian Fissure exposure was dime-size (1cm x 1cm) and no brain retractors were used for any of the cases reported. Gravity dependent brain relaxation was sufficient for excellent exposure of the soft tissue structures and vasculature needed to perform surgical clip ligation in the areas discussed above.

3.3) Using bimanual manipulation with surgical microinstruments gently open the arachnoid corridors, holding the brain tissue aside with the edge of the instrument handles or suction device as needed through this exposure. Note: The senior author's preference is to use 4-French Fukishima suction tip in the non-dominant hand and in the dominant hand bipolar bayonettes for blunt dissection or microscissors for sharp dissection. Moistened telfa strips are placed on the brain surface at the site of manipulation to prevent cortical injury. Cottonoids often stick to the brain surface and can’t be easily advanced deeper as the dissection progresses, without causing mild cortical injury.

3.4) Use the mouthpiece on the operating microscope frequently to adjust the scope and focus length as needed while keeping both hands in the field.

3.5) Secure the aneurysm in standard fashion, using the suction most often in the non-dominant hand to maintain the surgical corridor and visualization free of CSF.

3.6) After clip placement, perform intra-operative Doppler of the aneurysm dome to confirm cessation of flow as well as the inflow and outflow vessels to confirm flow and carefully examine the aneurysm neck and parent vessels. We reserve intra-operative digital subtraction angiography (DSA) for anterior communicating artery aneurysms and those clipped aneurysms where inflow, outflow, or aneurysm neck cannot be visualized completely or there is a concern with intra-operative Doppler. Intra-operative DSA is preferred over indocyanine green (ICG) angiography because when multiple aneurysm clips are used to reconstruct the aneurysm neck, the clip can obstruct visualization. Note: Once the aneurysm has been securely clipped, the microscope is removed from the field and the brain irrigated with normal saline solution to minimize the amount of pneumocephalus after closure.

3.7) After inspecting the clip for aneurysm occlusion with the Doppler, the aneurysm dome is perforated with a 22 gauge needle attached to intravenous tubing and a 10 milliliter syringe and manually suction aspirated to confirm aneurysm occlusion.

3.8) Reapproximate the native dura with 4-0 surgilon and cover with a synthetic dural substitute if a watertight closure is not able to be obtained properly.

3.9) Secure bone plates with a metal plating system per standard of care.
Note: Secure the frontal edge of the bone flap flush against the native bone to avoid space between the two which would not be cosmetically pleasing after the tissues heal.

3.10) Reapproximate the temporalis muscle fascia with interrupted 2-0 Vicryl sutures. Secure the top of the temporalis muscle with a 2-0 Vicryl stitch to the frontal metal plate to reapproximate it to the superior temporal line.

3.11) Reapproximate the galea using 3-0 Vicryl sutures and close the scalp in a standard fashion using either staples, nylon, or prolene. Dress with sterile bandages per surgeon preference.

4. Post-Treatment Care

4.1) Admit patient to the intensive care unit after treatment and mobilize with the nursing staff as soon as sedation or general anesthesia has worn off enough to do so, typically within 6 hours of extubation.

4.2) Order physical and occupational therapy to begin post-operative day one in order to assess the patient for safe discharge to home if there were any concerns by the nursing staff.

4.3) Discharge the patient when criteria are met: pain controlled with only oral medications, voiding independently, ambulating independently, and tolerating oral food intake.

REPRESENTATIVE RESULTS:

Currently, at our institution over 150 aneurysms are treated annually. From August 2008 to December 2012, 22 elective aneurysm clippings using this minimally invasive thumb-sized pterional craniotomy technique for supraclinoidal aneurysms on patient's ≤55 years of age were

performed by the same dual fellowship-trained cerebrovascular/endovascular neurosurgeon that developed this technique (EMD) (Table 1). This age group was chosen as earlier trials have shown that surgical treatment of aneurysms in patients above this age result in worse outcomes than endovascular treatment and hence, few patients older than 55 are treated with surgical clip ligation at our institution.

Only one patient (4.5%) treated for a right MCA aneurysm experienced a post-operative complication. A head CT scan was obtained due to decreased left upper extremity movement and revealed ischemic changes in the distribution of a right MCA branch most consistent with a thromboembolic event during clip ligation or transient vasospasm. The patient improved with physical and occupational therapy and was at baseline at two-month follow-up. 18 of 22 patients returned for follow-up imaging and there were no recurrences through an average duration of 22 months.

To represent the national average, we utilized the Nationwide Inpatient Sample (NIS) from 2008 to 2010. The NIS is a hospital discharge database that represents approximately 20% of all inpatient admissions to nonfederal hospitals in the United States. We obtained the NIS database from the Agency for Healthcare Research and Quality's Healthcare Cost and Utilization Project (Rockville, MD). For more information regarding the NIS database, please see http://www.hcup-us.ahrq.gov/nisoverview.jsp.

Hospitalizations for clipping of unruptured cerebral aneurysms were collected from the NIS by cross-matching the International Classification of Diseases (ICD-9-CM) diagnosis code for an unruptured cerebral aneurysm (437.3) with the procedure code for clipping (39.51) of a cerebral aneurysm. The ICD-9-CM codes used for aneurysm clipping have been previously studied and validated.[10–16] Only patients under 55 years of age were included, as to age-match the cases with our internal dataset. We excluded patients with "subarachnoid hemorrhage" (ICD-9-CM 430) and "intracerebral hemorrhage" (ICD-9-CM 431). In comparing total hospital charges across the years we assumed a 3% annual inflation rate for each year and used the adjusted charges in the analyses.

1,341 hospitalizations for surgical clip ligation of unruptured cerebral aneurysms were identified. Inpatient length of stay and hospital charges at our institution using the minimally invasive thumb-sized pterional technique were compared to NIS using Mann-Whitney U tests. Both outcome measures were significantly reduced at our institution in comparison to the national average (Table 2).

DISCUSSION:

Surgical clip ligation of intracranial aneurysms remains a relevant and important option in treating certain types of aneurysms, though this role has been diminishing over the past several years as endovascular technology becomes safer and more efficacious. Endovascular treatment has surpassed surgery for cerebral aneurysms, yet the higher recurrence rate after endovascular treatment, the occasional need for surgical treatment after aneurysm recurrence from failed endovascular treatment, specific morphologies making endovascular therapy higher risk requiring stent placement, and some recent literature reviewing the cumulative risk of

endovascular treatment being higher than for surgical treatment, all keep surgical clip ligation relevant to aneurysm treatment.[17]

The subfrontal approach was first described as a unilateral approach by Krause in 1908, and then modified by Dandy and Heuer for lesions of the pituitary gland and optic canal.[18] In 1933, Dott used this approach for clipping an aneurysm.[19] Through this technique there is minimal brain exposure and wide access to the suprasellar region with minimal need for brain retractors. Dandy and later Yasargil modified and used this technique to clip anterior communicating artery aneurysms.[20,21] Many other neurosurgeons have modified this technique describing it by different terms and have used this approach not only to reach vascular, but also anterior skull base lesions. Al-Mefti and Fox modified the supraorbital approach to the supero-lateral orbital exposure.[22] This extends the supraorbital craniotomy to include the lateral and superior orbital wall. This approach was used for orbital and skull base tumors as well as for complex anterior circulation aneurysm clipping. The advances in neurosurgery have been reflecting the size of the craniotomy and exposure not only for the cosmetic advantage but also to avoid complications such as epidural hematomas, unintended cortical injury, brain retraction, and the time of exposure to room air.

Van Lindert *et al* reported a series of 139 patients with a total of 197 aneurysms that were treated with clipping through the supraorbital keyhole approach.[18] In this study no complications related to the exposure were reported, and only four patients experienced aneurysmal rupture during clipping. The ruptures were attributed to aneurysm dissection or a result of clip application, and not due to brain retraction. The authors describe that multiple aneurysms can be safely clipped in the same procedure and that contralateral aneurysms can be safely reached. Petraglia *et al* reported a series of 28 patients with anterior communicating artery aneurysms that were treated with clipping through the subfrontal approach.[8] They describe this technique as safe and with fewer complications compared to the traditional pterional approach.

Some of the limitations related to the keyhole supraorbital approach are: (1) the keyhole is not always performed in the same anatomical location. The small incision and craniotomy requires good preoperative planning with MRI and CT reconstructions that depict the aneurysm orientation and the bony structures. In this way the incision and craniotomy need to be individualized for each patient's anatomy. (2) The direction of the instruments and light must be in the same plane and may require special clips that allow better visualization of the target. (3) There is a higher risk of opening of the frontal sinus, which may negate any cosmetic advantages compared to the pterional approach.[23] (4) Requires a well trained vascular neurosurgeon.

At our institution, the senior author's (EMD) approach for clipping anterior intracranial aneurysms involves thumb-sized pterional craniotomies without brain retractors. It is important to use a mouthpiece on the operative microscope for continuous readjustment of focus and angle of view to maintain constant bimanual manipulation of the brain tissues without retractors. This is considered less invasive than the standard approach and prevents many post operative complications and provides a faster recovery. We believe this is reflected in the shorter post-operative length of stay and lower total hospital charges, in comparison to the national average from NIS.

It is important to note that the patients treated at our institution had supraclinoid aneurysms. We do not treat aneurysms below the communicating segment of the internal carotid artery using the described clipping technique because drilling of the anterior clinoid process would require a larger craniotomy and cervical carotid cut-down for proximal arterial control. Additionally, none of the aneurysms treated in this study were considered giant aneurysms (> 20 mm). In our experience, these larger aneurysms typically require more extensive exposure to allow bypass and dissection to identify inflow and outflow zones and would not be treated well with a mini-craniotomy. Additionally, this smaller sized craniotomy does readily allow for multiple clip placements when needed and provides adequate exposure for proximal and distal control of the parent arteries associated with supraclinoid aneurysms in preparation for possible aneurysm rupture during dissection or clip placement. It avoids using the standard sized craniotomy flap to minimize any unnecessary exposure of the cortical surface which can be damaged during the approach. It also minimizes potential space for fluid and blood collections to form in the subdural and epidural spaces.

It is important to recognize however, that this is a single-center, single surgeon, retrospective study with a relatively small sample size. Treatment was not randomized and this could be a potential for selection bias. We tried to minimize bias by matching the groups with only patients under 55 years of age; knowing that advanced age is a contraindication to clipping of an unruptured cerebral aneurysm.[3] However, due to limitations of the NIS, we could not control for important confounders such as aneurysm size and location, limiting the conclusions that can be drawn in our comparisons with the national average. The lower costs and shorter length of stay at our institution, in comparison to the national averages, can also be partially attributed to institutional resources. Centers handling a large volume of cases for aneurysm treatment likely have a dedicated staff and a standardized set of protocols. A prospective randomized multicenter trial that includes the cost of long-term follow-up, recurrence rates, and return to work will better address these limitations and expand the scope of the study.

Lastly, we emphasize that this technique is being reported for the surgical treatment of unruptured supraclinoid anterior circulation aneurysms measuring no larger than 20mm. Larger or ruptured aneurysms, were not evaluated in this study because these aneurysms frequently require larger craniotomies for bypass and proper exposure and in the case of subarachnoid hemorrhage, larger craniotomies are required because of brain swelling, potential craniectomy, and access to lobar intraparenchymal hemorrhages. Though this exposure has been used in low Hunt-Hess grade subarachnoid hemorrhage patients with small and medium sized anterior circulation aneurysms in the locations described above, these data were not studied here and are not recommended until the surgeon has established a degree of comfort with surgical exposure first, with the unruptured aneurysms. The minimally invasive thumb-sized pterional craniotomy allows good exposure of small and medium-sized supraclinoid anterior circulation aneurysms. Additionally, minimal to no Sylvian Fissure dissection can be acquired with this craniotomy when approaching anterior communicating artery aneurysms. The senior author has found this approach to be very effective when approaching both ruptured and unruptured anterior communicating artery aneurysms, particularly those pointing inferiorly and anteriorly where the neck and inflow and outflow vessels could be readily identified. This thumb-sized craniotomy allows a subfrontal approach with minimal to no dissection of the Sylvian Fissure or resection of the Gyrus Rectus.

We recommend that neurosurgeons who do not routinely employ these surgical techniques, judiciously and progressively incorporate these minimally invasive and less tissue damaging maneuvers into their approach based upon comfort level. Cerebrospinal fluid drainage from key subarachnoid cisterns and constant bimanual microsurgical techniques avoid the need for retractors which can cause contusions, localized venous infarctions, and post-operative cerebral edema at the retractor sites. Utilizing this set of techniques has afforded our patients with a shorter hospital stay at a lower cost compared to the national average.

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DISCLOSURES:
Eric Deshaies is a physician consultant for MicroVention, Covidien Neurovascular, Integra LifeSciences Corporation.

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N/A

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Table

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Table 1: Internal dataset patient characteristics

Age, yrs	47.5 (44-52)
Male	4 (18%)
Aneurysm maximum dimension, mm	6.3 (5.6-9.0)
Location	
Internal carotid artery	4 (18%)
Middle cerebral artery	7 (32%)
Anterior cerebral artery	2 (9%)
Anterior communicating artery	6 (27%)
Posterior communicating artery	3 (14%)
Craniotomy size, mm^2	1835 (1370-2133)
Postoperative complications	1 (4.5%)
Duration of follow-up, months	22 (14-28)
Recurrence	0 (0%*)

Continuous variables presented as median (intequartile range)

Categorical variables presented as n (%)

*4 patients were not available for follow-up imaging

Table 2: Internal dataset compared to Nationwide Inpatient Sample (NIS)

	Internal dataset	NIS
Age, yrs	47.5 (44-52)	47 (42-52)
Length of stay, days	2 (1-3)	4 (3-6)
Hospital charges, $	49,040 (42,550-58,767)	77,178 (55,778-121,461)

Continuous variables presented as median (interquartile range)

P Value
0.561
<.001
<.001

*Excel Spreadsheet- Table of Materials/Equipment

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Name of Reagent/ Equipment	Company
Mayfield Infinity skull clamp	Integra
Mayfield table attachment	Integra
4-French Fukishima suction tip	Integra
Periosteal elevator (Langenbeck)	Codman
Metzenbaum scissors	Codman
Malis dissector, round angled	Codman
Penfield dissector, style 1	Codman
Lempert bone rongeur	Codman
Malis Irrigation Module	Codman
Bovie monopolar electrocautery device	Codman
Insulated blade for electrocautery device	Covidien
Fish-hook retractors	Lone Star
Pneumatic drill	Medtronic
Side-cutting drill	Medtronic
Fluted legend match head tool	Medtronic
Surgical scalpel No. 10,11,15	Bard-Parker
Intra-operative microscope with mouthpiece	Leica
Microscissors	V. Mueller
Rhoton dissector, #2	V. Mueller
Telfa strips	American Surgical
Aneurysm clip	Aesculap
Raney clip applier	Aesculap
Synthes Matrix metal plating system	Synthes
Braided absorbable surgical sutures (Vicyrl)	Ethicon
Braided nylon nonabsorbable surgical sutures (Nurolon) 4-0	Ethicon
Doppler System	Mizuho

Catalog Number

A-1114
A-1018
R-8986
65-1116
36-5023
80-1541
65-1015
19-1232
Module 1000

E1455
3350-8G
Midas Rex MR7
F2/8TA23
10MH30
0029064 (No.10), 0018291 (No.11), 0018043 (No.15)

NL3785-034(st), NL3785-035(cvd)
NL3785-002
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Author(s): Gentian Toshkezi MD, Mark R Villwock MS, Amit Singla MD, Eric M Deshaies MD

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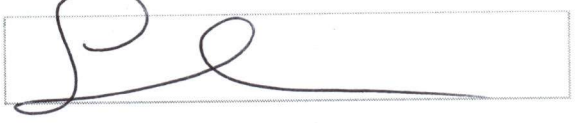
Signature:  Date: 9/25/13

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Reviewers' comments:

Reviewer #1:
The authors describe their experience with some modifications to the standard pterional approach for clip ligation of supraclinoid small to medium sized anterior circulation aneurysms. The modifications described are mainly focused in making the craniotomy smaller and to reduce unnecessary surgical tissue trauma during surgery, which in the paper is called minimally invasive. The authors compare their results in terms of complications, length of hospital stay and hospital charges with an age matched database of patients operated for unruptured intracranial aneurysms in other hospitals.

The paper is well written and the background, purpose and reasoning about reducing tissue trauma is well thought and explained. The step by step technique is very well described and detailed and easy to follow for the reader. However the modifications made to standard pterional approach is not so significant that this approach should be considered a separate entity as the authors have postulated: the "thumb sized" pterional craniotomy.

Furthermore, the strive for yet smaller craniotomies to achieve a cosmetically better result, may be hazardous if the craniotomy becomes so small that the maneuverability in and around the aneurysm becomes hindered or cumbersome because of the reduced space. This may lead to an intraoperative catastrophe if the aneurysm ruptures during dissection and if the view is obstructed may lead to that the surgeon can not deal with this event in an appropriate fashion, which contrary to the intent may lead to become a maximally invasive approach with increased tissue trauma and increased morbidity and even mortality.

Moreover, the comparison of the authors results to a database to "prove" the minimal invasive superiority in terms of in hospital length of stay and hospital costs is not a valid comparison. There are too many unknown confounding factors, that the authors have not controlled for, that can explain these differences. This is however to some extent discussed by the authors.

With these points of hesitance I recommend that this paper should be published in JoVE because it adds to the body of informative educational literature and the paper can be used as step by step guide to perform a pterional craniotomy of adequate size for clip ligation of aneurysms, but could also be used for other small or medium sized pathology in and around the suprasellar/parasellar region and pterion.

- **Thank you for your time in reviewing this manuscript. We have added an additional sentence to our limitation paragraph in the discussion (lines 382-384) to address our inability to control for important confounders such as aneurysm size and location in our comparison with the national average.**
- **Additionally, we have added to the discussion section (6th paragraph – Lines 370-372). This smaller sized craniotomy does readily allow for multiple clip placements when needed and provides adequate exposure for proximal and distal control of the parent arteries associated with supraclinoid aneurysms in preparation for possible aneurysm rupture during dissection or clip placement.**

Reviewer #2:
Manuscript Summary:
Dr. Toshkezi and his colleagues have presented an interesting approach in the management of unruptured intracranial anterior circulation aneurysms. As is mentioned in the body, with the evolution of endovascular neurosurgery, newer techniques have been adapted to decrease both the length of time with traditional cerebrovascular neurosurgery and decrease the length of stay post-operatively. Based on the description, this technique does appear to be one that would be interesting for other institutions to see. The rationale and limitations are adequately discussed. The text appears to provide a reasonable description of the procedure, but certainly video and/or photos would be necessary.

Major Concerns:
To coin this technique as "minimally invasive" may be a stretch. That being said, it is hard to truly define "minimally invasive" in cranial work. Based on the description I read, it appears that the incision is a standard pterional incision, but the "minimally invasive" portion is the smaller craniotomy. Many may argue that with a standard incision, why not proceed with a standard pterional craniotomy for easier access? But I do strongly agree with the techniques of opening the CSF cisterns early for brain relaxation, and avoiding placement of retractors to prevent cortical injury and venous congestion.

- **We have added to the discussion to further explain the benefits of a smaller sized craniotomy (Lines 370-376).**

The next question would be the comparison of length of stay and hospital cost. The average length of stay (LOS) following the thumb-sized pterional craniotomy was 3.2 days, while the LOS for the NIS group was 5.7 days. Given that the NIS population was in the hospital almost twice as long, it would make sense that the cost would be almost double as well. I feel most cerebrovascular neurosurgeons performing clippings of anterior circulation aneurysms expect patients to be in the hospital 2-7 days. I would be curious to know if there was any significant cost difference between the two groups if the LOS was equal.

- **The ability to do multivariate analysis with any statistical meaning is severely limited due to our small institutional sample size. Therefore we cannot make any statements about the effect of charges independent of length-of-stay. Anecdotally, if you only consider cases with a length-of-stay = 2 (the median at our hospital), the national average is $64K and our hospital is $51K. A much smaller difference than that presented in Table 2. So the extended length-of-stay is responsible for a large portion of the cost increase but institutional and operative factors likely play a key role too. The discussion on lines 384-387 was our attempt to address this factor.**

Minor Concerns:
Most were addressed in the body of the paper. This is a single center, single surgeon, small volume, non-randomized case series. That being said, it does provide a newer technique for cerebrovascular surgeons to use. The 22 month follow-up is somewhat low, but the bigger concern would be that only 18 of the 22 patients had follow-up. This means that almost 20% of the patients were lost to follow-up.

I would be curious to know if the authors use any techniques to confirm proper clip placement such as ICG, intra-operative angiography, aneurysm deflation.

- **Thank you for this suggestion. Section 3.6 now includes our protocol to verify clip placement.**

Additional Comments to Authors:
Errors that I found in the paper by section:

Protocol:
1.2 - Should be, radial arterial "line" (not plural; everyone just gets one).

1.9 "Electrocautery" is spelled incorrectly.

1.10 "Electrocautery" is spelled incorrectly.

1.11 "Electrocautery" is spelled incorrectly.

Dissection:
3.2 Spell out "posterior communicating artery" instead of p-comm

Discussion:
Line 376 "craniotomy" is spelled incorrectly.
Thank you for identifying these errors. All of the above changes have been made.

Table 1 says there were 2 post-operative complications; the body of the paper says only 1.

- **This was a mistake while drafting the manuscript. One patient was initially considered to have experienced a complication – but this was misclassified during chart extraction. The table has been modified to reflect the 4.5% complication rate.**

Reviewer #3:
This manuscript brings an interesting and important theme about minimally invasive approaches in the vascular neurosurgery. The technique described was clearly and thoroughly presented. The issues are listed below:

Major Concerns:
1 - The section REPRESENTATIVE RESULTS points that only one patient (4.5%) experienced postoperative complication, but the table 1 shows 9% (2 patients) of postoperative complications. What could explain this difference?

- **This was a mistake while drafting the manuscript. One patient was initially considered to have experienced a complication – but this was misclassified during chart extraction. The table has been modified to reflect the 4.5% complication rate.**

2 - The section REPRESENTATIVE RESULTS shows briefly about the data analysis and points that was used the T-Test to compare averages between independent samples. However the samples differ in size, one sample has n=22 and another n=1,341. It breaks with two assumptions of the T-TEST:
2.1 small sample (n=22) not normally distributed.
2.2 high difference between the samples size (22 vs 1,341)
I suggest use a non-parametric test like the Mann-Whitney U Test to compare continuous variables.

- **Thank you for identifying this. It has been modified and line 304 and Table 2 have been updated. Additionally, the continuous variables are now presented as median (interquartile range).**

3 - The casuistic includes 6 cases of anterior communicating artery aneurysms; it is important to discuss and explore the relation of the aneurysm with perforating arteries, the position and size of the aneurysms. These group of aneurysms have anatomical details that make them hard to manage even with standard pterional craniotomy and sometimes requiring the orbito-zygomatic craniotomy to be clipped.

- **We have added additional points to the discussion to address these concerns. Lines 402-408 address more explicit details regarding anterior communicating artery aneurysms.**

SW

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