Middle meningeal artery (MMA) embolization for patients with chronic subdural hematoma (cSDH)

PI: Joshua Osbun, MD
Institution: Washington University School of Medicine, St. Louis, MO
June 2, 2020

Background

Chronic subdural hematoma (CSDH) is one of the most common diseases in neurosurgery. Though conventional surgical methods like burr-hole irrigation and craniotomy have been the mainstay of treatment, middle meningeal artery (MMA) embolization has recently emerged as a promising adjunctive or alternative treatment, especially in patients with intractable CSDH or in patients where anticoagulation or antiplatelet therapy cannot be stopped.

The MMA gives rise to capillary feeders of hematomas. Embolization of this artery is thought to inhibit blood flow into pathological structures, control bleeding from the CSDH membrane, and enhance spontaneous resolution of the hematoma, thus potentially providing a minimally invasive alternative or adjunct to conventional surgical techniques.

Chronic subdural hematoma (CSDH) occurs in approximately 14 patients per every 100,000 people and becomes more prevalent in older patients, with an occurrence of 18 patients per every 100,000 between the ages of 71-80. It is currently one of the most common diseases treated by neurosurgeons, and as the population ages, the incidence of CSDHs is expected to double in slightly over 25 years. There is significant morbidity and mortality associated with this common disease.

Recent studies have shown the efficacy of endovascular MMA embolization in treating CSDH. There is emerging data to suggest that this minimally invasive therapy may be more efficacious and equally as safe compared to conventional more invasive surgery. If these results can be supported by more vigorous clinical data, this represents a revolutionary change in the treatment of this common disease in the elderly with major morbidity and mortality.

Prior Research

From recent meta-analysis, three dual-armed studies that compared embolization and conventional surgery groups and six single-armed case series were identified and analyzed. Hematoma recurrence rate was significantly lower in the embolization group compared to the conventional treatment group (2.1% vs 27.7%, OR .087, 95% CI .026-.292, $p<.001$, $I^2=0\%$), whereas surgical complication rates were similar between the two (2.1% vs 4.4%, OR 0.563, 95% CI 0.107-2.96, $p=.497$, $I^2=27.5\%$). Number of patients with mRS>2 in the embolization (12.5%) versus conventional treatment (9.1%) groups also showed no statistical difference ($p=.689$). A composite hematoma recurrence rate of 3.6% was found after summing the six-case series. Composite recurrence and complication rates in the embolization cohorts of the dual-armed studies as well as the case series were also lower than literature values for conventional surgical treatments. Since then, there has been one study with 60 embolizations showing a 90% success rate of avoiding subsequent surgery with no procedural-related complications.

Objective

Through the use of a prospective dual cohort, this study seeks to assess the safety and efficacy of middle meningeal artery embolization for subdural hematoma in addition to standard treatments, which include observation and surgical evacuation. Middle meningeal artery embolization has emerged recently as a minimally invasive and successful method of preventing re-accumulation of subdural hematoma, particularly for patients that are not obvious surgical candidates or those with recurrent or refractory hematomas. We will compare the outcomes of these two groups of patients who undergo middle meningeal artery embolization to matched historical controls from the past four years.

Specific Aim 1:

Determine the efficacy of middle meningeal artery embolization vs observation alone

The recurrence rate of patients that undergo the middle meningeal artery procedure will be compared to a number of medically managed patients that experience a clinically significant persistent or recurrent hematoma. This endpoint will be determined through a series of neurologic assessments and follow up imaging. Patients will be followed for 90 days. Secondarily, the number of patients in each treatment group that experience persistence or recurrence to the degree that surgical evacuation is required will be compared. Patients who prospectively undergo middle meningeal artery embolization will be compared to retrospective matched controls of patients that underwent medical management. We hypothesize that patients who undergo MMA embolization as compared to simple observation alone will be less likely to ultimately need surgery and have a higher likelihood of SDH resolution after 90 days.

Specific Aim 2:

Determine the safety and efficacy of middle meningeal artery embolization for recurrent and refractory subdural hematomas after initial surgical evacuation.

MMA embolization has emerged as an adjunct treatment for patients who experience recurrent or refractory SDH after initial surgical evacuation. These patients will require surgical evacuation of the hematoma for their condition regardless of the use of MMA embolization. For patients with a residual SDH or who develop recurrent SDH within 30 days of initial standard of care surgery, the patients that have adjunct treatment with MMA embolization will be compared to historical patients that are managed with continued observation versus repeat surgery. We hypothesize that patients who undergo MMA embolization will have a higher likelihood of demonstrating radiographic improvement of the SDH and have a lower rate of requiring additional surgery.

Methodology

Participants

Approximately 200 patients with chronic subdural hematoma are treated at Barnes-Jewish Hospital annually. Patients aged 18+ of any race, sex, and socioeconomic status undergoing treatment for subdural hematoma will be identified by screening of the inpatient neurosurgical units or identification by an investigator. Patients will be approached regarding enrollment in the study at the time a decision is made to treat the subdural hematoma. If a patient expresses interest, an investigator or coordinator will provide the written consent form and explain the

information gathered, time frame of participation, potential benefits, and risks of participation, including the risks of undergoing an interventional neuroradiology procedure. Treatment with middle meningeal artery embolization will be offered in addition to the standard surgical evacuation or observation by the physician in consideration of the patient's medical history and current condition. If patients are unable to provide informed consent, consent from the next of kin will be obtained in accordance with Missouri Statute Title XXVII, Section 431.064.

Patients will have as much time as they desire to think about the study, ask questions, and discuss with family. Any patient requiring emergent intervention or experiencing sudden neurologic deterioration is excluded from this study. The consent documentation contains a statement that consent is freely given, that the patient understands the potential risks and benefits of entering the study, and that the patient is free to withdraw from the study at any time. As the patient may experience a direct benefit from the study, the patient must initial yes/no to permission for future use of their data per policy. Patients who agree will then sign the IRB approved consent form prior to undergoing the procedure. The original signed consent will be maintained in a binder in a locked office. A copy will be given to the patient, with contact numbers if the patient has further questions or wishes to withdraw their consent. The expected duration of patient participation in the study is 90 days.

Based on a review of prior literature, we expect an effect size of 20% patients to meet the endpoint of recurrent or refractory subdural hematoma requiring surgery. With the addition of MMA embolization, we expect that only 5% of patients will meet this outcome. With equal numbers of patients in each arm, we estimate that 124 patients will be needed for a power of 80% using a two tailed alpha set at 0.5. In order to account for study dropout, we plan to study 200 patients who undergo MMA embolization. These patients will be compared to an additional 400 historical matched controls obtained via retrospective chart view from January 1st 2014 to December 31st 2018.

Inclusion/Exclusion Criteria

Must meet the following criteria for inclusion to undergo MMA embolization:

1. Patients 18 years or older undergoing treatment for a new diagnosis of chronic or acute subdural hematoma (cSDH)
   or
   Patients 18 year or older who have undergone surgical evacuation of a subdural hematoma and have a significant residual hematoma status post-surgery or who develop a recurrent subdural hematoma.
2. Minimal symptoms such as headache, altered mental status, or mild neurological deficit only
3. Ability to understand and sign written informed consent by patient or LAR

If any of the following criteria are met, the individual will be excluded from participation:

1. Significant midline shift and/or neurologic symptoms requiring urgent decompression.
2. Common carotid stenosis of over 50%.
3. Significant contraindication to angiography (eg. kidney failure, difficult anatomy).

4. SDH related to underlying condition

Groups:

1. Embolization Only
    a. Patients with new chronic or acute SDH with minimal symptoms only, or who are poor surgical candidates (dual antiplatelet therapy or systemic anticoagulation, ASA Class 4 or greater)
2. Embolization + Standard of Care Evacuation
    a. Patients with chronic or acute SDH who failed conventional surgery at any point needing additional intervention, not requiring urgent evacuation
    b. Recurrent SDH
3. Medical Management (Historical Cohort)
4. Surgery Alone (Historical Cohort)

Study Procedure

Middle meningeal artery embolization is ideal for patients with minimal symptoms or that are poor surgical candidates due to the need for continued anticoagulant or antiplatelet therapy. For patients who meet inclusion criteria, MMA embolization as an adjunct treatment will be offered. For patients that are medically managed, they will undergo MMA embolization to prevent growth or recurrence of the hematoma and have standard imaging follow up. For patients that require evacuation of the hematoma due to size or symptoms, they will undergo standard of care surgery via burr hole or craniotomy at the treating neurosurgeon's discretion and then at a later date during the same hospitalization receive MMA embolization. These patients may have already had multiple surgical evacuations with recurrence of the hematoma.

Once consented and enrolled, patients will undergo MMA embolization in the neuro-angiography suite via selective MMA catheterization and embolization with 150-250 micron polyvinyl alcohol (PVA) particles. The neurointerventional radiology department at BJH is a high volume center. Physicians and staff are experienced in neurovascular embolization for a variety of indications.

Middle meningeal artery embolization is a minimally invasive angiography procedure completed either under general anesthesia or conscious sedation (per preference of the performing physician) with use of fluoroscopy. Access is obtained through the femoral or radial artery and a catheter is advanced to the MMA. Polyvinyl alcohol particles are then injected to seal off this portion of the artery and prevent any further blood flow into the subdural hematoma. All catheters are then removed and hemostasis is obtained at the access site.
Patients will be followed post-procedure for 90 days to track any complications or recurrence/ persistence of the subdural hematoma. Further treatment following standard of care will be offered if the patient develops worsening symptoms or presents with radiographic recurrence or persistence of the subdural hematoma.

A head CT, NIHSS, and modified Rankin Score will be repeated on the following schedule. These non-invasive procedures are detailed in the consent:

- Pre-Procedure
- 30 days (±7) post procedure
- 90 days (±10) post procedure

Data Points

Patient demographic data including but not limited to age, sex, race, comorbidities, previous neuro history, and relevant medical history will be gathered from Epic and Clindesk. Pre-procedure information gathered about the current admission include the use of anticoagulants, date of presentation with the SDH, size and hemisphere of SDH, neurologic presenting symptoms, head CTs, and neuro exams, including mRS and NIHSS.

Post-procedure data gathered include the time to embolization, time to follow up, procedural complications, neuro exam results, head CTs and angiography images. Date of surgery and need for surgical removal of recurrent hematoma will be documented if relevant.
The modified Rankin Score (mRS) is a well-established scale used to classify outcomes on a 0 to 6 point scale where outcome is classified as: 0- no neurological deficits, 1-no significant disability, 2- slight disability, 3-moderate disability (requires assistance with activities of daily life, but able to walk unassisted), 4-moderately severe disability (requires assistance in activities of daily life and unable to walk unassisted), 5-severe disability (bedridden, incontinent), or 6-deceased.
The National Institutes of Health Stroke Scale (NIHSS) is an objective measure of impairment caused by a stroke. Eleven items are evaluated, with a potential score ranging from 0 to 42, with a higher score indicating more impairment.

Privacy/Data Protection

Patients will be assigned a unique study identification number at the time of consent. This number will link to identifying protected health information in a separate locked database accessible only to relevant research team members. Clinical study data will be entered into a secure database on RedCap under the study ID number to maintain patient data confidentiality.

Screening:

Study ID	MRN	Last Name	First Name	Admit Date	Enrolled Y/N	Date Consent Signed	Signed By Patient/ LAR	Exclusion

Initial Data:

Study ID	Birth Year	Sex	Race	(relevant comorbidities)	Use Anticoagulant y/n	Name of Med (aspirin, warfarin)	Procedure Date	Presenting neuro symptoms

Any neuro history	NIHSS Presentation	Baseline mRS	Size of SDH at Presentation	Laterality of SDH Left Right bilateral	Procedural Complications	

Follow up:

Study ID	Date of Follow Up	Time Point (30, 90 days)	NIHSS	mRS	Size of SDH at follow up	Neuro Deficit

Analysis

Endpoints

Two primary endpoints will be analyzed, related to the two main aims of the study. Aim 1 is to establish if middle meningeal artery embolization is more effective than observation alone at preventing recurrence of subdural hematoma. Aim 2 is to determine if adding on middle meningeal artery embolization reduces the need for further surgery in patients that initially undergo evacuation. The number of patients that experience a recurrent or refractory subdural hematoma will be compared, as well as the number of patients in each group that require surgery after undergoing embolization.

Primary Endpoints:

Recurrent or progressive SDH
Secondary surgical evacuation required

Secondary Endpoints:

Change in size of SDH at follow up
Procedure-related complications
New neuro deficit
NIHSS/mRS at follow-up intervals

Statistical Analysis

Statistical comparisons will be made for the number of patients that experience a recurrent or refractory subdural hematoma, as well as the number of patients in each group that require evacuation surgery after undergoing embolization, an indication that the embolization procedure failed. These primary endpoints will be compared with simple t-test. The secondary endpoint of the change in the size of the subdural hematoma on radiographic imaging will be analyzed by repeated measures ANOVA. Change in score on NIH Stroke Scale pre and post embolization will be compared to determine the functional outcome of the procedure. For a safety analysis, the rate of procedure-related complications between embolized patients and surgical controls will be compared by t-test. Rankin Score at the follow up intervals will be compared with a Chi Square analysis.

Safety Monitoring Plan

Research will be performed according to protocols approved by the Institutional Review Board at Washington University in St. Louis School of Medicine. An application to the IRB is currently pending.

Patients with subdural hematoma present with symptoms including confusion or altered mental status, decreased consciousness, weakness or numbness on one side of the body, headache, seizure, and difficulty with speech, swallowing, or walking.

During this study, assessment of medical history and physical examination will be performed at baseline and at stated follow up intervals to ascertain neurologic status, change in functional baseline, and occurrence of any AEs. Prior to interventional procedures, patients have coagulation tests performed to assess risk of bleeding. If the patient has an allergy to iodinated contrast, they will receive standard pre-medication. During the embolization procedure, patients undergo continuous vital sign monitoring and are assessed frequently by a dedicated, ACLS-certified procedural nurse. The patient will be monitored as an inpatient in the neuroICU or stepdown unit for a minimum of 24-48 hours after the procedure.

Adverse Events

An adverse event (AE) is any untoward medical occurrence in a subject during participation in the clinical study or with use of the experimental agent being studied. An adverse finding can include a sign, symptom, abnormal assessment (laboratory test value, vital signs, electrocardiogram finding, etc.), or any combination of these.
A serious adverse event (SAE) is any adverse event that results in one or more of the following outcomes:

- Death
- A life-threatening event
- Inpatient hospitalization or prolongation of existing hospitalization
- A persistent or significant disability/incapacity
- A congenital anomaly or birth defect
- An important medical event based upon appropriate medical judgment

AEs will be labeled according to severity, which is based on their impact on the patient. An AE will be termed “mild” if it does not have a major impact on the patient, “moderate” if it causes the patient some minor inconvenience, and “severe” if it causes a substantial disruption to the patient’s well-being. AEs will be categorized according to the likelihood that they are related to the study intervention. Specifically, they will be labeled definitely unrelated, definitely related, probably related, or possibly related to the study intervention.

Unanticipated events and deaths will be reported to the IRB within 10 days per institutional policy. Individual adverse events will be summarized and reported at continuing review without any subject level identifiable information. Any updates to study risks or benefits based on analysis of this study data or other new published research will be reported as a modification during continual review and may require updated consent. Determination of severity, SAE, and

unexpected event status will be decided by the PI. Adverse event documentation will be prepared and compiled by the research coordinator utilizing a standardized WUSTL reporting template.

Risks

Conventional burr hole craniotomy has a literature reported complication rate of 9%. The meta-analysis of middle meningeal artery embolizations demonstrated a composite complication rate of 2.1% in double arm studies[21], especially significant as a greater proportion of embolization patients are maintained on anticoagulant medications. The largest individual study to date included 60 embolizations with no procedural related complications[15]. A meta-analysis including 15 studies with 193 procedures additionally reported no procedure-related complications[25].

Expected risks to the subject due to the interventional procedure are minor pain and bruising at the catheter insertion site. About 5% of subjects may develop a hematoma, a collection of blood that may cause more bruising and pain than normal and may require intervention. Less likely, more serious risks of embolization procedures (<1%) include temporary neurologic deficits, blindness or cranial nerve palsy, or an anaphylactic reaction to the contrast dye.

There is a small risk (0.3%) of carotid artery dissection and/or stroke with permanent neurologic deficit from catheter injury or clot formation. Arterial perforation or brain hemorrhage is a life threatening but rare complication. Insertion site infection is exceedingly rare.

When procedures are performed through the radial artery, a combination of medications are used to prevent radial artery occlusion, which may be asymptomatic or may cause hand ischemia and the loss of the hand. Radial subjects receive a TR band at the conclusion of the procedure to maintain patent hemostasis. Radial artery occlusion is rare with these prevention measures. Femoral access subjects receive manual compression or a closure device and must be maintained on strict bedrest for 6 hours to prevent hematoma formation.

These risks are addressed in the consent form and are considered to be minimal or outweighed by the risk of multiple invasive surgical procedures or the risk to the patient by reaccumulation of the hematoma. Patients with known contraindications to angiography or comorbid conditions placing them at higher risk of procedural complications are excluded from study participation. The neurointerventional radiology department at BJH is a high volume center with experienced physicians and staff. Approximately 1200 outpatient diagnostic cerebral angiograms are performed each year and over 300 interventional procedures.

Study subjects will be followed for research purposes for 90 days and may continue long term follow up with their outpatient neurosurgeon. Study follow up visits occur at 30 days (±7) post procedure, and 90(±10) days post procedure. At each of these time points the subject will receive a head CT scan, neurologic assessment, and assessment of adverse events. Adherence to follow up visits will be tracked and reported.

The original signed consent will be maintained in a binder in a locked office. Subjects will be assigned a unique study identification number at the time of consent. Subject level hard copies of documents will be maintained in subject binders in a locked office with no personal identifying information, only the subject ID number. This number will link to identifying protected health

information in a separate locked database accessible only to relevant research team members. Clinical study data will be entered into a secure database on RedCap under the study ID number to maintain patient data confidentiality. Only engaged research team members will have access to the RedCap database.

Safety and Analysis

Study progress and safety, including patient recruitment, retention/attrition, and AEs, will be reviewed quarterly (or more frequently if needed). An Annual Report will be compiled and will include a list and summary of AEs. In addition, the Annual Report will address (1) whether AE rates are consistent with pre-study assumptions; (2) reason for dropouts from the study; (3) whether all participants met entry criteria; (4) whether continuation of the study is justified on the basis that additional data are needed to accomplish the stated aims of the study; and (5) conditions whereby the study might be terminated prematurely. This report will be made available to the IRB at continuing review.

No external monitoring committee will be utilized due to the nature of the study. The study will be collectively monitored for safety and adverse events by the three interventional neuroradiology faculty. Any adverse events will be reviewed at both the Department of Neurosurgery and Department of Radiology QA/QI committee meeting. Additionally any adverse events will be reported to the HSR QA/QI review board at Washington University. Each faculty reports to the Conflicts of Interest Review Committee (CIRC) at Washington University, and currently none have any financial conflicts of interest relevant to this study and are unlikely to develop any during the study duration given there is no funding source for the project and no industry sponsored product being utilized. Should any FCOI arise, that research member will be removed from study participation in accordance with policies recommended by CIRC.

Based on a review of prior literature, we expect an effect size of 20% of patients to meet the endpoint of recurrent or refractory subdural hematoma requiring surgery. With the addition of MMA embolization, we expect that only 5% of patients will meet this outcome. With equal numbers of patients in each arm, we estimate that 124 patients will be needed for a power of 80% using a two tailed alpha set at 0.5. In order to account for study dropout, we plan to study 200 patients who undergo MMA embolization.

This study will be stopped prior to its completion if: (1) the intervention is associated with adverse effects that call into question the safety of the intervention; (2) difficulty in study recruitment or retention will significantly impact the ability to evaluate the study endpoints; (3) any new information becomes available during the trial that necessitates stopping the trial; or (4) other situations occur that might warrant stopping the trial.

References

1. Ban, S. P., Hwang, G., Byoun, H. S., Kim, T., Lee, S. U., Bang, J. S., Oh, C. W. (2018). Middle Meningeal Artery Embolization for Chronic Subdural Hematoma. *Radiology, 286*(3), 992-999. doi:10.1148/radiol.2017170053
2. Chihara, H., Imamura, H., Ogura, T., Adachi, H., Imai, Y., & Sakai, N. (2014). Recurrence of a Refractory Chronic Subdural Hematoma after Middle Meningeal Artery Embolization That Required Craniotomy. *NMC Case Rep J, 1*(1), 1-5. doi:10.2176/nmccrj.2013-0343
3. Entezami, P., Boulos, A., Paul, A., Nourollahzadeh, E., & Dalfino, J. (2019). Contrast enhancement of chronic subdural hematomas after embolization of the middle meningeal artery. *Interv Neuroradiol*, 1591019919843354. doi:10.1177/1591019919843354
4. Entezami, P., Nourollahzadeh, E., & Dalfino, J. (2019). Embolization of Middle Meningeal Artery for the Treatment of Headaches Induced by Chronic Subdural Hematoma: A Case Report. *Headache, 59*(4), 615-618. doi:10.1111/head.13519
5. Fiorella, D., & Arthur, A. S. (2019). Middle meningeal artery embolization for the management of chronic subdural hematoma. *J Neurointerv Surg*. doi:10.1136/neurintsurg-2019-014730
6. Hashimoto, T., Ohashi, T., Watanabe, D., Koyama, S., Namatame, H., Izawa, H., Haraoka, J. (2013). Usefulness of embolization of the middle meningeal artery for refractory chronic subdural hematomas. *Surg Neurol Int, 4*, 104. doi:10.4103/2152-7806.116679
7. Hirai, S., Ono, J., Odaki, M., Serizawa, T., & Nagano, O. (2004). Embolization of the Middle Meningeal Artery for Refractory Chronic Subdural Haematoma. Usefulness for Patients under Anticoagulant Therapy. *Interv Neuroradiol, 10 Suppl 2*, 101-104. doi:10.1177/15910199040100s218
8. Kang, J., Whang, K., Hong, S. K., Pyen, J. S., Cho, S. M., Kim, J. Y., Oh, J. W. (2015). Middle Meningeal Artery Embolization in Recurrent Chronic Subdural Hematoma Combined with Arachnoid Cyst. *Korean J Neurotrauma, 11*(2), 187-190. doi:10.13004/kjnt.2015.11.2.187
9. Kim, E. (2017). Embolization Therapy for Refractory Hemorrhage in Patients with Chronic Subdural Hematomas. *World Neurosurg, 101*, 520-527. doi:10.1016/j.wneu.2017.02.070
10. Komiyama, M., Yasui, T., Tamura, K., Nagata, Y., Fu, Y., & Yagura, H. (1994). Chronic subdural hematoma associated with middle meningeal arteriovenous fistula treated by a combination of embolization and burr hole drainage. *Surg Neurol, 42*(4), 316-319.
11. Li, G., Zhang, Y., Zhao, J., Zhu, X., Yu, J., & Hou, K. (2019). Isolated subdural hematoma secondary to Dural arteriovenous fistula: a case report and literature review. *BMC Neurol, 19*(1), 43. doi:10.1186/s12883-019-1272-z
12. Link, T. W., Boddu, S., Marcus, J., Rapoport, B. I., Lavi, E., & Knopman, J. (2018). Middle Meningeal Artery Embolization as Treatment for Chronic Subdural Hematoma: A Case Series. *Oper Neurosurg (Hagerstown), 14*(5), 556-562. doi:10.1093/ons/opx154
13. Link, T. W., Rapoport, B. I., Paine, S. M., Kamel, H., & Knopman, J. (2018). Middle meningeal artery embolization for chronic subdural hematoma: Endovascular technique and radiographic findings. *Interv Neuroradiol, 24*(4), 455-462. doi:10.1177/1591019918769336
14. Link, . W., Schwarz, J. T., Paine, S. M., Kamel, H., & Knopman, J. (2018). Middle

Meningeal Artery Embolization for Recurrent Chronic Subdural Hematoma: A Case Series. *World Neurosurg, 118*, e570-e574. doi:10.1016/j.wneu.2018.06.241
15. Link, T. W., Boddu, S., Paine, S. M., Kamel, H., & Knopman, J. (2018). Middle Meningeal Artery Embolization for Chronic Subdural Hematoma: A Series of 60 Cases. *Neurosurgery*. doi:10.1093/neuros/nyy521
16. Matsumoto, H., Hanayama, H., Okada, T., Sakurai, Y., Minami, H., Masuda, A., Yoshida, Y. (2018). Which surgical procedure is effective for refractory chronic subdural hematoma? Analysis of our surgical procedures and literature review. *J Clin Neurosci, 49*, 40-47. doi:10.1016/j.jocn.2017.11.009
17. Mino, M., Nishimura, S., Hori, E., Kohama, M., Yonezawa, S., Midorikawa, H., Nishijima, M. (2010). Efficacy of middle meningeal artery embolization in the treatment of refractory chronic subdural hematoma. *Surg Neurol Int, 1*, 78. doi:10.4103/2152-7806.73801
18. Nakagawa, I., Park, H. S., Kotsugi, M., Wada, T., Takeshima, Y., Matsuda, R., Nakase, H. (2019). Enhanced Hematoma Membrane on DynaCT Images During Middle Meningeal Artery Embolization for Persistently Recurrent Chronic Subdural Hematoma. *World Neurosurg*. doi:10.1016/j.wneu.2019.02.074
19. Okuma, Y., Hirotsune, N., Sato, Y., Tanabe, T., Muraoka, K., & Nishino, S. (2019). Midterm Follow-Up of Patients with Middle Meningeal Artery Embolization in Intractable Chronic Subdural Hematoma. *World Neurosurg*. doi:10.1016/j.wneu.2019.02.121
20. Sirh, S., Park, H. R., & Park, S. Q. (2018). Usefulness of Middle Meningeal Embolization to Prevent Recurrent Spontaneous Chronic Subdural Hemorrhage. *J Cerebrovasc Endovasc Neurosurg, 20*(1), 40-46. doi:10.7461/jcen.2018.20.1.40
21. Srivatsan, A., Mohanty, A., Nascimento, F. A., Hafeez, M. U., Srinivasan, V. M., Thomas, A., Kan, P. (2019). Middle Meningeal Artery Embolization for Chronic Subdural Hematoma: Meta-Analysis and Systematic Review. *World Neurosurg, 122*, 613-619. doi:10.1016/j.wneu.2018.11.167
22. Srivatsan, A., Srinivasan, V. M., Thomas, A., Burkhardt, J. K., Johnson, J., & Kan, P. (2019). Perspective on Safety and Effectiveness of Middle Meningeal Artery Embolization for Chronic Subdural Hematoma. *World Neurosurg*. doi:10.1016/j.wneu.2019.03.210
23. Takahashi, K., Muraoka, K., Sugiura, T., Maeda, Y., Mandai, S., Gohda, Y., Matsumoto, Y. (2002). [Middle meningeal artery embolization for refractory chronic subdural hematoma: 3 case reports]. *No Shinkei Geka, 30*(5), 535-539.
24. Tempaku, A., Yamauchi, S., Ikeda, H., Tsubota, N., Furukawa, H., Maeda, D., Nishio, A. (2015). Usefulness of interventional embolization of the middle meningeal artery for recurrent chronic subdural hematoma: Five cases and a review of the literature. *Interv Neuroradiol, 21*(3), 366-371. doi:10.1177/1591019915583224
25. Waqas, M., Vakharia, K., Weimer, P. V., Hashmi, E., Davies, J. M., & Siddiqui, A. H. (2019). Safety and Effectiveness of Embolization for Chronic Subdural Hematoma: Systematic Review and Case Series. *World Neurosurg*. doi:10.1016/j.wneu.2019.02.208
26. Yu, J., Guo, Y., Xu, B., & Xu, K. (2016). Clinical importance of the middle meningeal artery: A review of the literature. *Int J Med Sci, 13*(10), 790-799. doi:10.7150/ijms.16489