Middle meningeal artery embolization treatment of nonacute subdural hematomas in the elderly: a multiinstitutional experience of 151 cases

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OBJECTIVE The incidence of already common chronic subdural hematomas (CSDHs) and other nonacute subdural hematomas (NASHs) in the elderly is expected to rise as the population ages over the coming decades. Surgical management is associated with recurrence and exposes elderly patients to perioperative and operative risks. Middle meningeal artery (MMA) embolization offers the potential for a minimally invasive, less morbid treatment in this age group. The clinical and radiographic outcomes after MMA embolization treatment for NASHs have not been adequately described in elderly patients. In this paper, the authors describe the clinical and radiographic outcomes after 151 cases of MMA embolization for NASHs among 121 elderly patients.

METHODS In a retrospective review of a prospectively maintained database across 15 US academic centers, the authors identified patients aged ≥ 65 years who underwent MMA embolization for the treatment of NASHs between November 2017 and February 2020. Patient demographics, comorbidities, clinical and radiographic factors, treatment factors, and clinical outcomes were abstracted. Subgroup analysis was performed comparing elderly (age 65–79 years) and advanced elderly (age > 80 years) patients.

RESULTS MMA embolization was successfully performed in 98% of NASHs (in 148 of 151 cases) in 121 patients. Seventy elderly patients underwent 87 embolization procedures, and 51 advanced elderly patients underwent 64 embolization procedures. Elderly and advanced elderly patients had similar rates of embolization for upfront (46% vs 61%), recurrent (39% vs 33%), and prophylactic (i.e., with concomitant surgical intervention; 15% vs 6%) NASH treatment. Transfemoral access was used in most patients, and the procedure time was approximately 1 hour in both groups. Particle embolization with supplemental coils was most common, used in 51% (44/87) and 44% (28/64) of attempts for the elderly and advanced elderly groups, respectively. NASH thickness decreased significantly from initial thickness

to 6 weeks, with additional decrease in thickness observed in both groups at 90 days. At longest follow-up, the treated NASHs had stabilized or improved in 91% and 98% of the elderly and advanced elderly groups, respectively, with > 50% improvement seen in > 60% of patients for each group. Surgical rescue was necessary in 4.6% and 7.8% of cases, and the overall mortality was 8.6% and 3.9% for elderly and advanced elderly patients, respectively.

CONCLUSIONS MMA embolization can be used safely and effectively as an alternative or adjunctive minimally invasive treatment for NASHs in elderly and advanced elderly patients.

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KEYWORDS elderly; nonacute subdural hematoma; chronic subdural hematoma; middle meningeal artery; endovascular embolization

NONACUTE subdural hematomas (NASHs) include subacute, acute-on-chronic, and chronic subdural hematomas (CSDHs) and disproportionally affect the elderly. As such, NASHs have become an ever more prevalent diagnosis, rising in concert with the aging population.[1] The estimated incidence of CSDHs in the general population is projected to nearly double from 10.35 to 17.6 per 100,000 over the next decade, likely making it the most commonly treated cranial neurosurgical condition in adults by 2030.[2] The projected increase in both incidence and prevalence reflects the aging population, with approximately 20%–25% of the population expected to be older than 65 years by the turn of the next decade.[3] Furthermore, the incidence of NASHs is dependent on age, and most cases occur in patients older than 65 years, with incidences estimated as high as 80.1 per 100,000 in those older than 65 years and 127.1 per 100,000 in those older than 80 years.[4,5] Diffuse cerebral atrophy, more frequent use of antiplatelet and anticoagulant medications, and increased frequency of minor trauma such as falls in the elderly patient population are all believed to be important factors contributing to NASH development.[1,6]

There is still no definitive consensus on the most appropriate treatment for NASHs, particularly in the elderly, and, as such, there remains wide variation in practice, ranging from conservative management to operative intervention.[7,8] Medical management of mildly symptomatic CSDHs has thus far also failed to improve outcomes. For example, the randomized, placebo-controlled ATOCH trial comparing an 8-week course of atorvastatin with placebo for mildly symptomatic CSDH reported neurological improvement in only 45% of patients receiving atorvastatin compared with 28% of the placebo group, and surgical rescue for neurological deterioration was needed in 11.2% and 23.5% of the atorvastatin and placebo groups, respectively.[9] Surgical management with twist-drill craniostomy, burr hole craniotomy, or standard craniotomy under general anesthesia remains the most common method for drainage for both asymptomatic and symptomatic subdural hematomas. Unfortunately, postoperative recurrence remains common, with estimates as high as 30%.[10] Another challenge complicating NASH treatment in the surgical perioperative period is deciding when and for how long antiplatelet or anticoagulation medications should be held.[11] The decision to operatively treat subdural hematomas in the elderly remains complicated: they have more medical complexity, are at increased risk of cardiac complications from general anesthesia, are more susceptible to postoperative infections, and are at risk of deconditioning during prolonged postoperative bed rest.[7,12–14]

Middle meningeal artery (MMA) embolization is a newly recognized technique used as an alternative or adjunctive minimally invasive treatment for NASHs. Early studies have uniformly demonstrated favorable outcomes with better efficacy and safety compared with conventional surgical evacuation.[15,16] In addition to decreased procedure-related morbidity, the benefits of MMA embolization are thought to be derived from improved targeting of the underlying pathophysiology of the subdural hematomas (i.e., devascularizing the immature capillary network supplying the fibrocellular neomembranes formed after subdural blood is reorganized), which is thought to decrease repeated cycles of subdural rebleeding, recurrence, and expansion over time.[17] Recent reports have primarily explored the use of MMA embolization for treating CSDHs in patients who are unable to stop anticoagulant therapy[18] or patients with recurrent hematomas;[19–22] however, aside from a few, larger single-center cohorts,[23,24] most reports comprise small case series. MMA embolization has yet to be adequately studied among the elderly. The purpose of this study was to analyze a cohort of elderly patients who underwent MMA embolization for NASH treatment at 15 academic centers across the US and describe the clinical and radiographic outcomes in this population.

Methods

We retrospectively reviewed a prospectively collected database of patients who underwent MMA embolization for NASHs between November 2017 and February 2020 across 15 US academic centers. Each center obtained appropriate local institutional review board approval before data collection.

The database was queried for patients aged 65 years and older who were further divided into two groups: age 65–79 years (elderly) and age ≥ 80 years (advanced elderly). Patient charts were reviewed for demographics, clinical data, and radiographic data, including age, sex, race, comorbidities, prior NASH, prior NASH evacuation, use of antiplatelet or anticoagulant medications, midline shift, laterality of hematoma, maximum hematoma width on axial imaging, and presence of membranes. Treatment data were also recorded, including embolization success, NASH treatment indication (upfront, recurrent, or prophylactic with concurrent surgical intervention), access location (transfemoral vs transradial), type of anesthesia (general anesthesia vs moderate sedation), procedure duration, and type of embolysate used (coils, liquid embolic, particles, or a combination). The maximum width of the subdural hematoma was measured initially, at 6 weeks, and

at 90 days and was also categorized as worse, improved, > 50% reduction, or 100% reduction at the latest recorded follow-up. The need for retreatment, adverse events, and mortality were assessed at the latest recorded follow-up.

Statistical analysis in the form of Student t-tests was conducted to compare midline shift and maximum subdural width between the two age groups, as well as to compare preprocedural width and width at 6-week and 90-day follow-ups. Welch's t-test was used to compare the average age between the groups. Chi-square analysis was conducted to compare preprocedure antiplatelet/anticoagulant use, sex, indication for procedure, outcome at latest follow-up, and mortality between the two age groups.

Results

In total, MMA embolization was attempted on 151 NASHs in 121 patients (30 bilateral procedures). Seventy elderly patients underwent a total of 87 embolization attempts (17 bilateral), and 51 advanced elderly patients underwent a total of 64 embolization attempts (13 bilateral) (Table 1). The average age for the elderly and advanced elderly patients differed significantly at 72.3 and 85.2 years old, respectively ($p < 0.005$). Both groups were predominantly white and male. Comorbid conditions were similar, with hypertension being the most common, followed closely by hyperlipidemia, coronary artery disease, and diabetes mellitus. Antiplatelet or anticoagulant agents were more common in the advanced elderly than in the elderly patients (69% vs 49%; $p = 0.03$). The initial maximum subdural width was significantly greater in the advanced elderly group (16.2 vs 14.5 mm; $p = 0.04$), whereas midline shift was significantly greater in the elderly group (2.0 vs 0.82 mm; $p = 0.006$). Subdural membranes were present in three-quarters of all NASHs (Table 2).

Of the 151 MMA embolization attempts, 98% (in 148 of 151 cases) were successful. The 3 cases with failed attempts occurred in the younger group (Table 3). NASH treatment was performed in three settings. Upfront treatment was performed in 46% (40/87) and 61% (39/64) of cases in the elderly and advanced elderly groups, respectively. In the elderly group, prior evacuation had been performed in 32 cases, primarily with either craniotomy (50%; 16/32) or burr holes (47%; 15/32). Similarly, in the advanced elderly group, prior evacuation had been performed in 21 cases, primarily with either craniotomy (29%; 6/21) or burr holes (52%; 11/21). Thus, MMA embolization was performed as a rescue treatment in 37% (32/87) and 33% (21/64) of cases in the elderly and advanced elderly groups, respectively. Finally, prophylactic treatment was performed in 15% (13/87) and 6% (4/64) of cases in the elderly and advanced elderly groups, respectively.

Transfemoral access was used more than 80% of the time for each group, and general anesthesia was used in about half of cases for both groups (Table 3). The average procedure duration was nearly identical between the groups at just over 1 hour. None of these were significantly different between the groups.

The choice of embolic agent was similar between the two groups, with the most common being particles plus coils (51% in the elderly group and 44% in the advanced

TABLE 1. Patient characteristics of 121 patients who underwent MMA embolization for NASH treatment

Variable	Age Group, Yrs		p Value
	65–79	≥80	
No. of patients	70	51	
Male sex	59 (84)	40 (78)	0.41
Mean age, yrs	72 ± 3.7	85 ± 4.4	**<0.005**
Race			
Hispanic	8 (11)	4 (8)	
White	52 (74)	34 (67)	
African American	4 (6)	5 (10)	
Asian	1 (1)	2 (4)	
Native American	1 (1)	0	
Comorbidities			
HTN	30 (43)	34 (67)	
HLD	23 (33)	19 (37)	
DM	14 (20)	9 (18)	
CAD	10 (14)	15 (29)	
CVD	8 (11)	4 (8)	
TBI	2 (3)	2 (4)	
PVD	1 (1)	3 (6)	
Factor VI deficiency	1 (1)	0 (0)	
Antiphospholipid syndrome	1 (1)	0 (0)	
Antiplatelet or anticoagulation medication use	34 (49)	35 (69)	**0.03**
81 mg aspirin	13 (19)	14 (27)	
325 mg aspirin	1 (1)	3 (6)	
Clopidogrel	6 (9)	2 (4)	
Warfarin	11 (16)	6 (12)	
Heparin	0 (0)	1 (2)	
Apixaban	2 (3)	4 (8)	
Dabigatran	0 (0)	1 (2)	
Rivaroxaban	1 (1)	1 (2)	

CAD = coronary artery disease; CVD = cerebrovascular disease; DM = diabetes mellitus; HLD = hyperlipidemia; HTN = hypertension; PVD = peripheral vascular disease; TBI = traumatic brain injury.
Values represent the number of patients (%) unless stated otherwise. The mean value is presented as the mean ± SD. Boldface type indicates statistical significance.

elderly group). Embosphere Microspheres (Merit Medical) were used in nearly two-thirds of the particle embolizations, most commonly in the 100- to 300-μm or 300- to 500-μm range, while polyvinyl alcohol particles were used in the remaining one-third, usually in the 150- to 250-μm range or 250- to 355-μm range (data not shown). Among liquid embolics, Onyx (18 or 34, Medtronic) was used in 90% of cases, while N-butyl cyanoacrylate (TRU-FILL, J&J Medical Devices) was used in the remaining cases (data not shown).

At the 6-week follow-up, the maximum subdural width was not significantly different between groups (10.9 vs 9.31 mm in the elderly and advanced elderly groups; $p = 0.28$); however, the decrease observed was significant when compared with the preprocedural subdural thick-

TABLE 2. Clinical and radiographic factors of 121 patients who underwent MMA embolization for NASH treatment

Variable	Age Group, Yrs		p Value
	65–79	≥80	
Mean maximum hematoma width	14.5 ± 6.0	16.2 ± 5.5	**0.04**
Mean midline shift	2.0 ± 3.2	0.82 ± 2.2	**0.006**
Left side	46 (53)	36 (56)	
Membranes	67 (77)	51 (80)	0.69
Prior NASH evacuation	32	21	0.62
Craniotomy	16 (50)	6 (29)	
Burr holes	15 (47)	11 (52)	
SEPS	1 (3)	4 (19)	

SEPS = subdural evacuating port system.
Values represent the number of cases (%) unless stated otherwise. Mean values are presented as the mean ± SD. Boldface type indicates statistical significance.

TABLE 3. Treatment characteristics of 121 patients who underwent MMA embolization for NASH treatment

Variable	Age Group, Yrs		p Value
	65–79	≥80	
Total no. of treatments			
Attempted	87	64	
Completed	84 (97)	64 (100)	0.13
Treatment type			
Upfront	40 (46)	39 (61)	0.07
Recurrent	34 (39)	21 (33)	0.43
Prophylactic	13 (15)	4 (6)	0.09
Access			0.86
TRA	14 (16)	11 (17)	
TFA	73 (84)	53 (83)	
Anesthesia			0.18
General anesthesia	38 (44)	35 (55)	
Moderate sedation	49 (56)	29 (45)	
Mean procedure duration, mins	67.6 ± 27.3	66.2 ± 30.6	0.38
Embolic agent			
Coils	3 (3)	3 (5)	
Liquid	18 (21)	12 (19)	
Particles	20 (23)	18 (28)	
Liquid + coils	1 (1)	1 (2)	
Particles + coils	44 (51)	28 (44)	
Particles + liquid	1 (1)	0 (0)	
Bilateral procedure	15 (20)	13 (20)	0.91

TFA = transfemoral access; TRA = transradial access.
Values represent the number of cases (%) unless stated otherwise. The mean value is presented as the mean ± SD.

ness (p = 0.04 and p < 0.001 for the elderly and advanced elderly groups) (Table 4). At the 90-day follow-up, a similar trend was observed, with NASH thickness similar between the groups (4.66 vs 6.13 mm; p = 0.22). Thickness was significantly decreased from the 6-week follow-up in the advanced elderly group (p = 0.002). At the longest follow-up of at least 6 weeks, the majority of patients in each group showed NASH improvement. Data were available for 92% (80/87) and 91% (58/64) of procedures in the elderly and advanced elderly groups, respectively. NASH stability or improvement was observed in 91% (73/80) and 98% (57/58) in the elderly and advanced elderly groups, respectively. Similarly, > 50% improvement was observed in the majority of elderly (61%) and advanced elderly (64%), while complete resolution was observed in 24% and 17%, respectively, for the two groups (Fig. 1). Worsening of the NASHs was infrequently observed (in 8.8% and 1.7% of the elderly and advanced elderly groups, respectively).

Adverse events were rare, at 2.3% (2/87) in the elderly group (one delayed seizure and one delayed infarction) and 1.6% (1/64) in the advanced elderly group (intermittent aphasia). The need for surgical rescue, defined by post-MMA embolization burr holes or craniotomy for worsening or persistent symptoms, did not differ between the two groups, with 4.6% (4/87) and 7.8% (5/64) in the elderly and advanced elderly groups, respectively. Mortality was not significantly different between the groups, at a rate of 8.6% (6/70) in the elderly group and 3.9% (2/51) in the advanced elderly group (p = 0.31). Three patient deaths (2.5%) occurred within 24 hours of the MMA embolization procedure, with only 1 neurological death due to the patient developing a cerebellar hematoma, remote from the subdural hematoma. The remaining 5 patient deaths (4.1%) occurred between 2 and 6 weeks after the procedure and were all related to progression of underlying neoplastic disease or withdrawal of care by family.

Discussion

In this study, we describe the clinical and radiographic outcomes in a robust series of 121 elderly patients undergoing 151 embolization procedures to treat NASHs. To the best of our knowledge, this is the first such report of MMA embolization for subdural treatment in elderly patients. Overall, MMA embolization was highly efficacious in treating the vast majority of NASHs. Hematoma size either stabilized or improved at the longest follow-up in 91% and 98% in the elderly and advanced elderly groups, respectively, with surgical rescue needed in only 4.6% and 7.8% of cases for persistent or worsening symptoms. This represents an improvement compared with conventional surgical management, where retreatment rates are expected to exceed 20%.[24] Furthermore, there was > 50% subdural improvement in > 60% of patients in each group. Our subgroups were fairly equivalent in clinical, radiographic, and outcome measures, although the advanced elderly group was significantly more likely to be taking antiplatelet or anticoagulant medication and had greater initial NASH width with less initial midline shift. Upfront hematoma treatments were slightly more common in the advanced elderly group, but the difference did not reach statistical significance.

Our study provides additional evidence reinforcing the results from other recent large, single-center MMA embolization cohorts.[15,23,24] In our patients, MMA embolization was both effective and safe in upfront subdural treatment,

TABLE 4. Outcomes of 121 patients who underwent MMA embolization for NASH treatment

Variable	Age Group, Yrs		p Value
	65–79	≥80	
Mean maximum width, mm			
Initial	14.5 ± 6.0	16.2 ± 5.5	**0.04**
No. of patients	87	64	
6-wk follow-up	10.9 ± 14.5*	9.3 ± 8.4*	0.28
No. of patients	55	38	
90-day follow-up	4.7 ± 10.0	6.1 ± 4.6*	0.22
No. of patients	42	34	
Longest follow-up			
Data available	80/87	58/64	
Worse	7 (8.8)	1 (1.7)	0.08
Stable to improved	73 (91)	57 (98)	0.08
>50% improvement	49 (61)	37 (64)	0.76
100% improvement	19 (24)	10 (17)	0.35
Adverse events	2 (2.3)	1 (1.6)	0.75
Intermittent aphasia	0	1	
Delayed seizure	1	0	
Delayed infarction	1	0	
Surgical rescue	4 (4.6)	5 (7.8)	0.41
Mortality, no. of patients (%)	6 (8.6)	2 (3.9)	0.31

Values represent the number of cases (%) unless stated otherwise. Mean values are presented as the mean ± SD. Boldface type indicates statistical significance.
* Significant difference from prior measurement.
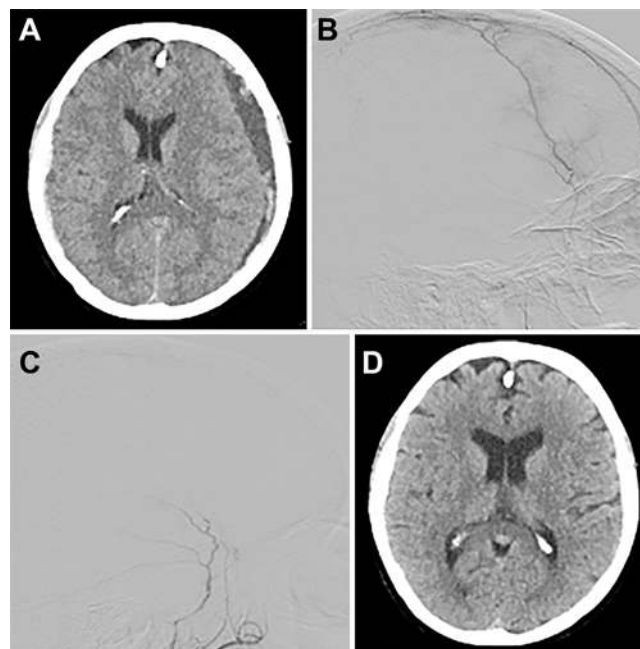
FIG. 1. Example of a left-sided NASH treated with MMA embolization. This 67-year-old female patient on a regimen of coumadin for a recent pulmonary embolism in the setting of antiphospholipid syndrome presented with headache and a supratherapeutic international normalized ratio of 4.2. The hematoma measured 11.0 mm at presentation on an axial noncontrast CT scan (**A**). It was treated with embolization of the anterior and middle branches of the MMA using 100- to 300-μm Embosphere Microspheres (Merit Medical) (**B and C**; digital subtraction angiograms, lateral view). At the 90-day follow-up, the NASH had completely resolved as seen on the axial noncontrast CT scan (**D**).

in recurrent hematomas, and as a prophylactic therapy at the time of surgical intervention. In 2019, Link et al.[23] reported their single-center experience of the first 60 cases of CSDHs treated with MMA embolization in 49 patients. Their cohort included 42 upfront, 8 recurrent, and 10 prophylactically treated subdural hematomas, and they reported comparable outcomes to those in our present study, with subdural stability or improvement in 91.1%, an 8.9% recurrence rate, and no procedural complications. Interestingly, the average age of their cohort was younger (average age 69 years) than that of our subgroups, but antiplatelet or anticoagulation medication use was higher (80%). Ban et al.[24] also recently reported a large, single-center series of 72 consecutive patients prospectively identified and treated with MMA embolization for CSDHs. They included patients ≥ 20 years of age and observed an average patient age of 69 years, as well as 40% taking antithrombotics. Enrollment criteria included CSDH thickness of at least 10 mm, and the average subdural maximum width was slightly larger than that in our patient cohort at 19.6 mm. MMA embolization was used alone (27/72) in asymptomatic patients or in combination with surgical hematoma evacuation (45/72) in symptomatic patients. At the 6-month follow-up, there were no cases of surgical rescue for those treated with embolization alone and in only 1 (2.2%) of 45 patients treated with embolization followed by surgery. Their cohort was compared with a historical control group of 469 patients with CSDH managed with conventional treatment (67 with conservative management and 402 with surgical evacuation), and they found significantly lower treatment failure rates as defined by residual hematoma thickness > 10 mm (1.4% vs 27.5%; p = 0.001), less frequent surgical rescue (1.4% vs 18.8%; p = 0.005), and no difference in treatment complications (0% vs 4.3%; p = 0.182). Recent systematic reviews have corroborated these excellent outcomes.[16,25–27] The hematoma resolution rate was estimated to be as high as 96.8%,[27] with recurrence ranging from 2.1% to 4.1%[16,25,26] and procedural complication rates from 0% to 2.1%.[16,25–27]

Surgery for CSDHs in the elderly carries unique challenges regarding effectiveness, recurrence rates, surgical complications, and medical perioperative complications.[14,28–35] A 2018 review of adults older than 65 years (2,831,274 cases in the NSQIP registry and 1,952,305 Medicare beneficiaries) found that the rate of postoperative hematoma recurrence requiring repeat surgery was between 5% and 10%.[36] For example, a Scandinavian population-based multicenter study of 1254 patients undergoing primary burr hole craniotomy found no statistically significant difference between surgical complications, perioperative morbidity, or perioperative mortality in patients older than 90 years versus those younger than 90 years.[29] Conversely, Krupa et al.[32] found a dramatic difference in outcome when comparing burr hole craniotomy and standard craniotomy in the young (age < 40 years)

and elderly (age > 75 years). Good outcome (Glasgow Outcome Scale score of 5) only occurred in 15.5% and 4.8% of their elderly patients treated with burr hole craniotomy and standard craniotomy, respectively, compared with a good outcome in approximately 70% of the younger group for each surgical method. Rohde et al.[35] also found a higher surgical complication rate and overall mortality rate in elderly patients who underwent burr hole craniotomy for CSDH. Still others have reported unique perioperative risks that need to be monitored for in the elderly, such as a higher risk of postoperative acute subdural hematoma requiring treatment,[34] higher risk of postoperative infection after craniotomy,[12] higher risk of mortality,[31] and decreased likelihood of a good functional outcome postoperatively.[31,34] In addition to operative risks, the elderly are also at higher risk of perioperative medical complications. A retrospective review of 106 patients aged 60 years or older treated with burr hole craniotomy for CSDHs saw a higher frequency of cardiac complications, and thus longer hospitalization, in those receiving general anesthesia when compared with local anesthesia.[14]

Endovascular MMA embolization offers several advantages over conventional open surgery for subdural evacuation that make it a particularly attractive minimally invasive treatment option in elderly patients. Percutaneous transradial or transfemoral access are both generally well tolerated under local anesthesia with a low risk of complications. Most patients in our study underwent transfemoral access; however, transradial access may soon prove to be a superior approach because it has been shown to be associated with a lower risk of major bleeding and vascular complications, shorter time to ambulation, and, in some instances, an improved ability to navigate tortuous cerebrovascular anatomy.[37,38] As such, MMA embolization procedures can often be done under moderate sedation or local anesthesia, thereby mitigating the risk of cardiac and respiratory complications from the stresses of endotracheal intubation and general anesthesia. Procedure times are also short; in the present study, the average duration was just over an hour in both subgroups. Postoperative bed rest is still practiced by clinicians as a way to allow brain re-expansion after subdural drain placement, but after MMA embolization, this is unnecessary as there is no subdural drain. Patients are typically ambulatory within a few hours after embolization, and in select asymptomatic patients, discharge to home may be appropriate after a short period of observation. Finally, infection risk is greatly reduced without the need for skin incision, craniotomy, and subdural drain placement.

A significant limitation of this study is that it is a nonrandomized, retrospective chart review of prospectively collected data and, as such, only demonstrates associations rather than causation. We also were unable to control for confounding variables, such as initial hematoma width, midline shift, and preprocedure antiplatelet or anticoagulation medication use. A unique strength of this cohort is the inclusion of 15 academic centers across the US. This helps increase the generalizability and external validity of our results; however, the wide variety of embolization agents used may make it challenging to draw meaningful conclusions as to which type of embolization is most ef-

fective in elderly patients. To the best of our knowledge, this study presents the outcomes on the largest cohort of elderly patients to have undergone MMA embolization for treatment of NASH.

Conclusions

MMA embolization appears to be both a safe and efficacious minimally invasive treatment option for NASHs in the elderly.

Acknowledgments

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Disclosures

Author Contributions

Supplemental Information

Videos

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