Image-guided embolization of arteriovenous malformations of the hand using Ethylene-vinyl Alcohol Copolymer

PURPOSE
This study aimed to evaluate the safety and outcome of image-guided embolization for treating arteriovenous malformations (AVMs) of the hand using ethylene-vinyl alcohol copolymer (EVOH).

METHODS
A retrospective, multicenter cohort of 15 patients with AVMs of the hand treated with 35 image-guided embolotherapies using EVOH was investigated. Clinical history, symptomatology, and imaging findings were assessed to evaluate clinical outcome (symptom-free, partial relief of pain, no improvement of pain, and clinical progression despite embolization), lesion devascularization (total, 100%; near-total, 90%-99%; substantial, 70%-90%; partial, 30%-70%; and failure, 0%-30%), and peri- and postprocedural complication rates (major complications classified according to CIRSE guidelines). Substratification analysis was performed with respect to the involvement of different anatomical compartments and the injected volume of the embolic agent.

RESULTS
Patients were treated for pain (93.3%), skin ulceration (46.7%), and local bleeding (33.3%). The mean number of embolotherapies was 2.3 (±1.1) in 3 patients, a planned surgical resection was conducted after embolization. Clinical outcome after a median follow-up of 18 months revealed an overall response of 11/15 patients (73.3%). Imaging at last follow-up revealed 70%-99% reduced vascularization in 12/15 patients (80%) including 2 patients (13.3%) with a near-total devascularization of 90%-99%. Peri- and postprocedural complications occurred in 8.5% and 31.5%, respectively, including 17.1% major complications, in 1 case requiring a previously unplanned resection. Involvement of the finger was associated with increased rates of persistent symptoms compared to the other groups (P = .049). No significant difference between the embolic agent volume injected and complication rates was found (P = .372).

CONCLUSION
Image-guided embolization using EVOH-based liquid embolic agents is effective for treating AVMs of the hand in the mid-term.

The classification of congenital vascular malformations into simple (venous, arteriovenous, capillary, and lymphatic malformations), combined vascular malformations, vascular malformations associated with other anomalies, and provisionally unclassified vascular anomalies was updated by the International Society for the Study of Vascular Anomalies in 2018 based on new insights in genetic involvement for the development of syndromes related to vascular anomalies. Arteriovenous malformations (AVMs) are composed of an abnormal vascular network with direct communications between dysplastic arterial and venous vessels consequently resulting in fast-flow lesions.

Although AVMs occur at any site of the body, it is important to be aware of the anatomical peculiarities and complexities depending on specific localizations. While commonly being small in size, AVMs of the hand can lead to substantial clinical impairment compared to malformations at other sites due to limited soft tissue coverage, the subtle biomechanics, and dense innervation of this anatomical area. The interventional treatment of these lesions located in small anatomical compartments involving dense neurovascular and articular...
structures is challenging due to the lesions’ diffuse and infiltrative nature, the limited compensation capabilities of blood flow in the terminal arterial vessels, and the need to preserve normal hand and wrist functionality. Previous studies reporting the outcome of embolization of hand AVMs with commonly used embolic agents such as pure ethanol have revealed high complication rates up to 76%. These include, besides systemic side effects, large skin necrosis and permanent sequelae such as joint contracture or neuropathic complications.

Though, there is a lack of reports with less aggressive embolic agents for treatment of AVMs affecting the hand and wrist. Therefore, the purpose of this multicenter study was to evaluate the safety and outcome of image-guided embolization using ethylene-vinyl alcohol copolymer (EVOH)-based liquid embolic agents for treating AVMs affecting the hand.

Methods
This multicenter, retrospective study was approved by the local ethics committee (protocol No: 21-0264) and was performed in accordance with relevant guidelines and regulations according to the Helsinki Declaration of 2013.

Study population
Fifteen consecutive patients with AVMs of the hand treated with image-guided embolotherapies in 3 interdisciplinary vascular anomalies centers at tertiary care university hospitals from 2011 to 2020 were analyzed. AVMs were diagnosed during the clinical presentation by a combination of anamnesis, physical examination, and imaging using magnetic resonance imaging (MRI) and ultrasound. Clinical and angiographical classifications were performed according to Schobinger (Table 1) and Cho, respectively, the latter performed in all pre-treatment imaging. All malformations had in common an extension into anatomically sensitive areas of the hand such as wrist, palm, and/or fingers. None of the patients presented with AVMs associated with syndromal anomalies (such as Parkes Weber syndrome) or combined vascular malformations. The indications for interventional treatment involved pain, swelling, bleeding, and peripheral ischemia presenting with local dystrophy or ulceration. There were no signs of right heart overload in any of the patients. Both therapy-naïve patients and patients after previously attempted treatments (conservative, surgery, and embolization) without sufficient symptom improvement were included.

Technique
All procedures were conducted under general intubation anesthesia. Postprocedural pain was managed applying piritramide intravenously using patient-controlled analgesia (PCA) pumps. The embolotherapies were performed under real-time ultrasound and fluoroscopic guidance using EVOH-based liquid embolic agents Onyx-18 (Onyx®, Medtronic) as well as Squid-18 and Squid-12 (Squid®, Emboflu, Balt). The choice of different embolic agents was based on personal preference of the operator. Embolic agents with lower viscosity were generally applied in case a more distal embolization was attempted, whereas more viscous EVOH was applied when higher control was required for embolization purpose. The procedures were mostly conducted using the plug-and-push technique via the transarterial route (26/35, 74.3%) including 2 cases with additionally used percutaneous direct access. Besides this, percutaneous only and transvenous only approaches were used in 8/35 patients (22.9%) and in 1/35 patients (2.9%), respectively. Plug-and-push technique was applied with 2 minutes waiting time between consecutive injections while building the plug. For arterial access, antegrade brachial route was applied. Here, 5 F sheath equipment was used routinely, followed by 4/5 F guiding catheters and subsequently using microcatheter with detachable tip in a triaxial manner (1.5 and 3 cm, Apollo™, Medtronic Inc.). Patients were discharged at day 3-5 following the procedure, with low-molecular-weight heparin for 7 days post-embolization. Repeated embolization sessions were performed depending on the extent of the lesion, clinical response to therapy, and course of clinical symptomatology.

Follow-up
The patients were seen within a standardized follow-up regime in the 3 centers involved. The first follow-up visit was performed at 1-3 months after each treatment session. In addition to detailed clinical re-examination, the patients routinely underwent MRI at 1-3 months, and in case of insufficient improvement of symptoms or residual perfused AVM being present, a new embolization session was planned. In case of no additional treatment, the next follow-up was scheduled at 6 months, again comprising a clinical examination as well as MRI. In case of no residual AVM left, a repeat follow-up was performed on an annual basis.

Outcome evaluation after treatment
Retrospective data collection was performed using electronic patient records and the Picture Archiving and Communication System at each department. All available pre-procedure and follow-up clinical data and findings were analyzed centrally to evaluate demographic patient data, lesion classification, procedural characteristics, clinical outcome, degree of lesion devascularization, and complication rates. For the clinical outcome of embolotherapies at final follow-up, an evaluation of patients’ pain was conducted using the following grading

| Schobinger classification | At diagnosis (n = 15) | At treatment initiation (n = 15) | At terminal follow-up (n = 15) |
|---------------------------|----------------------|---------------------------------|-------------------------------|
| Stage I                   | -                    | -                               | 3 (20.0%)                     |
| Stage II                  | 9 (60.0%)            | 1 (6.7%)                        | 7 (46.7%)                     |
| Stage III                 | 6 (40.0%)            | 14 (93.3%)                      | 5 (33.3%)                     |
| Stage IV                  | -                    | -                               | -                             |

Main points
- Image-guided embolization using ethylene-vinyl alcohol copolymer seems to be effective with both good clinical and objective outcome accompanied by acceptable peri- and postprocedural complication rates.
- Arteriovenous malformations including the fingers may be associated with increased rates of persistent symptoms compared to the involvement of more proximal hand compartments.
- Additional surgical treatments including amputations may be required and highlight the need for an interdisciplinary approach.
scale: symptom-free, partial relief of pain, no improvement of pain, and clinical progression despite embolization. Objective outcome was assessed (per patient) using pre-procedural MR angiography images compared to those obtained after the last embolization. Thereby, image findings (percentage of AVM devascularization) were subdivided into the following 5 categories according to Bouwman et al.²⁰: total (100%), near-total (90%-99%), substantial (70%-99%), partial (30%-70%), and failure (0%-30%). Complications were classified as peri- and postprocedural, whereas the latter was split into early postprocedural complications occurring within the first 30 days after the intervention and late postprocedural complications arising thereafter. Additionally, major complications were defined as grade 3 or higher applying the Cardiovascular and Interventional Radiological Society of Europe (CIRSE) classification system.²¹

**Statistical analysis**

Descriptive statistics were used to analyze the distribution of patients among the different categories. Substratification analyses were performed depending on the injected volume of the embolic agent and on the anatomical involvement of different compartments of the hand (wrist, palm, fingers, wrist and palm, and palm and fingers) using Pearson chi-squared test for categorial data and the Mann–Whitney U-test for metric data. All statistical testing was conducted using Statistical Package for the Social Sciences Statistics (Version 26.0, IBM Corp.), with P < .05 considered significant. Data are presented as means (± standard deviation) or medians (range, minimum – maximum).

**Results**

Fifteen patients, 5 males and 10 females, with a mean age of 32.7 years (±19.4 years) at treatment initiation who underwent a total of 35 image-guided embolotherapies, were included. Detailed patient characteristics are summarized in Table 2. Overall, 5/15 patients (33.3%) presented with multifocal appearance of AVMs while lesions included wrist (5/15, 33.3%, Figure 1), palm (9/15, 60.0%), and/or fingers (9/15, 60.0%). There was a mean time of 5.9 years (±6.78 years) between the initial diagnosis and first embolotherapy at our centers, whereas 7/15 patients (46.6%) had undergone previous treatment, either by partial debulking surgery (5/15, 33.3%) or incomplete embolization (2/15, 13.3%).

The mean number of image-guided embolotherapies per patient was 2.3 (±1.1). A total of 23/35 procedures (65.7%) were performed using Onyx-18, 8/35 (22.9%) using Squid-18, and 4/35 (11.4%) using Squid-12. The median injected volume of injected EVOH was 6.0 mL (range, 0.9-16.0 mL) per treatment session and 17.0 mL (range, 1.5-37.0 mL) per patient. The median follow-up period after the last embolization session was 18 months.

**Table 2. Patient characteristics and clinical data of the study cohort.**

| Patient no./gender | Age at diagnosis/age at first treatment | Location | Appearance | Clinical presentation |
|--------------------|----------------------------------------|----------|------------|-----------------------|
| 1/f                | 13/18                                  | cf       | Isolated   | Pain, peripheral ischemia, local bleeding |
| 2/f                | 8/16                                   | f        | Isolated   | Pain, swelling         |
| 3/f                | 11/13                                  | wc       | Multifocal | Pain, swelling         |
| 4/f                | 1/12                                   | wc       | Multifocal | Pain, peripheral ischemia, swelling |
| 5/f                | 26/27                                  | f        | Multifocal | Pain                   |
| 6/f                | 10/13                                  | c        | Isolated   | Pain, peripheral ischemia |
| 7/f                | 26/28                                  | wc       | Isolated   | Pain, local bleeding, swelling |
| 8/m                | 25/26                                  | f        | Isolated   | Swelling               |
| 9/m                | 15/37                                  | wc       | Multifocal | Pain, arterial aneurysma |
| 10/f               | 33/48                                  | wc       | Multifocal | Pain, venous aneurysma |
| 11/m               | 26/26                                  | w        | Isolated   | Pain                   |
| 12/f               | 58/60                                  | wc       | Isolated   | Pain, peripheral ischemia |
| 13/m               | 46/46                                  | f        | Isolated   | Pain, peripheral ischemia, local bleeding |
| 14/m               | 27/42                                  | f        | Isolated   | Pain, peripheral ischemia |
| 15/f               | 77/79                                  | cf       | Isolated   | Pain, peripheral ischemia, local bleeding |

cf = carpal and finger; f = finger; wc = wrist and carpal.

**Figure 1.** A 26-year-old female patient presenting with an AVM at the wrist of the right hand. (a) Clinical examination revealed peripheral ischemia with incipient local dystrophia of the surrounding soft tissue (arrow) and some superficially apparent vascular structures. (b) Negative roadmap images present the extent of the lesion predominantly involving dorsal wrist and carpal structures (arrow). (c, d) Periprocedural DSA via the transarterial route demonstrates multiple fine afferent arteries originating from the ulnar (arrow) and radial artery shunting to venous vascular structures. After 3 treatment sessions, the patient showed satisfying improvement of symptoms (Stage I, according to Schobinger classification) at terminal follow-up. AVM, arteriovenous malformation; DSA, digital subtraction angiography.
| Patient no./gender | Previously planned additional surgery | Number of embolization sessions | Volume of embolic agent [mL] | Approach | Peri-procedural complication | Postprocedural complication | Management of complications | Degree of devascularization | Pain at terminal follow-up |
|-------------------|--------------------------------------|---------------------------------|-----------------------------|----------|-----------------------------|-----------------------------|---------------------------|---------------------------|--------------------------|
| 1/f               | +                                    | 5                              | 13.5/3/4.5/10.5/6           | A/A/A/P/P | -                           | Prolonged pain > 7 days (second session), increasing skin necrosis (fourth session), late secondary bacterial infection with onyx extrusion (fifth session) | Surgery (onyx removal: ineffective, increased necrosis) (+ previously planned surgery) | 90%-99%                   | Partial relief            |
| 2/f               |                                      | 3                              | 3/3/10                      | A/A/P     | -                           | Early local infection with onyx extrusion and tattoo effect (first session), prolonged pain > 7 days (second session) | Conservative              | 70%-90%                   | No improvement            |
| 3/f               |                                      | 2                              | 6/10                        | A/P       | -                           | -                           | -                         | 70%-90%                   | Partial relief            |
| 4/f               |                                      | 2                              | 1.5/1.5                     | A/P       | -                           | Prolonged pain > 7 days (second session) | conservative            | 70%-90%                   | Partial relief            |
| 5/f               |                                      | 2                              | 4/3                         | A/A       | -                           | -                           | -                         | 30%-70%                   | No improvement            |
| 6/f               | +                                    | 2                              | 6/9                         | A/A       | -                           | Increasing skin necrosis (second session) | Conservative (+ previously planned surgery) | 70%-90%                   | Partial relief            |
| 7/f               |                                      | 2                              | 4.5/0.9                     | A/P       | -                           | -                           | -                         | 30%-70%                   | Partial relief            |
| 8/m               |                                      | 2                              | 7.5/6.5                     | A/P       | -                           | -                           | -                         | 70%-90%                   | No improvement            |
| 9/m               |                                      | 2                              | 16/15                       | A/A       | -                           | -                           | -                         | 70%-90%                   | Partial relief            |
| 10/f              |                                      | 3                              | 16/6/3                      | A/A/P     | -                           | -                           | -                         | 70%-90%                   | Partial relief            |
| 11/m              |                                      | 4                              | 7.5/4.5/6/1.2               | A/A/A/A   | Non-target embolization (third session) | -                           | -                         | 70%-90%                   | Partial relief            |
| 12/f              |                                      | 3                              | 7.5/13.5/9                  | A/A/A+P   | Non-target embolization (second session) | Increasing skin necrosis (third session) | Surgery (amputation of second finger and necrosectomy of third finger) | 70%-90%                   | Partial relief            |
| 13/m              |                                      | 1                              | 1.5                         | A+P       | Non-target embolization      | Tattoo effect               | -                         | 70%-90%                   | No improvement            |
| 14/m              | +                                    | 1                              | 15                          | V         | -                           | Increasing skin necrosis    | Conservative (+ previously planned surgery) | 90%-99%                   | Symptom-free              |
| 15/f              |                                      | 1                              | 4                           | A         | -                           | -                           | -                         | 30%-70%                   | Partial relief            |

a = transarterial; p = percutaneous; v = transvenous.
(range, 2-64 months). Final clinical follow-up (after last embolization ± surgical treatment) revealed an overall response of 11/15 patients (73.3%) including mainly partial relief of pain (10/15, 66.7%) and 1/15 symptom-free presentation (6.7%). The symptom-free patient had received 1 embolization session and, subsequently, a prior planned surgical amputation of the affected distal finger. Both patients, who underwent previously planned surgical resections of the AVM after the last embolotherapy as well as the patient whose post-procedural increasing necrosis after the 3 embolization was managed with surgical treatment, presented with partial relief, see Table 3. There was no improvement in pain in 4/15 patients (26.7%) at the last follow-up. No patient presented with clinical progression following embolization. We did not observe major differences with respect to the different access routes; however the cohort size did not allow a statistically valid stratification analysis here.

Pre-treatment imaging was as follows: MRI alone in 11/15 patients (73.3%), digital subtraction angiography (DSA) alone in 2/15 patients (13.3%), and both MRI and DSA in 2/15 patients (13.3%). Cho’s classification performed in all pre-treatment imaging (15/15, 100%) showed mostly type IIb (14/15, 93.3%) while 1 AVM (1/15, 6.7%) was categorized as type II. Post-treatment imaging at final follow-up revealed partial devascularization (30%-70%) in 3/15 patients (20%), substantial devascularization (70%-90%) in 10/15 patients (66.7%), and near-total devascularization (90%-99%) in 2/15 patients (13.4%) corresponding to an overall objective outcome of 100%.

Periprocedural complications in the form of non-target embolization occurred during 3/35 embolotherapies (8.5%, CIRSE grade 1). Hereof in 1 case, a non-target embolization of the radial artery occurred, whereupon intraprocedural percutaneous transluminal angioplasty was performed, as well as spasmyloitics and acetylsalicylic acid were administered. The radial artery was successfully recanalized angiographically but presented with distal occlusion during subsequent follow-up angiography, without any clinical sequelae. In the other 2 cases, there were neither therapeutic nor clinical consequences subsequently.

The postprocedural complication rate was 11/35 (31.5%): early postprocedural complications (<30 days) occurred after 10/35 procedures (28.6%) including prolonged pain >7 days (3/35, 8.5%, CIRSE grade 2), persistent skin darkening (tattoo effect, 2/35, 5.7%, CIRSE grade 2), minor local infection at the embolization site with EVOH cast extrusion (1/35, 2.9%, CIRSE grade 3, conservatively resolved), and (compared to pre-treatment status) progressive skin necrosis (4/35, 11.4%, CIRSE grade 3). Three patients of the latter had been scheduled for additional surgical resection following embolization, which was performed after adequate successful lesion devascularization (and not due to the post-procedural complication). Of note, each of these 3 patients had presented with apparent clinical signs of peripheral ischemia at initial presentation (Figure 2). In 1 extensive case of hand AVM primarily affecting palm

![Figure 2](image)

**Figure 2.** A 42-year-old male patient presenting with an AVM at the middle and distal phalanx of the right fourth finger. After near-total devascularization of the malformation, previously planned partial amputation of the affected digit was performed. (a, b) Clinical examination prior to therapy revealed severe peripheral ischemia with consecutive local dystrophy and necrosis of the surrounding soft tissue (arrow), Stage III, according to Schobinger classification. (c) Periprocedural DSA image using transarterial route by means of which the lesion could not be adequately reached. (d) Periprocedural negative roadmap image demonstrates inserted angiocatheter (arrow) after change to the transvenous route. (e, f) Periprocedural DSA while AVM embolization using the transvenous approach (arrow). (g) X-ray after previously planned amputation of the distal and part of the middle phalanx shows the amputation socket at the affected digit (arrow) and residual, embolized vascular structures. (h) Coronal MR angiography revealed near-total devascularization of the residual AVM 2 years after completed amputation. (i) Axial T2-weighted MR image presents residual, embolized vascular structures 2 years after amputation (arrow). (j, k) Clinical presentation of the amputation socket (arrow) at terminal follow-up (2 years after completed interdisciplinary treatment), here the patient presented painless. MR, magnetic resonance.
and wrist, which revealed postprocedural increasing skin necrosis including 2 fingers, additive surgical treatment (amputation of the second finger and necrosectomy at the third finger) had to be performed. No patient presented with impaired hand and wrist functionality or sensory loss. Concerning the patients with prolonged pain >7 days after embolization, these symptoms were self-limited in the further course and entirely resolved with conservative means. None of the patients developed a chronic pain syndrome. Regarding late postprocedural complications (>30 days), in 1 case (1/35, 2.9%, CIRSE grade 3) a secondary bacterial infection was observed with consecutive extrusion of the EVOH cast through the adjacent tissue of the finger, 6 weeks after the last embolization session. Subsequently attempted surgical removal of the cast at the extrusion site was ineffective followed by increased distal necrosis of the fingertip. Nevertheless, 5 months hereafter, the previously planned surgical resection (amputation of the 3 and 4 fingers including distal metacarpals) could be performed successfully (Figure 3).

In total, the major complication rate was 6/35 (17.1%).

While the anatomical involvement of different compartments of the hand (wrist, palm, fingers, wrist and palm, and palm and fingers) showed no significant influence on the complication rates (chi-squared test $P = 0.440$), there were significant differences of the clinical outcome after

**Figure 3.** A 18-year-old female patient presenting with an AVM at the right distal palm as well as third and fourth finger. Six weeks after the fifth embolization session of the malformation, a secondary bacterial infection with consecutive onyx cast extrusion was observed. (a) At pre-treatment clinical examination the patient's findings included signs of peripheral ischemia and local bleeding, Stage III, according to Schobinger classification. Initially, additive surgical resection was planned after sufficient devascularization. (b, c) Coronal MR angiography and periprocedural DSA image visualize the anatomical extension of the lesion at the distal carpal region and the two affected fingers of the right hand. (d) Angiogram of draining veins following direct puncture of the main outflow vein, used for subsequent retrograde EVOH embolization (arrow). (e) EVOH cast after retrograde embolization (f, g) Clinical presentation of postprocedural late complication (6 weeks after the fifth embolization session) with secondary bacterial infection and consecutive extrusion of the onyx cast through the adjacent tissue (arrows). Subsequent attempted surgical onyx removal at the extrusion site was ineffective resulting in increased distal necroses. (h) Clinical presentation 2 months after the previously planned surgical resection (amputation of 2 fingers and part of the metacarpals) which could be performed successfully 5 months after the postprocedural late complication. Here, the patient presented with relief of pain. EVOH, ethylene-vinyl alcohol copolymer.
embolization depending on the anatomical region involved (chi-squared test \( P = .049 \)). After treatment of AVMs in the group with involvement of 1 or more fingers \((n = 5)\), there was mainly no improvement of symptoms \((4/5, 80.0\%)\), whereas all other groups \((n = 10)\) mostly presented with improvement of symptoms \((9/10, 90.0\%)\), see Table 3. No significant differences between the embolic agent volume injected and the complication rates were detected (Mann-Whitney U test \( P = .372 \)).

**Discussion**

In this study investigating AVM embolization at the hand, we found an overall clinical response of 73% and an overall objective outcome of 100% accompanied by peri- and postprocedural complication rates of 9% and 32%, respectively, using EVOH-based liquid embolic agents.

Treatment of AVMs is associated with both high complication and recurrence rates.\(^9\) The risk for peripheral ischemia, necrosis and subsequent partial/distal limb loss is particularly high at the peripheral extremities.\(^9\) Although some hereditary forms with associated genetic mutations, as well as somatic mutations in sporadic lesions, have been identified for AVMs, targeted pharmacological therapy, as a future therapeutic option, is not yet established and further evidence is lacking.\(^22\) Both embolization and surgery aim at complete occlusion or removal of the nidus and, if possible, adjacent feeding and draining vessels. Especially around the hand, complete cure of AVM can hardly be achieved without significant impairment of peripheral vascularization, structure, and function.\(^14\)

Several concerns have been raised for the use of minimally invasive image-guided treatments in distal extremities while reporting relatively high complication rates in this locations, mostly using ethanol as embolic agent.\(^9,15,16,24\) Park et al.\(^9\) described a complication rate of 61% for ethanol embolization in AVMs of the hand in a retrospective study of 31 patients. In a further retrospective study, a complication rate of 49% was found in 41 patients in which ethanol embolization of AVMs of the hand was performed.\(^9\) In contrast to the previously mentioned studies regarding ethanol embolization, there is a lack of studies using novel embolic agents for treating AVMs of the distal extremities. Although EVOH has also been reported in extracranial applications,\(^19,25-36\) the data are still limited, especially with respect to distinct anatomical localizations.

In the recently published studies of EVOH embolization in peripheral AVMs, as well as the present study, which reveals 9% periprocedural and 32% postprocedural complications including 17% major complications, significantly fewer complications were described compared to pure ethanol in this distinct location.\(^10\) The non-adherent, polymerized EVOH-based liquid embolic agents show a low tendency to migrate beyond the target sites. In comparison to ethanol, they lead to decreased inflammatory reactions of the vessel wall, remaining intravascular with low permanent reaction of the surrounding interstitium. EVOH offers different formulations with different degrees of viscosity and radiopacity.\(^31,32\) In this study, we found non-target embolization in 3 cases and permanent tattoo effect in 2 patients, whereby the latter is difficult to avoid in very superficial lesions. Further early complications were prolonged pain, embolization-induced skin necrosis, and 1 minor local infection with consecutive EVOH extrusion that resolved conservatively. Another case of EVOH extrusion occurred as late complication 6 weeks post-treatment due to secondary bacterial infection. The extrusion sites in both cases were located at the finger, suggesting that these AVM lesions are more susceptible due to less soft tissue coverage. The overall complication rate was 40% which did not depend on the injected volume of embolic agents. These results are difficult to compare, as the limited studies published so far regarding image-guided embolization in use of EVOH presented heterogeneous patient cohorts and different anatomical regions involved. Saeed et al.\(^9\) reported 7 different complications in 28 EVOH embolotherapies of 19 patients with peripheral AVMs corresponding to an overall complication rate of 25%. Hereof, 6 events occurred periprocedurally including 1 embolic stroke.\(^25\) Albuquerque et al.\(^33\) recently assessed an overall complication rate of 16% in a retrospective study of 25 EVOH embolotherapies of peripheral AVMs in 14 patients while 3 patients presented with skin necrosis and 1 patient with a periprocedural small focus of active bleeding. In general, the safety in the present study is comparable to the previously mentioned studies on embolization using EVOH. In our cohort, 3 patients underwent additional surgical resection of the AVMs, which was not a consequence of postprocedural complications but primarily following the initial treatment plan. Here, based on the clinical presentation before treatment, a combined approach was considered the most appropriate.

In this series with hand AVMs, classified mostly as type IIIb according to Cho et al.,\(^17\) a near-total devascularization was achieved in 2 patients \((13\%)\). This constitutes a low rate compared to 63% or 79% of complete devascularization of peripheral AVMs in other parts of the body.\(^25,32\) In studies of hand AVMs, similar results have been obtained. Park et al. reported total obliteration of AVM vessels with ethanol in just 1 case of the entire cohort \((3\%)\). Moreover, in this study, no patient showed <30% devascularization (failure), so the overall objective response rate was 100%. This is high with regard to the large percentage of classification into type 3b, for which Cho et al.\(^17\) described a response rate of 83%. Regarding the relevance of the correct AVM classification, Bouwman et al.\(^20\) recently emphasized in a large cohort that the achievable degree of devascularization is significantly dependent on the AVM type. Clinical grading according to the Schobinger classification revealed stage III in 40% of patients at diagnosis and progression of the disease to stage III in 93% at treatment initiation, which was after a mean period of 6 years following initial diagnosis. Although a control group is missing within this cohort, this fact suggests that watch-and-wait is not favorable in AVMs affecting the hand. After treatment completion, only 33% of the patients showed persistent ulcer and tissue destruction at terminal follow-up. Regarding the clinical outcome within a mean follow-up of 20 months, overall response was seen in 74%, which is comparable to EVOH embolization of peripheral AVMs in other parts of the body.\(^25,33,35\) This suggests, that patients benefit even in the setting of a high risk for collateral damage. Considering hand AVMs, similar clinical results can be achieved with EVOH compared to the more aggressive embolic agent ethanol, for which symptom improvement is reported in up to 75\%.\(^8\) Though there may be more treatment sessions required for a comparable outcome when using EVOH, our cohort presented with a mean number of 2.3 sessions, compared to 1.5 or 1.9 in the reported ethanol cohorts.\(^15,35\)
The comparison between the anatomical involvement of different compartments of the hand showed a higher rate of persistent symptoms after treatment of cases with involvement of the fingers. Anatomical small compartments along the fingers showing contiguous proximity to neurovascular and articular structures as well as the skin may be responsible for persistent symptoms after devascularization of the lesions. Park et al. performing a similar categorization showed a higher complication rate in the group with finger involvement based on the same conclusions. However, in contrast to this study, he described increased improvement of symptoms in the group with finger involvement due to the small lesion size.8

This study had several limitations. First, this multicenter study presented a retrospective design with a consecutive lack of standardized follow-up information available for all patients. As no uniform follow-up intervals were predefined, for example, 12 or 24 months post-treatment, the inhomogeneity of the data must be taken into consideration when interpreting the results. Disease-specific questionnaires to evaluate specific symptoms and impairments were not used as a clinical outcome tool. In addition, due to the rarity of the disease, this study included a limited cohort size. Second, the methodological assessment of lesion devascularization with categorization in percentages is not validated, though it represents the most commonly used methodology in the literature. This limited indicator of success reflects the general problem concerning this rare disease, as currently no established and validated criteria for evaluation of the clinical and imaging outcome in vascular malformations exists. Third, regarding the inherently high recurrence rate of fast-flow vascular malformations, which is frequently manifesting after a longer term, our median follow-up time after the last embolotherapy (18 months) was rather short.

In conclusion, we were able to show that image-guided embolization using EVOH seems to be both effective and safe for treating AVM of the hand. Additional surgical treatments including amputations may be required and emphasize the need for an interdisciplinary approach. Overall, AVMs including the fingers were associated with higher rates of persistent symptoms and a higher risk for peripheral ischemia and ulceration following embolization, compared to the involvement of more proximal hand compartments.

Conflict of interest disclosure

The authors declared no conflicts of interest.

References

1. Wassef M, Borsik M, Cerceau P, et al. Classification of vascular tumours and vascular malformations. Ann. Pathol. 2021;41(1):58-70. [CrossRef]
2. Monroe EJ. Brief description of ISVSA classification for radiologists. Tech Vasc Interv Radiol. 2019;22(4):100628. [CrossRef]
3. Sadick M, Müller-Wille R, Wildgruber M, Wohlgemuth WA. Vascular anomalies (Part I): Classification and Diagnostics of Vascular Anomalies. Rofo. 2018;190(9):825-835. [CrossRef]
4. Al-Olabi L, Polubothu S, Dowsett K, et al. Mosaic RAS/MAPK variants cause sporicad vascular malformations which respond to targeted therapy. J Clin Invest. 2018;128(4):1496-1508. [CrossRef]
5. Martinez-Lopez A, Salvador-Rodriguez L, Montero-Vilchez T, Molina-Leyva A, Tercedor-Sanchez J, Arias-Santiago S. Vascular malformations syndromes: an update. Curr Opin Pediatr. 2019;31(6):747-753. [CrossRef]
6. Soulez G, Gilbert Md Frercp P, Giroux Md Frercp MF, Racicot Md Frercp JN, Dubois J. Interventional management of arteriovenous malformations. Tech Vasc Interv Radiol. 2019;22(4):100633. [CrossRef]
7. Yakes WF, Rossi P, Odlin H. How I do it. Arteriovenous malformation management. Cardiovasc Interv Radiol. 1996;19(2):65-71. [CrossRef]
8. Müller-Wille R, Wildgruber M, Sadick M, Wohlgemuth WA. Vascular anomalies (Part II): Interventional Therapy of Peripheral Vascular Malformations. Rofo. 2018. [CrossRef]
9. Park HS, Do YS, Park KB, et al. Ethanol embolotherapy of hand arteriovenous malformations. J Vasc Surg. 2011;53(3):725-731. [CrossRef]
10. Mendel T, Louis DS. Major vascular malformations of the upper extremity: long-term observation. J Hand Surg Am. 1997;22(2):302-306. [CrossRef]
11. Ek ET, Suh N, Carlson MG. Vascular anomalies of the hand and wrist. J Am Acad Orthop Surg. 2014;22(6):352-360. [CrossRef]
12. Drapé JL, Feydy A, Guerini H, et al. Vascular lesions of the hand. Eur J Radiol. 2005;56(3):331-343. [CrossRef]
13. Al-Qattan MM, Murray KA, El-Shayeb A. Arteriovenous vascular malformations confined to the hand: an algorithm of management based on a new classification. J Hand Surg Br. 2006;31(3):266-273. [CrossRef]
14. Lim CS, Evans N, Kaur I, et al. Incidence of major complication following embolo-sclerotherapy for upper and lower extremity vascular malformations. Vascular. 2021;29(1):69-77. [CrossRef]
15. Li X, Su L, Yang X, et al. Embolotherapy for high-flow arteriovenous malformations in the hands using absolute ethanol with coil-assisted dominant outflow vein occlusion. J Vasc Interf Radiol. 2019;30(6):813-821. [CrossRef]
16. Park UJ, Do YS, Park KB, et al. Treatment of arteriovenous malformations involving the hand. Ann Vasc Surg. 2012;26(5):643-648. [CrossRef]
17. Cho SK, Do YS, Shin SW, et al. Arteriovenous malformations of the body and extremities: analysis of therapeutic outcomes and approaches according to a modified angiographic classification. J Endovasc Ther. 2006;13(4):527-538. [CrossRef]
18. Finn MC, Glowacki J, Mulliken JB. Congenital vascular lesions: clinical application of a new classification. J Pediatr Surg. 1983;18(6):894-900. [CrossRef]
19. Wohlgemuth WA, Müller-Wille R, Teusch VI, et al. The retrograde transvenous push-through method: a novel treatment of peripheral arteriovenous malformations with dominant venous outflow. Cardiovasc Intervent Radiol. 2015;38(3):623-631. [CrossRef]
20. Bouwman FCM, Botden SMBL, Verhoeven BH, et al. Treatment outcomes of embolization for peripheral arteriovenous malformations. J Vasc Interv Radiol. 2020;31(11):1801-1809. [CrossRef]
21. Filippidi DK, Binkert C, Pellerin O, Hoffmann RT, Krajina A, Pereira PL. Cirse quality assurance document and standards for classification of complications: the cirse classification system. Cardiovasc Intervent Radiol. 2017;40(8):1141-1146. [CrossRef]
22. Nguyen HL, Boon LM, Vikkula M. Vascular anomalies caused by abnormal signaling within endothelial cells: targets for novel therapies. Semin Intervent Radiol. 2017;34(3):233-238. [CrossRef]
23. Couto JA, Huang AT, Konczyk DJ, et al. Somatic MAP2K1 mutations are associated with extracranial arteriovenous malformation. Am J Hum Genet. 2017;100(3):544-554. [CrossRef]
24. Hyun D, Do YS, Park KB, et al. Ethanol embolotherapy of foot arteriovenous malformations. J Vasc Surg. 2013;58(6):1619-1626. [CrossRef]
25. Saeed Kilani M, Lepennec V, Petit P, et al. Embolization of peripheral high-flow arteriovenous malformations with Onyx. Diagn Interv Imaging. 2017;98(3):217-226. [CrossRef]
26. Nassiri N, Cirillo-Penn NC, Crystal DT. Direct stick embolization of extremity arteriovenous malformations with ethylene vinyl alcohol copolymer. J Vasc Surg. 2017;65(4):1223-1228. [CrossRef]
27. De Beule T, Vranckx J, Verhammer P, et al. Transarterial embolization of peripheral arteriovenous malformations with ethylenevinyl alcohol copolymer - feasibility, technical outcomes, and clinical outcomes. Vasa. 2016;45(6):497-504. [CrossRef]
28. Cassinotto C, Lapujade B. Pancreatic arteriovenous malformations treated with onyx. J Vasc Interv Radiol. 2015;26(5):442-444. [CrossRef]
29. Numan F, Omeroglu A, Kara B, Cantasdemir M, Adaleti I, Kantarci F. Embolization of peripheral vascular malformations with ethylene vinyl alcohol copolymer (Onyx). J Vasc Interf Radiol. 2004;15(9):939-946. [CrossRef]
30. Do YS, Park KB, Park HS, et al. Extremity arteriovenous malformations involving the bone: therapeutic outcomes of ethanol embolotherapy. *J Vasc Interv Radiol*. 2010;21(6):807-816. [CrossRef]

31. Gioppo A, Faragò G, Caldiera V, Caputi L, Cusin A, Ciceri E. Medial tentorial dural arteriovenous fistula embolization: single experience with embolic liquid polymer SQUID and review of the literature. *World Neurosurg.* 2017;107(1):1050.e1-1050.e7. [CrossRef]

32. Pop R, Mertz L, Ilyes A, et al. Beam hardening artifacts of liquid embolic agents: comparison between SQUID and Onyx. *J Neurointerv Surg*. 2019;11(7):706-709. [CrossRef]

33. Albuquerque TVC, Stamoulis DNJ, Monsignore LM, et al. The use of dual-lumen balloon for embolization of peripheral arteriovenous malformations. *Diagn Interv Radiol*. 2021;27(2):225-231. [CrossRef]

34. Venturini M, Lanza C, Marra P, et al. Transcatheter embolization with SQUID, combined with other embolic agents or alone, in different abdominal diseases: a single-center experience in 30 patients. *CVIR Endovasc.* 2019;2(1):8. [CrossRef]

35. Sofocleous CT, Rosen RJ, Raskin K, Fioole B, Hofstee DJ. Congenital vascular malformations in the hand and forearm. *J Endovasc Ther.* 2001;8(5):484-494. [CrossRef]