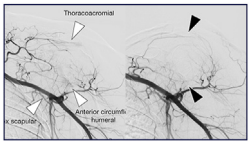


# Transarterial Embolization for Adhesive Capsulitis of the Shoulder: Midterm Outcomes on Function and Pain Relief

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## ABSTRACT

**Purpose:** To determine the safety and potential effectiveness of transarterial embolization for adhesive capsulitis of the shoulder.

**Materials and methods:** This prospective study analyzed consecutive adult patients with adhesive capsulitis referred for embolization between January 2018 and May 2023 after a poor response to treatment (symptoms and limitation of motion in ≥2 axes; ≤120° flexion, ≤50° external rotation and/or internal rotation with the shoulder abducted 90°) persisting for >3 months after having completed ≥6 weeks of analgesics and physical therapy. Different types of pain and mobility were measured before embolization and 1, 3, and 6 months after embolization. Overall upper limb function (Quick Disabilities of Arm, Shoulder, and Hand) and patient satisfaction were measured before and 6 months after embolization. Long-term follow-up comprised telephone interviews and clinical history reviews.

**Results:** A total of 20 patients (12 [60%] women; median age, 50.7; interquartile ranges [IQR], 45–55 years) were included; 6 (30%) had diabetes and 15 (75%) were off work. Median duration of symptoms before embolization was 39.4 weeks (IQR, 28–49 weeks), and median duration of rehabilitation therapy was 12.8 weeks (IQR, 8–16 weeks). Six months after embolization, significant improvements were observed in nocturnal pain ($P$ = .003), pain on moving ($P$ = .001), external rotation ($P$ < .001), internal rotation ($P$ < .001), active flexion ($P$ < .001), passive flexion ($P$ = .03), active abduction ($P$ < .001), passive abduction ($P$ < .001), and overall function ($P$ < .001). Despite objective improvements, patient satisfaction was nearly unchanged. Only 1 patient experienced a mild adverse event.

**Conclusion:** Transarterial embolization is safe and potentially effective in treating adhesive capsulitis of the shoulder refractory to conventional treatment. Clinical improvements were maintained in the mid to long term.

## ABBREVIATIONS

AE = adverse event, CS = cilastatin sodium, IMP = imipenem, MR = magnetic resonance, *Quick*DASH = Quick Disabilities of Arm, Shoulder, and Hand

Adhesive capsulitis is a painful shoulder condition in which the progressive loss of active and passive mobility results in functional disability. Most cases are idiopathic, and most patients respond partially to conventional treatment (physical therapy, nonsteroidal anti-inflammatory drugs, oral corticosteroids, and intra-articular injection of corticosteroid); however, up to 30% of cases are refractory to treatment, with most symptoms persisting chronically (1).

Based on the discovery of increased vascularization in adhesive capsulitis, various studies have assessed the effectiveness of embolizing the arterioles involved. Occluding arteriolar flow to induce ischemia in the inflamed tissue of the capsule reduces inflammation and pain (2). The safety and effectiveness of this technique for the treatment of adhesive capsulitis refractory to conventional interventions have been reported elsewhere (3).

The current study aimed to broaden experience in the use of transarterial embolization to treat adhesive capsulitis of the shoulder by including a larger sample of patients, evaluating safety by recording adverse events (AEs), and measuring potential effectiveness in terms of pain reduction and improved range of movement 6 months after the procedure as well as the long-term durability of these improvements.

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## RESEARCH HIGHLIGHTS

- Transarterial embolization of the shoulder is safe (only 1 patient [5%] experienced a mild adverse event—transient edema of the wrist/forearm).
- Six months after embolization, significant improvements were observed in nocturnal pain ($P = .003$), pain on moving ($P = .001$), external rotation ($P < .001$), internal rotation ($P < .001$), active flexion ($P < .001$), passive flexion ($P = .03$), active abduction ($P < .001$), passive abduction ($P < .001$), and overall function ($P = .001$).
- Clinical improvements were maintained during midterm to long-term follow-up (median, 18 months; interquartile range, 6–36 months). However, patient satisfaction was nearly unchanged.
- Long-term outcomes were worse in diabetic patients (the 6 diabetic patients continued to require analgesics).

## STUDY DETAILS

**Study type:** Prospective, observational, descriptive study

**Study phase:** Feasibility

**Level of evidence:** 4 (SIR-C)

## MATERIALS AND METHODS

This prospective study analyzes experience in embolizing consecutive patients with adhesive capsulitis referred by the authors' hospital's rehabilitation medicine department based on clinical and imaging criteria between January 2018 and May 2023. All patients had magnetic resonance (MR) imaging findings compatible with adhesive capsulitis. All patients referred for embolization showed a poor response to treatment, defined as the persistence of symptoms for >3 months with a persistent limitation of motion in at least 2 axes (≤120° flexion and ≤50° external rotation and/or internal rotation with the shoulder abducted 90°) after having completed conventional treatment (≥6 weeks of physical therapy, analgesics, and occasionally intra-articular infiltration or suprascapular nerve block). Patients aged <18 years, those with systemic disease, those with shoulder fractures, and those who underwent shoulder surgery were excluded.

### Embolization Technique

All procedures were performed by interventional radiologists with >3 years of experience. Under local anesthesia, percutaneous access was obtained either through the common femoral artery with a 5-F introducer sheath (Terumo, Tokyo, Japan) or through the radial artery with a 6-F introducer sheath. To obtain detailed information about the arterial supply to the glenohumeral capsule (thoracoacromial, suprascapular, scapular circumflex, and anterior and posterior humeral circumflex arteries), an arteriogram of the axillary artery was obtained using different types of catheters: 4-F or 5-F Glidecath C2, vertebral curve, or Simmons (Cook, Bloomington, Indiana, and Terumo). To selectively catheterize the artery or arteries supplying the hypervascularized area, identified by early vascular filling, hyperemia, anomalous vessels, or early venous return, a 1.9-F coaxial microcatheter (Parkway Soft; Asahi Intecc, Nagoya, Japan) was used; in a few difficult cases, a Progreat 2.4 (Terumo) or 45° curved-tip Carnelian 2.2-F microcatheter (Tokai Medical Products, Kasugai City, Aichi, Japan) was used as a second choice. To embolize the vessels, small amounts (0.2–0.4 mL) of suspended microparticles (10–70 μm) formed by diluting a mixture of 500-mg imipenem (IMP) and 500-mg cilastatin sodium (CS) (Aurovitas, Teramo, Italy) in 5–10 mL of iodinated contrast material were injected, and the vessels were flushed afterward with similar amounts of normal saline solution until the hypervascularized areas were excluded. All procedures were performed under fluoroscopic guidance. Embolization aimed to achieve complete or nearly complete stasis of flow in the feeding artery with no reflux of embolic agent to untargeted arteries.

After the procedure, patients remained under observation for a few hours and were discharged after their stability was confirmed. Between 72 and 96 hours after embolization, patients resumed rehabilitation with kinesiotherapy and physical therapy and continued until their clinical situation stabilized.

### Predefined Variables

The following variables were recorded demographics, such as age, sex, employment status, laterality of injury, dominance, and diabetes, and variables related to adhesive capsulitis, such as time since onset and duration of rehabilitation therapy before and after embolization.

Variables related to the embolization procedure included access (radial or femoral), arteriography findings, arteries embolized, and duration of the procedure. AEs during and after the procedure were classified according to the AE classification of the Society of Interventional Radiology (SIR) (4) and outcome variables as related to mobility: active flexion, passive flexion, active abduction, passive abduction, internal rotation, and external rotation. The range of motion was measured by goniometry and recorded in degrees before embolization and 1, 3, and 6 months after the procedure. Variables related to pain—active, nocturnal, and at rest—were measured with a visual analog scale ranging from 0 (no pain) to 10 (worst possible pain) before embolization and 1, 3, and 6 months after the procedure. Overall upper limb function was measured using the self-administered Quick Disabilities of Arm, Shoulder, and Hand (*Quick*DASH), which assessed patients' ability to perform 11 activities on a scale from 0 (no difficulty) to 100 (unable) (5) and was completed before embolization and 6 months after the procedure. Other variables measured included patient satisfaction, measured on a scale ranging

from 0 (completely dissatisfied) to 10 (completely satisfied) before embolization and 6 months after the procedure, and technical and clinical success. Technical success was defined as selective catheterization and embolization of at least 1 artery feeding the shoulder joint. Clinical success was defined as a >50% decrease in the different types of pain and >50% improvement in the range of joint motion 6 months after treatment.

### Long-Term Follow-up

After embolization, attending physicians from the rehabilitation department clinically followed up with patients who underwent rehabilitation (kinesiotherapy and physical therapy) until their clinical situation stabilized (up to 6 months). In monthly telephone interviews starting 6 months after the procedure, rehabilitation physicians reviewed patients' clinical histories and asked them about their symptoms, analgesic use, and overall satisfaction.

### Statistical Analysis

Categorical variables are reported as frequencies and percentages, and continuous variables are reported as medians and interquartile ranges (IQRs). To compare values of the variables before and after the procedure, the Wilcoxon signed-rank test was used, considering $P < .05$ significant. IBM SPSS for windows version 23 (IBM, Armonk, New York) was used for all analyses.

### Ethical Considerations

The ethics committee of the University Hospital of Toledo to which the authors' hospital is affiliated approved the study protocol. All participants provided written informed consent. Patients' confidentiality was ensured in accordance with current legislation.

## RESULTS

### Patients' Characteristics

This study included 20 patients (12 [60%] women; median age, 50.7 years; IQR, 45.5–55 years; 19 [95%] right-handed); of these, 6 (30%) had diabetes and 15 (75%) were on sick leave. Adhesive capsulitis affected the right shoulder in 10 (50%) patients and the left shoulder in 10 (50%) patients. Median duration of symptoms before embolization was 39.4 weeks (IQR, 28−49 weeks), and median duration of rehabilitation therapy before embolization was 12.8 weeks (IQR, 8–16 weeks).

### Embolization Procedures

Access was through the radial artery in 12 (60%) patients and through the femoral artery in 8 (40%). In all patients, arteriography identified hyperemia involving the joint, capsule, pannus, and/or plexus. All embolizations were performed with IMP/CS.

The most commonly embolized arteries (and their branches) were the anterior circumflex artery alone (n = 3; 15%), thoracoacromial artery alone (n = 3; 15%), and both anterior circumflex and thoracoacromial arteries (n = 14; 65%). Two arteries were embolized in 11 (55%) patients, 3 arteries in 7 (35%) patients, 1 artery in 3 (15%) patients, and 4 arteries in 1 (5%) patient. Only 1 (5%) patient had angiographic AEs, consisting of local extravasation of medication in the wrist and forearm that resolved with antihistamines, local ice packs, and intravenous normal saline solution. Median duration of the procedure was 33.2 minutes (IQR, 16−48.5 minutes). Median hospital stay was 1.6 days (IQR, 1−2 days). After the procedure, all patients were followed up clinically for 6 months.

### Clinical Outcomes and Patient Satisfaction

The Table summarizes the range of motion and overall shoulder function measured at each time point in the study (quantitative variables are expressed as medians and IQRs).

Six months after the procedure, significant improvements were observed in the range of motion in patients' shoulders in active flexion (80 %; $P < .001$), passive flexion (92%; $P = .03$), active abduction (67.5%; $P < .001$), passive abduction (70%; $P < .001$), internal rotation (59%; $P < .001$), and external rotation (72%; $P < .001$) and overall shoulder function as measured by the *Quick*DASH (164%; $P < .001$). Six months after the procedure, significant improvements were observed in patients' assessments of pain at night (320%; $P = .003$) and pain during movement (273%; $P = .001$) but not in pain at rest (0%; $P = .297$). Figures 1–3 illustrate these changes in boxplots.

Patients' satisfaction scores were 7.6 (IQR, 7.3–9.5) before the procedure and 7.8 (5–10) 6 months after the procedure.

Selective transarterial embolization in patients with adhesive capsulitis refractory is a safe technique. Only 1 patient (5%) experienced a minor AE (transient edema of the wrist/forearm), which was classified according to the AE classification of SIR (4) as a mild AE (category 3, causality, "no risk modifier," and preventable).

### Long-Term Outcomes and Durability of Effects

After embolization and 6 months of clinical follow-up, patients were followed up by telephone for a median of 18 months (IQR, 6–36 months). During long-term follow-up, 14 (70%) patients reported having stopped taking analgesics. Moreover, of the 6 (30%) who reported that they continued to take analgesics regularly or on demand, 5 were also receiving kinesiotherapy and physical treatment or joint infiltrations, and 2 of them were on the waiting list for arthrolysis. Among patients who required reintervention, the median time to new treatment was 18.4 months. The

**Table.** Mobility, Pain, and Quick Disabilities of Arm, Shoulder, and Hand on Assessments at Different Time Points in the Study

| | Before embolization | 1 mo | 3 mo | 6 mo | *P* value |
|---|---|---|---|---|---|
| Mobility, measured by goniometry and expressed in degrees | | | | | |
| Active flexion | 110 (95–112.5) | 115 (107–120) | 110 (100–130) | 130 (120–140) | <.001 |
| Passive flexion | 120 (102.5–120) | - | 130 (110–140) | 120 (120–130) | .03 |
| Active abduction | 100 (82.5–117) | 145 (120–160) | 160 (110–160) | 160 (150–170) | <.001 |
| Passive abduction | 110 (100–127.5) | - | 170 (160–180) | 170 (160–180) | <.001 |
| External rotation | 50 (40–60) | 65 (50–70) | 70 (60–80) | 70 (60–90) | <.001 |
| Internal rotation | 40 (30–50) | 60 (40–70) | 60 (40–70) | 80 (60–90) | <.001 |
| Pain, measured on a visual analog scale (0 = no pain; 10 = worst possible pain) | | | | | |
| Nocturnal pain | 2.9 (1.4–5.9) | 0.2 (0–2) | 0.2 (0–1.2) | 0 (0–0.9) | .003 |
| Pain at rest | 0 (0–1.9) | 0 (0–3) | 0 (0–0.5) | 0 (0–0.9) | .297 |
| Pain during movement | 4.8 (3.8–6.7) | 2.3 (1.2–3.8) | 1.1 (0.1–1.8) | 1 (0.1–2.3) | .001 |
| *Quick*DASH | 50 (40.9–61.5) | | | 25 (12.5–47.7) | <.001 |

Note–*P* values represent the comparison between pre-embolic values and values 6 months after the procedure. Quantitative variables are expressed as medians (interquartile ranges).
*Quick*DASH = Quick Disabilities of Arm, Shoulder, and Hand.

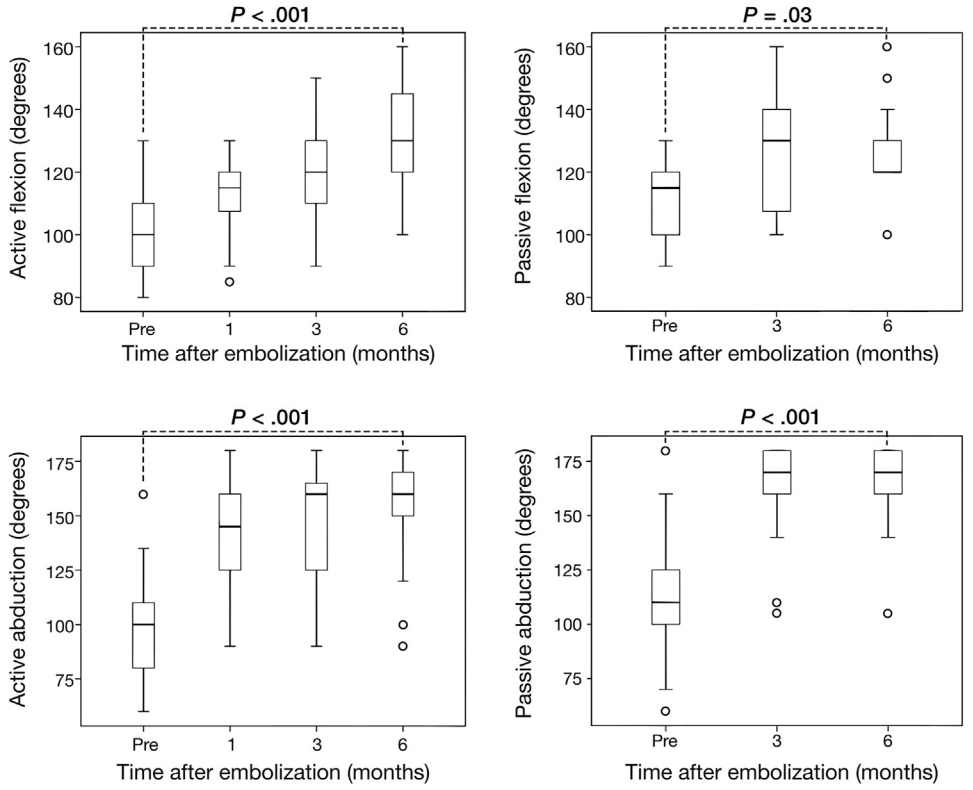


**Figure 1.** Boxplots showed patients' passive and active ranges of shoulder motion in flexion and abduction at different time points.

6 patients with the worst long-term response to embolization are all diabetic, and they continue to require analgesics for persistent pain despite additional treatment.

## DISCUSSION

Although yet to be validated with high-level evidence and included in treatment guidelines, musculoskeletal embolization is a promising new treatment that might become part of interventional radiologists' arsenal. Although the specifics of the treatment vary with the anatomic site, the basics of the procedure are similar. Embolization with IMP/CS was first proven effective in treating osteoarthritis of the knee, and the technique rapidly became used to treat other conditions such as lateral epicondylitis and adhesive capsulitis (6). With the aim of

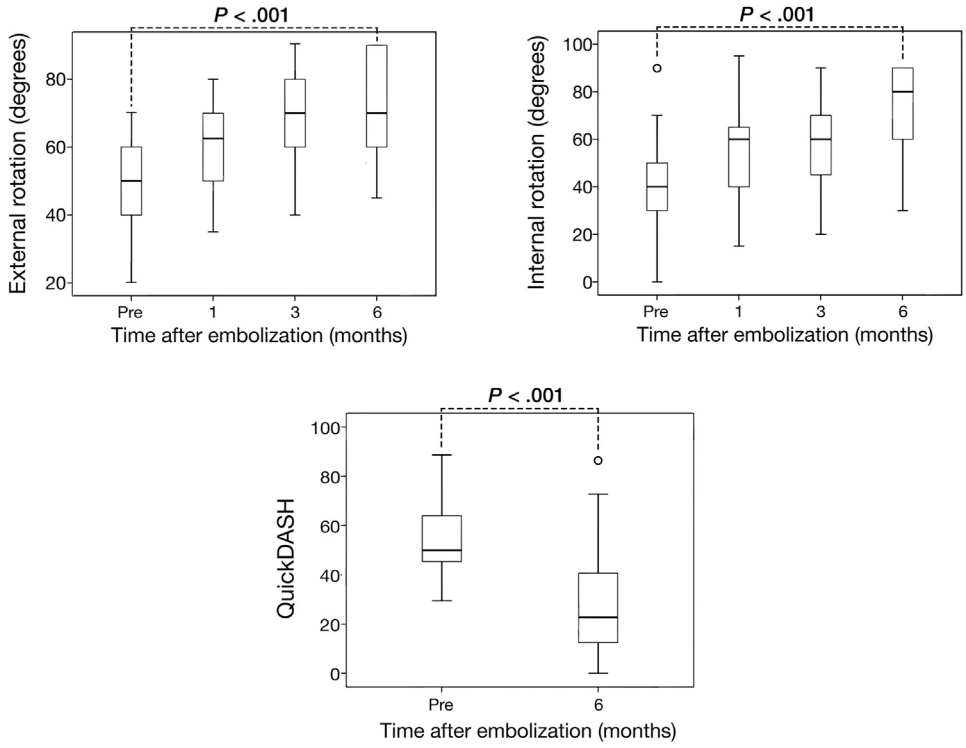


**Figure 2.** Boxplots showed the range of patients' internal and external shoulder rotation at different time points, illustrating the difference between patients' scores on the Quick Disabilities of Arm, Shoulder, and Hand (*Quick*DASH) questionnaire before and 6 months after embolization.

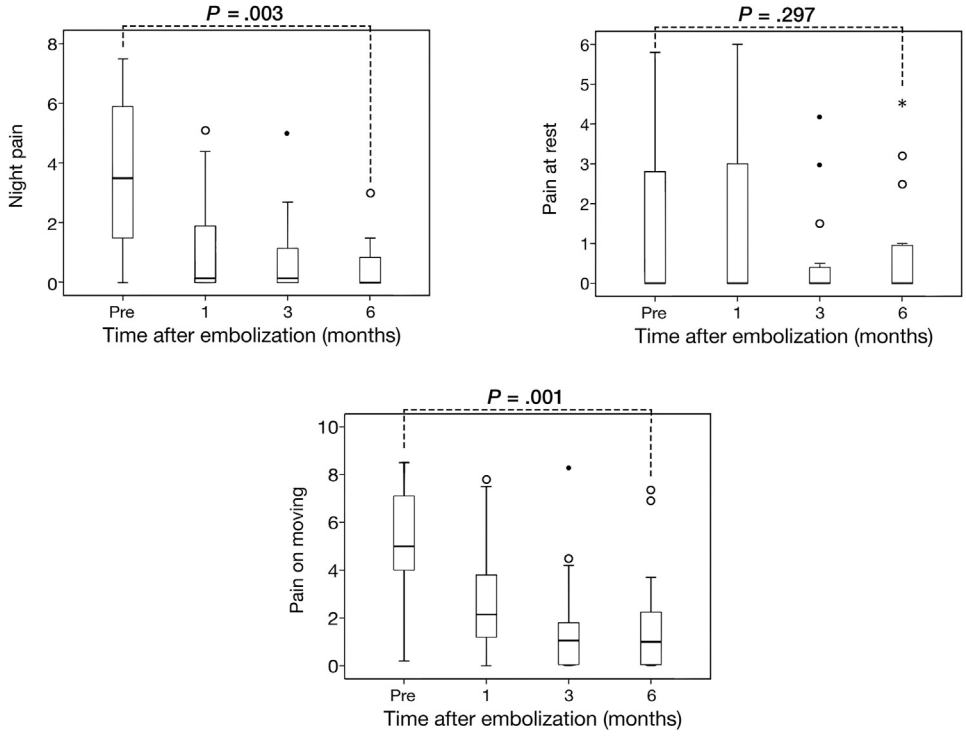


**Figure 3.** Boxplots showed the range of patients' nocturnal pain, pain at rest, and pain on movement at different time points.

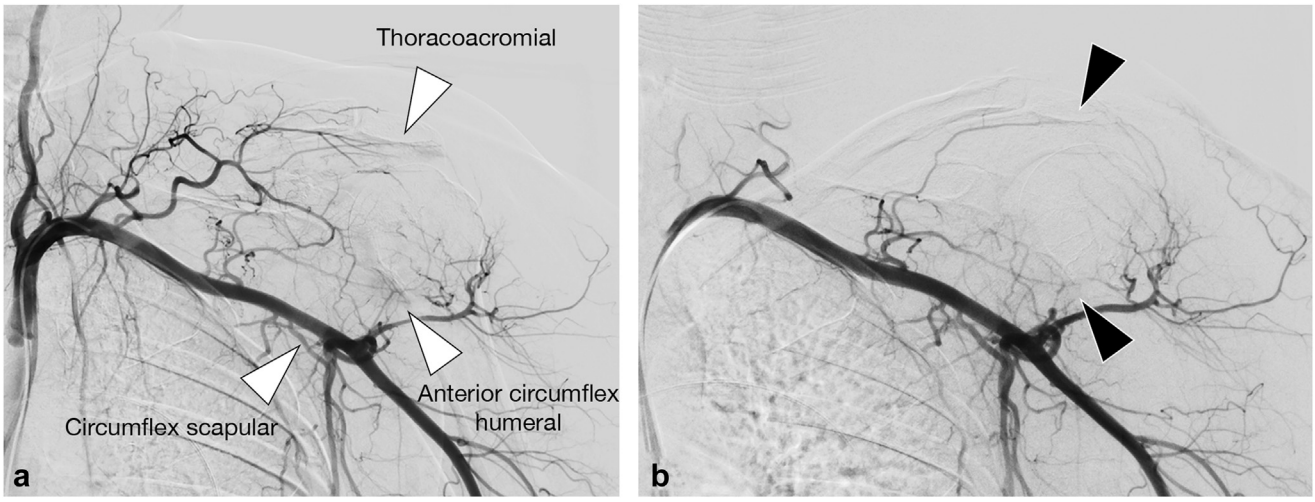


**Figure 4. (a)** Pre-embolic angiogram in the late arterial phase showed areas of hyperemia in territories dependent on the thoracoacromial and anterior humeral circumflex arteries (white arrowheads). **(b)** Postembolic angiogram showed resolution of the hyperemia after embolization with imipenem/cilastatin sodium (black arrowheads).

breaking the circle of hypervascularization, pain, and inflammation in cases where periarticular structures (eg, synovia, tendon, and capsule) are inflamed, this technique aims to temporarily occlude newly formed microvessels that are visible on angiography (7). In the current series, all patients had hypervascularization associated with inflammatory processes that lead to fibrosis in adhesive capsulitis (**Fig 4a, b**). The arteries most commonly involved in other series were the branches of the coracoid arteries (63%), thoracoacromial artery (33%), and scapular circumflex artery (4%) (8).

The cohort was representative of the population with adhesive capsulitis (9): all patients were middle-aged, there were more women than men, and 30% had a history of diabetes. Adhesive capsulitis had significant repercussions on the patients' functional capacity, with 3 of every 4 patients unable to work.

All patients had long been experiencing the symptoms of adhesive capsulitis (median time from onset, 39.3 weeks) and underwent extensive rehabilitation before embolization (median, 12.8 weeks), thus ensuring that the patients included established adhesive capsulitis that was refractory to conventional treatment. This is important because adhesive capsulitis first manifests as pain and functional limitations develop progressively. For this reason, only patients with restricted mobility indicating an advanced phase of disease were referred for embolization. The key clinical sign in adhesive capsulitis is a decreased range of both active motion (where the patient moves the limb) and especially passive motion (where the examiner moves the limb) (10).

Unlike the current study, most studies (11,12) assessed patients fundamentally on shoulder pain. Pain is undoubtedly an important complaint in patients with adhesive capsulitis, and pain relief is a valid treatment goal. However, the measurement of pain is subjective, and patients' perceptions of pain can be affected by many factors, including analgesic use. In contrast, goniometric measurements of passive and active ranges of motion in flexion and abduction and internal and external rotations are objective endpoints that can be compared over time and across series. Providing objective data about the range of motion before and at different time points after embolization is one of the major contributions of the current study.

The embolic agent IMP/CS is a combination of the antibiotic imipenem and cilastatin sodium, a nonpermanent embolic agent. Because this agent has a transient embolic effect, it was initially used for gastrointestinal bleeding to avoid bowel ischemia (13); however, it is now widely used in musculoskeletal embolization (14). In most procedures, 2–3 arteries need to be embolized to achieve the desired effect (15). IMP/CS forms polygonal particles ranging from 10 to 70 μm in diameter. Using agents composed of other types of microparticles, usually larger (100–250 μm) microspheres with longer-lasting effects, has not yielded better results. Indeed, microparticles that result in permanent embolization are associated with adverse effects such as transient osteomedullary edema (16) and cutaneous ischemia (11). Thus, embolic agents such as microspheres that can occlude vessels permanently may entail a greater risk when the goal is transient embolization (17). Along these lines, a recent study (18) comparing IMP/CS with calibrated microspheres in the management of chronic shoulder pain concluded that IMP/CS appears to be safer in this context. In the current study, no significant AEs were observed, corroborating the existing evidence for the safety of IMP/CS. However, unlike microspheres, IMP/CS is not readily available in many countries. Moreover, it is often contraindicated in patients with hypersensitivity or allergy to other antibiotics, and its safety as an embolic agent to block blood vessels has not been fully established.

Unlike other studies, the current study evaluated different types of pain. The intensity of pain at rest was low

even before embolization, and the decrease after the procedure did not reach significance. Pain on palpation decreased little over time. Active and nocturnal pain progressively improved and were significantly different 6 months after the procedure. Nocturnal pain is very characteristic of adhesive capsulitis, resulting in sleep deprivation and negatively impacting patients' lives. Nearly 90% of patients report sleep disturbances that decrease their quality of life (19). Nocturnal pain is the component of pain that improved most in the current series of patients. This component has an important impact on patients' satisfaction with the procedure (20). The mechanism underlying the improvement in pain is the destruction of nociceptors as a result of the occlusion of the neovessels (21). The findings of the current study are in line with those of all published studies, which reported that patients' pain, especially nocturnal pain, improved early after embolization (12).

The range of both active and passive motion improved in flexion, abduction, and rotation. The highest degree of improvement was in passive flexion, and the lowest was in internal rotation. It is crucial to assess the range of motion because pain usually precedes functional limitations. In the advanced stage of disease, pain tends to be better controlled, and patients' chief complaints are usually more related to limited mobility (10). Embolization decreases the number of vessels, improving patients' functional capacity (22).

Unlike many other studies about adhesive capsulitis, the current study also evaluated patients with *Quick*DASH, one of the most widely used instruments for assessing shoulder function. Because *Quick*DASH covers aspects related to pain as well as those related to mobility and function, this index provides important information about overall shoulder function in this context (5,23). In the current study, the *Quick*DASH scores improved significantly after embolization.

The results of the current study are comparable with those of other series, both regarding improvements in pain and functional recovery (19,24–26) and in the low rate of AEs. The important strengths of this study are the assessment of different types of pain and of mobility and the use of a comprehensive measurement of upper limb incapacity, which, taken all together, provide a complete view of patients' situations before and after the intervention. The current study expands earlier available evidence (3).

Some limitations of the current study warrant comment. Although the size of sample is similar to those reported in other studies, it is still small. Furthermore, the lack of a control group limits the authors' ability to reach firm conclusions. Multicenter studies would help ensure a larger and more heterogeneous group of patients, and a control group or comparator arm would help elucidate the true effects of embolization. Adhesive capsulitis was formerly considered a self-limiting disorder, but greater experience has shown that one-third of patients continue to have symptoms for at least 7 years (27–29). Nevertheless, the natural history of this disorder is to resolve over time; hence, it is difficult to determine to what extent the decrease in analgesic use observed is due to the procedure. Although most studies evaluate the effects of treatment on symptoms for 6 months, longer-term studies are necessary to determine in which patients adhesive capsulitis recurs and whether repeat embolization is effective (30,31). Larger studies would also enable subgroups of patients (eg, those with diabetes) to be evaluated. Thus, although arterial embolization is a very promising technique for adhesive capsulitis and forms part of the therapeutic arsenal of many interventional radiology teams, it is important to continue to produce high-quality scientific data to evaluate the effectiveness of this procedure (31–33).

In conclusion, selective transarterial embolization in patients with adhesive capsulitis refractory to conservative treatment has few AEs and improves different types of pain and the range of motion of the shoulder. These clinical improvements are observed early in the first weeks after the procedure and are maintained in the long term in most patients, justifying its utilization.

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