Key Papers in Embolotherapy

An overview of significant embolotherapy articles published in 2022 and summaries of the potential impact each may have on the field.

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The year 2022 was vibrant for embolotherapy papers—from small series suggesting early signal to large-scale multiyear projects that methodically moved evidence ahead. Given that choosing only four from across a substantial field is prone to complaints or failure at the outset, please accept our apologies. That said, we have intentionally selected four very different papers from the "edges" of embolization—excluding any oncology papers, as these have been addressed in dedicated recent interventional oncology overviews—to highlight points that risk being overlooked. Our selection includes a paper addressing an important question in the early days of a new investigatory area, genicular artery embolization (GAE); a culmination and compilation of work from a large study in a long-practiced area, uterine artery embolization (UAE); a large data set from a still-developing area, prostatic artery embolization (PAE); and, finally, a study focusing on the impact of spontaneous portosystemic shunt (SPSS) embolization for patients undergoing transjugular intrahepatic portosystemic shunt (TIPS) placement.

Long-Term Outcome of Prostatic Artery Embolization for Patients With Benign Prostatic Hyperplasia: Single-Centre Retrospective Study in 1072 Patients Over a 10-Year Period

Bilhim T, Costa NV, Torres D, et al. Cardiovasc Intervent Radiol. 2022;45:1324-1336. doi: 10.1007/s00270-022-03199-8

SUMMARY

This paper reports the results of a retrospective, single-center, 10-year study of 1,072 patients with symptomatic benign prostatic hyperplasia who underwent PAE. The average follow-up time was 4.4 years ± 2.4 years. The study also defined an evolution of practice at a center with one of the largest PAE experiences, from variations in technique to shifts in embolics from polyvinyl alcohol (PVA) to varied calibrated microspheres. Patient data were reported in tertiles of 1 to 3, 4 to 6, and 7 to 10 years, where data on 929, 352, and 153 patients were available. Reintervention rates were 3.4%, 21%, and 58% at 1, 5, and 10 years, respectively. Although higher rates of clinical failure were noted with PVA, the authors note that this earliest agent paralleled early PAE learning curves—points noted in multiple other studies, where embolization technique and endpoints emphasizing dense distal embolization have proven important for durable effect. Indeed, reintervention rates proved lower in later patients treated with spherical embolics. Prostatectomy rates were 1% at 1 year and 11.6% at 5 years, while one-third of patients continued using prostate medications. As with other series, adverse events were low, and incontinence and ejaculatory dysfunction were near-absent (< 1%). Ninety-seven patients underwent repeat PAE and achieved quality-of-life and International Prostate Symptom Score improvements similar to those at initial PAE.

WHY THIS ARTICLE IS IMPORTANT

Despite a decade of experience, multiple systematic and meta-analyses, and comparative trials demonstrating relevant outcomes for patients with lower urinary tract symptoms (LUTS), most patients continue to have to discover this option on their own, uninformed or misinformed by urologists. This study provides the longest-duration follow-up on one of the largest cohorts of patients undergoing PAE. It further affirms the very safe nature of PAE and its ability to achieve meaningful improvements in LUTS that are durable to 5 years at rates comparable to endourologic interventions, without feared ejaculatory or incontinence concerns. Although comparative studies of transurethral resection of the prostate have suggested better 2-year control of LUTS compared with PAE, treated prostates were notably smaller (eg, mean, 51 mL) compared with a mean prostate volume of 83 mL in this study. This reflects the real-world experience, where larger prostates are more likely to be referred for—and are perhaps better suited to, PAE (even to mega sizes)—especially given that endourologic options become more limited in larger sizes, short of open or laser prostatectomies. This study emphasizes the ability to achieve meaningful improvements for patients with acceptable tradeoffs in 5-year recurrence, offsetting concerns about endourologic complications, as well as the option for later, unimpeded, repeat PAE or prostatectomy if needed. Overall, the study provides defining evidence that PAE is a viable alternative to traditional surgical treatments for benign prostate hyperplasia, with comparable multiyear outcomes and fewer risks and complications.

Multicenter Randomized Sham Controlled Study of Genicular Artery Embolization for Knee Pain Secondary to Osteoarthritis

Bagla S, Piechowiak R, Sajan A, et al. J Vasc Interv Radiol. 2022;33:2-10.e2. doi: 10.1016/j.jvir.2021.09.019

SUMMARY

This patient-blinded, 2:1, randomized controlled trial evaluated knee osteoarthritis (OA) symptom improvement after GAE (n = 14) versus a sham procedure (n = 7).

Enrollees had Kellgren-Lawrence grade 1 to 3 radiography findings, visual analog scale (VAS) scores > 50/100, and pain refractory to 3 months of conservative therapies, including medications, physical therapy, or intra-articular injections. Embolization was performed using 100–300-µm, 4-week resorbable particles (OptiSphere; Medtronic). Sham patients crossed over to GAE at 1 month. All patients were followed to 12 months.

At 1 month, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and VAS scores showed statistically significant greater pain reduction in the GAE group. Crossover GAE-treated patients also reported VAS improvement compared to scores after index sham procedures, although not WOMAC. Overall, five of 21 (24%) patients did not improve in pain after GAE and required increased pain medication.

WHY THIS ARTICLE IS IMPORTANT

This is the first sham-controlled trial reporting clinical outcomes focusing on early pain relief after GAE for OA. A placebo effect has been identified in many OA therapies, including physiotherapy, medications, and intra-articular injections. The study is lauded for undertaking and overcoming the challenges of enrolling and completing a sham-controlled interventional procedure. By its nature, sample sizes would be expected to be small, and early crossover offered, to accommodate and encourage enrollees' participation. Thus, it was limited to detecting "early" 1-month signal of GAE effect over the control group, which it did. It is arguable that these limitations prevented detecting changes in WOMAC score. Notably, VAS score improvement did not occur in the control group, but WOMAC scores showed a mean 5-point reduction in the sham group. Regardless of these notable limitations, the study shows clear "signal" for early pain improvement in the GAE group, setting aside concerns about the often-discussed placebo effects in OA therapies.

Uterine Artery Embolisation Versus Myomectomy for Premenopausal Women With Uterine Fibroids Wishing to Avoid Hysterectomy: The FEMME RCT

Daniels J, Middleton LJ, Cheed V, et al. Health Technol Assess. 2022;26:1-74. doi: 10.3310/ZDEG6110

SUMMARY

This 74-page document provides all relevant information from the FEMME multicenter randomized trial comparing UAE with myomectomy, the 2-year published data (2020), the 4-year data (2021), and the cost-utility data (2021). The FEMME trial (2012-2015) included 105 myomectomy patients and 98 UAE patients (mean ages, 40 and 43 years, respectively). There was a small (8 points) but statistically significant difference in health-related quality-of-life scores between groups on a 100-point scale (using the validated health-related quality-of-life domain questionnaire of the Uterine Fibroid Symptom Quality of Life tool), favoring myomectomy at 2-year assessment. This difference dropped to 5 points and lost significance at 4 years.

Patients in the UAE group sustained more fibroid-related residual symptoms; there were more repeat interventions after UAE versus myomectomy (24% vs 13%), but this difference did not reach significance. Improvement in menorrhagia was similar, as were adverse events. There were no differences in postprocedural amenorrhea (14% vs 17% at 2 years and 27% vs 35% at 4 years) or in ovarian reserve by hormonal assessments. Hospital stay was shorter, and recovery was faster after UAE.

There were 15 pregnancies in the UAE group (15%) versus seven in the myomectomy group (6%), not reaching statistical significance. UAE was slightly more expensive and less cost-effective than myomectomy, but the differences were small and nonsignificant. The authors agreed that both UAE and myomectomy should be offered to women with fibroids, including those desiring future pregnancies, and that the level of evidence suggesting that myomectomy is associated with better fertility is very low and unsupported by this study.

WHY THIS ARTICLE IS IMPORTANT

This is a landmark study for women, as it presents the largest and most robust comparison between the two existing uterus-preserving techniques to treat symptomatic uterine fibroids. Almost half of patients had fibroids > 7 cm, and one-third of patients had more than three fibroids, with uterine volumes of approximately 1,200 mL. These represent "real-world" fibroid patients; most enrollees would not be suitable for other approaches such as thermal ablation and ultrasound- or MR-guided, high-intensity, focused ultrasound techniques. UAE and myomectomy proved similar regarding quality of life, safety profiles, ovarian function preservation, and preservation of future fertility. The nonsignificant trend for greater residual symptoms and interventions in UAE patients is arguably offset by its lower invasiveness and faster recovery. This trial lays to rest the ongoing argument that UAE induces more ovarian dysfunction than myomectomy. Thus, UAE is not relatively contraindicated in women wishing to conceive, which is perhaps this trial's most important message.

Concurrent Large Spontaneous Portosystemic Shunt Embolization for the Prevention of Overt Hepatic Encephalopathy After TIPS: A Randomized Controlled Trial

Lv Y, Chen H, Luo B, et al. Hepatology. 2022;76:676-688. doi: 10.1002/hep.32453

SUMMARY

This single-center 1:1 randomized trial compared TIPS alone versus TIPS plus SPSS embolization in patients for the prevention of variceal bleeding. Twenty-nine patients underwent TIPS versus 27 who underwent TIPS plus embolization of the large SPSS (TIPS+E). Follow-up was to 2 years or transplant or death. The primary outcome measure was the new onset of hepatic encephalopathy (HE) after the procedure; patients with

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preprocedural spontaneous recurrent HE were excluded. The SPSSs embolized included splenorenal, portocaval, mesorenal/caval, or gastroparaesophageal shunts or recanalized (para)umbilical veins. Large SPSS was defined as the sum of SPSS diameters being more than half the diameter of the main portal vein. TIPS with diameters of 8 mm were created with Fluency covered stents (BD Interventional), and embolization was performed with coils or Amplatzer vascular plugs (Abbott), adding approximately 30 minutes to procedural duration (1 vs 1.5 hours).

The probability of developing HE was significantly higher in the TIPS group (n = 15; 52%) compared to the TIPS+E group (n = 6; 22%; *P* = .045). HE was severe (grades 3 or 4) in five TIPS patients versus one TIPS+E patient. All TIPS+E HE patients were medically managed, whereas three TIPS HE patients required reinterventions due to refractory HE (one SPSS embolization, two SPSS embolization plus TIPS reduction). The 2-year incidence of recurrent bleeding, shunt dysfunction, death, and other adverse events was similar in both groups.

WHY THIS ARTICLE IS IMPORTANT

This study highlights two points. First, the incidence of HE after TIPS in patients with large SPSSs is notably higher (52%) than the overall reported rates after TIPS. Second, and perhaps unsurprisingly, concomitant shunt embolization minimizes HE incidence and severity by reducing the global degree of portosystemic diversion (and deprivation of nutrient portal flow).

These shunts proved relatively infrequent. In this study, 349 of 425 patients (82%) were excluded due to absent or small SPSS during the 3-year enrollment. Despite decades of shunt creation, the role of empiric embolization of large competitive shunts remains one of ongoing dialogue and debate. This study serves to emphasize the meaningful effect on subsequent HE in TIPS patients with such shunts and the rationale for their occlusion at shunt creation. ■

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