Decoding the complexity of benign prostatic hyperplasia therapies in the PARTEM trial

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We have read the paper titled "Prostatic Artery Embolization Versus Medical Treatment In Patients With Benign Prostatic Hyperplasia (PARTEM): A Randomized, Multicentre, Open-label, Phase 3, Superiority Trial"[1] with great interest.

The authors found superiority of prostatic artery embolization (PAE) over combination therapy (CT) with dutasteride and tamsulosin treating men with bothersome lower urinary tract symptoms (LUTS) resistant to alpha-blocker monotherapy, measured by validated questionnaires to assess LUTS, quality of life, and erectile function up to 2 years. We congratulate the authors on this well written paper and beautifully executed trial. We, however, have some concerns related to the interpretation of their results considering the study design and existing literature.

The study enrolled 90 patients over 42 months, averaging to enrolling little over 2 patients monthly across 10 French hospitals. Patients in the CT arm who had poor tolerance to CT were allowed to continue treatment with tamsulosin alone. At 9 months, 76.7% of patients were adherent to CT. Although non-adherence to medication is a complex problem with multifactorial causation, the 23.3% non-adherence rate at 9 months in the CT arm is quite high compared to 18% and 31% reported at 4 years in the MTOPS[2] and CombAT[3] studies, respectively. In our opinion, an insufficient control group that included patients unable to tolerate CT and those who were non-compliant would make it difficult to draw meaningful conclusions from a study, and represents a major design weakness.

The per-protocol analysis (Table S4 in the article)[1] done with 30 patients who were compliant with CT as well as modified intention-to-treat analysis both showed PAE is not better than CT reducing prostate size and PSA at 9 months. Despite that, the mean baseline-adjusted difference in IPSS and QOL between the two groups at 9 months was 4.2 and 1.7, respectively, favoring PAE. This subjective improvement in favor of PAE cannot be explained objectively, as non-invasive urodynamic parameters of Qmax and post-void residual urine were similar in both groups at 9 months. As rightly pointed out by the authors in their limitations, with no other scientific explanation for superior improvement in subjective parameters, detection bias appears as the most likely cause of this perceived difference.

In this study, of the 38 patients from the CT group who completed 2-years of follow-up, 18 (47.36%) needed invasive therapy at the end of 2 years. This incidence is alarmingly high compared with the long-term data from the MTOPS and CombAT studies. In the MTOPS study, 12 out of 786 patients in the CT arm needed invasive therapy at 4 years, at a rate of 0.4/100 patients-year.[2] In the CombAT study, only 38 (2.4%) out of 1610 patients needed a BPH surgical procedure.[3] Unfortunately, there is no data available regarding the indication for invasive therapy for the reader to understand this high need for surgical intervention in the CT group.

Regarding PAE, retreatment rate at 2 years in the 42 patients completing follow up was extremely high at 38.09%. This includes 11.9% (5 patients) needing surgical treatment and 26.1% necessitating medical management. This high retreatment rate coupled with a 4-fold higher 9-month treatment cost of PAE compared with CT raises doubts about cost-effectiveness of PAE in today's economically overburdened healthcare system. Additionally, a significant part of the procedure time is likely done under active fluoroscopy, with mean fluoroscopy time of 34.75 min (ranging 16.8–54.3 min), a non-negligible radiation dose to the pelvic area. With a reported overall mean dose area product of 181.6 Gy cm^2, ranging from 33.2 to 863.4 Gy cm^2 in the literature, this might be a relevant radiation exposure especially for younger men, and warrants discussion with patients before PAE.[4]

To summarize, this study reveals PAE is not better than CT in reducing prostate size, PSA and post-void residual urine or improving Qmax at 9 months. Despite similar objective effects, subjective parameters of IPSS and QOL show statistically significant improvement of 4.2 and 1.7, respectively, favoring PAE, probably due to detection bias. This comes at a cost of 30.09% retreatment rate, a 4-fold higher expense, and a non-negligible radiation exposure. The trial failed to show stability of PAE results over a medium follow-up period of 2 years.

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In our humble opinion, these two treatment modalities have inherently different indications and target populations as summarized in the main practice guidelines (AUA and EAU),[5,6] challenging the conceptual validity of a comparison between them. We would advise caution to readers when interpreting the findings showcasing superiority of outcomes of PAE over CT.

Contributors

Diana M Lopategui MD led the original draft writing and literature review. Ansh Bhatia MD assisted in the review and editing of the manuscript and the conceptualization of the project. Joao G Porto MD assisted in the data curation and writing of the original draft. Robert Marcovich MD assisted in the project supervision and the review and editing of the manuscript. Hemendra N Shah MD led the project conceptualization, project supervision and review and editing of the manuscript.

Declaration of interests

The authors have no financial or personal conflicts of interests to declare.

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