Editorial

Prostatic artery occlusion: a new strategy to improve clinical outcomes of prostatic artery embolization?

Julien Frandon[1]^, Julien Ghelfi[2], Stephane Droupy[3], Jean-Paul Beregi[1]

[1]Department of Medical Imaging, Nîmes University Hospital, University of Montpellier, Medical Imaging Group Nîmes, IMAGINE, Nîmes, France; [2]Department of Diagnostic and Interventional Imaging, CHU Grenoble Alpes, Université Grenoble Alpes, La Tronche, France; [3]Department of Urology, Nîmes University Hospital, University of Montpellier, Nîmes, France

Correspondence to: Julien Frandon. Department of Medical Imaging, Nîmes University Hospital, University of Montpellier, Medical Imaging Group Nîmes, IMAGINE, 30029 Nîmes, France. Email: jfrandon38@gmail.com.

Comment on: Lucas-Cava V, Sánchez-Margallo FM, Moreno-Lobato B, *et al.* Prostatic artery occlusion: initial findings on pathophysiological response in a canine prostate model. Transl Androl Urol 2022;11:1655-66.

Keywords: Prostate artery embolization; ischemia; occlusion

Submitted Dec 31, 2022. Accepted for publication Feb 01, 2023. Published online Feb 13, 2023.
doi: 10.21037/tau-22-878
View this article at: https://dx.doi.org/10.21037/tau-22-878

Prostatic artery embolization (PAE) is an interventional radiology treatment for lower urinary tract symptoms related to benign prostatic hyperplasia. Initially described in the 1970s for the treatment of bleeding after prostatic surgical resection (1), PAE was first reported in the treatment of prostatic hyperplasia in animals in 2008 (2), then in men in 2010 (3). Since then, the technique has developed exponentially and is now recognized as an alternative treatment for lower urinary tract symptoms with very few side effects (4,5).

The technique consists in selective catheterization of the prostatic arteries under imaging control (Digial substraction angiography, Cone Beam-CT, angio-CT) and gentle injection of calibrated microparticles, generally between 300 and 500 microns according to the recognized standards of practice (6). One hypothesis is that the ischemia induced leads to a softening and decrease of the prostate size, thus reducing its obstructive effect on the lower urinary tract. A recent multicenter study showed a clinical efficacy of around 80%, independent of the center, of the initial prostate volume and of technical parameters (7). The mechanisms of action of embolization, allowing a better selection of patients, are not yet elucidated.

Lucas-Cava *et al.* studied the effects of PAE on a canine model (8). They described a new technique of embolization with a complete occlusion of the prostatic arteries by a liquid agent, ethylene-vinyl alcohol copolymer or Onyx®, an agent originally used for the embolization of vascular malformations (9). They proposed to study the mechanisms of action at the angiographic, histological and hormonal levels.

Their hypothesis is that with Onyx®, the prostatic arteries will be completely occluded, hence the choice of the term "occlusion of the prostatic arteries", unlike with particles which leave the proximal carrier artery permeable. They expect with this agent a greater ischemic effect thus avoiding repermeabilization of the arteries in the long-term. This hypothesis matches with report in clinical practice of repermeabilization of the prostatic arteries as one of the causes of non-efficiency or recurrence of symptoms, then inducing further increase in the prostate size (10,11). To study this point, other teams have assessed embolization with another liquid agent, N-Butyl Cyanoacrylate Glue, and showed the same clinical efficacy as with microparticles, with no more complications and shorter duration of embolizations, therefore less X-rays exposition (12). However, Lucas-Cava *et al.* showed on angiographic controls at 6 months that, despite an initial complete occlusion by the liquid agent, either the prostatic arteries

^ ORCID: 0000-0001-7816-8178.

had repermeabilized or the prostate had recruited other arteries, highlighting the limits of this new technique (8). In addition, studies on repeated embolizations of prostatic arteries showed much lower efficacy, suggesting another unresolved mechanism at stake in the treatment of prostates possibly resistant to ischemia (10,11).

Histological analysis showed major necrosis with an impressive reduction of the prostate size. Animal studies using particles loaded with chemotherapy (13) or a radioactive agent (14) have also shown significant necrosis of the prostate in other canine models. Although massive necrosis is interesting, these histological results raise questions about the safety of embolization performed with Onyx®. Indeed, these studies found severe oedema during the first week after embolization, which could temporarily aggravate urinary symptoms, and associated necrosis in the bladder and rectum at 2 weeks. These results should be considered in the light of the fact that no protective measures for the collateral vascularization were taken. It was shown in clinical studies that protective embolization of these large anastomoses with non-target territories such as the rectum, bladder or penis allowed these complications to be avoided (15). It is important that the choice of the embolization agent allows PAE to remain a technique with very few side effects as it addresses a functional pathology for which many therapeutic alternatives are available (16).

The temporal analysis of induced necrosis showed an early ischemic necrosis during the first two weeks with very little apoptotic effect at long-term. These results are encouraging because they are in favor of an acute effect, reversible in the long-term and which should therefore not hinder future therapies. PAE could then be associated with other therapies without interfering on their mechanisms of action. For example, PAE has been described before permanent interstitial brachytherapy for patients with a large prostate, reporting the same oncological efficacy and fewer side effects (17).

Finally, by completely occluding the prostatic arteries, Lucas-Cava *et al.* hoped to limit the inflow of testosterone into the prostatic bloodstream and thus have an additional anti-hormonal effect (8). The authors studied the effects of embolization on the blood concentration of canine testosterone and dihydrotestosterone. They showed a decrease in dihydrotestosterone after embolization with an unexpected increase in plasmatic testosterone concentration. The decrease in dihydrotestosterone was small and a small long-term apoptotic effect, expected with the anti-hormonal effect, was reported at 6 months. Other teams have based their approach mainly on this hypothesis of hormonal deprivation by developing venous embolization of the spermatic vein with results equivalent to PAE on lower urinary tract symptoms (18). Indeed, with embolization of the spermatic vein, they avoided stagnation of testosterone in the prostatic veins because the prostatic outflow is pushed to divert the spermatic venous return. Prostatic testosterone purification is then increased, thereby decreasing dihydrotestosterone production. There seems to be a definite but yet unknown hormonal mechanism.

To conclude, Lucas-Cava *et al.* proposed a very interesting study which, thanks to a promising canine model, allows a better understanding of the mechanisms of prostate embolization. They also raised new interesting questions, notably with regards to complex vascular and hormonal mechanisms.

Acknowledgments

The authors thank Hélène de Forges, PhD, for substantive editing of this editorial.
Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the editorial office, *Translational Andrology and Urology*. The article did not undergo external peer review.

Conflicts of Interest: The authors have completed the ICMJE uniform disclosure form (available at https://tau.amegroups.com/article/view/10.21037/tau-22-878/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

1. Wolf KJ, Hippéli R, Haumer M. Therapeutic embolization of severe hemorrhages from the prostatic bed after transurethral prostatic resection. Rofo 1979;130:366-8.
2. Sun F, Sánchez FM, Crisóstomo V, et al. Benign prostatic hyperplasia: transcatheter arterial embolization as potential treatment--preliminary study in pigs. Radiology 2008;246:783-9.
3. Carnevale FC, Antunes AA, da Motta Leal Filho JM, et al. Prostatic artery embolization as a primary treatment for benign prostatic hyperplasia: preliminary results in two patients. Cardiovasc Intervent Radiol 2010;33:355-61.
4. Ray AF, Powell J, Speakman MJ, et al. Efficacy and safety of prostate artery embolization for benign prostatic hyperplasia: an observational study and propensity-matched comparison with transurethral resection of the prostate (the UK-ROPE study). BJU Int 2018;122:270-82.
5. McWilliams JP, Bilhim TA, Carnevale FC, et al. Society of Interventional Radiology Multisociety Consensus Position Statement on Prostatic Artery Embolization for Treatment of Lower Urinary Tract Symptoms Attributed to Benign Prostatic Hyperplasia: From the Society of Interventional Radiology, the Cardiovascular and Interventional Radiological Society of Europe, Société Française de Radiologie, and the British Society of Interventional Radiology: Endorsed by the Asia Pacific Society of Cardiovascular and Interventional Radiology, Canadian Association for Interventional Radiology, Chinese College of Interventionalists, Interventional Radiology Society of Australasia, Japanese Society of Interventional Radiology, and Korean Society of Interventional Radiology. J Vasc Interv Radiol 2019;30:627-637.e1.
6. Cornelis FH, Bilhim T, Hacking N, et al. CIRSE Standards of Practice on Prostatic Artery Embolisation. Cardiovasc Intervent Radiol 2020;43:176-85.
7. Frandon J, Belaouni A, Pellerin O, et al. Efficacy and safety of prostate artery embolization for patients with lower urinary tract symptoms and indwelling urinary catheter: A retrospective multicenter study. Diagn Interv Imaging 2022;103:601-6.
8. Lucas-Cava V, Sánchez-Margallo FM, Moreno-Lobato B, et al. Prostatic artery occlusion: initial findings on pathophysiological response in a canine prostate model. Transl Androl Urol 2022;11:1655-66.
9. Molyneux AJ, Coley SC. Embolization of spinal cord arteriovenous malformations with an ethylene vinyl alcohol copolymer dissolved in dimethyl sulfoxide (Onyx liquid embolic system). Report of two cases. J Neurosurg 2000;93:304-8.
10. de Assis AM, Moreira AM, Carnevale FC. Angiographic Findings during Repeat Prostatic Artery Embolization. J Vasc Interv Radiol 2019;30:645-51.
11. Kenny AG, Pellerin O, Moussa N, et al. Repeat Prostatic Artery Embolization. J Vasc Interv Radiol 2020;31:1090-1095.e1.
12. Loffroy R, Guillen K, Salet E, et al. Prostate Artery Embolization Using N-Butyl Cyanoacrylate Glue for Urinary Tract Symptoms Due to Benign Prostatic Hyperplasia: A Valid Alternative to Microparticles? J Clin Med 2021;10:3161.
13. Pellerin O, Déan C, Reb P, et al. Prostate artery chemoembolization in prostate cancer: A proof of concept study in spontaneous prostate cancer in a canine model. Diagn Interv Imaging 2021;102:709-15.
14. Mouli SK, Raiter S, Harris K, et al. Yttrium-90 Radioembolization to the Prostate Gland: Proof of Concept in a Canine Model and Clinical Translation. J Vasc Interv Radiol 2021;32:1103-1112.e12.
15. Amouyal G, Chague P, Pellerin O, et al. Safety and Efficacy of Occlusion of Large Extra-Prostatic Anastomoses During Prostatic Artery Embolization for Symptomatic BPH. Cardiovasc Intervent Radiol 2016;39:1245-55.
16. Lebdai S, Chevrot A, Doizi S, et al. Do patients have to choose between ejaculation and miction? A systematic review about ejaculation preservation technics for benign prostatic obstruction surgical treatment. World J Urol 2019;37:299-308.
17. Haddad H, Hermani H, Bischoff P, et al. Permanent interstitial brachytherapy for prostate cancer implementing neoadjuvant prostatic artery embolization. Brachytherapy 2022;21:308-16.
18. Strunk H, Meier M, Schild HH, et al. Treatment of benign prostatic hyperplasia by occlusion of the impaired urogenital venous system - first experience. Rofo 2015;187:180-6.

Cite this article as: Frandon J, Ghelfi J, Droupy S, Beregi JP. Prostatic artery occlusion: a new strategy to improve clinical outcomes of prostatic artery embolization? Transl Androl Urol 2023;12(2):152-154. doi: 10.21037/tau-22-878

