POLITECNICO DI TORINO
Repository ISTITUZIONALE

Shockwaves delivery for aortic valve therapy—Realistic perspective for clinical translation?

Original
Shockwaves delivery for aortic valve therapy—Realistic perspective for clinical translation? / Curini, L., Pesce, M.. - In: FRONTIERS IN CARDIOVASCULAR MEDICINE. - ISSN 2297-055X. - 10:(2023). [10.3389/fcvm.2023.1160833]

Availability:
This version is available at: 11583/2999779 since: 2025-05-02T13:49:30Z

Publisher:
Frontiers Media

Published
DOI:10.3389/fcvm.2023.1160833

Terms of use:

This article is made available under terms and conditions as specified in the corresponding bibliographic description in the repository

Publisher copyright

(Article begins on next page)

25 November 2026

frontiers | Frontiers in Cardiovascular Medicine

TYPE Mini Review
PUBLISHED 11 April 2023
DOI 10.3389/fcvm.2023.1160833

Check for updates

OPEN ACCESS

EDITED BY
Peter Zilla,
University of Cape Town, South Africa

REVIEWED BY
Johannes Holfeld,
Innsbruck Medical University, Austria

*CORRESPONDENCE
Maurizio Pesce
maurizio.pesce@ccfm.it

SPECIALTY SECTION
This article was submitted to Heart Valve Disease, a section of the journal Frontiers in Cardiovascular Medicine

RECEIVED 07 February 2023
ACCEPTED 23 March 2023
PUBLISHED 11 April 2023

CITATION
Curini L and Pesce M (2023) Shockwaves delivery for aortic valve therapy—Realistic perspective for clinical translation? Front. Cardiovasc. Med. 10:1160833. doi: 10.3389/fcvm.2023.1160833

COPYRIGHT
© 2023 Curini and Pesce. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.

Shockwaves delivery for aortic valve therapy—Realistic perspective for clinical translation?

Lavinia Curini and Maurizio Pesce*

Unità di Ricerca in Ingegneria Tissutale Cardiovascolare, Centro Cardiologico Monzino, IRCCS, Milan, Italy

Calcific aortic valve disease (CAVD) is the most frequent valvular heart disorder, and the one with the highest impact and burden in the elderly population. While the quality and standardization of the current aortic valve replacements has reached unprecedented levels with the commercialization of minimally-invasive implants and the design of procedures for valve repair, the need of supplementary therapies able to block or retard the course of the pathology before patients need the intervention is still awaited. In this contribution, we will discuss the emerging opportunity to set up devices to mechanically rupture the calcium deposits accumulating in the aortic valve and restore, at least in part, the pliability and the mechanical function of the calcified leaflets. Starting from the evidences gained by mechanical decalcification of coronary arteries in interventional cardiology procedures, a practice already in the clinical setting, we will discuss the advantages and the potential drawbacks of valve lithotripsy devices and their potential applicability in the clinical scenario.

KEYWORDS

calcific aortic valve disease, ultrasound, lithotripsy, decalcification, medical device

1. The role of cells-depositing calcium in CAVD

Calcific aortic valve disease (CAVD) is the most frequent heart valve disorder in the aging population, associated with increased morbidity and mortality (1). The underlying process of CAVD is typically illustrated by a complex and multifaceted course, characterized by endothelial dysfunction, inflammation, increased oxidative stress, sub-endothelial lipid accumulation, valve fibrosis and, ultimately, calcification of valve leaflets (2). The clinical evolution of the valve pathology starts with aortic sclerosis, characterized by mild valve thickening; it evolves into symptomatic aortic stenosis (AS), characterized by obstruction of blood flow, severe calcification preventing leaflet movement, and heart failure (3, 4). This process occurs in a typically biphasic fashion. The sclerotic phase is slow with mild or no symptoms, followed by severe calcification with dyspnea, angina and myocardial decompensation (5).

Mechanistically, the deposition of calcific nodules in the aortic valve generally begins in the fibrosa, a layer that is predominantly abundant of type I and III collagen forming anisotropically-deposited thick fibers necessary to absorb the load generated by the blood filling the aorta during the valve closure at diastole (6). This establishes a relationship between the non-uniform distribution of strain forces on the leaflets and the pathologic programming of valve-resident cells.

Calcific lesions are mainly produced from valve-resident cells, whose the most important type are the so-called valve interstitial cells (VICs) (7). These cells are normally deputed to the renewal of the extracellular matrix, but under specific pathophysiologic conditions, they can differentiate into myofibroblasts (8) and finally into calcium depositing cells (9), under

the control of genes (e.g., Bmp2, Runx2), at least in part, in common with the canonical osteogenic pathway. Despite the similarity with the bone calcification process, valve and vessel-specific mineralized tissues show a different organization. Indeed, in an interesting work, Bertazzo and colleagues, using nano-analytical electron microscopy techniques, detected spherical calcium phosphate particles, made of highly crystalline hydroxyapatite and structurally different from mineralized bone (10). They showed that, unlike tissue presenting calcific lesions that clearly express bone-specific factors, the deposition of spherical microparticles in the extracellular matrix precedes the accumulation of the large calcific nodules present in the pathologic valves (10). Interestingly, the same Authors showed that deposition of these particles was more abundant in the fibrosa layer in positions subjected to the maximal mechanical stress (11). These evidences, together with experiments *in vitro* showing that secretion of calcified particles by VICs is subjected to mechanical control (12), and that these cells are sensitive to mechanical cues (13), confirm the primary relevance of valve mechanics for pathologic evolution, and suggest that removing the calcium deposits by a debridement technique, could be a viable strategy to recover a normal phenotype in valve resident cells, other than restoring the mechanical function of the valve.

Other cell types that contribute to calcific evolution of the aortic valves are the endothelial cells that cover the leaflet surface, the so-called valve endothelial cells (VECs), which similarly to the VICs can participate in the calcification of the valve by differentiating into mesenchymal cells through endothelial-mesenchymal transition (14). Several conditions such as altered shear stress, inflammation and modifications in the extracellular matrix (15–17) can favor VECs differentiation into myofibroblasts and, subsequently into calcium-depositing cells.

A last relevant cell type participating in valve calcification has been recently highlighted by the finding that somatic blood cell-derived clones bearing somatic mutations in *DNMT3A* or *TET2* loci predominate in the peripheral blood of patients with an increased mortality rate following TAVI implantation. This expansion, named "clonal hematopoiesis of indeterminate potential" (CHIP) is supposed to create a proinflammatory environment characterized by increased pro-inflammatory leukocyte subsets and a pro-inflammatory T-cell polarization likely favoring rapid progression of aortic stenosis and its complications (18–20).

2. Use of shockwaves in treatment of cardiovascular diseases

2.1. Intravascular lithotripsy

The term lithotripsy refers originally to a technique that employs sonic pressure waves—or shockwaves—to disintegrate and remove hard deposits such as renal and ureteral calculi or gallstones, whose remnants are later washed out by urinary or biliary secretion (21–23). Shockwaves are in use also in cardiovascular therapy. However, opposite to the original destination of use, the effect of the mechanical treatment is not that of removing the calcium from the tissues, but to reduce the size of the deposits with the aim at facilitating interventional cardiology procedures in heavily calcified coronary arteries (24–31), or to create easier vascular access for minimally-invasive procedures in case of calcifications in the iliac arteries (32–34). Given that the final aim of the treatment is to restore the softness of the tissue, in these applications, the calcium deposits remain *in situ* and are not expected to be washed-out by the blood giving rise to thromboembolic events. The delivery of shockwaves to the vessels is named "intravascular lithotripsy" (IVL). It is performed exploiting the minimally-invasive procedure and setup available in the interventional cardiology room contextually with the revascularization (35). Technically, the shockwaves are generated by piezoelectric lithotripters inserted into balloon catheters connected to a generator producing adjustable doses and intensities to optimize the treatment of the arteries for each specific patient (25). The sonic waves are transmitted from the balloon-based catheter to the vascular wall by physical contact to reach the media of the vessels, where they break more superficial or deeper calcium deposits, allowing optimal artery expansion and stent implantation. In the clinical practice, IVL has been successfully employed in balloon angioplasty and plaque ablation and as an adjuvant to prevent post-procedure complications, such as accelerated restenosis, damage of the arterial wall, or catheter overstretching and rupture (36–39). In a trial by Tepe et al., the authors tested the efficiency of IVL on percutaneous transluminal angioplasty (PTA) in two cohorts of patients with femoropopliteal artery calcification (40). Data reported a greater success in the patient group who received IVL before PTA compared to the PTA-only group, thus confirming IVL as an effective vessel preparation method facilitating endovascular treatment (40). In another trial, Hill and colleagues showed the safety and effectiveness of IVL to allow stent implantation in 431 patients with calcified coronary lesions (30). The percentage of procedural success was 92.4%, with no adverse events (e.g., myocardial infarction, cardiac death). The IVL safety was also evaluated in stents under-expansion and in-stent restenosis in 60 patients who underwent percutaneous coronary intervention with intravascular lithotripsy system for severe calcified lesions (41). This analysis showed that the IVL balloon easily reached the lesion, and the application of the treatment was feasible in 92.3% of cases, with high angiographic success and no differences in complications or major cardiac adverse events at 30-days, confirming IVL as a safe strategy to adjuvate stent expansion (41, 42).

2.2. Shockwave treatment in minimally-invasive aortic valve replacement

Similarly to the use in coronary revascularization, setups for IVL have been successfully employed to facilitate the intravascular access to the aortic valve for easier insertion of large-dimension sheaths in TAVI procedures (43–46).

Shockwaves are delivered by a piezoelectric device to the iliac artery or the aortic wall to break up the calcifications hardening the tissue, allowing the insertion of the catheters for TAVI implantation and reducing the risks of arterial wall damage to optimize TAVI deployment (46). For example, in two studies in patients aged 75–89 years with AS and presenting more than one lesion that required pre-procedural intervention, IVL simplified the femoral access and TAVI implantation (47, 48). Another use of lithotripsy for facilitating valve replacement was described by Sharma and colleagues, who performed transcatheter aortic valve lithotripsy directly in the valve before TAVI implantation to decrease the risk of paravalvular aortic regurgitation and annular rupture. The results showed that the procedure did not affect the motion of the leaflets in the prosthetic valve and favored the expansion of the TAVI stent (49). Similarly, a post TAVI dilatation lithotripsy was performed in a patient carrying a previously implanted TAVI to allow a new expansion of the TAVI stent in order to reduce the risk of stroke or annular rupture (50). Results showed an effectively post-dilated valve and a more symmetric expansion of the supporting stent.

2.3. Shockwaves delivery for direct calcium disruption in human calcified leaflets

A new application of shockwaves delivery, as an adjuvant or even a stand-alone treatment, for aortic valve disease concerns the disintegration of the calcific deposits reducing the pliability and the motion of the leaflets in terminally calcified stenotic valves. This interesting possibility was prospected in a report from our group (51), in which we described the feasibility of treating aortic valve leaflets using an *ad-hoc* device that was specifically designed to deliver shockwaves in a very localized and concentrated fashion, by direct physical contact with the leaflet of a tricuspid valve. Conceived to be part of an all-in one "trans-catheter debridement device" (TDD), to treat the valves with low-intensity ultrasound shockwaves with alternate 100 kHz/3 MHz pulses with a minimally-invasive trans-catheter approach, we showed the efficiency of the emitted waves in reducing the dimensions of the calcific nodules in pathologic human leaflets *ex vivo*, and the safety of the shockwaves administration to the aortic valves in living pigs (51). The absence of major histologically detectable damages witnessed that for their extreme focalization to penetrate the large calcium deposits from the aortic leaflets, the shockwaves did not cause large ruptures maintaining the integrity of the tissue (51, 52). For the whole duration of the procedure, the animals remained with one of the valve leaflets immobilized by the piezoelectric transducer, even if the motion of the other leaflets during the procedure, as well as of the treated leaflet after the procedure were not compromised, suggesting an overall clinical feasibility of the procedure. The biological safety of the procedure was finally confirmed in another report in which the same device was employed to treat an *in vitro* reconstituted valve tissue, where no major ruptures and no changes in cell viability were observed (53). At the moment, it is not known whether the delivery of shockwaves to the leaflets results into an induction of inflammation and/or cellular apoptosis (54) and the permanence of smaller deposits resulting from the fragmentation of the large calcific nodules causes long-term effects on mechanical performance of the valve. Another important aspect of this potentially new treatment will probably be the necessity to employ, concomitantly to shockwaves delivery, embolic protection devices able to filter out from the blood the debris deriving from the calcium deposits fragmentation. In this respect, several types of these devices have been designed to capture debris that embolizes distally during vascular surgeries in specific vascular districts particularly critical such as, for example, carotid stenting (55).

3. Conclusion

The growing interest for minimally-invasive procedures to reduce the extent of calcification in vessels and valves, and to increase the efficiency of vessel reperfusion and valve substitution, is prompting the design of a new class of devices that will be employed in the future to minimize the clinical consequences of cardiovascular aging. Prompted by pioneering studies on isolated cases or small trials, delivery of shockwaves is progressing in preclinical testing in preparation for possible large human translation. Before the release of a regulatory-compliant procedure to debride the large calcific nodules present in the natural valves, or even in implanted biological valves, this technology should be validated for safety in terms of long-term biological effects and should be designed according to quality criteria. In addition, the risks should be minimized, for example, by combining the new shockwaves delivery system with distal protection devices able to collect eventual debris originating from the calcium disintegration activity.

Author contributions

LC and MP concieved the manuscript and wrote the paper. All authors contributed to the article and approved the submitted version.

Funding

LC and MP are supported by funds of the Italian Ministry of Health (Ricerca Corrente and 5 per mille).

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

References

1. Alushi B, Curini L, Christopher MR, Grubitzch H, Landmesser U, Amedei A, et al. Calcific aortic valve disease-natural history and future therapeutic strategies. *Front Pharmacol.* (2020) 11:685. doi: 10.3389/fphar.2020.00685

2. Kraler S, Blaser MC, Aikawa E, Camici GG, Luscher TF. Calcific aortic valve disease: from molecular and cellular mechanisms to medical therapy. *Eur Heart J.* (2022) 43:683–97. doi: 10.1093/eurheartj/ehab757

3. Lindman BR, Clavel M-A, Mathieu P, Iung B, Lancellotti P, Otto CM, et al. Calcific aortic stenosis. *Nat Rev Dis Primers.* (2016) 2:16006. doi: 10.1038/nrdp.2016.6

4. Cho J, Lee H, Rah W, Chang HJ, Yoon YS. From engineered heart tissue to cardiac organoid. *Theranostics.* (2022) 12:2758–72. doi: 10.7150/thno.67661

5. Lindman BR, Bonow RO, Otto CM. Current management of calcific aortic stenosis. *Circ Res.* (2013) 113:223–37. doi: 10.1161/CIRCRESAHA.111.300084

6. Balguid A, Driessen NJ, Mol A, Schmitz JP, Verheyen F, Bouten CV, et al. Stress related collagen ultrastructure in human aortic valves–implications for tissue engineering. *J Biomech.* (2008) 41:2612–7. doi: 10.1016/j.jbiomech.2008.06.031

7. Taylor PM, Batten P, Brand NJ, Thomas PS, Yacoub MH. The cardiac valve interstitial cell. *Int J Biochem Cell Biol.* (2003) 35:113–8. doi: 10.1016/S1357-2725(02)00100-0

8. Schroer AK, Merryman WD. Mechanobiology of myofibroblast adhesion in fibrotic cardiac disease. *J Cell Sci.* (2015) 128:1865–75. doi: 10.1242/jcs.162891

9. Liu AC, Joag VR, Gotlieb AI. The emerging role of valve interstitial cell phenotypes in regulating heart valve pathobiology. *Am J Pathol.* (2007) 171:1407–18. doi: 10.2353/ajpath.2007.070251

10. Bertazzo S, Gentleman E, Cloyd KL, Chester AH, Yacoub MH, Stevens MM. Nano-analytical electron microscopy reveals fundamental insights into human cardiovascular tissue calcification. *Nat Mater.* (2013) 12:576–83. doi: 10.1038/nmat3627

11. Yabusaki K, Hutcheson JD, Vyas P, Bertazzo S, Body SC, Aikawa M, et al. Quantification of calcified particles in human valve tissue reveals asymmetry of calcific aortic valve disease development. *Front Cardiovasc Med.* (2016) 3:44. doi: 10.3389/fcvm.2016.00044

12. Bouchareb R, Boulanger MC, Fournier D, Pibarot P, Messaddeq Y, Mathieu P. Mechanical strain induces the production of spheroid mineralized microparticles in the aortic valve through a RhoA/ROCK-dependent mechanism. *J Mol Cell Cardiol.* (2014) 67:49–59. doi: 10.1016/j.yjmcc.2013.12.009

13. Santoro R, Scaini D, Severino LU, Amadeo F, Ferrari S, Bernava G, et al. Activation of human aortic valve interstitial cells by local stiffness involves YAP-dependent transcriptional signaling. *Biomaterials.* (2018) 181:268–79. doi: 10.1016/j.biomaterials.2018.07.033

14. Xu K, Xie S, Huang Y, Zhou T, Liu M, Zhu P, et al. Cell-type transcriptome atlas of human aortic valves reveal cell heterogeneity and endothelial to mesenchymal transition involved in calcific aortic valve disease. *Arterioscler Thromb Vasc Biol.* (2020) 40:2910–21. doi: 10.1161/ATVBAHA.120.314789

15. Dahal S, Huang P, Murray BT, Mahler GJ. Endothelial to mesenchymal transformation is induced by altered extracellular matrix in aortic valve endothelial cells. *J Biomed Mater Res A.* (2017) 105:2729–41. doi: 10.1002/jbm.a.36133

16. Zhong A, Mirzaei Z, Simmons CA. The roles of matrix stiffness and ß-catenin signaling in endothelial-to-mesenchymal transition of aortic valve endothelial cells. *Cardiovasc Eng Technol.* (2018) 9:158–67. doi: 10.1007/s13239-018-0363-0

17. Deng G, Zhang L, Wang C, Wang S, Xu J, Dong J, et al. AGEs-RAGE axis causes endothelial-to-mesenchymal transition in early calcific aortic valve disease via TGF-β1 and BMPR2 signaling. *Exp Gerontol.* (2020) 141:111088. doi: 10.1016/j.exger.2020.111088

18. Abplanalp WT, Mas-Peiro S, Cremer S, John D, Dimmeler S, Zeiher AM. Association of clonal hematopoiesis of indeterminate potential with inflammatory gene expression in patients with severe degenerative aortic valve stenosis or chronic postischemic heart failure. *JAMA Cardiol.* (2020) 5:1170–5. doi: 10.1001/jamacardio.2020.2468

19. Mas-Peiro S, Hoffmann J, Fichtlscherer S, Dorsheimer L, Rieger MA, Dimmeler S, et al. Clonal haematopoiesis in patients with degenerative aortic valve stenosis undergoing transcatheter aortic valve implantation. *Eur Heart J.* (2020) 41:933–9. doi: 10.1093/eurheartj/ehz591

20. Vieceli Dalla Sega F, Palumbo D, Fortini F, D'agostino Y, Cimaglia P, Marracino L, et al. Transcriptomic profiling of calcified aortic valves in clonal hematopoiesis of indeterminate potential carriers. *Sci Rep.* (2022) 12:20400. doi: 10.1038/s41598-022-24130-8

21. Chaussy C, Schmiedt E, Jocham D, Brendel W, Forssmann B, Walther V. First clinical experience with extracorporeally induced destruction of kidney stones by shock waves. *J Urol.* (1982) 127:417–20. doi: 10.1016/S0022-5347(17)53841-0

22. Powers CJ, Tinterow MM, Burpee JF. Extracorporeal shock wave lithotripsy: a study of renal stone differences. *Kans Med.* (1989) 90:19–22. PMID: 2709649

23. Nahrwold DL. Gallstone lithotripsy. *Am J Surg.* (1993) 165:431–4. doi: 10.1016/S0002-9610(05)80935-3

24. Cleveland RO, Sapozhnikov OA. Modeling elastic wave propagation in kidney stones with application to shock wave lithotripsy. *J Acoust Soc Am.* (2005) 118:2667–76. doi: 10.1121/1.2032187

25. Ali ZA, Brinton TJ, Hill JM, Maehara A, Matsumura M, Karimi Galougahi K, et al. Optical coherence tomography characterization of coronary lithoplasty for treatment of calcified lesions: first description. *JACC Cardiovasc Imaging.* (2017) 10:897–906. doi: 10.1016/j.jcmg.2017.05.012

26. Ali ZA, Nef H, Escaned J, Werner N, Banning AP, Hill JM, et al. Safety and effectiveness of coronary intravascular lithotripsy for treatment of severely calcified coronary stenoses: the disrupt CAD II study. *Circ Cardiovasc Interv.* (2019) 12:e008434. doi: 10.1161/CIRCINTERVENTIONS.119.008434

27. Brinton TJ, Ali ZA, Hill JM, Meredith IT, Maehara A, Illindala U, et al. Feasibility of shockwave coronary intravascular lithotripsy for the treatment of calcified coronary stenoses. *Circulation.* (2019) 139:834–6. doi: 10.1161/CIRCULATIONAHA.118.036531

28. Dini CS, Tomberli B, Mattesini A, Ristalli F, Valente S, Stolcova M, et al. Intravascular lithotripsy for calcific coronary and peripheral artery stenoses. *EuroIntervention.* (2019) 15:714–21. doi: 10.4244/EIJ-D-18-01056

29. Sorini Dini C, Nardi G, Ristalli F, Mattesini A, Hamiti B, Di Mario C. Contemporary approach to heavily calcified coronary lesions. *Interv Cardiol.* (2019) 14:154–63. doi: 10.15420/icr.2019.19.R1

30. Hill JM, Kereiakes DJ, Shlofmitz RA, Klein AJ, Riley RF, Price MJ, et al. Intravascular lithotripsy for treatment of severely calcified coronary artery disease. *J Am Coll Cardiol.* (2020) 76:2635–46. doi: 10.1016/j.jacc.2020.09.603

31. Laricchia A, Colombo A. New interventional solutions in calcific coronary atherosclerosis: drill, laser, shock waves. *Eur Heart J Suppl.* (2020) 22:L49–52. doi: 10.1093/eurheartj/suaa134

32. Di Mario C, Chiriatti N, Stolcova M, Meucci F, Squillantini G. Lithotripsy-assisted transfemoral aortic valve implantation. *Eur Heart J.* (2018) 39:2655. doi: 10.1093/eurheartj/ehy021

33. Di Mario C, Goodwin M, Ristalli F, Ravani M, Meucci F, Stolcova M, et al. A prospective registry of intravascular lithotripsy-enabled vascular access for transfemoral transcatheter aortic valve replacement. *JACC Cardiovasc Interv.* (2019) 12:502–4. doi: 10.1016/j.jcin.2019.01.211

34. Armstrong EJ, Soukas PA, Shammas N, Chamberlain J, Pop A, Adams G, et al. Intravascular lithotripsy for treatment of calcified, stenotic iliac arteries: a cohort analysis from the disrupt PAD III study. *Cardiovasc Revasc Med.* (2020) 21:1262–8. doi: 10.1016/j.carrev.2020.02.026

35. Kereiakes DJ, Virmani R, Hokama JY, Illindala U, Mena-Hurtado C, Holden A, et al. Principles of intravascular lithotripsy for calcific plaque modification. *JACC Cardiovasc Interv.* (2021) 14:1275–92. doi: 10.1016/j.jcin.2021.03.036

36. Neville RF, Sidawy AN. Myointimal hyperplasia: basic science and clinical considerations. *Semin Vasc Surg.* (1998) 11:142–8.

37. Rigatelli G, Dell'avvocata F, Giordan M, Cardaioli P. Air embolism caused by balloon rupture resolved by manual thrombectomy catheter aspiration. *Cardiovasc Revasc Med.* (2011) 12:129–30. doi: 10.1016/j.carrev.2010.06.007

38. Stanek F. Laser angioplasty of peripheral arteries: basic principles, current clinical studies, and future directions. *Diagn Interv Radiol.* (2019) 25:392–7. doi: 10.5152/dir.2019.18515

39. Sofidis G, Kartas A, Karagiannidis E, Stalikas N, Sianos G. A case of balloon rupture during coronary angioplasty: slow flow requiring swift action. *Cureus.* (2020). doi: 10.7759/cureus.9335

40. Tepe G, Brodmann M, Werner M, Bachinsky W, Holden A, Zeller T, et al. Intravascular lithotripsy for peripheral artery calcification: 30-day outcomes from

the randomized disrupt PAD III trial. *JACC Cardiovasc Interv*. (2021) 14:1352–61. doi: 10.1016/j.jcin.2021.04.010

41. Pham V, Bonnet M, Varenne O, Lafont A, Darmon A, Feldman L, et al. In-Stent use of intravascular coronary lithotripsy for restenosis and stent underexpansion: a multicentre experience. *Can J Cardiol*. (2022) 38:1474–5. doi: 10.1016/j.cjca.2022.05.020

42. Tovar Forero MN, Sardella G, Salvi N, Cortese B, Di Palma G, Werner N, et al. Coronary lithotripsy for the treatment of underexpanded stents: the international & multicentre CRUNCH registry. *EuroIntervention*. (2022) 18:574–81. doi: 10.4244/EIJ-D-21-00545

43. Chiam PTL, Lim YT, Sivathasan C. Transfemoral transcatheter aortic valve implantation facilitated by intravascular ultrasound-guided shockwave lithotripsy: TAVI facilitated by IVUS guided lithotripsy. *AsiaIntervention*. (2021) 7:116–7. doi: 10.4244/AIJ-D-21-00026

44. Ciardetti N, Ciatti F, Nardi G, Di Muro FM, Demola P, Sottili E, et al. Advancements in transcatheter aortic valve implantation: a focused update. *Medicina*. (2021) 57(7):711. doi: 10.3390/medicina57070711

45. Ricottini E, Carpenito M, Nusca A, Melfi R, Rinaldi R, Grigioni F, et al. Combined procedure of transcatheter aortic valve replacement and coronary intravascular lithotripsy. *J Cardiovasc Med*. (2022) 23:487–92. doi: 10.2459/JCM.0000000000001321

46. Nuyens P, Wong I, Vanhaverbeke M, Wang X, Bieliauskas G, Sondergaard L, et al. Intravascular lithotripsy-assisted transfemoral transcatheter aortic valve implantation. *J Vis Exp*. (2022). doi: 10.3791/63556

47. Blackstone EH, Suri RM, Rajeswaran J, Babaliaros V, Douglas PS, Fearon WF, et al. Propensity-matched comparisons of clinical outcomes after transapical or transfemoral transcatheter aortic valve replacement: a placement of aortic transcatheter valves (PARTNER)-I trial substudy. *Circulation*. (2015) 131:1989–2000. doi: 10.1161/CIRCULATIONAHA.114.012525

48. Kempton H, Roy A, Watson A, Evans D, Muller D, Roy D. Using intravascular lithotripsy to facilitate transfemoral arterial access for transcatheter aortic valve implantation. *Heart Lung Circ*. (2022) 31:e135–9. doi: 10.1016/j.hlc.2022.07.016

49. Sharma A, Bertog S, Mbai M. Transcatheter aortic valve lithotripsy in severely calcified bicuspid aortic stenosis prior to transcatheter aortic valve implantation. *Eur Heart J*. (2020) 42:358. doi: 10.1093/eurheartj/ehaa829

50. Belluschi I, Buzzatti N, Denti P, Maisano F. Transcatheter lithotripsy to facilitate post-dilatation of underexpanded aortic transcatheter heart valve. *Eur Heart J*. (2022) 43:2081. doi: 10.1093/eurheartj/ehac044

51. Bernava G, Fermi E, Gelpi G, Rizzi S, Benettin D, Barbuto M, et al. Lithotripsy of calcified aortic valve leaflets by a novel ultrasound transcatheter-based device. *Front Cardiovasc Med*. (2022) 9:850393. doi: 10.3389/fcvm.2022.850393

52. Fermi E, Benettin D, Bernava G, Pesce M, Pasquino E. Trans-catheter double-frequency ultrasound ablator for the treatment of aortic valve leaflets calcification. *Biomed J Sci Tech Res*. (2021) 33:25952–7. doi: 10.26717/BJSTR.2021.33.005429

53. Tiengo E, Fermi E, Zanolla I, Zanotti F, Trentini M, Pasquino E, et al. In vitro model for the evaluation of innovative transcatheter debridement device (TDD): pericardium-based scaffold and stem cells to reproduce calcificated valves. *Biomedicines*. (2022) 10. doi: 10.3390/biomedicines10102352

54. Gardiner R, Muradagha H, Kiernan TJ. Intravascular lithotripsy during percutaneous coronary intervention: current concepts. *Expert Rev Cardiovasc Ther*. (2022) 20:323–38. doi: 10.1080/14779072.2022.2069561

55. Giannopoulos S, Sagris M, Giannopoulos S, Tzoumas A, Kokkinidis DG, Texakalidis P, et al. Embolic protection devices for carotid artery stenting: a network meta-analysis. *Vascular*. (2022). doi: 10.1177/17085381221140616