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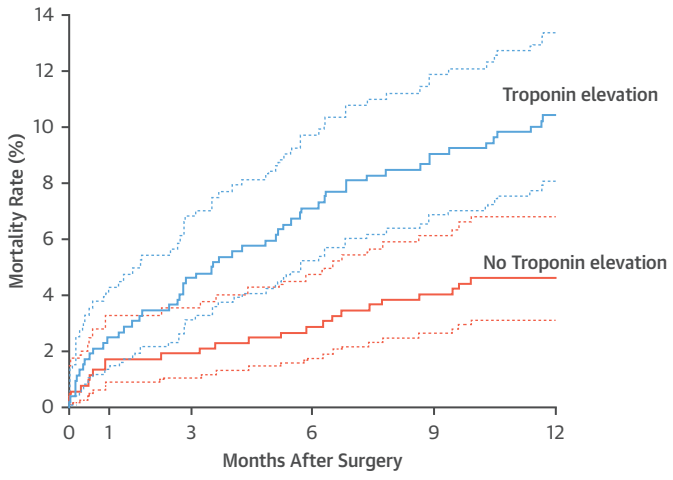
FIGURE 1 1-Year Mortality in the Propensity Score–Matched Cohort of 1,042 Patients Without Adverse Post-Operative Event



Blue lines indicate mortality in patients with a post-operative finding of isolated myocardial injury during the 3 days after surgery. **Orange lines** indicate patients without troponin elevation. **Dotted lines** indicate the upper and lower 95% confidence limits.

*Department of Anesthesia and Pain Management
University Health Network
200 Elizabeth Street, 3n-464
Toronto, Ontario M5G 2C4
Canada
E-mail: scott.beattie@uhn.ca

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Safety and Performance of Lithoplasty for Treatment of Calcified Peripheral Artery Lesions

Percutaneous transluminal angioplasty of calcified peripheral artery lesions often results in suboptimal vessel expansion. Angioplasty of calcified lesions is often associated with acute loss of patency due to residual stenosis or dissection, often requiring stenting (1,2). A high rate of chronic failure due to restenosis is also seen, resulting in target-lesion revascularization. Plaque modifying devices, including atherectomy, remove atheroma and have shown improved lumen diameter and reduced bailout stenting. However, vascular complications and significantly higher rates of procedural distal embolization requiring adjunctive tools still persist along with suboptimal patency (3). Lithotripsy is a well-characterized treatment adopted for calcified renal calculi, in which calcifications are fragmented by high-power acoustic shockwaves. Lithoplasty is a technology based on lithotripsy, in which multiple emitters mounted on a traditional balloon catheter provide circumferential pulsatile energy to disrupt calcified plaque and improve acute gain while minimizing vessel injury. The goal of this study was to demonstrate the safety and performance of the Peripheral Lithoplasty System (Shockwave Medical, Fremont, California) for treatment of calcified, stenotic peripheral arteries.

We prospectively enrolled 35 patients with calcified, stenotic, de novo femoropopliteal arterial lesions. The balloon, sized 1:1 to the reference vessel diameter, was inflated to 4 atm, and 30 pulses were delivered followed by further dilation to nominal pressures. The procedure was repeated providing a minimum of 60 pulses in the target lesion per vessel segment with interval deflation to allow for distal perfusion. Investigators were initially trained using a bench model, and all cases had clinical specialist support. Key inclusion criteria included moderate or severe calcification, reference vessel diameter 3.5 mm to 7.0 mm, stenosis ≥70%, lesion length ≤150 mm and 1 patent runoff vessel to the foot. Key exclusion criteria included Rutherford category 5 or 6, untreated significant inflow disease, and significant renal disease or dialysis. Procedural angiograms along with duplex ultrasounds at discharge, 30 days, and 6 months were analyzed by a

core laboratory. Calcification was identified by the angiographic core laboratory as readily apparent densities at the site of stenosis extending at least one-half the lesion length and defined as moderate or severe on the basis of single side or bilateral involvement, respectively.

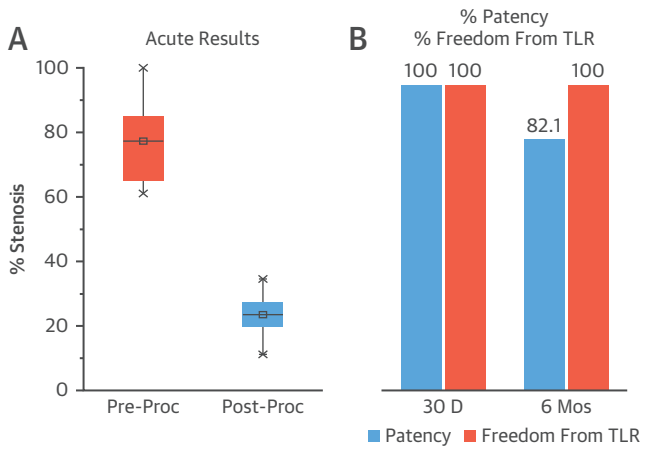
The primary performance endpoint was procedural success defined as post-treatment residual diameter stenosis of <50% with or without adjunctive percutaneous angioplasty per the core laboratory. Loss of vessel patency was defined as ≥50% restenosis by duplex ultrasound core laboratory review. Major adverse events were assessed at 30 days and 6 months, and defined as emergency surgical revascularization, target-limb amputation, thrombus or distal emboli requiring treatment, or perforation/flow-limiting dissections requiring intervention including stenting. Functional outcomes including improvement in ankle brachial index and Rutherford category were assessed through 6 months.

Initial stenosis was 76.3% with an average lesion length of 61.5 mm. Calcium burden was significant with severe calcification reported in 64.1% of patients, and an average calcified length of 80.3 mm. The balloon was delivered successfully in all patients and required minimal use of pre- and post-dilation (8.6% and 14.3%). Procedural success occurred in all patients, and the final residual stenosis was 23.4% with an acute gain of 2.9 mm. The average number of pulses was 104, mean balloon pressure 7.1 mm Hg, and average treatment time of 11 min per patient. There were no vascular complications at index procedure adjudicated by the core laboratory, and no stents were implanted. Distal embolic filters were used at the discretion of the investigator in a total of 6 cases, and thrombus was present in 1 filter. Vessel patency at 30 days and 6 months was 100% and 82.1%, respectively with no target lesion revascularizations within 6 months (Figure 1). There were no major adverse events reported through 6 months. The ankle brachial index and Rutherford category were improved from pre-procedure examination and sustained through 6 months.

The DISRUPT PAD I (Safety and Performance Study of the Shockwave Lithoplasty System) was the first study to investigate lithotripsy on a traditional balloon catheter to treat calcified, stenotic lesions. The system successfully treated calcified femoropopliteal lesions, traditionally challenging and time consuming to treat, with limited adjunctive balloon use and no implants. The results show a dramatic reduction in stenosis severity with high acute gain and minimal vessel injury. There were no major adverse events or revascularizations after the index procedure, and vessel patency was durable out to 6 months. Importantly, the system appeared to change vessel wall compliance in this study as evidenced by balloon expansion during sonic pulsing while maintaining the same low pressure. This result suggests disruption of both superficial and deep calcium in the vessel wall.

Finally, the study suggests that lithoplasty for the treatment of calcified femoropopliteal arteries is safe and effective. These positive results indicate lithoplasty may play an important role in the management of calcified peripheral arterial disease. Further evaluation and procedural optimization is warranted.

FIGURE 1 Study Results



(A) Pre-procedural (Pre-Proc) stenosis (76.3 ± 13.5%) measured at baseline, post-procedural (Post-Proc) (23.4 ± 5.7%) measured post-index procedure. **(B)** Patency and freedom from TLR. TLR = target-lesion revascularization.

Marianne Brodmann, MD
Martin Werner, MD
Todd J. Brinton, MD
Uday Illindala, MS
Alexandra Lansky, MD
Michael R. Jaff, DO, RPVI
***Andrew Holden, MD**

*Vascular Offices, Level 4/Building 32
Auckland City Hospital
2 Park Road, Grafton
Auckland 1023
New Zealand
E-mail: AndrewH@adhb.govt.nz

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Low-Risk Lifestyle Is a Strong Predictor of Outcomes Across Populations With Different Cardiovascular Health Manifestations

Lv et al. (1) sought to examine the association of a combination of modifiable healthy lifestyle factors with the risk of ischemic cardiovascular disease. They observed that adherence to a healthy lifestyle might substantially lower the burden of cardiovascular diseases in the Chinese, and this would prevent approximately two-thirds of major coronary events and two-fifths of ischemic strokes over a period of <10 years.

The difference between their definition of healthy lifestyle components based on cited papers (2,3) and the American Heart Association (AHA) definition (4) (referenced elsewhere in their paper) raised some concerns. For instance, the low-risk group for smoking was defined as "nonsmokers or those who had stopped smoking for reasons other than illness for ≥6 months." The rationale for this cutpoint is not clear, especially because the Chinese population may have a high proportion of heavy smokers. The AHA defined ideal smoking status as "stopped smoking ≥12 months or never smoked."

Lv et al. defined the low-risk group for diet as "those who eat vegetables and fruits every day." It should be made clear that those who ate vegetables and fruits every day could include people consuming 7 servings per week, which is lower than the recommended 30 servings per week (4.5 servings per day) (4).

Taking into account these 2 definitions, we acknowledge that the investigators might be underestimating the true effect of adhering to healthy factors.

Furthermore, low-risk lifestyle appears to be a strong predictor of outcomes across populations with different cardiovascular health manifestations (i.e., Western countries vs. China).

*Bamba Gaye, PhD
Luc Djousse, MD, ScD, MPH
Jean Philippe Empana, MD, PhD

*INSERM, U970
Paris Cardiovascular Research Center
University Paris Descartes
Sorbonne Paris Cité
56 Rue Leblanc
Paris, #75015
France
E-mail: bamba.gaye@inserm.fr

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REPLY: Low-Risk Lifestyle Is a Strong Predictor of Outcomes Across Populations With Different Cardiovascular Health Manifestations

We thank Dr. Gaye and colleagues for raising thoughtful points. In the present China Kadoorie Biobank (CKB) study, we defined the low-risk lifestyle according to previous studies, recent guidelines for cardiovascular health, and the distribution of the related variables in the CKB population.

For smoking, we included former smokers who had stopped smoking because of illness in the current smoker category, because approximately one-half of former smokers in the CKB population quit due to illness (1). Such a definition might minimize potential bias of spuriously elevated risk related to this group. We followed our previous publications to define former smokers as those who had stopped smoking for reasons other than illness for ≥6 months (1,2). In addition, we changed the definition of smoking cessation from ≥6 months to ≥12 months. Of 13,112