procedure. In 6 cases, a stent was deployed prophylactically and in 1 patient, an acute partial obstruction developed which was treated with PCI. In 5 cases the "chimney" stenting technique was used. Therefore, the use of stents with greater radial strength or chimney stenting needs investigating for evidence of benefit. At present, there is no recommendation to change practice from conventional guidewire and/or stent protection. Interestingly though, the BASILICA procedure has been recently shown to be feasible in lacerating both surgical or native valve leaflets prior to TAVR and seems a promising strategy to prevent both acute and DCO that is currently under investigation in a prospective clinical trial (NCT03381989) [11]. In summary, the newly recognised syndrome of DCO is thankfully rare, but clinicians should be aware of this complication that is similar to acute coronary obstruction and is associated with a high mortality rate. As there is a natural movement towards TAVR in lower risk patients with longer life expectancies, DCO will be less tolerable in this group. Ongoing research studies should specifically recognise DCO as a complication so data can be gathered to characterise this phenomenon further. Also, in cases of sudden cardiac death out of hospital, post mortem studies where possible could help shed light further on the real incidence and pathogenesis of this condition.

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Changing the paradigm in renal denervation: Is trans-urethral access the key to effective blood pressure reduction?

To the Editor:

We read with interest the article by Petrov et al. [1], in *Cardiovascular Revascularization Medicine* entitled, "Comparison of standard renal denervation procedure versus novel distal and branch vessel ablation with brachial arterial access." The authors should be congratulated on their publication demonstrating greater blood pressure (BP) improvement with 'Y-pattern' compared to standard renal denervation (RDN) in patients with resistant hypertension, and the feasibility of brachial access for such procedures.

The key to success with percutaneous RDN is ablation of the renal nerves, with resultant reduction in sympathetic outflow and improvement in BP. The SYMPLICITY HTN 3 [2] trial failed to demonstrate a benefit of RDN for blood pressure control over placebo. One hypothesis for the study's failure was that there was inadequate ablation of renal nerves [3–5]. The SPYRAL HTN-OFF MED [6] trial where RDN was performed in both the main and branch arteries resulted in significant reduction in BP compared to placebo supporting this hypothesis. This study by Petrov et al. [1] elegantly compares 'Y-pattern' with standard RDN, and further validates that the putative factor for RDN success in achieving blood pressure control is effective renal nerve ablation.

We propose that RDN via trans-urethral approach may be more efficacious than the peri-arterial approach. To understand why requires a brief review of renal physiology. The kidneys are innervated by both afferent (kidney ➔ brain) and efferent (brain ➔ kidney) nerve fibers. Both types of fibers can in theory mediate blood pressure control. Ablation of afferent renal nerves can decrease arterial pressure by decreasing sympathetic drive to the kidney and other organs. On the other hand, ablation of efferent renal nerves can reduce blood pressure by reducing renal vascular resistance, renin release, and sodium and water reabsorption [7]. However, recent studies in the rat model suggest it is ablation of the afferent nerves that mediate the antihypertensive effects of RDN [8,9].

Histopathologic studies suggest that the majority of afferent nerves controlling sympathetic tone are in the renal collecting system [10–14]. This intuitively makes sense since the presence of afferent renal sensory nerves in the renal pelvic wall is ideal for sensing stretch of the renal pelvic wall. Within the renal pelvis, there is also an abundance of efferent nerves, and afferent and efferent nerves are in close proximity and often intertwined [10]. This is in stark contrast to the peri-arterial area where the renal nerves are predominantly composed of efferent with few afferent fibers [15]. This begs the question whether

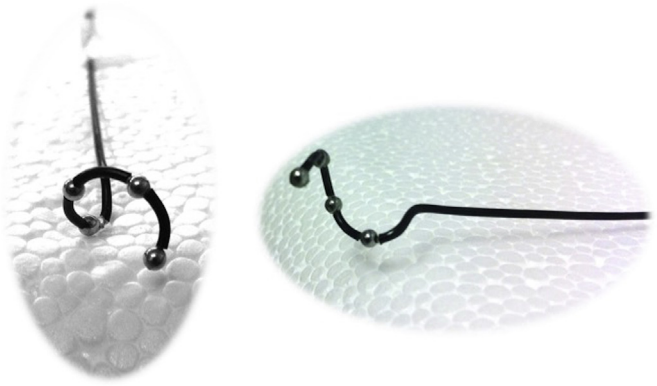

Fig. 1. The NephroBlate™ device with its helical probe.

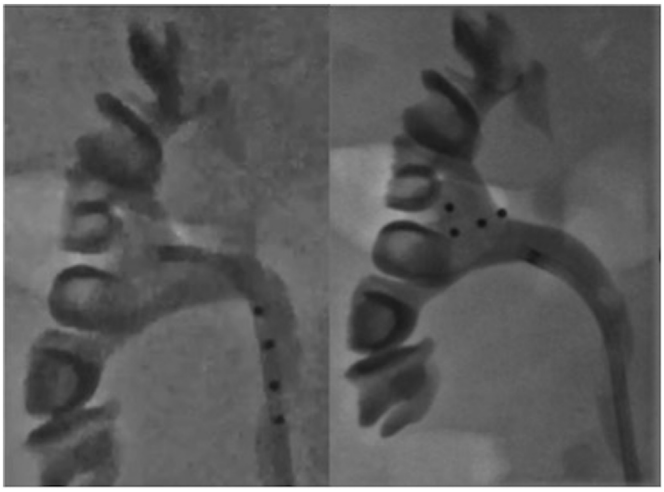

Fig. 2. Cinematography of the NephroBlate™ device in the swine renal pelvis.

a trans-urethral approach targeting the collecting system would result in greater blood pressure reduction. We therefore developed NephroBlate™ (Verve Medical, Scottsdale, AZ), a radiofrequency catheter system that is introduced trans-urethrally to the renal pelvis, using standard urologic techniques, and exploits the proximity of the renal nerves to the renal pelvis (Figs. 1–2). We first tested this hypothesis in a swine model whereby animals underwent renal pelvic denervation via urethral access. We found that swine that underwent ablation had a 60.4% reduction in their renal cortical norepinephrine levels compared to control. Histopathology also confirmed nerve ablation in the treated zones [16]. We took this proof-of-concept and applied it to human studies. At a urologic center in India, patients who had renal disease, in whom nephrectomy was planned, underwent RDN with the NephroBlate™. These patients underwent nephrectomy 1 month later. Histopathology demonstrated superficial nerves that were fully ablated in treated areas [17] (Fig. 3). To our knowledge, only one study has examined the renal histopathology after peri-arterial renal denervation, which in contrast, showed suboptimal denervation of renal nerve fibers in part because the renal nerves were deeper than depth that could be reached with ablation [18]. We also then treated patients with resistant hypertension via trans-urethral RDN and found we were able to drop their blood pressure by a mean systolic of 44 mm Hg and a mean diastolic of 18 mm Hg [17].

RDN via trans-urethral access with NephroBlate™ is safe and utilizes techniques that are common in urology practice. The renal pelvis is a potential space, so no additional manipulation of the ablation catheter is necessary when treating the collecting system. Our procedure times averaged between 9 and 15 min [17]. Via a peri-arterial approach Petrov et al. [1] had procedural times of 56 ± 15 min for the standard group and 85 ± 27 min for Y-pattern group. In the SPYRAL HTN-ON MED [3] study, the denervation time itself took over 60 min (60.8 ± 25.3). This is a long interventional procedure despite being in skilled operators' hands. In addition to the potential shorter procedure time, RDN via a trans-urethral approach has the added advantages of avoidance of systemic contrast, anti-platelet, or heparin administration, which can be an issue in patients with chronic kidney disease and bleeding diatheses respectively.

Besides resistant hypertension, an overactive sympathetic drive has been implicated in other disease processes such as congestive heart failure, type 2 diabetes mellitus, and obstructive sleep apnea [19–21]. RDN has the potential to aid in all of these diseases. We feel that RDN, especially, renal nerve ablation via a trans-urethral approach merits further exploration.

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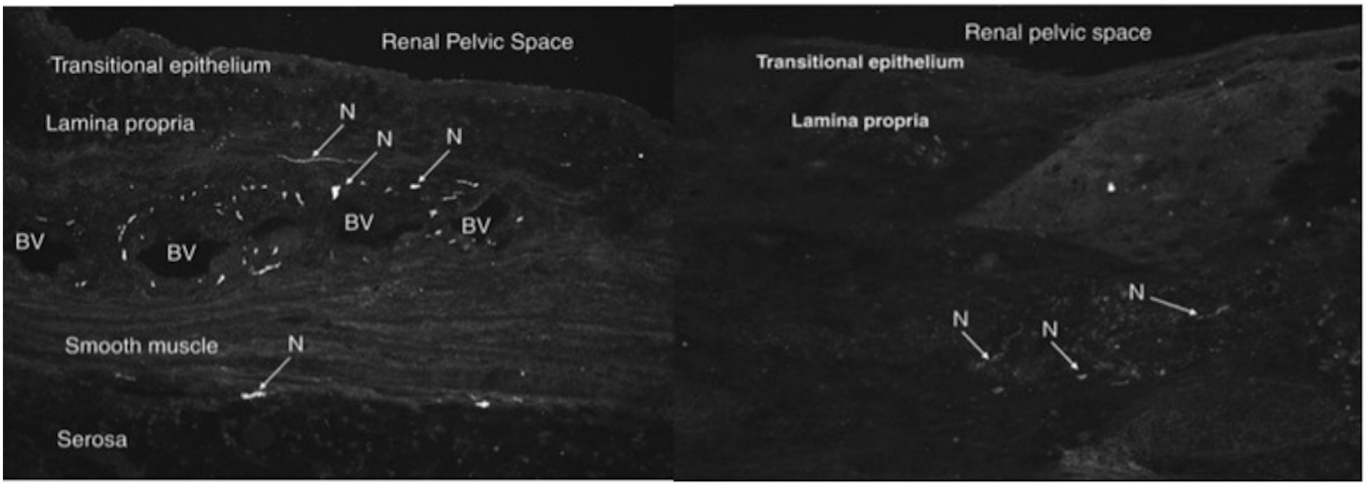

Fig. 3. Pelvis wall distal to the ablation zone (left). Pelvis wall in the ablation zone showing effective ablation of renal nerves (right). BV-blood vessel; N-nerve.

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Letter by Dérimay et al. regarding the article, "A randomized trial comparing two stent sizing strategies in coronary bifurcation treatment with bioresorbable vascular scaffolds – The Absorb Bifurcation Coronary (ABC) trial" by Rampat et al.☆

We read with great interest the study by Rampat et al. [1], comparing two stent sizing strategies (proximal vs. distal) in coronary bifurcation provisional stenting with ABSORB bioresorbable vascular scaffolds (BVS) (Abbott Vascular). In 37 patients, they concluded that stent sizing according to the proximal vessel leads to less stent malapposition, and advised this strategy. However, we disagree with these conclusions.

In classic metallic stents, a distal sizing is clearly recommended, to decrease the risk of distal dissection and/or carina shifting [2]. This strategy involves correcting the systematic proximal malapposition due to fractal geometry [3]. A proximal post-dilatation or Proximal Optimization Technique (POT) demonstrated perfect apposition and side-branch ostium optimization [4]. However, the specific mechanical properties of bioresorbable poly-L-lactic (PLLA) are its viscoelasticity and low elongation at break (with scaffold fracture risk) [5]. These properties could put in doubt the strategy proposed by Rampat et al. Foin et al. [6], however, demonstrated that BVS can be post-dilated up to 1 mm beyond the nominal diameter without fracture. In a bifurcation bench study, we confirmed that a provisional strategy with distal BVS sizing followed by POT provided excellent mechanical results without significant fracture on micro-CT analysis [7]. The ABC trial excluded left main coronaries, so the physiological stepwise differences between proximal and final vessels were systematically all <1 mm [8]. In fact, the only case of BVS fracture occurred after a kissing balloon inflation with balloon juxtaposition that probably exceeded this threshold.

In this study, the authors concluded that proximal stent sizing was probably better, mostly because proximal apposition was judged worse in case of distal sizing. However, this difference was probably due to technical points more than to the choice of vessel for sizing. In distal sizing, POT balloon diameter and inflation pressure were lower than for proximal sizing. Thus, given the post-dilatation capability of BVSs up to 1 mm, it seems that the malappositions were probably due to stent under-expansion after POT. Moreover, malapposition threshold is threshold defined by summing stent thickness and OCT resolution (<170 μm); in this study, however, the malapposition threshold was higher than usual (300 μm) [9]. This higher threshold could easily underestimate intermediate malapposition (between 170 μm and 300 μm), which are more frequent with proximal sizing. Conversely, the authors observed an unsurprising trend for excess of distal dissection with proximal sizing (which was probably non-significant only because of the small sample size). Moreover, it is interesting to know that the ABSORB 2.5 mm and 3.0 mm models are in fact the same scaffold. A specific analysis taking account of this might change the final interpretation.

Thus, in our opinion, it cannot be concluded that a proximal sizing is preferable for BVS implantation in bifurcations. Given the possibility of BVS post-dilatation up to 1 mm without fracture, it seems that the same strategy as metallic stent with distal BVS sizing and systematic POT could be recommended most of the time to avoid distal dissection. The key point concerning final proximal malapposition is primarily the technical characteristics of the POT. The choice of balloon diameter and pressure, the mechanical properties (compliance or not) and inflation time according to PLLA viscoelasticity are essential factors. We look forward to reading Dr. Rampat's response to the above.

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