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Deep vein insufficiency, not the method choice, determines the outcome of endovascular treatment in CEAP 6 patients

We have read two interesting reports recently published in *JVS-VLD* by O'Banion et al.[1,2] In the first paper, the authors described a short-term outcome of superficial venous reflux treatment using cyanoacrylate (CA) or radiofrequency (RF) ablation in CEAP 6 patients.[1] The second paper concerned the auxiliary perforator treatment in the same patients in the follow-up period.[2] In both papers, the authors concluded that CA shows superiority over RF in time required to wound healing[1] and requires less perforator interventions.[2]

Although both papers contain valuable observations, in our opinion, they provide the surprising interpretation of attached results.

The authors concluded that CA is better than RF ablation because, in contrast to the latter, it enables the perforator treatment in the primary approach. However, this statement is unfounded, as the authors did not include the calf segment in the primary RF procedure. They explained their decision by intention to avoid nerve injury, although, actually, it is the matter of accurate and careful vein separation from the adjacent nerve by tumescent anesthesia.[3] Moreover, in the follow-up period, the authors used RF to close incompetent perforators, even in the CA group.[2] Interestingly, if patients from the RF group were treated including the calf segment, would they require any auxiliary procedures for their perforators?

The main limitation of both studies is the significant difference in the venous insufficiency severity between the treated groups. It is noteworthy that the insufficiency of the superficial system alone affected 41% patients from the CA group, whereas in the RF-treated patients, it concerned 9% individuals only.[1]

It is obvious that deep vein insufficiency is a much worse condition compared with the sole involvement of the superficial system. Because of higher venous hypertension, those patients reveal the increased risk of ulceration, decreased healing rate, and higher risk of ulcer recurrence.[4] Also, to enable sufficient blood outflow, they require much higher compression compared with others.[5] Thus, to evaluate the impact of particular treatment on wound healing, the assessment of healing rate in each patient before and after the procedure would be required.

In our opinion, the treatment outcome depends mainly on the vein condition and, to a lesser extent, on the method choice. Although the authors identified this issue, unexpectedly, they missed it in final conclusions.

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REFERENCES

1. O'Banion LA, Reynolds KB, Kochubey M, Cutler B, Tefera EA, Dirks R, et al. A comparison of cyanoacrylate glue and radiofrequency ablation techniques in the treatment of superficial venous reflux in CEAP 6 patients. J Vasc Surg Venous Lymphat Disord 2021;9:1215-21.
2. Kiguchi MM, Reynolds KB, Cutler B, Tefera E, Kochubey M, Dirks R, et al. The need for perforator treatment after VenaSeal™ and ClosureFast™ endovenous saphenous vein closure in CEAP 6 patients. J Vasc Surg Venous Lymphat Disord 2021;9:1510-6.
3. Rodriguez-Acevedo O, Elstner KE, Martinic K, Zea A, Diaz J, Martins RT, et al. Hydrodisplacement of sural nerve for safety and efficacy of endovenous thermal ablation for small saphenous vein incompetence. Phlebology 2017;32:482-7.
4. Raffetto JD, Ligi D, Maniscalco R, Khalil RA, Mannello F. Why venous leg ulcers have difficulty healing: overview on pathophysiology, clinical consequences, and treatment. J Clin Med 2020;10:29.
5. Szary C, Wilczko J, Grzela T, Partsch H. Which pressure of adjustable compression wrap system is necessary to reduce deep vein cross section area in post-thrombotic patients? A proof-of-concept study. Phlebology 2020;35:207-14.

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Reply

We appreciate Szary et al's interest and letter to the editor regarding our papers comparing outcomes of CEAP 6 patients undergoing cyanoacrylate vs thermal ablative techniques.

It should be noted that there was no conclusion of superiority between devices within either of the papers as Szary et al reported. Rather, we concluded from our review of retrospectively collected data in CEAP 6 patients that those treated with VenaSeal had a shorter time to wound healing compared with radiofrequency ablation (RFA). In addition, VenaSeal treatment was associated with the decreased need for perforator intervention.[1,2] To evaluate overall superiority, a prospective, randomized trial would be necessary. Currently, Spectrum, a global post-market randomized controlled trial, is underway in efforts to answer these important questions.

Thermal saphenous nerve injury is a well-documented risk of RFA. A review of 17 randomized controlled trials reported nerve injury in the distribution of the endothermal treated saphenous vein in 12% of limbs acutely, which improved over time. However, symptoms persisted in 2.6% of patients at 5 years. Notably, in great saphenous vein (GSV) below-knee treated segments, the incidence of persistent symptoms was 7.7% at 5 years, likely due to the proximity of the saphenous nerve to the GSV below the knee.[3] Because of the above significant

risk, most physicians, including the authors, limit thermal ablation to the proximal 1/3 of the GSV below the knee.

As pathologic medial calf perforators are often located in the distal third of the calf, as Szary et al mention, the question arises that if patients from the RFA group are treated through the calf segment, would these patients require any auxiliary procedures to achieve wound healing? Unfortunately, to compare noninferiority between these two procedures for below the calf segments would be difficult, as the risk of nerve injury is fundamentally higher for endothermal ablation than cyanoacrylate. From the results of our studies, we feel that when there is an equally efficacious nonthermal technique for saphenous vein closure in a pathologic GSV in the distal 2/3 of the calf, this should be preferred to avoid the aforementioned thermal nerve injury risk.

In addition, as mentioned in the limitations of the papers, more patients in the RFA-treated group had deep venous reflux, which could have contributed to a higher proportion of refluxing perforators. However, on multivariate analysis, deep venous reflux was not an independent predictor of prolonged wound healing.[2] Another acknowledged limitation was the nonroutine identification of pathologic perforators on initial duplex ultrasound (which has fortunately now been adopted as IAC standard in the updated 2020 guidelines). Thus, it is difficult to ascertain how thermal vs cyanoacrylate closure affected the below-knee segment perforator veins independently or in the presence/absence of deep venous reflux. Conversely, if perforators are preprocedurally identified in CEAP 6 patients, perhaps cyanoacrylate may be the better-suited method of venous closure than other thermal modalities to eliminate the potential risk of thermal nerve injury and allow for complete closure of the entire GSV from saphenofemoral junction to the ankle in one procedure.

Unfortunately, because of financial insurance constraints, the applicability of cyanoacrylate procedures to all patients is limited, and thus, with a more inclusive multicenter, randomized trial (Spectrum), the authors envision a robust diversified cohort with the ability to address the limitations raised in either paper.

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REFERENCES

1. Kiguchi MM, Reynolds KB, Cutler B, Tefera E, Kochubey M, Dirks R, et al. The need for perforator treatment after VenaSeal and ClosureFast endovenous saphenous vein closure in CEAP 6 patients. J Vasc Surg Venous Lymphat Disord 2021;9:1510-6.
2. O'Banion LA, Reynolds KB, Kochubey M, Cutler B, Tefera EA, Dirks R, et al. A comparison of cyanoacrylate glue and radiofrequency ablation techniques in the treatment of superficial venous reflux in CEAP 6 patients. J Vasc Surg Venous Lymphat Disord 2021;9:1215-21.
3. Dermody M, O'Donnell TF, Balk EM. Complications of endovenous ablation in randomized controlled trials. J Vasc Surg Venous Lymphat Disord 2013;1:427-36.e1.

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High colloid osmotic pressure as a proposed mechanism of acute renal injury after pharmacomechanical thrombectomy

The article titled "Risk factors for acute kidney injury after pharmacomechanical thrombolysis for acute deep vein thrombosis" aimed to identify patients at the highest risk of developing acute kidney injury after pharmacomechanical thrombolysis (PMT) and represents a pioneer study of this topic.[1-4]

A retrospective study analysis could lead to confounding or the exclusion of certain variables. In response, we would like to suggest a separate theory in which high oncotic pressure produces acute kidney injury after PMT. It is our hope that this will improve further research on the causation and, ultimately, solution for PMT-induced acute kidney injury, by identifying additional variables for analysis.

Colloid osmotic pressure (COP) is one of the four Starling forces determining the movement of fluids across a capillary. Proteins, notably albumin, play an important role in this particular context. In addition to albumin, other proteins also contribute to COP.[5,6]

A thrombus is an aggregation of platelets and red blood cells that form a plug in a mesh of cross-linked fibrin protein. The PMT procedure produces zones with the Bernoulli effect where the thrombus is macerated, thereby releasing D-dimers or fibrin degradation products with molecular weight of 180 kDa or 195 kDa to the blood.[7,8]

We theorized that these products are unable to permeate through the glomerular membrane and play a role in increasing the COP and, thereby, lead to fluid retention in the intravascular compartment and decrease the glomerular filtration rate.[5] Our theory is based on Starling's original model of semipermeable capillaries and does not exclude other theories, which, instead, could be acting in association. We acknowledge that recent research has considered the contributions of the endothelial glycocalyx layer toward changes in the pressure gradients and fluid exchange.[9]

Based on our theory, we consider it necessary to include the following variables for analysis in future studies: plasma osmolality, electrolytes in urine and serum, D-dimer levels, urinary rate per hour, detailed fluid intake during the procedure, and the pre- and postprocedure total serum protein levels. The inclusion of the