MINIREVIEWS

5934 Development of clustered regularly interspaced short palindromic repeats/CRISPR-associated technology for potential clinical applications
Huang YY, Zhang XY, Zhu P, Ji L

5946 Strategies and challenges in treatment of varicose veins and venous insufficiency
Gao RD, Qian SY, Wang HH, Liu YS, Ren SY

5957 Diabetes mellitus susceptibility with varied diseased phenotypes and its comparison with phenome interactome networks
Rout M, Kour B, Vuree S, Lulu SS, Medicherla KM, Suravajhala P

ORIGINAL ARTICLE

Clinical and Translational Research

5965 Identification of potential key molecules and signaling pathways for psoriasis based on weighted gene co-expression network analysis
Shu X, Chen XX, Kang XD, Ran M, Wang YL, Zhao ZK, Li CX

5984 Construction and validation of a novel prediction system for detection of overall survival in lung cancer patients

Case Control Study

6001 Effectiveness and postoperative rehabilitation of one-stage combined anterior-posterior surgery for severe thoracolumbar fractures with spinal cord injury
Zhang B, Wang JC, Jiang YZ, Song QP, An Y

Retrospective Study

6009 Prostate sclerosing adenopathy: A clinicopathological and immunohistochemical study of twelve patients
Feng RL, Tao YP, Tan ZY, Fu S, Wang HF

6021 Value of magnetic resonance diffusion combined with perfusion imaging techniques for diagnosing potentially malignant breast lesions
Zhang H, Zhang XY, Wang Y

6032 Scar-centered dilation in the treatment of large keloids
Wu M, Gu JY, Duan R, Wei BX, Xie F

6039 Application of a novel computer-assisted surgery system in percutaneous nephrolithotomy: A controlled study
## Contents

**Thrice Monthly Volume 10 Number 18 June 26, 2022**

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>6050</td>
<td>Influences of etiology and endoscopic appearance on the long-term outcomes of gastric antral vascular ectasia</td>
<td>Kwon HJ, Lee SH, Cho JH</td>
</tr>
<tr>
<td></td>
<td><strong>Randomized Controlled Trial</strong></td>
<td></td>
</tr>
<tr>
<td>6060</td>
<td>Evaluation of the clinical efficacy and safety of TST33 mega hemorrhoidectomy for severe prolapsed hemorrhoids</td>
<td>Tao L, Wei J, Ding XF, Ji LJ</td>
</tr>
<tr>
<td>6069</td>
<td>Sequential chemotherapy and icotinib as first-line treatment for advanced epidermal growth factor receptor-mutated non-small cell lung cancer</td>
<td>Sun SJ, Han JD, Liu W, Wu ZY, Zhao X, Yan X, Jiao SC, Fang J</td>
</tr>
<tr>
<td></td>
<td><strong>Randomized Clinical Trial</strong></td>
<td></td>
</tr>
<tr>
<td>6082</td>
<td>Impact of preoperative carbohydrate loading on gastric volume in patients with type 2 diabetes</td>
<td>Lin XQ, Chen YR, Chen X, Cai YP, Lin JX, Xu DM, Zheng XC</td>
</tr>
<tr>
<td></td>
<td><strong>META-ANALYSIS</strong></td>
<td></td>
</tr>
<tr>
<td>6091</td>
<td>Efficacy and safety of adalimumab in comparison to infliximab for Crohn's disease: A systematic review and meta-analysis</td>
<td>Yang HH, Huang Y, Zhou XC, Wang RN</td>
</tr>
<tr>
<td></td>
<td><strong>CASE REPORT</strong></td>
<td></td>
</tr>
<tr>
<td>6105</td>
<td>Successful treatment of acute relapse of chronic eosinophilic pneumonia with benralizumab and without corticosteroids: A case report</td>
<td>Izhakian S, Pertzov B, Rosengarten D, Kramer MR</td>
</tr>
<tr>
<td>6119</td>
<td>Hepatic epithelioid hemangioendothelioma after thirteen years’ follow-up: A case report and review of literature</td>
<td>Mo WF, Tong YL</td>
</tr>
<tr>
<td>6128</td>
<td>Effectiveness and safety of ultrasound-guided intramuscular lauromacrogol injection combined with hysteroscopy in cervical pregnancy treatment: A case report</td>
<td>Ye JP, Gao Y, Lu LW, Ye YJ</td>
</tr>
<tr>
<td>6136</td>
<td>Carcinoma located in a right-sided sigmoid colon: A case report</td>
<td>Lyu LJ, Yao WW</td>
</tr>
</tbody>
</table>
Contents

Thrice Monthly Volume 10 Number 18 June 26, 2022

6148 Overlapping syndrome of recurrent anti-N-methyl-D-aspartate receptor encephalitis and anti-myelin oligodendrocyte glycoprotein demyelinating diseases: A case report
Yin XJ, Zhang LF, Bao LH, Feng ZC, Chen JH, Li BX, Zhang J

6156 Liver transplantation for late-onset ornithine transcarbamylase deficiency: A case report

6163 Disseminated strongyloidiasis in a patient with rheumatoid arthritis: A case report
Zheng JH, Xue LY

6168 CYP27A1 mutation in a case of cerebrotendinous xanthomatosis: A case report
Li ZR, Zhou YL, Jin Q, Xie YY, Meng HM

6175 Postoperative multiple metastasis of clear cell sarcoma-like tumor of the gastrointestinal tract in adolescent: A case report
Huang WP, Li LM, Gao JB

6184 Toripalimab combined with targeted therapy and chemotherapy achieves pathologic complete response in gastric carcinoma: A case report

6192 Presentation of Boerhaave’s syndrome as an upper-esophageal perforation associated with a right-sided pleural effusion: A case report
Tan N, Luo YH, Li GC, Chen YL, Tan W, Xiang YH, Ge L, Yao D, Zhang MH

6198 Camrelizumab-induced anaphylactic shock in an esophageal squamous cell carcinoma patient: A case report and review of literature

6205 Nontraumatic convexal subarachnoid hemorrhage: A case report
Chen HL, Li B, Chen C, Fan XX, Ma WB

6211 Growth hormone ameliorates hepatopulmonary syndrome and nonalcoholic steatohepatitis secondary to hypopituitarism in a child: A case report
Zhang XY, Yuan K, Fang YL, Wang CL

6218 Vancomycin dosing in an obese patient with acute renal failure: A case report and review of literature
Xu KY, Li D, Hu ZJ, Zhao CC, Bai J, Du WL

6227 Insulinoma after sleeve gastrectomy: A case report
Lobaton-Ginsberg M, Sotelo-González P, Ramirez-Renteria C, Juárez-Aguilar FG, Ferreira-Hermosillo A

6234 Primary intestinal lymphangiectasia presenting as limb convulsions: A case report
Cao Y, Feng XH, Ni HX

6241 Esophagogastric junctional neuroendocrine tumor with adenocarcinoma: A case report
Kong ZZ, Zhang L
### Contents

**World Journal of Clinical Cases**  
Thrice Monthly Volume 10 Number 18 June 26, 2022

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>6247</td>
<td>Foreign body granuloma in the tongue differentiated from tongue cancer</td>
<td>Jiang ZH, Xu R, Xia L</td>
</tr>
<tr>
<td>6261</td>
<td>Management of type IIIb dens invaginatus using a combination of root canal treatment, intentional replantation, and surgical therapy: A case report</td>
<td>Zhang J, Li N, Li WL, Zheng XY, Li S</td>
</tr>
<tr>
<td>6277</td>
<td>De novo brain arteriovenous malformation formation and development: A case report</td>
<td>Huang H, Wang X, Guo AN, Li W, Duan RH, Fang JH, Yin B, Li DD</td>
</tr>
<tr>
<td>6283</td>
<td>Coinfection of <em>Streptococcus suis</em> and <em>Nocardia asiatica</em> in the human central nervous system: A case report</td>
<td>Chen YY, Xue XH</td>
</tr>
<tr>
<td>6289</td>
<td>Dilated left ventricle with multiple outpouchings — a severe congenital ventricular diverticulum or left-dominant arrhythmogenic cardiomyopathy: A case report</td>
<td>Zhang X, Ye RY, Chen XP</td>
</tr>
<tr>
<td>6307</td>
<td>Thyroid follicular renal cell carcinoma excluding thyroid metastases: A case report</td>
<td>Wu SC, Li XY, Liao BJ, Xie K, Chen WM</td>
</tr>
<tr>
<td>6314</td>
<td>Appendiceal bleeding: A case report</td>
<td>Zhou SY, Guo MD, Ye XH</td>
</tr>
<tr>
<td>6319</td>
<td>Spontaneous healing after conservative treatment of isolated grade IV pancreatic duct disruption caused by trauma: A case report</td>
<td>Mei MZ, Ren YF, Mou YP, Wang YY, Jin WW, Lu C, Zhu QC</td>
</tr>
<tr>
<td>6325</td>
<td>Pneumonia and seizures due to hypereosinophilic syndrome—organ damage and eosinophilia without synchronisation: A case report</td>
<td>Ishida T, Murayama T, Kobayashi S</td>
</tr>
</tbody>
</table>

**LETTER TO THE EDITOR**

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>6338</td>
<td>Stem cells as an option for the treatment of COVID-19</td>
<td>Cuevas-González MV, Cuevas-González JC</td>
</tr>
</tbody>
</table>
ABOUT COVER
Editorial Board Member of World Journal of Clinical Cases, Cristina Tudoran, PhD, Assistant Professor, Department VII, Internal Medicine II, Discipline of Cardiology, "Victor Babes" University of Medicine and Pharmacy Timisoara, Timisoara 300041, Timis, Romania. cristina13.tudoran@gmail.com

AIMS AND SCOPE
The primary aim of World Journal of Clinical Cases (WJCC, World J Clin Cases) is to provide scholars and readers from various fields of clinical medicine with a platform to publish high-quality clinical research articles and communicate their research findings online.

WJCC mainly publishes articles reporting research results and findings obtained in the field of clinical medicine and covering a wide range of topics, including case control studies, retrospective cohort studies, retrospective studies, clinical trials studies, observational studies, prospective studies, randomized controlled trials, randomized clinical trials, systematic reviews, meta-analysis, and case reports.

INDEXING/ABSTRACTING
The WJCC is now indexed in Science Citation Index Expanded (also known as SciSearch®), Journal Citation Reports/Science Edition, Scopus, PubMed, and PubMed Central. The 2021 Edition of Journal Citation Reports® cites the 2020 impact factor (IF) for WJCC as 1.337; IF without journal self cites: 1.301; 5-year IF: 1.742; Journal Citation Indicator: 0.33; Ranking: 119 among 169 journals in medicine, general and internal; and Quartile category: Q3. The WJCC’s CiteScore for 2020 is 0.8 and Scopus CiteScore rank 2020: General Medicine is 493/793.

RESPONSIBLE EDITORS FOR THIS ISSUE
Production Editor: Ying-Yi Yuan; Production Department Director: Xu Guo; Editorial Office Director: Jin-Lei Wang.
Strategies and challenges in treatment of varicose veins and venous insufficiency

Rong-Ding Gao, Song-Yi Qian, Hai-Hong Wang, Yong-Sheng Liu, Shi-Yan Ren

Abstract

Patients with varicose veins can be treated with conservative or surgical approaches based on the clinical conditions and patient preferences. In the recent decade, the recommendations for managing symptomatic varicose veins have changed dramatically due to the rise of minimally invasive endovascular techniques. The literature was systematically searched on Medline without language restrictions. All papers on the treatment of varicose veins and venous insufficiency with different procedures were included and reviewed. Endovenous laser ablation (EVLA) and radiofrequency ablation (RFA) both are same safe and effective in terms of occlusion rate, and time to return to normal activity. In comparison with RFA or EVLT, Cure conservatrice et Hemodynamique de l’Insufficience Veineuse en Ambulatoire (CHIVA) may cause more bruising and make little or no difference to rates of limb infection, superficial vein thrombosis, nerve injury, or hematoma. In terms of recurrence of varicose veins, there is little or no difference between CHIVA and stripping, RFA, or EVLT. Great saphenous vein recanalization is highest in the ultrasound-guided foam sclerotherapy (FS) group (51%) during 1 year of follow-up. The 2013 National Institute for Health and Care Excellence clinical guidelines recommend surgery as a third-line therapeutic option after EVLA or RFA and sclerotherapy. Although the mechano-chemical endovenous ablation (MOCA) is a non-thermal, non-tumescent option and appears to be of similar efficacy to stab avulsion with no potential risk of nerve damage, the overall success rate of MOCA is lower than those of other procedures such as EVLA, RFA, or high ligation and stripping. EVLA is the most...
cost-effective therapeutic option, with RFA being a close second for the treatment of patients with varicose veins. Endovenous thermal ablation (EVLA or RFA) is recommended as a first-line treatment for varicose veins and has substituted the high ligation of saphenofemoral junctional reflux and stripping of varicose veins. Ultrasound-guided FS is associated with a high recurrence rate and can be used in conjunction with other procedures. MOCA and cyanoacrylate embolization appear promising, but evidence of their effectiveness is required.

Key Words: Varicose veins; Venous insufficiency; High ligation and stripping; Endovenous laser ablation; Radiofrequency ablation; Cure conservatrice et Hemodynamique de l’Insufficience Veineuse en Ambulatoire

©The Author(s) 2022. Published by Baishideng Publishing Group Inc. All rights reserved.

Core Tip: Endovenous laser ablation (EVLA) is the most cost-effective therapeutic option, with radiofrequency ablation (RFA) being a close second for the treatment of patients with varicose veins. Endovenous thermal ablation (EVLA or RFA) is recommended as a first-line treatment for varicose veins and has substituted the high ligation of saphenofemoral junctional reflux and stripping of varicose veins. In terms of recurrence of varicose veins, there is little or no difference between Cure conservatrice et Hemodynamique de l’Insufficience Veineuse en Ambulatoire and EVLA, RFA, or stripping. Ultrasound guided foam sclerotherapy is associated with a high recurrence rate and can be used in conjunction with other procedures. Mechanochemical endovenous ablation and cyanoacrylate embolization appear promising, but evidence on their effectiveness is warranted.

INTRODUCTION
Varicose veins are tortuous, twisted, or elongated veins dilated to at least 3 mm in diameter evaluated when a patient in standing status with a prevalence of 10% in the population[1], and serious conditions such as deep venous thrombosis (DVT) and pulmonary embolism may occur if untreated[2,3]. Patients with varicose veins can be treated with conservative or surgical options based on the clinical conditions and patient preferences[4-6]. In the recent decade, there has been a dramatic change in the recommendations for managing symptomatic varicose veins due to the rise of minimally invasive endovascular techniques[6,7]. Therefore, we searched the literature and summarize the strategies and challenges in the treatment of varicose veins and venous insufficiency.

STRATEGIES IN TREATMENT OF VARICOSE VEINS AND VENOUS INSUFFICIENCY
The decision and the choice of treatment for varicose veins are based on the severity of the venous insufficiency, cost, risk of postoperative complications, and patient preferences. Management options for varicose veins include conservative treatment and surgical intervention. Asymptomatic patients with varicose veins are initially managed with conservative treatment options that include medicine, compression therapy, and lifestyle modifications, while symptomatic patients are suggested to consider surgical options[1] that include endovenous laser ablation (EVLA), radiofrequency ablation (RFA), high ligation and stripping (HL/S) of the incompetent great saphenous vein (GSV), Cure conservatrice et Hemodynamique de l’Insufficience Veineuse en Ambulatoire (CHIVA), mechanochemical ablation (MOCA), cyanoacrylate embolization (CAE), etc. (Table 1)[6-8].

COMPRESSION THERAPY
Compression therapy is the mainstay of conservative management and is effective in the treatment of varicose veins with venous ulcers[9]. Compression bandaging helps manage ankle edema. However, many patients can barely tolerate bandaging because of itching, pain, and difficulty in putting on shoes. Thus, medical stockings are more welcomed than compression bandaging[10]. Compression stockings
**Table 1 Strategies for management of varicose veins**

<table>
<thead>
<tr>
<th>Name of treatment</th>
<th>Mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conservative</td>
<td></td>
</tr>
<tr>
<td>Medicine</td>
<td>Enhancing venous tone and reducing inflammation</td>
</tr>
<tr>
<td>Compression</td>
<td>External pressure, bandages, or graduated stockings</td>
</tr>
<tr>
<td>Surgery</td>
<td></td>
</tr>
<tr>
<td>HL/S</td>
<td>Ligation of the conjunction of reflux, stripping veins</td>
</tr>
<tr>
<td>AP</td>
<td>Removal of veins via small incision</td>
</tr>
<tr>
<td>CHIVA</td>
<td>Ligation of the escape point and preserving veins</td>
</tr>
<tr>
<td>HIPP</td>
<td>Destroying veins and sucking out with vacuum pressure</td>
</tr>
<tr>
<td>Thermal</td>
<td></td>
</tr>
<tr>
<td>EVLA</td>
<td>Sealing the veins by laser energy</td>
</tr>
<tr>
<td>RFA</td>
<td>Sealing the veins by radiofrequency</td>
</tr>
<tr>
<td>Nonthermal</td>
<td></td>
</tr>
<tr>
<td>Sclerotherapy</td>
<td>Destroying the venous wall by sclerosants or chemical agents and sealing veins by external pressure</td>
</tr>
<tr>
<td>MOCA</td>
<td>Rotating the venous wall and sealing veins with a clue</td>
</tr>
<tr>
<td>CAE</td>
<td>Sealing veins with a clue</td>
</tr>
</tbody>
</table>

HL/S: High ligation and stripping; EVLA: Endovenous laser ablation; RFA: Radiofrequency ablation; MOCA: Mechanochemical ablation; CAE: Cyanoacrylate embolization; CHIVA: Cure conservatrice et Hemodynamique de l’Insufficience Veineuse en Ambulatoire.

With graded compression produce graded external compression directly to the legs and oppose the venous blood pressure.

When choosing compression stockings, patients are educated to prefer compression stockings with graduated compression to non-graded ones. Patients with varicose veins involving the main axial superficial veins above and below the knee should choose thigh-length graduated compression stockings rather than knee-length ones. Stockings with moderate pressure (20-30 mmHg) are recommended for patients with varicose veins (C2 to C3), stockings with pressure around 30 to 40 mmHg for people with skin change or an ulcer (C4 to C6), and stockings with a pressure between 40 and 50 mmHg for patients with a recurrent ulcer as an adjuvant treatment to prevent ulcer recurrence \[10,11\].

At least 1-wk compression stocking therapy after EVLA is suggested because a long time (1-2 wk) of using compression therapy is better than a short-term (24-48 h) of application in terms of reducing postoperative pain at 1 wk and recovery for work \[11\]. Yet, a trial of compression therapy is unnecessary before endovenous thermal ablation\[9\] as there is no strong evidence to support compression stockings in the cure of varicose veins C1-C4\[9\]. Limitations to the use of compression stockings include arterial insufficiency, application difficulty, and patient preferences.

**MEDICAL THERAPY**

Venoactive drugs are prescribed for symptomatic patients with varicose veins, ankle swelling, and venous ulcers to improve venous tone and capillary permeability. The commonly used drugs are spooning, e.g., horse chestnut seed extract, the micronized purified flavonoid fraction (MPFF), and flavonoids\[12-14\]. Pentoxifylline is reported to target inflammatory cytokine release, leukocyte activation, and platelet aggregation at the microcirculatory level. The use of pentoxifylline or MPFF in combination with compression therapy may improve the closure of venous ulcers compared with compression and placebo\[13\]. A Cochrane meta-analysis shows that vasoactive drugs may relieve pain and swelling caused by chronic venous insufficiency, but their precise mechanism is not clear. Long-term studies of the safety and effectiveness of phlebotomists are warranted\[12-15\].
SURGICAL THERAPY

Historically, surgery with hig h ligation of saphenofemoral junction (SFJ) or saphenopopliteal junction with or without vein stripping (HL/S) has been the gold standard of care for varicose veins[1]. Specifically, following general or lumbar anesthesia, an incision is made at the groin or upper calf, the GSV is located and incised, the proximal end is ligated below the SFJ, a stripping wire with a probe is put into the GSV and advanced distally, and the proximal part of the GSV is tied to the wire and stripped. Recently, a growing number of research data do not consistently favor surgery as the standard treatment option due to postoperative complications, and the 2013 National Institute for Health and Care Excellence clinical guidelines recommend surgery as a third-line therapeutic option after EVLA or RFA and sclerotherapy[8,16-18].

HL/S of the GSV and their respective junctions are indicated when the saphenous veins themselves dilate greater than 1 cm in diameter. In a cohort study, Navarro et al[19] evaluated the relationship of GSV diameter measured in the thigh and calf to the clinical severity of reflux in 112 legs of 85 consecutive patients with SFJ and truncal GSV incompetence[19] and found that a GSV diameter of 5.5 mm or less predicted having no abnormal reflux, with a sensitivity of 78%, specificity of 87%, positive and negative predictive values of 78%, and accuracy of 82%[19].

The surgical outcome of HL/S is relatively satisfactory; HL/S is associated with higher anatomic closure rates at 30 d and 5 years than RFA and ultrasound-guided foam sclerotherapy (UGFS)[8,16]. HL/S has similar long-term saphenous vein closure rates with EVLA at 5 years[8,16-18]. However, the postoperative complications are DVT, bleeding, hematoma, wound infection, nerve injury, pain, and delayed return to normal activity. The injury of femoral arteries, such as ligation and or stripping of the femoral artery, occurred in the hands of inexperienced operators, which is underreported. Ligation alone is usually associated with a high recurrence rate of the varicose vein that may necessitate re-operation[20]. Stripping of the GSV below the knee or the SSV is not usually performed to avoid the risk of nerve injury.

AMBULATORY PHLEBECTOMY

Ambulatory phlebectomy (AP), also known as hook phlebectomy, mini-phlebectomy, microphlebectomy, or stab phlebectomy, is a minimally invasive procedure operated under local anesthesia as an outpatient procedure, and it can excise most varicose veins except the proximal long saphenous vein[21]. AP has a technically better outcome in terms of recurrence of GSV and SFJ reflux than UGFS in the long term. Specifically, a small stab wound or puncture is made to remove varicose veins. Administering a certain volume of saline around the target veins before making a stab may help retrieve a longer section of unwanted veins. AP is usually performed in conjunction with other procedures.

Notwithstanding, recurrence rates can be high if the junctional reflux is untreated[21]. The junctional reflux should be managed by HL/S or EVLT rather than simple AP[21]. Patients can walk right away after AP. The proportion of complications associated with AP such as localized thrombophlebitis and hemorrhage is much lower than that of HL/S. The postoperative complications are reduced dramatically after the application of broad compression pads over the wounds following AP.

CHIVA

CHIVA is ambulatory conservative hemodynamic management of varicose veins that preserves deliberately the saphenous vein and collaterals based on venous hemodynamics[22]. CHIVA is an office-based treatment for varicose veins performed under local anesthesia. The main advantages are the preservation of the saphenous vein, local anesthesia, low cost, low pain, and less bruising, nerve damage, and recurrence than stripping saphenectomy[23] (Figure 1). CHIVA seemed to have superior clinical benefits in long-term efficacy for treating varicose veins[24]. Practically, CHIVA procedure is most likely similar to AP. Patients can walk out of the theatre immediately after CHIVA surgery and go home following observing for a while.

However, the recent Cochrane review[25] included six randomized controlled trials (RCTs) with 1160 patients and compared CHIVA with RFA, vein stripping, and EVLT, respectively, for their effects. In terms of recurrence of varicose veins, there is little or no difference between CHIVA and stripping, RFA, or EVLT. In comparison with RFA or EVLT, CHIVA may cause more bruising and make little or no difference to rates of limb infection, superficial vein thrombosis, nerve injury, or hematoma. Three RCTs comparing CHIVA with vein stripping showed that CHIVA may reduce slightly nerve injury and hematoma in the legs, but make little or no difference to the side effects of limb infection, and superficial vein thrombosis or bruising[25]. One RCT comparing CHIVA with compression dressings in patients with venous ulcers shows uncertainty on whether CHIVA can reduce recurrence.
It is necessary to map and find the escape point (EP) of the veins before CHIVA. Most (82.3%) EPs are located below the knee, and 65.8% are located from the knee to midcalf. The diameter of tributary veins (TVs) near the EP is about 90% of that of the GSV. Thermal ablations of the below-knee varicose vein may damage the nerve[26].

**TRANSILLUMINATION POWERED PHLEBECTOMY**

Transilluminated powered phlebectomy (TIPP) is reported as a minimally invasive procedure that is often performed under spinal or general anesthesia for the treatment of varicose veins[27], and it was once considered cosmetic for veins less than 2.5 mm in diameter due to few incisions. However, TIPP has been associated with a higher incidence of hematoma, postoperative pain, and paresthesia[28] due to damage to tissue and nerve around the veins; it has not been proven to be superior to other procedures to remove varicose veins[27]. Aremu et al.[27] compared conventional stab avulsions to TIPP and found that recurrence at 52 wk in the TIPP group is higher than that in the stab avulsion group (21.2% vs 6.2%)[28].

TIPP cannot be performed for all the varicose veins, especially for truncal varicose veins. In combination with RFA, a more satisfactory outcome at a 1-year follow-up[29] can be achieved. Passman et al.[30] divided their patients into three groups to evaluate the effect of TIPP: Saphenous stripping-stab avulsion phlebectomy (STRIP-AP), combined saphenous vein stripping-TIPP (STRIP-TIPP), and combined EVLT-TIPP. The rate of complications was higher in procedures involving TIPP (STRIP-AP 5.6%, STRIP-TIPP 6.5%, and EVAB-TIPP 2.0%; P = NS), and more hematomas occurred in procedures involving TIPP (STRIP-AP 5.6%, STRIP-TIPP 16.3%, and EVAB-TIPP 6.9%; P < 0.05)[30].

**ENDOVENOUS THERMAL ABLATION THERAPY**

Endovenous thermal ablation (EVLA or RFA) is recommended as a first-line treatment and has substituted the surgical procedure to destroy the veins by heat and occlude the veins for symptomatic varicose veins[9,31,32].

EVLA was initially reported by Dr. Carlos Bone for the treatment of varicose veins at the International Union of Phlebology in 1999. The laser fiber is inserted into the target vein, a heat generator emits laser energy, and the thermal light emitting out of the fiber tip induces local thermal injury to the veins, leading to vein contraction, blood thrombosis, and venous fibrosis. EVTA with or without HL/S appeared to be a safe and effective treatment for patients with incompetent saphenous veins[33].

One systematic evidence review reported that the occlusion rates of the GSV and small saphenous vein within 6 mo after EVLA were all greater than 90%[20]. A study by Wallace et al.[34] showed that the SFJ anatomical success closure rate detected by DUS 5 years after treatment is similar between HL/S
A range of laser wavelengths can be used to achieve occlusion, and the radial fibers and lasers with high wavelengths (1470–1940 nm) are introduced for homogeneous damage of the vein wall to improve the efficacy and reduce the side effect of procedures [36]. The temperature produced by a 1470-nm laser with a radial probe is 120–140 °C (± 20 °C) [36], and less pain is noticed in the first week after the use of a 1470-nm wavelength fiber than a 940-nm fiber. At the 48-mo follow-up, the recurrence rate of treated veins followed by ultrasound was less with the 1470-nm wavelength laser than with 940-nm fibers (8.3% vs 15.9%, P = 0.017) [37]. Another RCT indicated that patients treated with the 1470-nm catheter had a higher occlusion rate than those with the 1920-nm system (94.7% vs 87.5%; P = 0.05) at 1-year follow-up. Patients treated with the 1920-nm EVLA catheter had less ecchymosis, induration, and analgesic use. However, a systematic review and meta-analysis show that commonly used EVLA parameters do not influence efficacy, no particular wavelength is superior to any other [20], and no statistically significant differences were found for wavelengths [short (810, 940, and 980 nm), long (1470, 1500, and 1920 nm)], high or low administered energy (≤ 50 J/cm and > 50 J/cm), or follow-up (≤ 1 year and > 1 year). The overall success rate of EVLA was 92% [38]. An RCT study by Malskat et al. [39] showed that treatment success and adverse event rates between a 1470-nm wavelength fiber and a 940-nm fiber for the treatment of varicose veins were similar [39].

The common complications after EVLA are bruising (24%-75%), thrombophlebitis (5%), superficial vein thrombosis, DVT, hematomas and ecchymoses, skin burn, pigmentation, nerve injury, recurrence, and retained fragment of catheter [40,41]. Arteriovenous fistula has been reported after perforator ablation. The risk of nerve lesions increases when the endovenous treatment is carried out on the lower leg. Recurrence can be treated with the second ablation, and the occlusion rate was 93.3% 1 year after the second ablation [42,43].

RFA

RFA is an ultrasonography-guided minimally invasive treatment that ablates the refluxing vein segment using thermal energy delivered through a radiofrequency catheter. RFA can be segmental procedures that induce heat to 120 °C. Ultrasonography is used to guide to insert a guidewire into the target vein, and an introducer sheath is advanced through the guidewire which will be pulled away followed by inserting the RFA catheter into the sheath into the target position.

A tumescent anesthetic solution is injected around GSV to reduce pain, provide good hemostasis, and prevent burn and nerve damage. After injection of a tumescent solution, the RF generator is then activated and the catheter is slowly pulled along the length of the vein. Compression therapy is used to reduce the risk of vein thrombosis, postoperative bruising, and tenderness. Patients are encouraged to walk immediately after RFA [44].

There is a difference among the RFA devices. F-Care (F Care Systems, Antwerp, Belgium) is a relatively new RFA technique for the treatment of venous insufficiency. The 30-d total occlusion rates in the F-Care and Closurefast groups were 96.2% and 98.1%, respectively (P = 0.3). The 1-year full occlusion rates in the F-Care and Closurefast groups were 71.7% and 90.6%, respectively (P = 0.013) [45]. The 3-RF trial is the first RCT of Venefit, radiofrequency induced thermal therapy (RFITT), and endovenous radiofrequency (EVRF) to compare outcomes of RFA devices. At 6 mo, complete GSV closure was significantly better after Venefit and RFITT treatment (100% and 98%, respectively) compared with EVRF treatment (79%, P < 0.001). However, clinical outcomes did not differ significantly at 1 year [46].

RFA is associated with a high satisfaction rate and quality of life score. Although operative time in RFA was significantly longer than that in surgery, recovery after RFA was significantly quicker than that after surgery in terms of returning to usual activity and work in 1 wk with fewer major adverse events. Complete obliteration of GSV was obtained in 98.2% of 135 patients (164 limbs) at a median follow-up of 11 mo [47]. RFA was shown to be non-inferior in terms of recurrence of CHIVA and HL/S 2 years after treatment. No differences in postoperative complications or pain were found among HL/S, RFA, and CHIVA [48].

COMPARISON OF RFA AND EVLA

EVLA and RFA seem to be the same safe and effective modalities in clinical efficacy in terms of occlusion rate, time to return to normal activity, and complications such as thrombophlebitis, hematoma, and recanalization [31,49,50]. A 10-year follow-up with duplex ultrasound for 240 patients treated with a 1470-nm diode laser with radial fibers found stable and valuable long-term results [36]. EVLA is the most cost-effective therapeutic option, followed by RFA, in patients with the incompetence of the GSV [8]. EVLA can manage almost all the varicose veins both above and below the knee; in contrast, RFA is used to ablate the truncal varicose vein above the knee, and cannot treat the varicose...
veins below the knee that can be managed by EVLA. Thus, RFA is usually performed in conjunction with other procedures such as HIPP to achieve a better outcome[29].

An RCT comparing the endovenous treatment of primary GSV in 159 patients using RFA or 810 nm EVLT showed complete occlusion (100%) by duplex ultrasound in both groups at 1 wk, and 97% for RFA and 96% for EVLT at 3 mo follow-up. No significant adverse event was observed. Even though RFA showed less pain, ecchymosis, and hematoma[30,51], EVLA and RFA demonstrated comparable outcomes in terms of venous occlusion rates and return to normal activities. Both radiofrequency-powered segmental ablation and EVLA using bare-tip fibers have similarly high GSV obliteration rates in the first 5 years, and the treatments are equally effective clinically and have similar minimal postoperative pain scores and short recovery times[32].

SCLEROTHERAPY

Sclerotherapy is a less invasive percutaneous approach to administering sclerosants into the target veins [52] that will be closed subsequently after immediate external pressure. Anesthesia is generally not required during sclerotherapy. Compression stockings or bandages should be applied immediately after sclerotherapy. Patients are encouraged to walk to reduce the complications of sclerotherapy.

Sclerotherapy is recommended to treat varicose tributaries or the incompetent saphenous vein[9] and is considered cosmetic for treatment of veins less than 2.5 mm in diameter and all other indications. As sclerotherapy alone has not been proven to be effective for the treatment of SFJ or saphenopopliteal junctions reflux, patients with reflux should be treated with EVLA or HL/S to reduce the risk of recurrence.

Currently available sclerosants include detergents (e.g., polidocanol and sodium morrhuate), osmotic agents, and chemical agents. No reliable evidence is available to support that one type of sclerosant is better than any other. Instead of using sclerosant as a liquid, foam sclerotherapy (FS) is performed using mixed sclerosant with air (usually 1:4) with or without UGFS, and it is used primarily or in conjunction with other procedures. The closure rate of veins with FS is higher (68%) than that with liquid sclerotherapy (17.5%) at 12 mo of follow-up[53]. UGFS is associated with faster recovery and less postoperative pain compared with EVLA and surgical stripping. The common complications are superficial venous thromboembolism, recurrence, hyperpigmentation, telangiectasia matting, etc. Patients often complain of nodular or linear hardness alone in the varicose veins with tenderness. DVT, tissue necrosis, or even arterial thrombosis has been observed after FS, especially with the use of liquid sodium morrhuate.

GSV recanalization was highest in the UGFS group (51%) during 1 year of follow-up[53]. A prospective RCT involving more than 580 legs compared four treatments: EVLA, RFA, UGFS, and surgical stripping for GSVs. UGFS was associated with a higher technical failure (16.3%) compared with other treatments (P < 0.001) at the 5-year follow-up. A total of 288 limbs of 233 patients were treated with UGFS, and the mean follow-up interval was 37.8 mo. Occlusion was achieved for 89.6% of the incompetent veins in two sessions of UGFS. The internal diameters of the treated veins were reduced to 66.9% at 3 mo and 32.7% at 12 mo. It is worthy to know that UGFS is unable to seal incompetent GSV segments completely and may be repeated several times in cases of recurrence[54].

MECHANOCHEMICAL ENDOVENOUS ABLATION

MOCA was conducted in 2010 using the ClariVein device. A wire tip is introduced into the targeted veins and rotated to abrade the intimal layer of the venous wall mechanically (3500 rpm), and a liquid sclerosant is simultaneously injected into the damaged venous wall below the catheter tip to seal the veins.

The MOCA is a non-thermal-non-tumescent option (NTNT) and appears to be of similar efficacy with stab avulsion with no potential risk of nerve damage.

A recent multi-center randomized study comparing MOCA with RFA for truncal vein reflux demonstrated that MOCA was significantly less painful than RFA (P = 0.003). There were no significant differences between MOCA and RFA for occlusion rates, clinical severity scores, time to return to normal activities, and adverse effects such as DVT and superficial thrombophlebitis[55].

The anatomical closure rate of MOCA is higher with 3% POL liquid than with 2% POL liquid at the 6-mo follow-up. A multicenter RCA study showed that the technical success rate at 6 mo was 69.8% in the 2%-group vs 78.0% in the 3%-group (P = 0.027). The overall closure rate was higher in GSVs < 5.9 mm than in GSVs > 5.9 mm (84.3% vs 59.5%, P < 0.001). Regardless of the concentration of sclerosant, the overall success rate of MOCA is lower than that of EVAL, RFA, or HL/S[55].
CAE

CAE is a novel endovascular NTNT ablation technique for treatment of incompetent truncal veins with n-butyl-2-cyanoacrylate (NBCA) glue[56-58]. Multiple studies have shown the effectiveness of CAE since its first use in 2013. Current available two techniques are the VenaSealTM Closure System and the VariCloseR vein sealing system[56]. A catheter is used to pull back segmentally in a former system or, continuously in the latter technique. NBCA glue is an adhesive that rapidly polymerizes during endovenous treatment to cause rapid occlusion of veins and initiate vein fibrosis.

In a review of 2910 patients (3220 veins) in 17 studies, 1981 patients received NBCA, 445 RF, and 484 EVLA. The mean follow-up was 12.3 mo (1-36 mo). Two-year occlusion rates were 93.7, 90.9, and 91.5% for NBCA, RFA, and EVLA, respectively[58]. CAE had higher anatomic closure rates at 30 d than EVLA[16]. Patients treated with CAE had less postoperative ecchymosis than those with RFA (P < 0.01). Pain during the procedure was comparable for both groups. Patients treated with NBCA had the fewest complications, e.g., bruising, phlebitis, and pain. NBCA is simple to administer, safe, and effective even without compression stockings[58].

However, complications of CAE treatment are phlebitis, cellulitis, and DVT. The adhesive is presumably not degraded and remains in the vein over many years. In rare instances, cyanoacrylate glue embolization can extravasate and cause chronic foreign body reactions necessitating surgical intervention[57,58]. A thread-like thrombus extension has been reported with the VenaSeal system, which resolved spontaneously without additional adjunctive treatment after 6 mo of follow-up. Occlusion of the treated vein is incomplete with recanalization in the peripheral region after CAE. In this case, USFS can be used to achieve the complete occlusion of the veins. MOCA and CAE appear promising but evidence of their effectiveness is needed[6].

CONCLUSION

EVLA is the most cost-effective therapeutic option, with RFA being a close second for the treatment of patients with varicose veins. Endovenous thermal ablation (EVLA or RFA) is recommended as a first-line treatment for varicose veins and has substituted the high ligation of saphenofemoral junctional reflux and stripping of varicose veins. The 2013 National Institute for Health and Care Excellence clinical guidelines recommend surgery as a third-line therapeutic option after EVLA or RFA and sclerotherapy. In terms of recurrence of varicose veins, there is little or no difference between CHIVA and EVLA, RFA, or stripping. Ultrasound-guided FS is associated with a high recurrence rate and can be used in conjunction with other procedures. Currently, no strong evidence is available to show whether MOCA or cyanoacrylate embolization is similar or superior to any other procedures in the treatment of varicose veins.

FOOTNOTES

Author contributions: Qian SY and Gao RD contributed equally to this manuscript by composing the manuscript; Ren SY searched and studied the references and designed, wrote, revised, and submitted the manuscript; Wang HH and Liu YS discussed the manuscript; all authors have read and approved the final manuscript.

Conflict-of-interest statement: No conflict of interest exists.

Open-Access: This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: https://creativecommons.org/Licenses/by-nc/4.0/

Country/Territory of origin: China

ORCID number: Rong-Ding Gao 0000-0002-4516-1575; Song-Yi Qian 0000-0001-9258-5621; Hai-Hong Wang 0000-0002-7126-7138; Yong-Sheng Liu 0000-0002-9560-5875; Shi-Yan Ren 0000-0003-4528-2307.

S-Editor: Fan JR
L-Editor: Wang TQ
P-Editor: Fan JR
REFERENCES


20. MSAC. Endovenous laser therapy (ELT) for varicose veins. Assessment report. MSAC Application 1113 Canberra, ACT: MSAC; March. 2008

21. MSAC. Consultation Decision Analytic Protocol (DAP) to guide the assessment of radiofrequency ablation for the treatment of varicose veins due to chronic venous insufficiency. MSAC Application 1166 Canberra, ACT: MSAC; November 11, 2011


Chan SS, Tang TY, Chong TT, Choke EC, Tay HT. Retrograde technique for great saphenous vein ablation using the VenaSeal™ closure system - Ideal approach for deep seated or small below the knee refluxing truncal veins. Phlebology 2020; 35: 102-109 [PMID: 31132940 DOI: 10.1177/0268355519853412]

