International Journal of Surgery and Surgical Research
www.surgeryjournals.net
Online ISSN: 2664-9179
Received: 02-02-2026, Accepted: 03-03-2026, Published: 19-03-2026
Volume 6, Issue 1, 2024, Page No. 14-19

Ozone Sclerobliteration Vs polidocanol sclerotherapy in Ceap C1 venous disease

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Abstract
Objective: To perform a comprehensive evaluation of sclerotherapy outcomes in patients with reticular varicose veins (C1 according to CEAP) using both objective digital analysis and subjective patient assessment, comparing the efficacy and tolerability of ozone sclerobliteration and the traditional polidocanol method.
Materials and Methods: This prospective comparative study included 70 patients (two equal groups of 35 each) with chronic venous disease classified as C1 (telangiectasias and reticular veins). Group 1 underwent ozone sclerobliteration using an ozone-oxygen mixture (ozone concentration 70 µg/mL), while Group 2 received conventional microsclerotherapy with 0.5% polidocanol. The objective dynamics of the vascular network were assessed using the author-developed digital photo-analysis software VesselAnalyzerPRO, which provides automatic vein segmentation and calculation of the affected area before treatment and 30 days after sclerotherapy. At the 30-day follow-up, patients were also surveyed using a dedicated questionnaire that included five parameters for tolerability and one rating for the cosmetic outcome.
Results: Both techniques demonstrated comparable efficacy: the mean reduction in visible vein area was 78.4 ± 6.2% in the ozone group and 76.9 ± 6.8% in the polidocanol group ($p > 0.05$). Differences in subjective tolerability were minimal: the mean total tolerability score was 4.34 ± 0.96 in the ozone group and 4.49 ± 1.00 in the polidocanol group ($p > 0.05$), indicating equally high patient comfort. The cosmetic outcome, according to patient self-assessment, was significantly higher in the ozone group (2.57 ± 0.50 vs. 2.20 ± 0.62 points, $p < 0.001$). This difference was attributed to side effects observed only after polidocanol sclerotherapy: 7 patients (20%) developed transient hyperpigmentation and/or matting, while no such complications occurred after ozone sclerobliteration. The use of VesselAnalyzerPRO provided reproducible quantitative indicators and enabled an objective comparison of cosmetic outcomes.
Conclusion: Ozone sclerobliteration is not inferior to polidocanol in terms of efficacy for eliminating the vascular network and can be considered a safe alternative for patients with telangiectasias (C1 CEAP). The absence of pigmentation and matting, combined with similar levels of patient comfort, confirms the high safety and tolerability profile of ozone therapy. The implementation of VesselAnalyzerPRO demonstrated the value of an integrated assessment approach that combines objective quantification of the cosmetic effect with patient feedback.

Keywords: Reticular varicose veins, sclerotherapy, ozone, polidocanol, VesselAnalyzerPRO, quantitative analysis, computer vision.

Introduction

Chronic venous diseases (CVD) of the lower extremities are among the most prevalent vascular pathologies, affecting up to 40% of adults. In one-third of patients, CVD manifests in cosmetically significant forms such as telangiectasias and reticular veins (classified as C1 by the CEAP classification). While these changes are not life-threatening, they can significantly diminish quality of life, particularly in women.

Conventional microsclerotherapy using detergent sclerosants (e.g., polidocanol) is recognized as the treatment of choice for C1 disease. However, the injection of a chemical agent is often accompanied by side effects such as burning sensations, skin hyperpigmentation, the appearance of new fine capillaries (telangiectatic matting), and local inflammatory reactions [7].

In the search for a method without these drawbacks, ozone sclerobliteration emerged—a technique involving the intraluminal injection of a medical ozone-oxygen gas mixture into pathologically altered venules. The use of ozone for treating telangiectasias is approved by official Russian methodological guidelines [1, 2] and is successfully employed in several phlebology and cosmetic centers. However, from a scientific perspective, it has not been rigorously investigated until now. Clinically, ozone causes vascular injury leading to subsequent thrombosis and fibrosis, but without the introduction of foreign chemical substances.

The challenge of objectively quantifying treatment efficacy remains pertinent. Until recently, sclerotherapy outcomes were assessed visually (through physician examination or comparison of before-and-after photographs), which is subjective and reduces the reliability of studies [3]. The software package VesselAnalyzerPRO (certificate № 2025687611 dated 15.10.2025), developed by the authors, aims to address this limitation. The program utilizes computer vision methods for high-precision measurement of the vascular network area and other parameters, allowing for objective comparison of treatment results [4].

Objective of the Study: To compare the efficacy of ozone sclerobliteration and traditional sclerotherapy with

polidocanol in patients with telangiectasias and reticular veins (C1 CEAP), and to evaluate the potential of the VesselAnalyzerPRO software for objective quantitative analysis of the cosmetic effect. A secondary objective was to incorporate subjective patient opinions on procedure tolerability and the cosmetic result.

Materials and methods

Patient Population: The study included 70 patients with chronic venous disease of the lower limbs, class C1 (multiple telangiectasias and reticular veins) (C1sEpAsPn LI). The cohort comprised 58 women (82.8%) and 12 men (17.2%) aged 28 to 54 years (mean 39 ± 7 years). All patients complained of visible "spider veins" on their legs and sought cosmetic improvement.

Inclusion Criteria

- Presence of multiple telangiectasias and reticular veins with a diameter of 0.5–3 mm.
- Absence of pathological venous reflux in the major truncal veins (confirmed by duplex ultrasound scanning).
- Patient's informed consent for treatment.

Exclusion Criteria

- Varicose veins C2 and above according to CEAP.
- History of deep or superficial vein thrombosis.
- Hemostasis disorders.
- Pregnancy or lactation.
- Allergy to ozone or polidocanol.
- Severe concomitant diseases.

Treatment Methods: Patients were randomized into two equal groups of 35. Group I (ozone) received intravascular injections of an ozone-oxygen mixture with an ozone concentration of 70 µg/mL, generated by a medical ozone generator (Medozon, Germany) immediately before the procedure. Injections were performed using a fine needle (28–30G) into the dilated venules under visual control; the volume per injection was 0.5–2 mL, with a total volume of up to 20 mL of the gas mixture per session. Group II (polidocanol) underwent microsclerotherapy with a 0.5% polidocanol solution; the injection technique was identical (1–3 mL per injection, up to a total of 10 mL of sclerosant per session).

All procedures were performed on an outpatient basis. Post-procedure, patients wore class II compression stockings continuously for the first 72 hours, followed by daytime use for two weeks. A 30-minute walk immediately after the procedure was recommended. Typically, one session was sufficient; for extensive vascular networks, 2–3 sessions were performed at 7–10 day intervals.

Digital Image Analysis: For objective efficacy assessment, standardized photographs of the affected areas were taken before treatment and 30 days post-treatment. Images were captured under standard diffused lighting (≈5500 K) from a distance of ~60 cm, including a scale ruler within the frame. A smartphone camera with consistent settings was used, and images were saved in high-quality JPEG format. Analysis was performed using the VesselAnalyzerPRO software (version 2.1), developed by the authors. The program automatically segments the vascular network in the photograph and calculates quantitative parameters: total visible vessel area (S, mm $^{[2]}$), number of vascular fragments (N), mean vessel diameter (D, mm), and the relative change in vascular network area (ΔS, %). The software suite allows batch loading of image series, scale calibration, adaptive segmentation with artifact filtering, statistical analysis (t-test, ANOVA, correlation), and report generation with tables and graphs. In this study, 140 pairs of images (2 per patient for 70 patients) were analyzed using the program; the resulting data were exported and further processed in IBM SPSS Statistics v28.

Assessment of Tolerability and Outcomes: Thirty days after sclerotherapy, patients completed an author-developed questionnaire to subjectively assess procedure tolerability and the cosmetic result. The questionnaire included 5 items related to tolerability (pain/burning during injection, systemic reactions, subjective perception of procedure duration, local post-procedural reactions, need for additional medication) and 1 item for evaluating the cosmetic effect. Each of items 1–5 was scored from 0 (no symptom) to 3 (severe). The sum of these five scores (range 0–15) served as an integrated tolerability score (lower score indicates better tolerability). The cosmetic result was rated on a scale from -1 (worse than baseline) to 3 (excellent).

Statistical Analysis: Quantitative data are presented as mean ± standard deviation (M ± SD). Normality of distribution was checked using the Shapiro–Wilk test. Student's t-test was used for comparing means (paired t-test for before-and-after comparisons within groups, and unpaired t-test for between-group comparisons). Differences were considered statistically significant at $p < 0.05$.

Results

At baseline, the groups showed no statistically significant differences in key characteristics. The mean vascular network area was 112.3 ± 17.9 mm $^{[2]}$ in the ozone group and 110.8 ± 19.4 mm $^{[2]}$ in the polidocanol group ($p > 0.05$). The groups were also comparable in terms of sex, age, number of vascular fragments per image, and other parameters; the mean diameter of reticular veins before treatment was ≈1.1 mm in both groups.

At 30 days post-treatment, clear positive dynamics were observed in all cases (Table 1).

Table 1: Comparison of Quantitative Parameters Obtained from VesselAnalyzerPRO (M ± SD)

Parameter	Group I (Ozone) Before Treatment	Group I (Ozone) After 30 Days	Group II (Polidocanol) Before Treatment	Group II (Polidocanol) After 30 Days	p (between groups at 30 days)
Total Vessel Area, mm $^{[2]}$	112.3 ± 17.9	24.2 ± 8.5	110.8 ± 19.4	25.7 ± 9.2	> 0.05
Mean Diameter, mm	1.1 ± 0.3	0.5 ± 0.2	1.0 ± 0.4	0.6 ± 0.2	> 0.05
Number of Vessel Segments	30 ± 8	9 ± 3	28 ± 9	10 ± 4	> 0.05
Reduction in Area, %	--	78.4 ± 6.2%	--	76.9 ± 6.8%	> 0.05

Note: Within-group differences ("before / after") were statistically significant ($p < 0.001$).

All quantitative parameters of the vascular network significantly decreased compared to baseline ($p < 0.001$ in each group). The visible vessel area was reduced by more than 75%: to ~24 mm $^{[2]}$ in the ozone group and ~26 mm $^{[2]}$ in the polidocanol group. The relative reduction in vascular area was 78.4 ± 6.2% with ozone and 76.9 ± 6.8% with polidocanol; the difference between groups was not significant ($p > 0.05$). The mean vein diameter decreased from ~1.0 mm to ~0.5 mm, and the number of vessel segments decreased from ~30 to ~9–10 ($p < 0.001$ vs. baseline in both groups); no between-group differences were found.

Clinically, similar improvement was observed in both groups: telangiectasias began to fade by the second week, and by day 15, the vascular network was barely noticeable in most patients. By day 30 post-sclerotherapy, only isolated, faint vessels remained (primarily in areas with the densest initial vasculature). Digital analysis confirmed the elimination of >75% of the vascular network, which correlated well with the visual assessment of the effect by both the physician and the patient.

Comments on Figures

1. **Figure 1.** Appearance of an area with reticular varicose veins before treatment. An extensive bluish-purple vascular network is visible, with venule diameters of 1–2 mm.
2. **Figure 2.** The same area 30 days after ozone sclerobliteration. A marked reduction in the number of visible vessels and uniform lightening of the skin are noted.
3. **Figure 3.** Interface of the *VesselAnalyzerPRO* software: automatic segmentation of venous structures, a quantitative table of parameters (area mm $^{[2]}$, diameter, ΔS %), and a dynamics graph.

Both techniques were generally safe and well-tolerated; no serious adverse reactions were observed. However, the side effect profiles differed. In Group I (ozone), there were no cases of hyperpigmentation or matting; 2 patients (5.7%) developed minor hematomas at injection sites, which resolved within 7–10 days. In Group II (polidocanol), 4 patients (11.4%) had minor hematomas, 3 (8.6%) developed mild transient skin hyperpigmentation, and another 3 (8.6%) developed matting (the appearance of numerous fine capillaries in the sclerosed area). No cases of skin necrosis, ulcers, or thrombosis were recorded. All adverse events were reversible and had completely regressed by the end of the 30-day follow-up period without specific treatment.

Patients reported that ozone sclerobliteration was not more difficult to tolerate than traditional sclerotherapy. Many in Group I noted less pain and the virtual absence of the burning sensation typical of detergent sclerosants during injection. However, 4 patients (13%) in Group I experienced a brief (1–2 min) episode of dry cough immediately after ozone injection, which resolved spontaneously.

At 30 days, subjective satisfaction with the result was high in both groups. Mean scores for individual tolerability items were similar for ozone and polidocanol: pain 1.24 vs. 1.49; systemic reactions 0.46 vs. 0.46; procedure duration ≈1 vs. ≈1; local reactions ≈1 vs. ≈1; additional medication 0.43 vs. 0.43 ($p > 0.05$ for all parameters). The mean total tolerability score was 4.34 ± 0.96 in Group I and 4.49 ± 1.00 in Group II ($p > 0.05$), corresponding to an "excellent" level in both groups. However, patients in the ozone group rated the cosmetic effect significantly higher: 2.57 ± 0.50 vs. 2.20 ± 0.62 ($p < 0.01$). This difference was attributed to the cosmetic side effects (pigmentation, matting) observed in the polidocanol group.

Discussion

In terms of efficacy for eliminating reticular varicose veins, ozone sclerobliteration is not inferior to microsclerotherapy with polidocanol. The mean reduction in vessel area (~78% for ozone vs. ~77% for polidocanol) aligns with literature data for standard sclerotherapy (≈75–80%) [5, 6].

The main difference between ozone and chemical sclerobliteration lies in the mechanism of action. Detergent sclerosants (polidocanol, sodium tetradecyl sulfate) cause endothelial destruction through chemical protein denaturation, followed by aseptic inflammation and vessel obliteration. While effective, this process carries a risk of side effects. Hyperpigmentation after sclerotherapy of small veins is reported in 10–30% of cases, and matting in 15–24%, which is consistent with our findings (matting in ~8.6% with polidocanol) [7]. The presence of pigmentation and matting in Group II patients led to a lower cosmetic outcome score. Furthermore, detergent agents often cause burning during injection, leading to patient discomfort; our data support this (pain/burning scores were higher in Group II, although the difference was not statistically significant). Thus, in terms of tolerability, ozone sclerobliteration is at least non-inferior to the traditional method, and based on subjective sensations, it may even be somewhat superior, providing greater comfort.

Ozone sclerobliteration, in contrast, does not involve aggressive chemicals. Its action is attributed to a combination of mechanical and oxidative endothelial damage. At low doses, ozone possesses angioprotective and anti-inflammatory properties: it improves microcirculation, reduces levels of pro-inflammatory cytokines, and induces an adaptive antioxidant response without damaging healthy cells [8, 9, 10]. It also modulates the release of growth factors and signaling pathways, stimulating neoangiogenesis and vascular remodeling while simultaneously reducing chronic inflammation [11, 12, 13]. Due to this combination of direct sclerosing action with a mild biomodulatory effect, ozone sclerotherapy may enhance tissue repair. This was reflected in the absence of cosmetic complications (pigmentation, matting) in the ozone group, unlike the polidocanol group.

A key feature of our study was the use of the VesselAnalyzerPRO system to objectify results. Traditionally, sclerotherapy efficacy is assessed subjectively—based on the physician's impression during examination or comparison of photographs—which fails to provide reproducible quantitative criteria. In 2006, Rocha *et al*. first demonstrated the feasibility of quantitative analysis of photographs after sclerotherapy [3]. Nearly 20 years later, Bertanha *et al*. (2023) confirmed the value of automated analysis for telangiectasias, showing a high correlation with clinical efficacy [4]. Our software employs modern computer vision algorithms for accurate segmentation and measurement of vascular structures, minimizing subjectivity in cosmetic outcome assessment: repeated analysis of the same images yielded a discrepancy of no more than 1–2%. Moreover, we found a high concordance between objective and subjective outcomes: the Pearson correlation coefficient between the percentage reduction in vascular network area

(from the software) and the patient's cosmetic outcome score was r = 0.86 ($p < 0.001$). In other words, patients perceived improvement proportionally to what the software recorded. Similar findings have been reported by other authors [14].

A comprehensive (objective + subjective) evaluation of outcomes allows for a more complete characterization of treatment success. In our study, both aspects—digital and questionnaire—showed consistent improvement: the software documented a >75% reduction in visible veins, and patients rated the cosmetic effect as "good" to "excellent" on average. Such a dual approach captures nuances: objectively incomplete vessel elimination might still be associated with high patient satisfaction if the residual venules are inconspicuous; conversely, a good digital result accompanied by patient dissatisfaction could indicate unrealistic expectations or complications (e.g., pigmentation). Thus, parallel assessment by both the physician (via objective tools) and the patient ensures a comprehensive understanding of treatment effectiveness. It is noteworthy that in modern phlebology, increasing attention is paid to patient-reported outcomes—subjective measures like satisfaction and quality of life. For instance, Pasek *et al*. (2023) showed that in patients with venous ulcers, local ozone therapy not only accelerated healing but also significantly improved quality of life [15]. In less severe pathology (telangiectasias), patient satisfaction is a key success criterion, as the treatment goal is aesthetic. Our work demonstrated that ozone sclerobliteration provides a cosmetic result in the eyes of patients that is comparable to the "gold standard" (polidocanol), while avoiding cosmetic complications. The combination of digital analysis and a patient questionnaire convincingly demonstrated this. We believe that the adoption of such questionnaires and digital analysis methods for standardizing outcome assessment in aesthetic phlebology is promising.

Our observations reflect the global trend of searching for optimal methods to eliminate spider veins with minimal side effects. Besides sclerotherapy, laser and combined technologies are evolving (e.g., the CLaCS method, combining a transcutaneous laser with cooling and sclerotherapy) [Ianoși *et al*., 2020; Fonseca *et al*., 2023; Miyake *et al*., 2020] [5, 16, 17].

Our study is the first to directly compare a chemical and a non-chemical method of sclerobliteration. It was shown that ozone is not inferior to polidocanol in efficacy, while its safety profile is superior (no persistent hyperpigmentation or matting). Moreover, a single session of ozone sclerobliteration was sufficient for most patients, whereas some combined methods (e.g., CLaCS) may require 2–3 procedures for an optimal effect. Thus, ozone represents a promising alternative, particularly for patients with intolerance to standard sclerosants or those preferring a more "natural" approach [18].

The implementation of digital image analysis (VesselAnalyzerPRO) opens new avenues for objective evaluation of treatment results. Furthermore, such objectification enhances the physician-patient interaction: by providing patients with a quantitative report on progress (e.g., "the vascular network area decreased by 78%"), the physician increases trust and satisfaction with the treatment.

Our data support recommending ozone sclerobliteration as a modern, safe alternative to traditional sclerotherapy for telangiectasias. This is particularly relevant for patients who have experienced complications from chemical sclerotherapy (pigmentation, matting) or who prefer to avoid synthetic agents. Ozone is an inexpensive gas generated on-site; with the necessary equipment, the procedure is technically simple. Ozone therapy is already used in dermatology and surgery, and its integration into phlebology seems logical [9, 10, 19]. Future research perspectives include expanding the sample size and extending the follow-up period (to 6–12 months) to assess the durability of the cosmetic effect, as well as investigating the combination of ozone with other methods (e.g., transcutaneous laser) to enhance outcomes [20].

Fig 1: Appearance of an area with reticular varicose veins before treatment. An extensive bluish-purple vascular network is visible, with venule diameters of 1–2 mm.

Fig 2: The same area 30 days after ozone sclerobliteration. A marked reduction in the number of visible vessels and uniform lightening of the skin are noted.

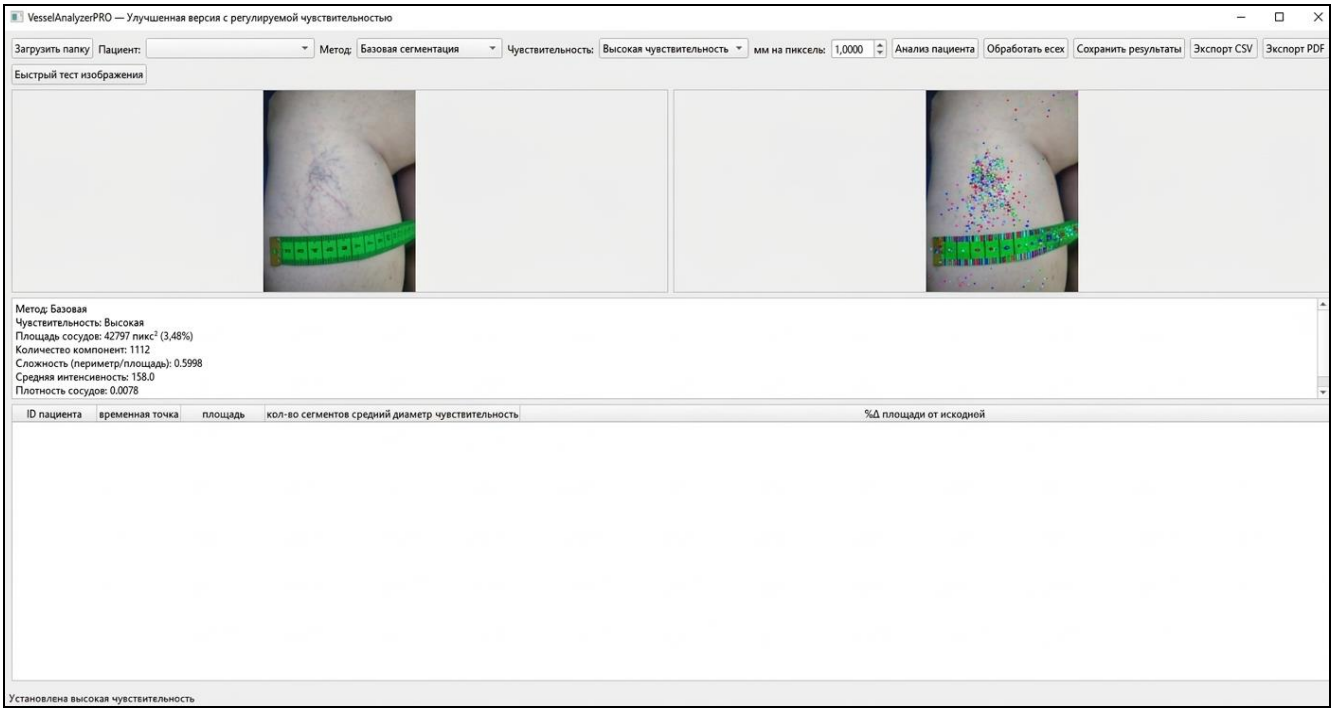

Fig 3: Interface of the *VesselAnalyzerPRO* software: automatic segmentation of venous structures, a quantitative table of parameters (area mm², diameter, ΔS %), and a dynamics graph.

Conclusion

- **Efficacy:** Ozone sclerobliteration for reticular varicose veins (C1 CEAP) achieves a significant reduction in vascular network area (~78%) and is non-inferior to conventional microsclerotherapy with 0.5% polidocanol (~77%, $p > 0.05$) [6, 21].

- **Safety and Tolerability:** Ozone sclerobliteration is characterized by a lower incidence of side effects compared to polidocanol. No cases of hyperpigmentation or matting occurred in the ozone group (vs. ~8.6% each in the polidocanol group), confirming the high safety profile and good tolerability of the ozone technique (non-inferior to the traditional method). The pain reaction during ozone injection was also less pronounced than with the detergent sclerosant.

- **Objectification of Results:** The use of the VesselAnalyzerPRO software enabled objective quantitative assessment of the cosmetic effect, eliminating the subjectivity of visual evaluation. Automatic calculation of the vascular network area and the percentage of its reduction allows for comparison of the effectiveness of different methods, facilitates multicenter studies with unified criteria, and enables the creation of large patient registries, thereby enhancing the level of evidence [22]. The calculated percentage of vascular network reduction showed a high correlation with the clinical outcome assessment (including patient evaluation) ($r = 0.86$; $p < 0.001$) [3, 4, 14].

- **Standardization:** The adoption of digital image analysis systems creates prerequisites for standardizing research and building a more robust evidence base in aesthetic phlebology. Objective criteria (e.g., the percentage of telangiectasia elimination) can serve as unified efficacy endpoints when comparing different methods, including in multicenter trials.

- **Practical Significance:** Ozone sclerobliteration represents a modern, physiologically based alternative to traditional chemical sclerotherapy for telangiectasias and reticular veins (C1 CEAP). It provides comparable cosmetic results with a more favorable safety profile, making this method an attractive addition to the armamentarium of aesthetic vein medicine. The use of ozone is particularly suitable for patients with intolerance or inadequate response to standard sclerosants, as well as for those wishing to avoid the injection of chemical agents [8–12, 19].

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