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A systematic review and meta-analysis of comparative studies comparing nonthermal versus thermal endovenous ablation in superficial venous incompetence

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ABSTRACT

Objective: Endovenous thermal ablation (TA) offers an effective initial treatment option for superficial venous incompetence of the lower limb. These techniques offer lower complication rates with similar efficacy to traditional open surgery. In recent years, nonthermal ablation (NTA) in the form of mechanochemical ablation and cyanoacrylate vein ablation has been suggested to further reduce perioperative morbidity. This study aimed to compare the use of both thermal and nonthermal endovenous ablative techniques in the management of superficial venous incompetence.

Methods: A search of online databases including MEDLINE, Embase, Cumulative Index to Nursing and Allied Health Literature, and Cochrane database was last performed in January 2019. Comparative studies comparing NTA with TA were included. The primary outcome was technical success. Secondary outcomes included operative pain, complications, modification of disease severity, and quality of life.

Results: Six studies describing the outcomes of 1236 participants and 1256 truncal ablations were included for analysis. Follow-up ranged from 6 weeks to 36 months. With regard to overall technical success, 458 of 483 (94.8%) receiving NTA and 521 of 553 (94.2%) undergoing TA had successful truncal ablation on follow-up ultrasound imaging at the study end point (pooled risk ratio, 1.01; 95% confidence interval [CI], 0.99-1.04). Subgroup analysis identified no difference in success between groups during immediate, 6-month, 12-month, or >12-month follow-up periods. Postprocedural pain was generally lower in those undergoing NTA with a mean difference of −18.11 (95% CI, −36.7 to 0.48). Techniques experienced significantly lower rates of ecchymosis (risk ratio, 0.43; 95% CI, 0.23-0.78), with no difference identified with regard to rates of paresthesia, phlebitis, and skin pigmentation. Further assessment of quality of life (mean difference, −0.27; 95% CI, −0.57 to 0.04) and Venous Clinical Severity Score (−0.52; 95% CI, −1.05 to 0.01) revealed no difference between groups. Included data were deemed of moderate methodologic quality.

Conclusions: Nonthermal techniques are as effective as standard TA in the first year and, in some studies, may be associated with less procedural pain. These data suggest that NTA offers an alternative and safe means to treat superficial venous disease. There is, however, a need for further powered trials with larger numbers of patients and longer follow-up to definitively examine this hypothesis. (J Vasc Surg: Venous and Lym Dis 2019;7:902-13.)

Keywords: Thermal; Nonthermal; Endovenous ablation; Varicose veins

Chronic venous insufficiency represents a significant health care burden affecting up to 30% of the general population.[1] In recent years, endovenous thermal ablation (TA) has emerged as a reliable alternative to traditional open approaches in the treatment of superficial venous reflux.[2-5]

Open surgery for great saphenous vein (GSV) incompetence may frequently be associated with significant early morbidity, including ecchymosis, hematoma, and perioperative pain.[3] Endothermal modalities in the form of endovenous laser ablation (EVLA) and radiofrequency ablation (RFA) offer effective truncal ablation with lower rates of morbidity[4-6] and are now widely recommended as first-line therapy.[2]

These thermal techniques use heat transfer to ablate incompetent venous trunks, with local infiltration of tumescent anesthesia used to protect surrounding structures from heating injury, to induce venous compression, and to limit procedural pain. Despite this, thermal injury may increase the rates of periprocedural pain, skin burns, and nerve injury.[7,8]

Nonthermal techniques including mechanochemical ablation (MOCA; ClariVein [Vascular Insights, Madison, Conn]) and cyanoacrylate vein ablation (CAVA; VenaSeal [Medtronic, Santa Rosa, Calif] and VariClose [Biolas, Ankara,

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Turkey]) have been developed with a view to removing thermal injury risk.[9,10] These techniques preclude the risk of nerve damage, whereas cyanoacrylate closure obviates the need for postinterventional compression stockings.[11] To date, a number of randomized and observational trials[12-17] have examined the merits of these nonthermal approaches compared with thermal venous ablation. Meta-analysis data comparing nonthermal ablation (NTA) and TA are yet to be established.

This meta-analysis and systematic review of comparative trials aimed to assess the efficacy of endovenous nonthermal and thermal ablative procedures in the management of lower limb superficial venous incompetence.

METHODS

Statement of design

This meta-analysis and systematic review was carried out in accordance with guidance provided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (http://www.prisma-statement.org/).

Study eligibility

All studies comparing endovenous thermal and nonthermal techniques for lower limb superficial venous ablation were included. Thermal approaches included EVLA and RFA; nonthermal techniques included cyanoacrylate closure and mechanochemical ablative techniques. Studies examining both GSV and small saphenous vein (SSV) incompetence were considered, and eligible studies were required to report at least one of the defined study end points. No search limitation was set for publication date or status of an article.

Population, intervention, comparator, and outcome

Population. Patients with either GSV or SSV incompetence undergoing endovenous intervention were included.

Intervention. Nonthermal superficial venous ablative techniques included MOCA and CAVA (NTA).

Control. The comparator was thermal superficial venous ablation (TA).

Primary outcomes. Overall technical procedural success was determined by follow-up ultrasound examination at the study end point. Subgroup analysis examined technical success as determined by ultrasound examination at various time points from the index procedure. These included immediate (up to 1 month) and up to and including 6-, 12-, and >12-month assessments. Where multiple assessments were undertaken, the latest assessment in any time frame was included for analysis.

Secondary outcomes.

- Procedural pain: reported immediately after the procedure on a numeric scale (0-10) or by means of a visual analog scale
- Periprocedural complications
  - Minor: ecchymosis or hematoma, paresthesia, phlebitis, pigmentation, or skin burns
  - Major: deep venous thrombosis (DVT)
- Quality of life at study end point assessed by the Aberdeen Varicose Vein Questionnaire (AVVQ)[18]
- Modification of disease severity at study end point by the Venous Clinical Severity Score (VCSS)[19]

Search methodology

The Cochrane Central Register of Controlled Trials, MEDLINE through PubMed, Embase, and Cumulative Index to Nursing and Allied Health Literature were last systematically searched for relevant articles in January 2019. We searched PubMed using the following MeSH words: "varicose veins," "saphenous vein," "VenaSeal," "cyanoacrylate," "mechanochemical," "endovenous ablation," "ClariVein," "radiofrequency ablation," "endovenous laser ablation," "comparison," and "randomized controlled trials." Other databases were searched in a similar fashion. All applicable abstracts were assessed, and full texts of relevant articles were assessed completely. Bibliographies of full texts were cross-referenced for further relevant studies.

Data collection

Data were assessed by two independent reviewers (A.H., T.A.). Any disagreements were discussed and resolved in conjunction with the senior author (S.A.). Study authors were contacted to obtain the full data where needed. When this was unsuccessful, data were reported per the original publication or statistical methods were employed to extrapolate the mean and standard deviation from median and interquartile ranges.[20,21]

Data management

Extracted data were compiled and analyzed using the Review Manager version 5.3.5.[22] Funnel plots were used to assess for publication bias. Comparative data were displayed as pooled risk ratios (RRs), and these were calculated using the random-effects model of Dersimonian and Laird.[23] Heterogeneity was established using the Cochran Q statistic, and a P value $<.05$ was considered statistically significant. Continuous variables (pain, VCSS, quality of life) were analyzed using the mean and standard deviation. Risk of bias and confounding factors were assessed using the Downs and Black quality assessment tool for both randomized and nonrandomized studies.[24] Per-protocol data were used where available.

RESULTS

Study selection

An initial search identified 313 abstracts for review. After the application of inclusion and exclusion criteria, 13 full-text articles were assessed, yielding 6 comparative trials for analysis. Excluded studies were protocols for

proposed trials,[25-27] with five articles[28-32] providing preliminary results of included trials. Outcome data from preliminary results were extracted for meta-analysis where not available in included articles. The study selection process is summarized in Fig 1.

Study characteristics and description

All studies compared nonthermal and thermal endovenous ablative techniques; six comparative studies were included for meta-analysis. Publication dates ranged from 2013 to 2018. Three studies[14,15,17] compared MOCA with endothermal ablative techniques, whereas three[12,13,16] examined the merits of CAVA in comparison with EVLA[12,16] and RFA.[13] All ablations were performed under local anesthesia save for one study, which did not report mode of anesthesia.[12] All laser ablations were performed at a standard wavelength of 1470 nm.[12,16,17] The characteristics of included trials are summarized in Tables I and II.

Risk of bias

The risk of bias and methodologic scores for included studies are summarized in Table III using the Downs and Black quality assessment tool.[24] Four studies[13-16] were deemed of satisfactory quality with a mean Downs and Black score of 20 across all studies. However, a majority of included studies[12,15-17] were weakened by their nonrandomized approach assessing small cohorts of patients. Of note, two studies[13,14] reported industry support.

Participants

Included studies described the outcomes of 1236 participants undergoing 1256 truncal ablations. Of these, 590 underwent NTA, which comprised 412 CAVA and 178 MOCA procedures; another 666 patients underwent TA, comprising 281 RFA and 385 EVLA procedures. All patients had ultrasound-confirmed GSV, SSV, or dual saphenous incompetence. Further demographic, follow-up, and inclusion criteria are reported in Tables I and II.

Effects of interventions

Technical success. A total of five studies[12-14,16,17] examined the technical success outcomes for both NTA and TA. These articles provided the outcomes of 1060 truncal ablations for meta-analysis. With regard to overall technical success, 458 of 483 (94.8%) receiving NTA and 521 of

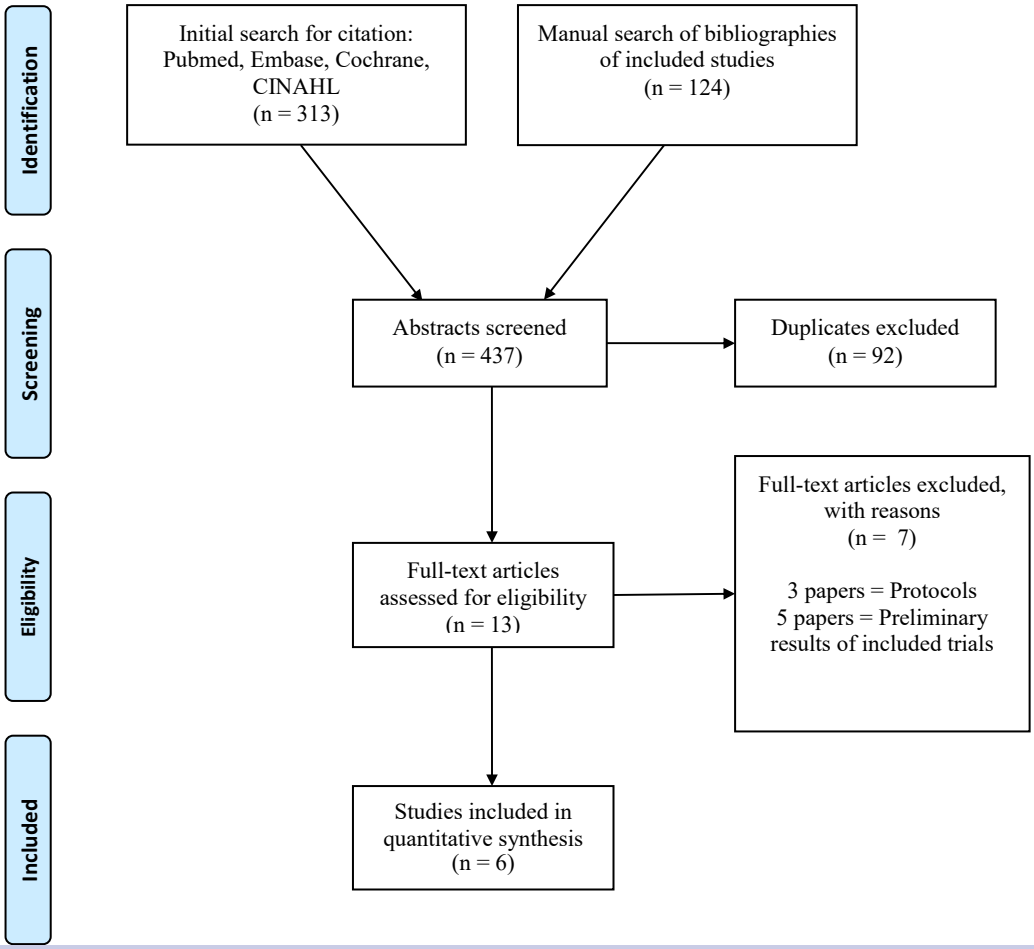

Fig 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram. *CINAHL,* Cumulative Index to Nursing and Allied Health Literature.

Table I. Characteristics of included trials

Study	Morrison,[13] 2019	Lane,[14] 2017	Koramaz,[12] 2017	Bozkurt,[16] 2016	Vun,[17] 2015	Van Eekeren,[15] 2013
Study design	RCT	RCT	Retrospective	Prospective (nonrandomized)	Prospective (nonrandomized)	Prospective (nonrandomized)
Duration	36 months	6 months	12 months	12 months	6 weeks	6 weeks
No. of participants	222	170	339	310	127	68
Interventions (randomized)	CAVA (n = 108) RFA (n = 114)	MOCA (n = 87) RFA (n = 83)	CAVA (n = 150) EVLA (n = 189)	CAVA (n = 154) EVLA (n = 156)	MOCA (n = 57) RFA (n = 50) EVLA (n = 40)	MOCA (n = 34) RFA (n = 34)
Adjunct treatment of nontruncal varicosities	None (in the first 3 months)	Phlebectomies	Phlebectomies	Staged sclerotherapy or phlebectomies at 3 months	None	None
Mode of anesthesia	Local	Local	Not reported	Local	Local	Local
Postoperative compression	Yes	Yes	Yes	Yes	Yes	Yes
Lost to follow-up	76	49	Not reported	27	9	None
Age, years, mean	49.5	50	46.08	41.35	50[a]	58
Proportion female, %	79.5	58.8	50.2	50.95	66	63.5

CAVA, Cyanoacrylate vein ablation; *EVLA*, endovenous laser ablation; *MOCA*, mechanochemical ablation; *RCT*, randomized controlled trial; *RFA*, radiofrequency ablation.
[a]Represents interquartile range.

553 (94.2%) undergoing TA had successful truncal ablation on follow-up ultrasound imaging at the study end point (pooled RR, 1.01; 95% confidence interval [CI], 0.99-1.04; Fig 2, *A*). No statistical heterogeneity was identified ($\chi^2 = 3.27$; $df = 4$; $P = .5$; $I^2 = 0\%$).

Subgroup analysis identified no significant difference in technical success rates between groups at immediate (RR, 1.07; 95% CI, 0.95-1.20) evaluation. Furthermore, assessment at both ≤6-month (RR, 1.01; 95% CI, 0.98-1.05) and 12-month intervals (RR, 1.02; 95% CI, 0.99-1.04) and in those with >12-month follow-up imaging (RR, 1.03; 95% CI, 0.94-1.12) displayed no significant difference between groups (Fig 2, *B-E*).

Further subgroup analysis identified no significant difference in technical success rates (at the latest recorded time point) when MOCA was compared with TA (RR, 0.96; 95% CI, 0.89-1.03; Supplementary Fig 1, online only) or when CAVA was compared with thermal techniques (RR, 1.02; 95% CI, 0.94-1.11; Supplementary Fig 2, online only).

Procedural pain. Five studies[13-17] reported periprocedural pain outcomes, with three[14-16] providing data for meta-analysis. Incompete data were excluded from meta-analysis and reported in the original form. One trial[14] reported pain using both scales. Four articles[14-17] reported pain using a visual analog scale, whereas two[13,14] used a rating scale of 0 to 10.

When pain of NTA was compared with that of TA by a visual analog scale, a mean difference of −18.11 (95% CI, −36.7 to 0.48) favoring NTA was identified (Fig 3, *A*). Vun et al[17] reported heterogeneous data but identified significantly lower median pain scores in the MOCA group compared with RFA and EVLA, respectively (1 vs 5 vs 6; $P < .01$).

Two studies[13,14] reported intraoperative pain data using a numeric pain scale (0-10), with Lane et al providing data for analysis. The authors identified significantly lower pain scores in patients undergoing NTA with a mean difference of −1.52 (95% CI, −2.39 to −0.67), although direct comparisons were available for fewer than 100 patients in each group (Fig 3, *B*). Morrison et al[13] reported no significant mean difference between groups for procedural pain in their preliminary report (2.2 vs 2.4; $P = .11$).[29]

Further subgroup analysis revealed significantly less pain in those undergoing MOCA compared with RFA (mean difference, −9.83; 95% CI, −19.4 to −0.25; Fig 3, *C*) and in those undergoing CAVA compared with EVLA (mean difference, −34; 95% CI, −38.41 to −29.59; Fig 3, *D*). One study[13] compared pain scores for CAVA and RFA, identifying no significant difference between groups.

Procedural complications.

Minor complications. Five studies[12-16] examined the effects of each intervention on minor periprocedural

Table II. Inclusion and exclusion criteria and outcomes of included trials

Study	Morrison,[13] 2019	Lane,[14] 2017	Koramaz,[12] 2017	Bozkurt,[16] 2016	Vun,[17] 2015	Van Eekeren,[15] 2013
Inclusion criteria	Primary GSV incompetence CEAP 2-4b	Primary GSV or SSV incompetence	Primary GSV incompetence CEAP 2-5 Vein >5.5 mm, <15 mm	Primary GSV incompetence CEAP 2-4b	GSV or SSV incompetence Nontortuous veins (3-10 mm)	Primary GSV incompetence CEAP 2-6
Exclusion criteria	Secondary incompetence Previous DVT or PE Peripheral artery disease SSV incompetence GSV >12 mm	Secondary incompetence DVT Peripheral artery disease Hypercoagulability Veins <3 mm	Tortuous Peripheral artery disease DVT or PE Deep venous incompetence Thrombophlebitis Secondary incompetence Malignant disease Pregnancy	DVT Deep venous incompetence SSV or anterior accessory vein incompetence Vasculopathies Coagulopathies GSV diameter >15 mm Pregnancy Severe systemic illness	Unsuitable anatomy	Pregnancy Lactation Anticoagulant use DVT Recurrent varicosities
Primary outcomes	Technical success	Pain by the visual analog scale and number scale	Technical success	Technical success	Technical success	Not defined
Secondary outcomes	Recanalization rates Quality of life (AVVQ) VCSS Adverse events	Technical success Quality of life (AVVQ) VCSS	Adverse events VCSS Pain score	Procedural time Procedural pain Ecchymosis Adverse events Quality of life (AVVQ) VCSS	Procedural time Procedural pain	VCSS Quality of life (AVVQ, SF-36) Periprocedural pain Complication rate Return to normal activity Procedural time

AVVQ, Aberdeen Varicose Vein Questionnaire; *CEAP*, Clinical, Etiology, Anatomy, and Pathophysiology class; *DVT*, deep venous thrombosis; *GSV*, great saphenous vein; *PE*, pulmonary embolus; *SF-36*, 36-Item Short Form Health Survey; *SSV*, small saphenous vein; *VCSS*, Venous Clinical Severity Score.

complications, with NTA associated with a significant reduction in rates of ecchymosis and hematoma formation compared with TA (RR, 0.43; 95% CI, 0.23-0.78; Fig 4, *A*). No significant difference was identified between groups for rates of phlebitis (pooled RR, 0.70; 95% CI, 0.32-1.54), paresthesia (RR, 0.31; 95% CI, 0.07-1.51), and skin pigmentation (RR, 0.42; 95% CI, 0.10-1.77; Fig 4, *B-D*).

Of note, subgroup analysis identified a significantly lower ecchymosis rate in those undergoing CAVA compared with TA (RR, 0.41; 95% CI, 0.2-0.83; Supplementary Fig 3, online only); however, this effect was not identified when MOCA and TA were compared (Supplementary Fig 4, online only). Furthermore, no difference was identified between groups when CAVA and MOCA were respectively compared with TA for rates of phlebitis, paresthesia, and pigmentation (Supplementary Figs 5-10, online only).

Major complications (DVT). Four studies[12-15] reported rates of DVT, with no significant difference identified between treatment cohorts (RR, 0.45; 95% CI, 0.06-3.36; Fig 4, *E*).

Quality of life. Four studies[13-16] assessed postoperative quality of life using the AVVQ score up to 1 year. Preliminary (3-month) results were extracted from one trial as data were not available from final results.[29] At baseline, no significant difference in AVVQ score was identified between groups in any trial. Comparison of both groups revealed a mean difference between groups of −0.27 (95% CI, −0.57 to 0.04), which did not reach statistical significance (Fig 5).

Modification of disease severity. Five studies[12-16] assessed the modification of disease severity as a result of interventions. Again, preliminary (3-month) results were extracted from one study,[29] and no difference was identified between cohorts at baseline and on completion, with a mean difference between groups of −0.52 (95% CI, −1.05 to 0.01; Fig 6).

DISCUSSION

Open surgery and thermal endovenous ablation offer safe and effective options to treat lower limb superficial venous incompetence. Endovenous interventions obviate the need for a saphenofemoral cutdown and the inherent risks associated with groin dissection. As a result, RFA and EVLA are associated with fewer perioperative morbidities and superior quality of life and as such have emerged as first-line treatment options in many locations.[2-6]

Table III. Downs and Black quality assessment tool for included randomized and nonrandomized studies

Question	Morrison,[13] 2019	Lane,[14] 2017	Koramaz,[12] 2017	Bozkurt,[16] 2016	Vun,[17] 2015	Van Eekeren,[15] 2013
Hypothesis/objective clear?	Yes	Yes	Yes	Yes	Yes	Yes
Main outcomes clearly described in introduction or methods?	Yes	Yes	Yes	Yes	Yes	Yes
Are patients' characteristics clearly described?	Yes	Yes	Yes	Yes	No	Yes
Are interventions clearly described?	Yes	Yes	Yes	Yes	Yes	Yes
Are confounders equally distributed?	Yes	Yes	Yes	Yes	No	No
Are the main findings clearly described?	Yes	Yes	Yes	Yes	Yes	Yes
Are estimates or variability provided?	Yes	Yes	Yes	Yes	Yes	Yes
Are important adverse events reported?	Yes	Yes	Yes	Yes	No	Yes
Are the characteristics of those lost to follow-up described?	No	No	No	No	No	Yes
Are specific *P* values reported?	Yes	Yes	Yes	Yes	Yes	Yes
Were potentially eligible subjects representative of the population?	Yes	Yes	Yes	Yes	Yes	Yes
Were participating subjects representative of the population?	Yes	Yes	Yes	Yes	Yes	Yes
Were staff, places, and facilities representative of the treatment most patients receive?	Yes	Yes	Yes	Yes	Yes	Yes
Was an attempt made to blind subjects to the intervention they received?	No	No	No	No	No	No
Was an attempt made to blind main outcome assessors?	No	No	No	No	No	No
If any results reflect data dredging, is this clear?	Yes	Yes	Yes	Yes	UTD	Yes
Do analyses adjust for length of follow-up differences?	Yes	Yes	Yes	Yes	Yes	Yes
Were appropriate statistical analyses used?	Yes	Yes	Yes	Yes	Yes	Yes
Was compliance with the intervention reliable?	Yes	Yes	Yes	Yes	Yes	Yes
Were the main outcome measures valid and reliable?	Yes	Yes	Yes	Yes	Yes	Yes
Were study groups recruited from the same population?	Yes	Yes	Yes	Yes	Yes	Yes
Were subjects recruited over similar time periods?	Yes	Yes	No	Yes	Yes	No
Were study subjects randomized to intervention groups?	Yes	Yes	No	No	No	No
Was treatment assignment concealed?	No	No	No	No	No	No
Was there adequate adjustment for confounders in the analysis?	Yes	Yes	Yes	Yes	No	Yes
Were losses of patients to follow-up taken into account?	Yes	Yes	UTD	Yes	UTD	Yes
Was an appropriate sample size calculation carried out?	No	Yes	No	No	No	Yes
No. of yes results	22	23	19	21	15	21

UTD, Unable to determine.
An overall score of 20 or more is deemed acceptable methodologic quality.

NTA represents the next generation of endovenous therapy. These techniques quickly ablate superficial veins chemically without the need for heat transfer, thus hypothetically reducing the risk of procedural morbidity. To date, no review data have compared their use with standard endovenous thermal approaches in the management of superficial venous incompetence.

This review consists of six studies including 1236 participants. Trial design varied, with two randomized controlled trials,[13,14] three prospective studies,[15-17] and

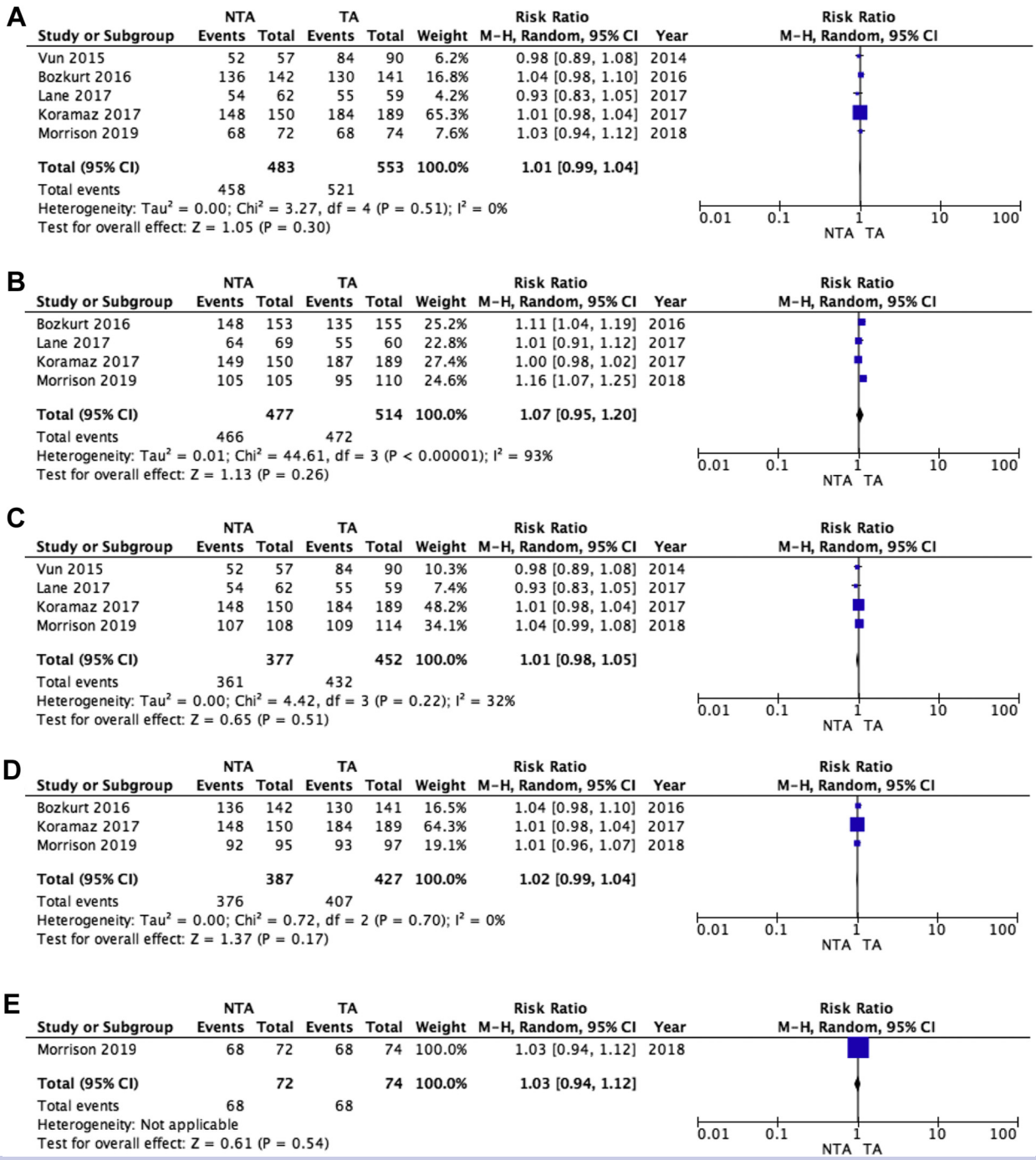

Fig 2. A, Forest plot depicts results of meta-analysis comparing nonthermal ablation (*NTA*) and thermal ablation (*TA*) with regard to overall technical success (at the latest recorded study time point) for all studies. The *solid squares* represent the relative risk, the *horizontal lines* represent the 95% confidence intervals (*CIs*), and the *diamond* represents the pooled relative risk. *M-H*, Mantel-Haenszel. **B-E,** Forest plot depicts results of meta-analysis comparing NTA and TA with regard to immediate, ≤6-month, ≤12-month, and >12-month follow-up periods.

one retrospective review[12] included. Four further studies[28-31] provided preliminary results from included trials. Assessment of bias using the Downs and Black tool revealed a majority of studies to be of moderate quality; however, a number were potentially exposed to methodologic bias because of trial design and small cohorts of patients.

This meta-analysis suggests that NTA offers equivalent truncal ablation rates to the existing standard TA in the short term with significantly lower rates of ecchymosis.

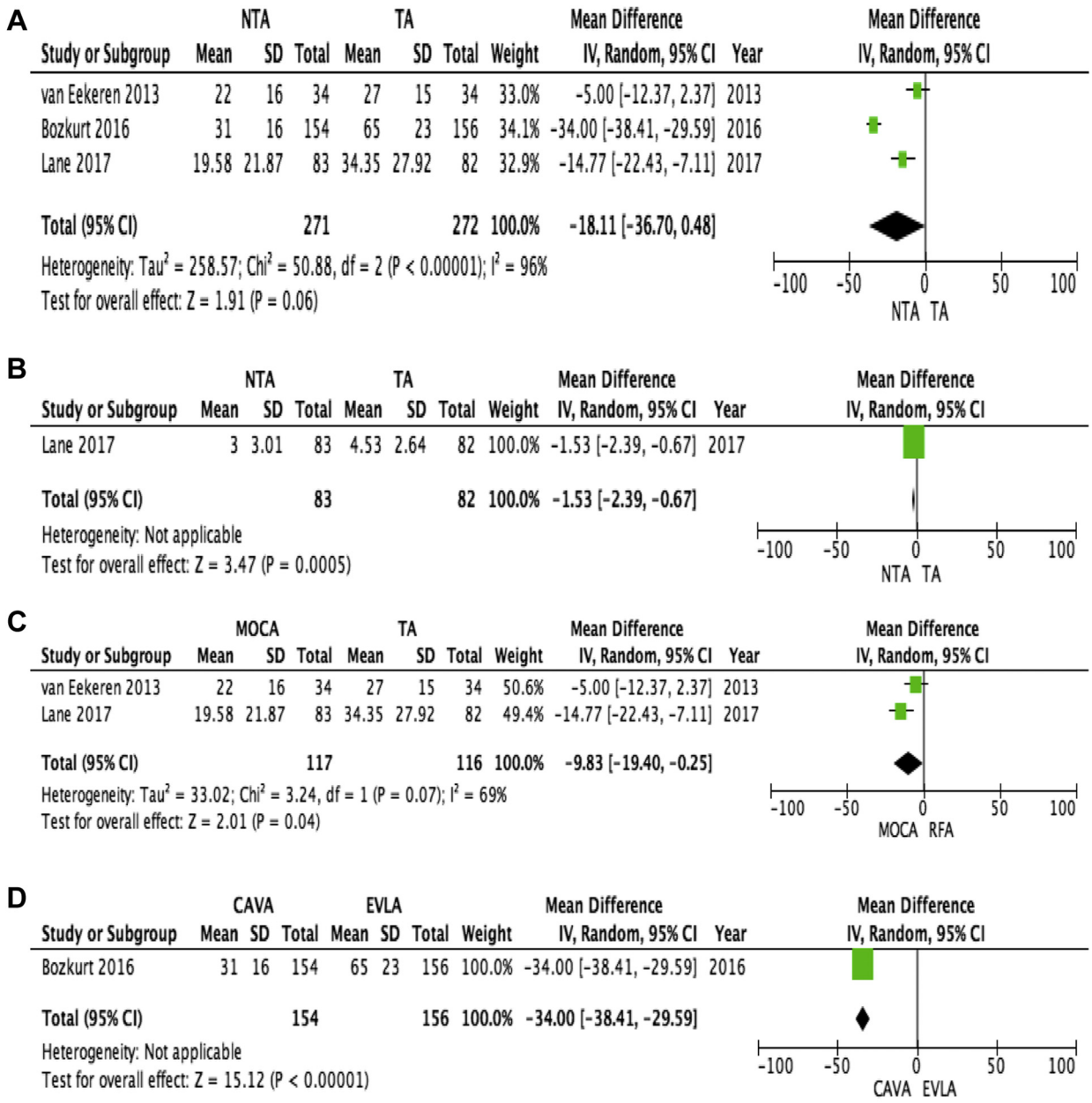

Fig 3. A, Forest plot depicts results of meta-analysis comparing nonthermal ablation (*NTA*) and thermal ablation (*TA*) with regard to procedural pain as measured using a visual analog scale. The *solid squares* represent the mean difference, the *horizontal lines* represent the 95% confidence intervals (*CIs*), and the *diamond* represents the pooled mean difference. Data from Lane (2017) depict maximal procedural pain. *IV,* Inverse variance; *SD,* standard deviation. **B,** Forest plot depicts results of meta-analysis comparing NTA and TA with regard to procedural pain as measured using numeric scale of 0 to 10. **C** and **D,** Forest plot depicts results of meta-analysis comparing mechanochemical ablation (*MOCA*) with TA and cyanoacrylate vein ablation (*CAVA*) with endovenous laser ablation (*EVLA*), respectively, with regard to procedural pain as measured using visual analog scale. *RFA,* Radiofrequency ablation.

Subgroup analysis assessing NTA treatments individually compared with TA identified that MOCA and CAVA offered significantly lower procedural pain (visual analog scale) compared with RFA and EVLA, respectively, whereas patients undergoing CAVA had significantly less ecchymosis compared with those having TA. Of note, MOCA offered no additional benefit to ecchymosis rates compared with TA.

With this in mind, these data would suggest that CAVA and MOCA offer an innovative and effective adjunct to venous surgeons, with longer term data to be established. The absence of TA appears to offer

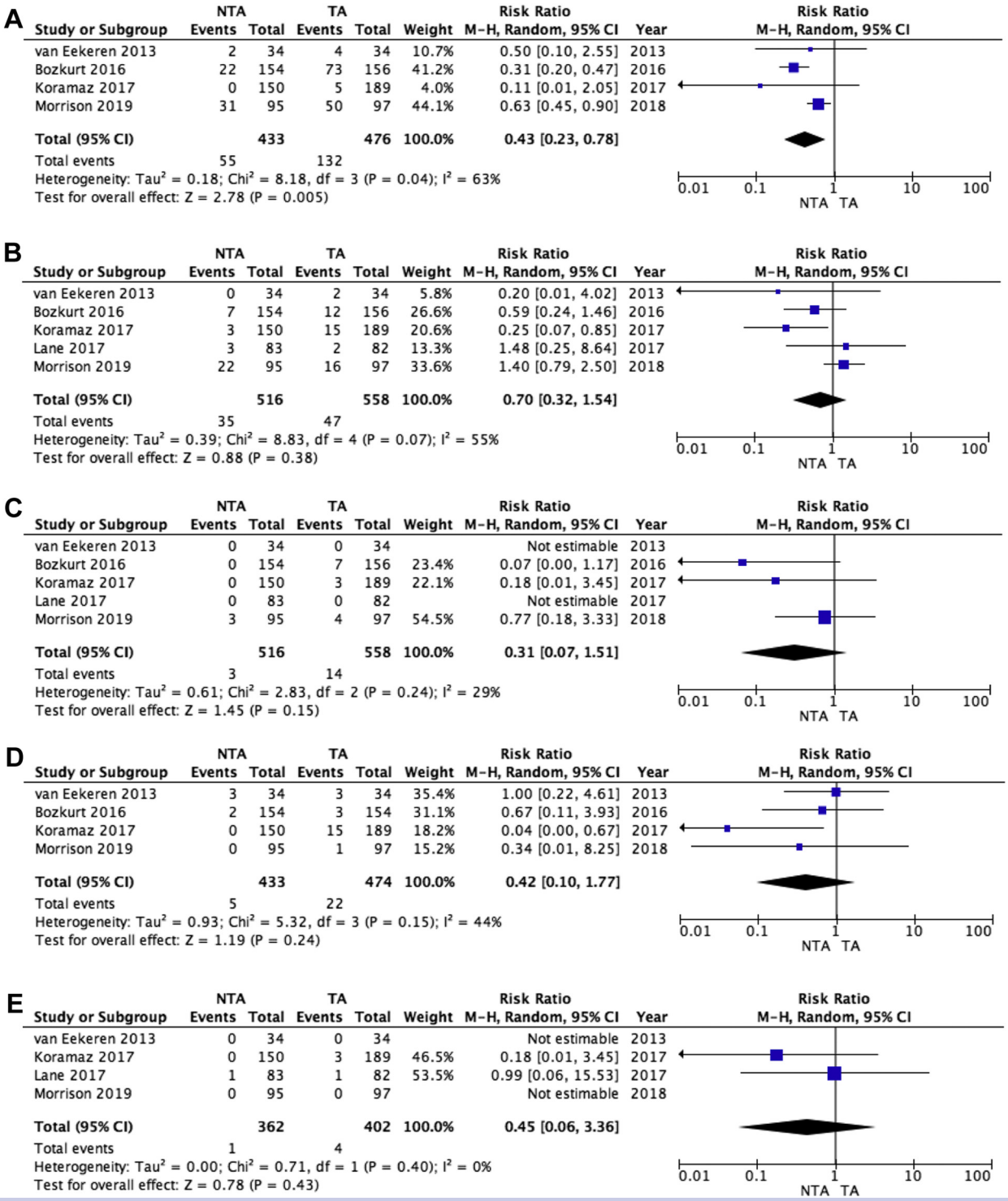

Fig 4. A, Forest plot depicts results of meta-analysis comparing nonthermal ablation (*NTA*) and thermal ablation (*TA*) with regard to postoperative ecchymosis. The *solid squares* represent the risk ratio (RR), the *horizontal lines* represent the 95% confidence intervals (*CIs*), and the *diamond* represents the pooled ratio. *M-H,* Mantel-Haenszel. **B-D,** Forest plot depicts results of meta-analysis comparing NTA and TA with regard to postoperative phlebitis, paresthesia, and skin pigmentation. **E,** Forest plot depicts results of meta-analysis comparing NTA and TA with regard to rates of deep venous thrombosis (DVT).

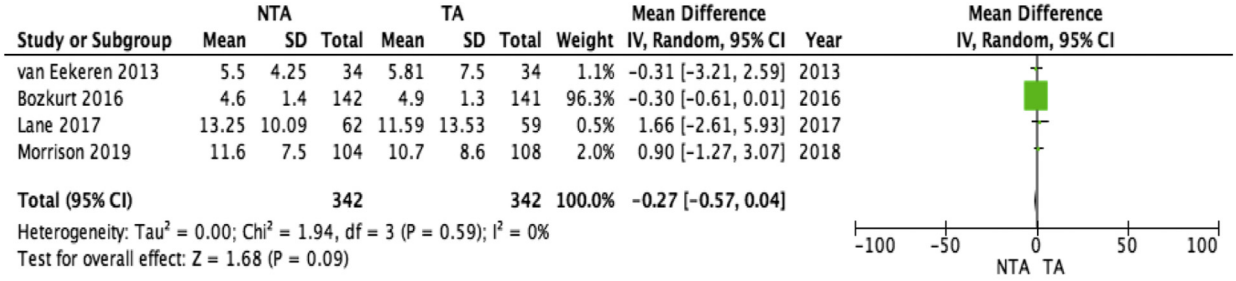

Fig 5. Forest plot depicts results of meta-analysis comparing nonthermal ablation (*NTA*) and thermal ablation (*TA*) with regard to postprocedural quality of life (Aberdeen Varicose Vein Questionnaire [AVVQ] score). The *solid squares* represent the mean difference, the *horizontal lines* represent the 95% confidence intervals (*CIs*), and the *diamond* represents the pooled mean difference. *IV,* Inverse variance; *SD,* standard deviation.

less direct tissue trauma and hence lower rates of pain and morbidity. Furthermore, avoiding the heat transfer involved with TA removes the requirement for tumescent anesthesia, which is time and labor intensive. This has been identified in a number of trials that suggest TA to be significantly more time-consuming than NTA.[12,15-17] The absence of the repeated skin punctures associated with tumescent anesthesia may also be associated with the reduced ecchymosis rates seen in the CAVA group. However, thermal techniques may be associated with a greater cost; recent data from Epstein et al[33] suggested that RFA (followed by MOCA and subsequently EVLA) remains the treatment with the greatest cost and outcome benefit to the patient. The authors did note that CAVA is not cost-effective because of its expense and similar efficacy to existing cheaper options. Nevertheless, this added expense might be countered by an ability to simultaneously treat multiple trunks with CAVA, something not possible with MOCA because of the dosing limitations of sclerosing agents. Importantly, this analysis confirms that thermal approaches were not significantly associated with higher rates of DVT, which had previously been hypothesized because of heat-induced injury of the deep venous system.

These findings are consistent with previous review data from Vos et al,[34] who reported the outcomes of 15 articles assessing the technical success of NTA. The authors identified excellent rates of technical success at 1 year for MOCA and CAVA (94.1% vs 89%, respectively), with significant improvements in quality of life score and VCSS.

Of note, whereas catheter-directed ultrasound-guided foam sclerotherapy offers an additional nonthermal ablative technique, trial data assessing its use in comparison to TA were excluded from this analysis. This was incorporated in the study design as existing data from Davies et al[35] have already established it to be associated with significantly lower rates of anatomic success compared with TA.

This review offers a systematic and comprehensive review of the literature comparing the outcomes of NTA and TA for superficial venous incompetence. Significantly, it offers an initial insight into the rapidly evolving, widely used approaches to endovenous surgery and represents the first comparative review of data of these interventions. It is, however, subject to limitations. A number of studies reported the outcomes of nonrandomized, industry-funded, small cohorts of patients. Furthermore, heterogeneity of diagnosis, intervention, and follow-up suggests that cautious interpretation of outcomes is required. Finally, it must be considered

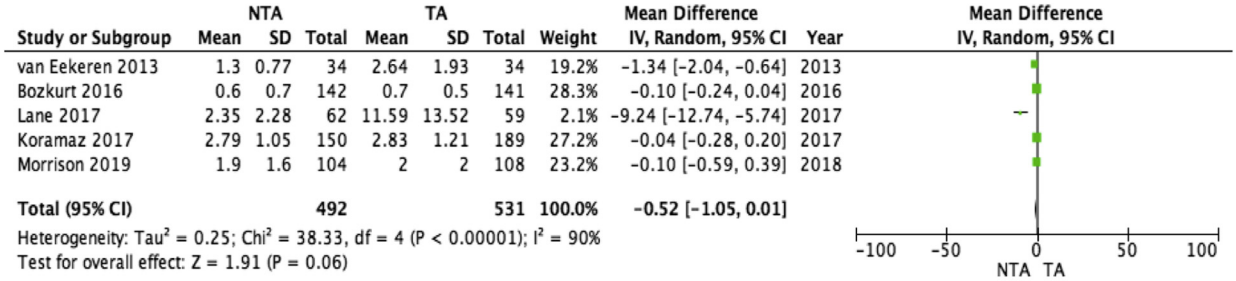

Fig 6. Forest plot depicts results of meta-analysis comparing nonthermal ablation (*NTA*) and thermal ablation (*TA*) with regard to modification of disease severity (Venous Clinical Severity Score [VCSS]) as a result of intervention. The *solid squares* represent the mean difference, the *horizontal lines* represent the 95% confidence intervals (*CIs*), and the *diamond* represents the pooled mean difference. *IV,* Inverse variance; *SD,* standard deviation.

that the efficacy and safety of thermal techniques are widely established in both the literature and surgical practice, whereas NTA remains in its infancy, with only short-term data assessing a small number of patients available to date.

The promising early-stage efficacy and safety profiles of NTA, seen in this review, require consolidation with prolonged clinical use and further level I evidence. From the perspective of TA, higher frequency lasers and variations in fiber type may offer potential improvements in treatment efficacy; initial studies suggest lower rates of periprocedural pain and ecchymosis.[36,37] Further comparative data examining NTA, higher frequency laser probes, and various fiber tips may offer insight into this evolving area of venous treatment.

CONCLUSIONS

Nonthermal ablative techniques are as effective as standard TA in the first year. Of note, data were exposed to potential biases, and as such, there is a need for further powered trials to definitively examine this hypothesis.

AUTHOR CONTRIBUTIONS

Conception and design: AH, TA, GG, BE, ST, SM, SA
Analysis and interpretation: AH, TA, EB, SW, SA
Data collection: AH, TA, SA
Writing the article: AH, TA
Critical revision of the article: TA, GG, EB, BE, ST, SW, SM, SA
Final approval of the article: AH, TA, GG, EB, BE, ST, SW, SM, SA
Statistical analysis: AH, TA, GG
Obtained funding: Not applicable
Overall responsibility: AH
AH and TA contributed equally to this article and share co-first authorship.

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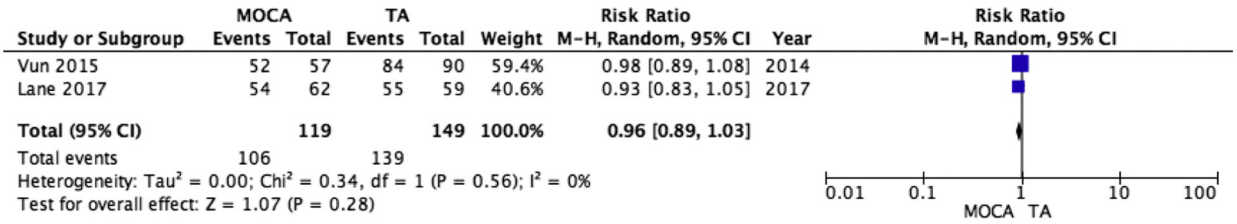
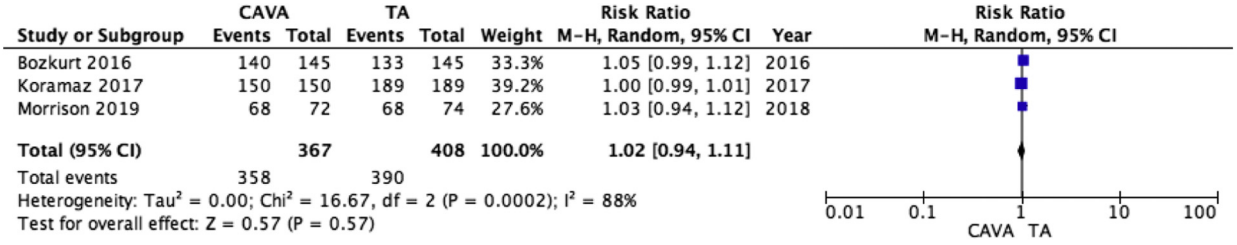
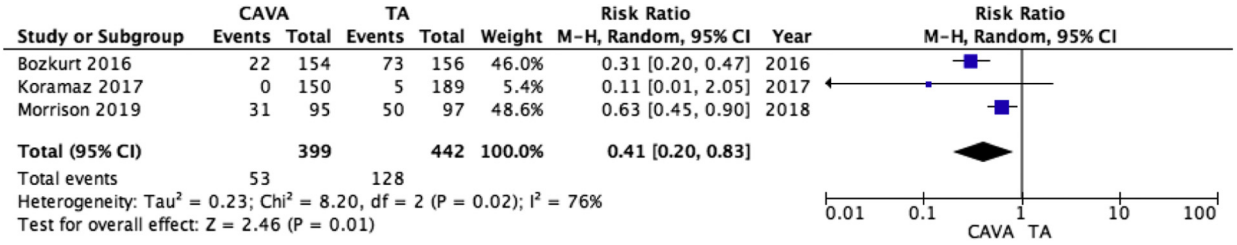


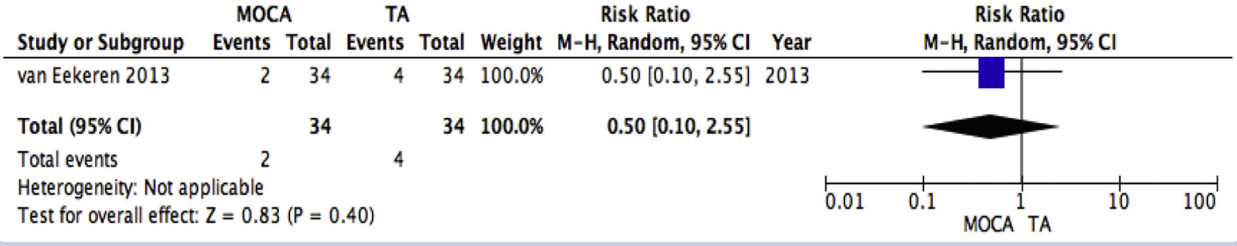
Supplementary Fig 1 (online only). Forest plot depicts results of meta-analysis comparing mechanochemical ablation (*MOCA*) and thermal ablation (*TA*) with regard to overall technical success (at the latest study time point). The *solid squares* represent the relative risk, the *horizontal lines* represent the 95% confidence intervals (*CIs*), and the *diamond* represents the pooled relative risk. *M-H,* Mantel-Haenszel.



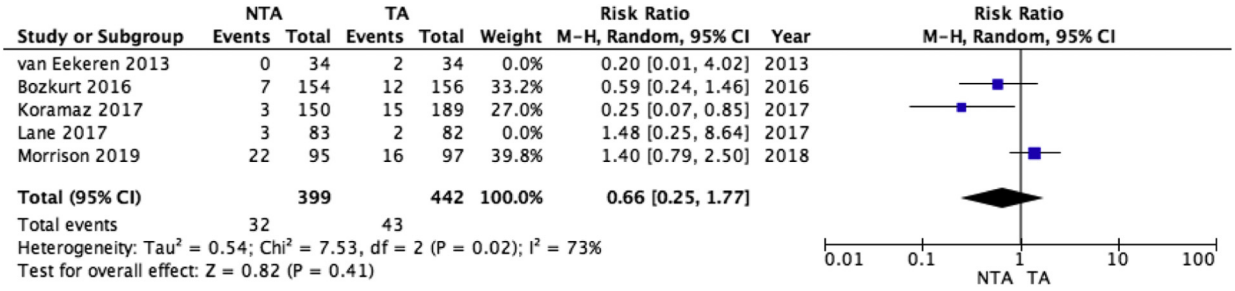
Supplementary Fig 2 (online only). Forest plot depicts results of meta-analysis comparing cyanoacrylate vein ablation (*CAVA*) and thermal ablation (*TA*) with regard to overall technical success (at the latest study time point). The *solid squares* represent the relative risk, the *horizontal lines* represent the 95% confidence intervals (*CIs*), and the *diamond* represents the pooled relative risk. *M-H,* Mantel-Haenszel.



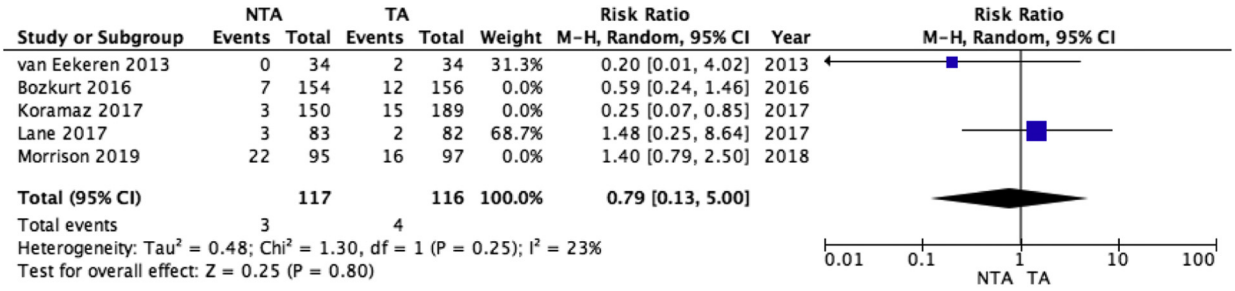
Supplementary Fig 3 (online only). Forest plot depicts results of meta-analysis comparing cyanoacrylate vein ablation (*CAVA*) and thermal ablation (*TA*) with regard to rates of ecchymosis. The *solid squares* represent the relative risk, the *horizontal lines* represent the 95% confidence intervals (*CIs*), and the *diamond* represents the pooled relative risk. *M-H,* Mantel-Haenszel.



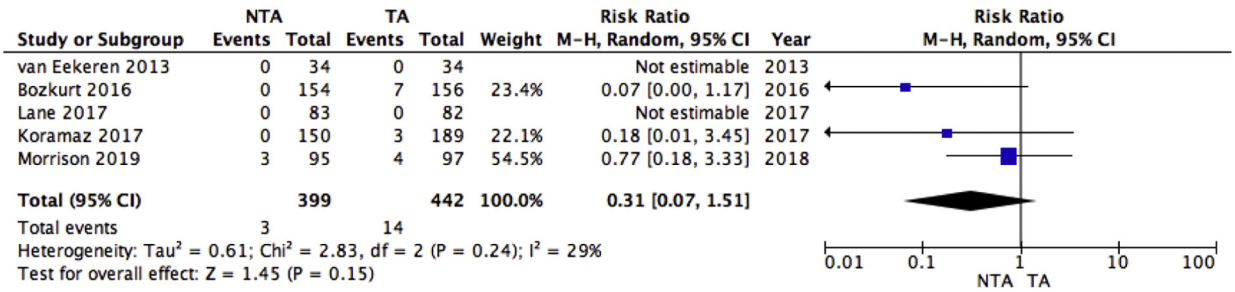
Supplementary Fig 4 (online only). Forest plot depicts results of meta-analysis comparing mechanochemical ablation (*MOCA*) and thermal ablation (*TA*) with regard to rates of ecchymosis. The *solid squares* represent the relative risk, the *horizontal lines* represent the 95% confidence intervals (*CIs*), and the *diamond* represents the pooled relative risk. *M-H,* Mantel-Haenszel.



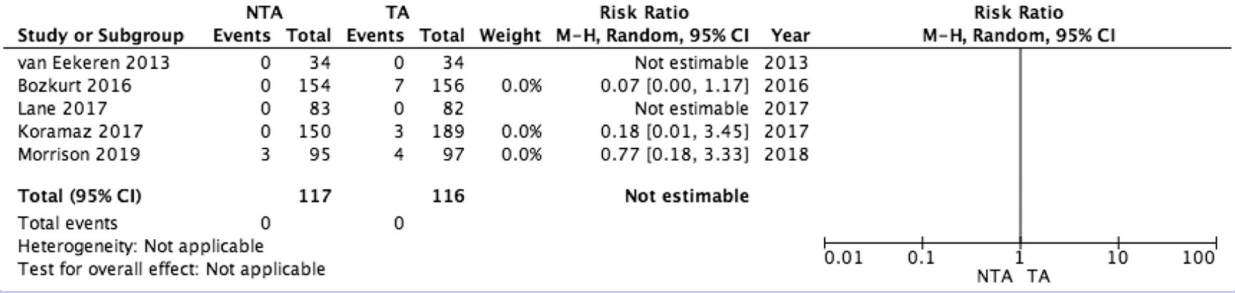
Supplementary Fig 5 (online only). Forest plot depicts results of meta-analysis comparing cyanoacrylate vein ablation (*NTA*) versus thermal ablation (TA) with regard to rates of phlebitis. The *solid squares* represent the relative risk, the *horizontal lines* represent the 95% confidence intervals (*CIs*), and the *diamond* represents the pooled relative risk. *M-H*, Mantel-Haenszel.



Supplementary Fig 6 (online only). Forest plot depicts results of meta-analysis comparing mechanochemical ablation (NTA) versus thermal ablation (*TA*) with regard to rates of phlebitis. The *solid squares* represent the relative risk, the *horizontal lines* represent the 95% confidence intervals (*CIs*), and the *diamond* represents the pooled relative risk. *M-H*, Mantel-Haenszel.



Supplementary Fig 7 (online only). Forest plot depicts results of meta-analysis comparing cyanoacrylate vein ablation (*NTA*) versus thermal ablation (*TA*) with regard to rates of parasthesia. The *solid squares* represent the relative risk, the *horizontal lines* represent the 95% confidence intervals (*CIs*), and the *diamond* represents the pooled relative risk. *M-H*, Mantel-Haenszel.



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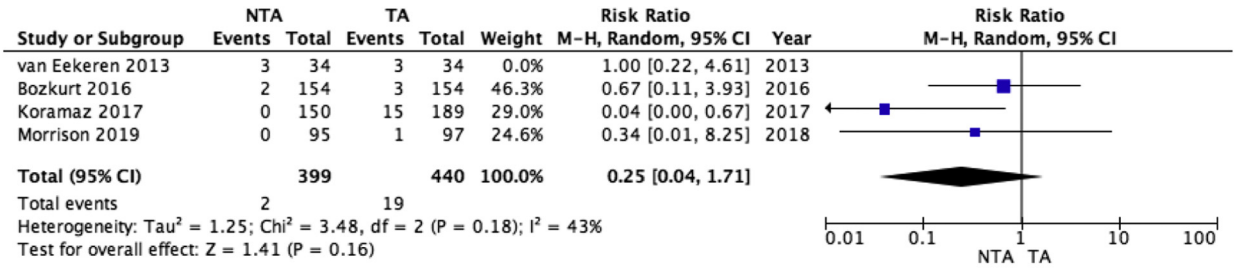
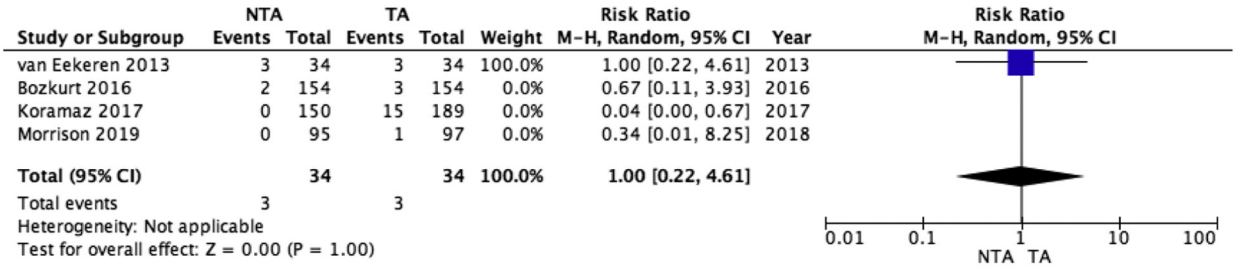


Supplementary Fig 9 (online only). Forest plot depicts results of meta-analysis comparing cyanoacrylate vein ablation (NTA) versus thermal ablation (TA) with regard to rates of skin pigmentation. The solid squares represent the relative risk, the horizontal lines represent the 95% confidence intervals (*CIs*), and the diamond represents the pooled relative risk. *M-H,* Mantel-Haenszel.



Supplementary Fig 10 (online only). Forest plot depicts results of meta-analysis comparing mechanochemical ablation (NTA) versus thermal ablation (TA) with regard to rates of skin pigmentation. The solid squares represent the relative risk, the horizontal lines represent the 95% confidence intervals (*CIs*), and the diamond represents the pooled relative risk. *M-H,* Mantel-Haenszel.