RANDOMIZED CONTROL TRIALS (RCT's) in VARICES ENDOVENOUS TREATMENT

M. PERRIN Lyon - France
B. EKLOF Helsinborg- Sweden

Forty seven articles(38 RCT's) comparing Open surgery, Radiofrequency Ablation (RFA), Endovenous Laser Ablation (EVLA) and Chemical Ablation (CA) have been identified

Conventional open Surgery (COS) vs. RFA	(# 9/7)
Conventional open Surgery (COS) vs. EVLA	(#14/12)
EVLA vs. RFA	(# 5/5)
EVLA vs. EVLA	(# 5/5)
EVLA vs. Cryostripping	(# 3/1)
EVLA vs. foam	(# 2/1)
Open Surgery vs CA	(# 7/5)
Phlebectomy vs. CA	(# 1/1)
COS vs. Thermal vs. Chemical ablation	(# 1/1)

Conventional open Surgery (COS) versus

Radiofrequency ablation (RFA) # 7 RCT's, 9 articles

Rautio T. Endovenous obliteration versus conventional stripping operating in the treatment of primary varicose veins : a randomized controlled trial with comparison of the costs. *J Vasc Surg* 2002;35:958-65

Lurie F. Prospective randomized study of endovenous radiofrequency Obliteration (Closure procedure) vs ligation and stripping in a selected patient population (EVOLVES Study) *J Vasc Surg* 2003;38:207-14

Lurie F. Prospective randomized study of endovenous radiofrequency obliteration (Closure) versus ligation and vein stripping (EVOLVeS) Two-year follow-up. *Eur J Vasc Endovasc Surg* 2005;29:67-73

Perala J. Radiofrequency endovenous obliteration vs stripping of the long saphenous vein in the management of primary varicose veins:3-year outcome of a randomized study. *Ann Vasc Surg* 2005;19:1-4

Hinchliffe RJ. A prospective randomized controlled trial of VNUS Closure versus surgery for the treatment of recurrent long saphenous varicose veins. *Eur J Vasc Endovasc Surg* 2006;31:212-8

Kianifard B. Radiofrequency ablation (VNUS Closure) does not cause neo-vascularisation at the groin at one year : results of a case controlled study. S*urgeon* 2006 ;4 :71-74

Stötter L. Comparative outcomes of radiofrequency endoluminal ablation, invagination stripping and cryostripping in the treatment of great saphenous vein. *Phlebology* 2006;21:60-4

Subramonia S. Radiofrequency ablation versus conventional surgery for varicose veins-a comparison of treatment costs in a randomized trials. *Eur J Vasc Endovasc Surg* 2009;39:104-11

Elkaffas KH. Great saphenous vein radiofrequency ablation versus standard stripping in the management of primary varicose veins- a randomized clinical trial. Angiology 2010;62:49-54

Summary results on COS versus RFA

- Almost all RCT's conclude that after radiofrequency ablation there was less postoperative pain, faster recovery and earlier return to work and normal activities, as well as higher patient satisfaction.

- The longest follow-up is 3 years and there is no difference in terms of clinical result between classical surgery and radiofrequency ablation.

Comments on COS versus RFA

- **It must be noted that in all series the bipolar catheter (Closure Plus) was used, knowing that the new ClosureFast® catheter has given better results in case series.**

- **It should however be pointed out that modern less invasive open surgery under local anesthesia in the office setting is showing similar good outcomes in case series report.**

Conventional open Surgery (COS) versus Endovenous laser ablation EVLA. # RCT's 12, articles 14

de Medeiros CAF. Comparison of endovenous treatment with an 810 nm laser versus conventional stripping of the great saphenous vein in patients with primary varicose veins. *Dermatol Surg*. 2005;31:1685-94

Vuylstecke M. Endovenous laser obliteration for the treatment of primary varicose veins. *Phlebology* 2006;21:80-87

Ying L. A random, comparative study on endovenous laser therapy and saphenous veins stripping for the treatment of great saphenous vein incompetence. Zhonghua-Yi-Xue-Za-Zhi 2007;87(43):3043-3046.

Rassmussen LH. Randomized trial comparing endovenous laser ablation of the great saphenous vein with ligation and stripping in patients with varicose veins : short-term results *J Vasc Surg* 2007;46:308 15

Darwood RJ. Randomized Clinical trial comparing endovenous laser ablation with surgery for the treatment of primary great saphenous veins. *Br J Sug* 2008;95:294-301

Kalteis M. High ligation combined with stripping and endovenous laser ablation of the great saphenous vein: Early results of a randomized controlled study. *J Vasc Surg* 2008;47:822-9

Theivacumar NS. Neovascularization and recurrence 2 years after treatment for sapheno-femoral and great saphenous reflux : a comparison of surgery and endovenous laser. *Eur J Vasc Endovasc Surg* 2009;38:203-207

Conventional open Surgery (COS) versus Endovenous laser ablation EVLA. # RCT's 12, articles 14

Christenson JT. Prospective randomized trial comparing endovenous laser ablation and surgery for treatment of primary great saphenous varicose veins with a 2 year follow-up.
***J Vasc Surg* 2010;52:1234-41**

Rassmussen LH. Randomized trial comparing endovenous laser ablation with stripping of the great saphenous vein : clinical outcome and recurrence after 2 years. Eur *J Vasc Endovasc Surg* 2010;39:630-5

Caradice D. Randomized clinical trial of endovenous laser ablation compared with conventional surgery for great saphenous varicose veins. *BJS* 2011.

Caradice D. Clinical and technical outcomes from a randomized clinical trial of endovenous laser ablation compared with conventionalsurgery for great saphenous varicose veins. *BJS* 2011

Pronk P. Randomised Controlled Trial Comparing Sapheno-Femoral Ligation and Stripping of the Great Saphenous Vein with Endovenous Laser Ablation (980 nm) Using Local Tumescent Anaesthesia: One Year Results. *Eur J Vasc Endovasc Surg* 2010;40:649-656

Rass K. Comparable Effectiveness of Endovenous Laser Ablation and High Ligation With Stripping of the Great Saphenous Vein. *Arch Dermatol.*2012 ;148:49-58

Samuel N. Randomized Clinical Trial of Endovenous Laser Ablation Versus Conventional Surgery for Small Saphenous Varicose Veins. *Ann Surg*. 2012 Nov 15.PMID: 23160149

Summary results on COS versus EVLA

- All RCT's used bare tipped fibers 980 nm except three 810 nm.
- Only one RCT concerns the SSV

- Almost all RCT's conclude that after EVLA there was less postoperative pain, faster recovery and earlier return to work and normal activities

- Observation time was 1 year or less in 10 studies and 2-year in 4 studies.
- After two years no significant difference was found in clinical or DUS recurrence, clinical severity or QOL.

Comments on COS versus EVLA

No RCT has been reported with the new radial or jacket-tipped laser fibers compared to open surgery.

EVLA versus cryostripping. # RCT 1, articles 3

Disselhoff BC. Is there a risk for lymphatic complications after endovenous laser treatment versus cryostripping of the great saphenous vein? A prospective study. *Phlebology* 2008;23:10-14

Disselhoff BC. Randomized clinical trial comparing endovenous laser with cryostripping for great saphenous varicose veins. *Br J Surg* 2008;95:1232-1238

Disselhoff BC. Randomized comparison of Costs and Cost-effectiveness of cryostripping and Endovenous Laser ablation for Varicose veins: 2-Year results. *Eur J Vasc Endovasc Surg* 2009;37:357-63

Summary results EVLA vs. cryostripping

- Cryostripping was significantly faster (P<0.001) while EVLA was associated with significantly less postoperative pain (P=0.003) and quicker retun to normal activities (P<0.001) .
- Cryostripping was less costly but cost effectiveness ratio was non significant (P=0.788).
- No difference in terms of recurrence and QoL VCSS, AVVSS at 2-year.

EVLA versus EVLA. # RCT's 5, articles 5

Disselhoff BC. Randomized clinical trial comparing endovenous laser ablation of the great saphenous vein with and without ligation of the saphenofemoral junction : 2-year results. *Eur J Vasc Endovasc Surg* 2008;36: 713-18

Theivacumar NS. Endovenous laser ablation : does standard above –knee great saphenous vein ablation provide optimum results in patients with above –and below-knee reflux. A randomized controled trial. *J Vasc Surg* 2008 ;48 :173-8

Doganci S. Comparison of 980 nm Laser and Bare-tip fibre with1470 nm Laser and radial Fibre in the treatment of great Saphenous vein varicosities : A prospective randomized controlled trial. *Eur. J Vasc Endovasc Surg* 2010;40:254-9

Pannier F. 1470 nm diode laser for endovenous ablation (EVLA) of incompetent saphenous veins – a prospective randomized pilot study comparing warm and cold tumescence anesthesia. *Vasa* 2010;39:249-55

Vuylstecke M. Endovenous laser treatment : is there a clinical difference between using a 1500 nm and a 980 nm diode laser. Amulticenter randomisqed clinical trial. *Intern. Angio* 2011;30:327-34

Summary results EVLA versus EVLA

- HL combined with EVLA does not improve the outcome compared to EVLA withous HL.

- EVLA 1500 nm vs. 980 nm. Immediate post operative course fewer clinical side-effects with 1500 nm. P: ns At 6-month similar occlusion rate.

- EVLA 1470 nm radial fibre gives at one month follow-up less post operative pain and better VCSS compared to EVLA 980 nm bare fiber.

EVLA versus Ultra sound-guided Foam Sclerotherapy

Lattimer CR. Validation of a New Duplex Derived Haemodynamic Effectiveness Score, the Saphenous Treatment Score, in Quantifying Varicose Vein Treatments. EJEVS 2012 ;43 :348-54

Lattimer CR. Cost and Effectiveness of Laser with Phlebectomies Compared with Foam Sclerotherapy in Superficial Venous Insufficiency. Early Results of a Randomised Controlled Trial. EJEVS 2012 ;43 :594-600

Summary and Comments

Outcome was evaluated both clinically and by DUS

At short-term (3 weeks-3 months) UGFS is 3.15 times less expensive than EVLA with comparable effectiveness in terms of AK GSV obliteration, AVVQ, AVCSS ,VFI but 56% in UGFS group versus 6% in the EVLA group required additional foam.

Open Surgery versus Chemical Ablation (CA).
RCT's 6 , articles 7

Bountouroglou DG. Ultrasound-guided foam sclerotherapy combined with sapheno-femoral ligation compared to surgical treatment of varicose veins: early results of a randomised controlled trial. *Eur J Vasc Endovasc Surg*. 2006;31:93-100

Wright D. Varisolve® polidocanol microfoam compared with surgery or sclerotherapy in the management of varicose veins in the presence of trunk vein incompetence: European randomized controlled trial. *Phlebology* 2006;21:180-90.

Abela R. Reverse foam sclerotherapy of the great saphenous vein with sapheno-femoral ligation compared to standard and invagination stripping: a prospective clinical series. *Eur J Vasc Endovasc Surg* 2008;36:485-90

Figueiredo M. Results of surgical treatment compared with ultrasound guided foam sclerotherapy inpatients with varicose veins: a prospective randomised study. *Eur J Vasc Endovasc Surg* 2009;38:758-63

Liu X . Ultrasoud-guided sclerotherapy of the great saphenous vein with sapheno-femoral ligation compared to standard stripping*. Intern Angiology* 2011;30:321-26

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Open Surgery versus Chemical Ablation (CA).
RCT's 7 , articles7

Kalodiki E. **Long Term Results of a Randomized Controlled Trial on Ultrasound Guided Foam Sclerotherapy Combined with sapheno femoral Ligation versus standard Surgery for Varicose Veins.** ***J Vasc Surg*** **2012;55: 451-7**

Shadid N. **Randomized clinical trial of ultrasoundguided foam sclerotherapy versus surgery for the incompetent great saphenous vein.** ***Br J Surg*** **2012;99:1062-70**

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Comments on OS versus CA

The 5 first RCT's comparing ultrasound-guided foam sclerotherapy to conventional surgery and in one case also to liquid sclerotherapy *with short-term follow up* (max 1 year) do not give any conclusive results. It looks that HL+ Foam (Liu) gives less post operative discomfort and results in more rapid recovery.

Comments on OS versus CA (ctd)

Conversely the 6th article Kalodiki is a full documented 3-5 year follow-up RCT concluded that the treatment was equally effective between the surgical and foam groups, as demonstrated with the VCSS, VSDS, and the physical component of the SF-36 Score improvements. The AVVQ was significantly better in the surgery group, but the margins were small and this may not have any clinical significance.

Comments on COS versus CA (ctd)

The only surprising point in this trial is the complementary high ligation as it is generally admitted that HL enhances neovascularization at the groin.
Besides complementary HL brings up a question, should the outcome be equivalent in absence of HL.

Comments on COS versus CA (ctd)

The Shadid RCT, a multicenter study is interesting as USGFS was performed without HL.

At 2 years F-U

No difference in terms of PREVAIT. P= 0,407

Persistence of Reflux more frequent after USGS. P=0.003.

Total Cost in favor of USGFS COS €1824. USGFS €774

Adding that foam is less expensive one can conclude that cost effectiveness ratio is in favor of foam as far as the patient is informed that multisession USGFS is frequently necessary and accept to comply with.

Phlebectomy versus CA

De Roos KP. Ambulatory phlebectomy versus compression sclerotherapy: results of a randomized controlled trial. *Dermatol Surg* 2003;29:221-226

Summary results and Comment

At 2-year Follow-up recurrence rates were lower with Phlebectomy. P<0,001

But as liquid sclerotherapy was used we need RCT with foam that gives by far better results.

EVLA versus RFA. # RCT's 5, articles 5

Almeida JI. Radiofrequency Endovenous Closure FAST® versus Laser Ablation for the Treatment of Great Saphenous Reflux : A Multicenter, Single-blinded, Randomized Study (RECOVERY Study). ***J Vasc Interv Radiol*** **2009;20:752-759**

Shepherd AC. Randomized clinical trial of VNUS Closure FAST radiofrequency ablation versus laser for varicose veins. ***Br J Surg*** **2010;97;810-8**

Gale SS. A randomized, controlled trial of endovenous thermal ablation using the 810-nm wavelength laser and the ClosurePLUS radiofrequency ablation methods for superficial venous insufficiency of the great saphenous vein. ***J Vasc Surg*** **2010;52:645-50**

Goode SD. Laser and Radiofrequency ablation Sudy : a randomized Study comparing Radiofrequency Ablation and Endovenous Laser Ablation (810 nm). ***Eur J Vasc Endovasc Surg*** **2010;40:246-53**

Nordon IM. EVVERT comparing laser and radiofrequency: An update on endovenous treatment options. ***In Greenhalgh R, editor. BIBA publishing*****, UK. 2011:381-388**

Summary results on EVLA versus RFA

Material used

For RFA: four Closure catheters

(3 ClosureFast®, one ClosurePlus®)

and one CELON RFIT

For EVLA Three 810 and two 980-nm bare fiber.

Less bruising and less pain with ClosureFast.

Comments on EVLA versus RFA

- New laser fibers are developed e.g. radial or jacket-tip fibers.

- Kabnick has reported on a pilot study comparing RF (ClosureFast in 50 patients) versus EVLA (980 nm jacket-tipped fiber in 35 patients).

His conclusion was that the most current RF and jacket-tip laser methods and devices are indistinguishable in efficacy and short-term side-effects.
With procedure time and tumescent anesthesia also equivalent, these procedures present no genuinely significant difference to patients.

OPERATIVE PROCEDURE	ARTICLE	CONCLUSIONS
OS versus EVLA versus RFA Versus CA	Rasmussen LA, Lawaetz M, Bjoern L, Vennits B, Blemings A, Eklof B. A randomized clinical trial comparing endovenous laser ablation, radiofrequency ablation, foam sclerotherapy and surgical stripping for great saphenous varicose veins. *BJS* 2011;98:1079-87	GSV with SFJ reflux 580 lower limbs OS (group 1) versus EVLA 980 and 1470 nm, bare fiber versus (group 2) RFA Closure Fast ™ (group 3) versus UGFS, one or 2 sessions when needed (group 4) All procedures under local anesthesia and completed by phlebectomy Follow-up *3 days and 1 month* Better QoL (SF 36) as well as less pain score (P<0.001) and shorter time off work (P<0.001) in group 3 and 4 *1 year* DS examination: GSV occlusion better in group 1,2,3 compared to group 4 (P<0.001) Clinical recurrence: No significant difference

Abbreviations:
DS = duplex ultrasound ; EVLA = endovenous laser ablation ; GSV= great saphenous vein ; OS= Open Surgery: saphenofemoral ligation+ stripping, +/- perforator ligation+/- tributary phlebectomy ; QoL= quality of life ; RFA= radiofrequency ablation ; UGFS= ultrasound guided sclerotherapy.

COS versus Thermal ablation (RFA and EVLA) versus CA

This is the only RCT comparing the four operative procedures in 571 lower limbs performed under tumescent anesthesia

Results after one year showed that all treatments are efficacious *with a higher technical failure rate after foam sclerotherapy.*

RFA and foam sclerotherapy leads to faster recovery less postoperative pain and superior QOL scores Compared with EVLA and open surgery

However the follow-up is short and a bare laser fibre was used. A 5 year follow-up is ongoing.

DISCUSSION

Firstly, when long- or medium- term outcomes comparing new thermal ablation techniques become available, the development is so rapid that the material or device employed in the RCT is frequently no more used.

DISCUSSION (ctd)

Most new procedures are operator dependent and when two or more new techniques are tested in RCT's it is important that the investigators are well trained in all of them.

Behind the brief description of a procedure we don't know precisely how it was performed. For example HL + stripping technique has evolved and is presently less aggressive and invasive than it was in the past.

DISCUSSION (ctd)

RCTs are important in the evaluation of new procedures. Skepticism about conventional RCTs in non-pharmacological interventions such as surgery remains and so called expertise-based RCTs are suggested as an alternative where participants are randomized to clinicians with expertise in intervention A or clinicians with expertise in intervention B, and the clinicians perform only the procedure they are experts in.

DISCUSSION (ctd)

Accurate analysis of the presented RCTs is difficult as hidden bias can be hard to identify. For illustrating this point in some RCT's, operative procedures were performed either under local tumescent anesthesia or general anesthesia that should influence short-term evaluation.

CONCLUSION

The final conclusion based on the presented RCT's with the caveats mentioned above is that the differences between modern open classical surgery and the new endovenous procedures are insignificant in terms of midle-term FU and that no treatment modality can be recommended as superior to another.

Final Comment

In practice, in most cases the choice procedure is not made on evidence based -data but on others factors such as

-Personal mastery of the different techniques : the Practitioner will favor the one he/she masters best

-Cover/reimbursement by the Health Services/Health Insurance which varies from country to country.

- **The patient's own choice, influenced by :**
  - **possible postoperative problems**
  - **recovery time and time off work**
  - **which procedure allows easiest control of recurrences**