Title: Safety and effectiveness of early compression of free flaps following lower limb reconstruction: a systematic review

Authors: Juan Enrique Berner^{1,2}, Patrick Will^{3,4}, Luke Geoghegan⁵, Luigi Troisi⁶, Jagdeep Nanchahal⁷, Abhilash Jain^{5,8}

Affiliations:

1. Queen Victoria Hospital NHS Foundation Trust. East Grinstead, United Kingdom
2. Kellogg College, University of Oxford. Oxford, United Kingdom
3. BG Klinik Ludwigshafen. Ludwigshafen am Rhein, Germany
4. Ruprecht Karl University of Heidelberg. Heidelberg, Germany
5. Imperial College Healthcare NHS Trust. London, United Kingdom
6. University Department of Hand Surgery and Rehabilitation, San Giuseppe Hospital, IRCCS MultiMedica Group. Milan, Italy.
7. The Kennedy Institute of Rheumatology. Nuffield Department of Orthopaedic, Rheumatology and Musculoskeletal Sciences, University of Oxford. Oxford, United Kingdom.
8. Nuffield Department of Orthopaedic, Rheumatology and Musculoskeletal Sciences, University of Oxford. Oxford, United Kingdom

Corresponding author:

Mr Juan Enrique Berner MD MSc MRCS

Address: Kellogg College, University of Oxford. Oxford, United Kingdom. OX2 6PN.

Telephone: +447427074300

E-mail: juan.berner@nhs.net

Disclosure: All authors have no conflict of interest.

A protocol for this systematic review was registered with PROSPERO (CRD42019154393)

Abstract

Introduction: Early postoperative compression of free flaps for lower limb reconstruction remains controversial. It may reduce venous congestion and promote resolution of oedema. However, concerns remain regarding inadvertent pedicle compression, which may lead to flap failure. The aim of this systematic review was to determine the safety and effectiveness of this intervention.

Methods: A systematic review was designed in compliance with PRISMA. MEDLINE and EMBASE databases were searched. Parallel screening, selection of eligible studies and data gathering was carried out by two independent authors. A formal risk of bias assessment was included along with appraisal of outcomes.

Results: A total of 847 abstracts were retrieved and 262 free flaps for lower limb reconstruction were identified in 10 eligible articles. The overall flap failure rate for patients that underwent early postoperative compression was 1.6%. Apart from flap failure rates, there were no other outcomes consistently reported and none of the studies included a no-compression group for comparison.

Discussion: All the included studies had methodological flaws, resulting in a high risk of bias. Nevertheless, there was consistent reporting of flap failure as a postoperative outcome. Compression of free flaps in the context of lower limb reconstruction does not appear to be associated with a higher flap failure rate compared with other series. Compression bandages may reduce the pain associated with dangling regimes. However, there is no evidence to support that free flap compression in the context of lower limb reconstruction is associated with any other clinical benefit.

Introduction

In order to reduce the incidence and allow early identification of lower limb free flap threatening complications, several postoperative management protocols have been proposed¹. Postoperative compression of free flaps is an aspect of these practices for which there is currently no consensus.

It has been proposed that elevation could reduce acute swelling facilitated by a gradient of hydrostatic pressure², that dangling may act as an acclimatising factor increasing oxygenation, reducing venous pooling and improving flow³, and that compression optimises venous blood flow in the extremities⁴. For flap inset it is crucial to position the vascular pedicle safely to avoid inadvertent compression that might later affect blood flow⁵. Intrinsic compression caused by internal metalwork and bony prominences, or extrinsic compression caused by splints and pressure areas, can result in complete flap failure if due care is not taken⁶, as demonstrated in a recent survey of microsurgical centres in Austria, Germany and Switzerland⁷.

Traditionally, flaps have been protected with soft, tension-free dressings to avoid any unnecessary compression that might compromise flap perfusion. However, several authors have recently questioned this assumption. It has been argued that controlled, evenly-distributed, compression would not have a detrimental effect by causing direct pedicle compression, but it could also enhance recovery by reducing swelling, congestion and oedema⁸. The most common modality to deliver this therapeutic approach has been the use of postoperative compressive bandages⁹.

The aim of this systematic review was to assess the safety and effectiveness of early compression of free flaps for lower limb reconstruction. All compression modalities were investigated, along with reported results and complications.

Materials and Methods

This systematic review was designed, conducted and reported following PRISMA statement guidance¹⁰.

Before any searches were conducted, clear inclusion and exclusion criteria were defined (Table 1) and a copy of the study protocol was registered in PROSPERO (CRD42019154393).

Randomised and non-randomised controlled trials, cohort and case-control studies, case series and case reports were considered. Previous systematic and narrative reviews, and reports of techniques that did not include patient data were excluded. All studies reporting the use of a defined postoperative free flap compression modality in the context of lower limb reconstruction were included.

With the aid of a senior librarian with experience in systematic reviews, a search strategy was designed using the following free search terms: “free flap”, “free tissue flap”, “free tissue transfer”, “microsurgical flap” and “perforator flap”. These were then combined with “bandage*”, “compress*”, “wrap*”, “flap training” and “dangling”, along with “lower extremity” and their associated terms (Appendix 1). Searches were conducted on the 27th of January 2020, scrutinising EMBASE and MEDLINE databases. No filters or limitations in regard to publication time and language were used. Abstract and conference proceedings were also considered.

EndNote X8 reference management software (Clarivate Analytics, Pennsylvania, USA) was used to identify and discard duplicate entries. Two authors (JB and LT) independently screened titles and abstracts using the Rayyan QCRI software (Qatar Computing Research Institute, Qatar). Full text-reviews

was then undertaken for eligible studies looking for compliance with inclusion and exclusion criteria. A senior author (AJ) had the role to resolve any outstanding disagreements.

The obtained list of publications was then independently reviewed by two authors (LG and PW) with the aid of a pre-agreed data gathering pro-forma. Information regarding patient demographics, specific compression modalities, outcomes and complication rates were included. Formal risk of bias assessment was performed for individual publications using either the Cochrane risk of bias tool for randomised controlled trials (RoB2)¹¹ or the National Institute of Health (NIH) Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies¹², depending on the respective study design¹³.

Results

A total of 847 entries were obtained from the systematic searches, of which 498 were retrieved from MEDLINE and 349 from EMBASE. Following identification of 223 duplicate items, 624 publications were reviewed further. Of these, only 10 met the pre-defined inclusion criteria (Figure 1).

The final list of eligible articles included publications between 2008 and 2019. Of these, 2 were randomised controlled trials (RCTs), while the remainder were non-randomised studies, including 4 retrospective cohorts and 4 case series. Eight articles were available in English, while two were published in German (Table 2).

A total of 268 free flaps were reported among eligible studies, which included mainly lower limb, but also upper limb and trunk reconstruction cases. Only the data regarding lower limb cases were extracted, obtaining a total of 262 flaps that underwent a form of compression, with a median age of 54 years (range 6-88 years).

The eligible articles used extrinsic flap compression at different stages in the postoperative period. Early flap compression, defined as interventions commenced within the first postoperative week, was reported in 7 studies that included a total of 253 patients. All of these used elastic bandages to achieve compression at this stage, starting as early as post-operative day 1^{8,9,14–18}. Out of these, 4 complete flap failures were reported, resulting in an overall flap failure rate of 1.6% for early flap compression.

The remaining three eligible publications^{19–21} initiated compression by means of elastic bandages and custom-made stockings between post-operative day 14 and 28. These papers reported a smaller sample of patients with a total of 9 free tissue transfers and no flap failures.

Apart from flap failure rates, there were no other outcomes consistently reported in the included articles. Decrease in postoperative oedema²⁰ and pain reduction during dangling⁹ were reported. Near-infrared spectroscopy^{9,19,22} and micro-dialysis monitoring¹⁶ were used to measure flap perfusion parameters of compressed flaps during dangling, showing a lower drop in tissue oxygenation when compared to unwrapped limbs.

Due to the design of the studies included in this systematic review, all had moderately to high risk of bias. GRADE assessments were Moderate and Low for all of the studies included in our review.

Discussion

Postoperative interventions to optimise recovery of these patients could not only have an impact on quality of life and return to normal activities, but could also reduce overall inpatient stay and complication rates with associated cost savings²³. Limb compression is a simple and low-cost intervention that potentially could help with oedema control, while optimising venous return and lymphatic drainage^{24,25}. However, there is a rationale for avoiding deliberate compression over free flaps to avoid inadvertent pedicle compression, although this assumption has been questioned over the last decade¹⁹.

Based on the data in the studies included in this review, compression of free flaps was not associated with higher failure rates when compared to other large series. Although the quality of the articles included in this systematic review was variable, acceptable flap survival rates were consistently reported in all eligible studies. Out of the 262 cases, only 4 complete free flap failures were reported (1.6%), two secondary to deep venous thrombosis, while in the remaining five no clear cause was documented. This complication rate is well within the expected for this type of procedures, with a recent systematic review including 43 studies and 1,090 free flaps for lower limb reconstruction, reporting an overall flap failure rate of 8.3%²⁶.

Besides the reduction in pain during dangling that was reported by Kolbensschlag et al⁹, no other publications presented any other clinical benefits of compression versus lack of compression for these patients. Previous studies have demonstrated that when a free flap is first dangled, a decrease in superficial oxygen saturation follows. Flap training regimes intend to repeat dangling over a period of time, so that after a few days no drop in oxygen saturation is noted³. Compressed flaps seem to present a milder drop of oxygen saturation levels compared to non-compressed limbs^{9,19}. It has been hypothesised

that this finding could be explained by the physiological venoarteriolar response phenomenon, involving a decrease in cutaneous blood flow in the context of increased interstitial pressures in order to limit oedema formation²⁷. However, it is difficult to ascertain if these findings are clinically relevant. This is the case, especially considering that other factors that can also affect pedicle flow, such as poor microvascular technique, hypercoagulability states and systemic hypotension were not appraised in the articles included in this review. None of the studies reported standardised long-term outcomes. It would be interesting to know if these therapies are able to improve flap bulk and scarring outcomes, thereby reducing revision rates.

To our knowledge, this is the first systematic review that has examined effectiveness and the safety of early free flap compression in the lower limb. Limitations to this review are inherently related to the quality of the eligible studies. Most of the articles were non-randomised cohort studies and case series, not allowing comparison with standardised control groups. Application of compressive bandages is a complex intervention, where technique, operator and the characteristics of the bandaging influencing on the resulting compression. Consistent pressure measurements are difficult to obtain, which was reflected in the included studies.

It was not possible to conduct a subgroup analysis comparing the effects of compression on muscle versus fasciocutaneous flaps due to the fact that several studies included both types of flaps, without specifying specific results for each group. Further studies are required, ideally randomised controlled trials, comparing early limb compression versus no compression using these or similar standardised outcome measures, to fill in the gaps in evidence.

Standardisation of free flap postoperative care protocols is still an unmet goal for the ortho-plastic community. Although previous systematic reviews have addressed aspects related to these, such as dangling²⁸ and monitoring of free flaps²⁹, this is the first to focus on compression of free flaps. Considering the quality of evidence, no therapeutic recommendations can be made in relation to this intervention as there is limited evidence to support that this could lead to a clinically relevant reduction of venous congestion and oedema. However, we can conclude that according to the reports in the literature compression of free flaps is not associated with a higher flap failure rate and may be associated with a reduction in pain on dangling.

Acknowledgements

The authors would like to acknowledge Tatjana Petrinic, Bodleian Health Care Librarian, for her aid in designing the systematic search strategy used in this study.

Conflicts of interest

All authors have no conflict of interest.

Funding disclosure

No funding received

References

1. Xipoleas G, Levine E, Silver L, Koch RM, Taub PJ. A survey of microvascular protocols for lower extremity free tissue transfer II: postoperative care. *Ann Plast Surg.* 2008;61(3):280-284.
doi:<http://dx.doi.org/10.1097/SAP.0b013e3181579900>
2. Villeco JP. Edema: A silent but important factor. *J Hand Ther.* 2012;25(2):153-162.
doi:10.1016/j.jht.2011.09.008
3. Henton JMD, Simmons JMH, Hettiaratchy S, Jain A. Perfusion dynamics in lower limb reconstruction: Investigating postoperative recovery and training using combined white light photospectroscopy and laser Doppler (O2C). *J Plast Reconstr Aesthetic Surg.* 2015;68(9):1286-1292. doi:<https://dx.doi.org/10.1016/j.bjps.2015.05.006>
4. Ibegbuna V, Delis KT, Nicolaides AN, Aina O. Effect of elastic compression stockings on venous hemodynamics during walking. *J Vasc Surg.* 2003;37(2):420-425. doi:10.1067/mva.2003.104
5. Salgado CJ, Smith A, Kim S, et al. Effects of late loss of arterial inflow on free flap survival. *J Reconstr Microsurg.* 2002;18(7):579-583. doi:10.1055/s-2002-35095
6. Koul AR, Patil RK, Nahar S. Unfavourable results in free tissue transfer. *Indian J Plast Surg.* 2013;46(2):247-255. doi:10.4103/0970-0358.118600
7. Cerny M, Schantz J-T, Erne H, et al. [Overview and Introduction of a Treatment Concept for Postoperative Care and Mobilisation After Free Flap Transplantation in the Lower Extremity]. *Handchirurgie, Mikrochirurgie, Plast Chir.* 2016;48(6):363-369. doi:<https://dx.doi.org/10.1055/s-0042-120275>
8. Suh HP, Jeong HH, Hong JPJ. Is Early Compression Therapy after Perforator Flap Safe and Reliable? *J Reconstr Microsurg.* 2019;35(5):354-361. doi:10.1055/s-0038-1676604
9. Kolbensschlag J, Ruikis A, Faulhaber L, et al. Elastic Wrapping of Lower Extremity Free Flaps during

Dangling Improves Microcirculation and Reduces Pain as well as Edema. *J Reconstr Microsurg*. 2019;35(7):522-528. doi:<http://dx.doi.org/10.1055/s-0039-1688451>

10. Moher D, Liberati A, Tetzlaff J, Altman DG, Group TP. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *PLoS Med*. 2009;6(7):e1000097. doi:10.1371/journal.pmed.1000097
11. Higgins J, Sterne J, Savovic J, et al. A revised tool for assessing risk of bias in randomized trials. *Cochrane Database Syst Rev*. 2016;(10 (Suppl 1)). doi:dx.doi.org/10.1002/14651858.CD201601
12. Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies. National Institutes of Health. <https://www.nlm.nih.gov/health-topics/study-quality-assessment-tools>. Accessed June 30, 2019.
13. Dekkers OM, Egger M, Altman DG, Vandembroucke JP. Distinguishing case series from cohort studies. *Ann Intern Med*. 2012;156(1):37-40. doi:10.7326/0003-4819-156-1-201201030-00006
14. Smith TO, Hazelden S, Parker L, Jha B, Youatt M, Haywood R. The use of Coban™ compression bandage following below-knee free-flap surgery. *Int J Nurs Pract*. 2012;18(6):604-609. doi:<https://dx.doi.org/10.1111/ijn.12004>
15. Jokuszies A, Neubert N, Herold C, Vogt PM. Early start of the dangling procedure in lower extremity free flap reconstruction does not affect the clinical outcome. *J Reconstr Microsurg*. 2013;29(1):27-32. doi:<http://dx.doi.org/10.1055/s-0032-1326736>
16. Neubert N, Vogt PM, May M, et al. Does an Early and Aggressive Combined Wrapping and Dangling Procedure Affect the Clinical Outcome of Lower Extremity Free Flaps? - A Randomized Controlled Prospective Study Using Microdialysis Monitoring. *J Reconstr Microsurg*. 2016;32(4):262-270. doi:<http://dx.doi.org/10.1055/s-0035-1568882>
17. Hierner R. [The gastrocnemius muscle flaps]. *Die Musculus-gastrocnemius-Lappenplastiken*.

2008;20(2):128-144. doi:<https://dx.doi.org/10.1007/s00064-008-1236-8>

18. Knobloch K, Herold C, Vogt PM. Free latissimus dorsi flap transfer for reconstruction of soft tissue defects of the lower extremity. *Oper Orthop Traumatol*. 2012;24(2):122-130.
doi:<https://dx.doi.org/10.1007/s00064-011-0094-y>
19. Ridgway EB, Kutz RH, Cooper JS, Guo L. New insight into an old paradigm: Wrapping and dangling with lower-extremity free flaps. *J Reconstr Microsurg*. 2010;26(8):559-566.
doi:<https://dx.doi.org/10.1055/s-0030-1263292>
20. Campione E, Chuckwu C. Multi-layered short stretch compression is safe and effective in tailoring the contour of surgical flaps by expediting edema reduction: A pilot study. *Wound Repair Regen*. 2011;19(2):A17. doi:<http://dx.doi.org/10.1111/j.1524-475X.2010.00670.x>
21. Unal C, Gercek H. Use of custom-made stockings to control postoperative leg and foot edema following free tissue transfer and external fixation of fractures. *J Foot Ankle Surg*. 2012;51(2):246-248. doi:<https://dx.doi.org/10.1053/j.jfas.2011.10.029>
22. Dornseifer U, Kleeberger C, Kargl L, et al. Perfusion Controlled Mobilization after Lower Extremity Free Flaps-Pushing the Limits of Time and Intensity. *J Reconstr Microsurg*. 2017;33(3):179-185.
doi:<https://dx.doi.org/10.1055/s-0036-1594296>
23. Townley WA, Urbanska C, Dunn RLR, Khan U. Costs and coding--free-flap reconstruction in lower-limb trauma. *Injury*. 2011;42(4):381-384. doi:10.1016/j.injury.2010.10.006
24. Tzani I, Tsihlaki M, Zerva E, Papathanasiou G, Dimakakos E. Physiotherapeutic rehabilitation of lymphedema: State-of-the-art. *Lymphology*. 2018;51(1):1-12.
25. Stücker M, Link K, Reich-Schupke S, Altmeyer P, Doerler M. Compression and venous ulcers. *Phlebology*. 2013;28(1_suppl):68-72. doi:10.1177/0268355512475120
26. Haykal S, Roy M, Patel A. Meta-analysis of Timing for Microsurgical Free-Flap Reconstruction for

Lower Limb Injury: Evaluation of the Godina Principles. *J Reconstr Microsurg*. 2018;34(4):277-292.

doi:10.1055/s-0037-1621724

27. Crandall CG, Shibasaki M, Yen TC. Evidence that the human cutaneous venoarteriolar response is not mediated by adrenergic mechanisms. *J Physiol*. 2002;538(2):599-605.
doi:10.1113/jphysiol.2001.013060
28. McGhee JT, Cooper L, Orkar K, Harry L, Cubison T. Systematic review: Early versus late dangling after free flap reconstruction of the lower limb. *J Plast Reconstr Aesthetic Surg*. 2017;70(8):1017-1027. doi:http://dx.doi.org/10.1016/j.bjps.2017.04.001
29. Kagaya Y, Miyamoto S. A systematic review of near-infrared spectroscopy in flap monitoring: Current basic and clinical evidence and prospects. *J Plast Reconstr Aesthetic Surg*. 2018;71(2):246-257. doi:10.1016/j.bjps.2017.10.020

Table 1: Systematic review inclusion and exclusion criteria

Inclusion Criteria	Exclusion Criteria
<ul style="list-style-type: none"> - Studies reporting outcomes following lower limb reconstruction with free flaps - Patients underwent postoperative flap compression by any means 	<ul style="list-style-type: none"> - Studies focusing soft tissue transfer for upper limb, head and neck or trunk reconstruction only - Pre-clinical studies - Negative pressure wound therapy

Table 2: Included studies in systematic review

Reference	Study type	Location of reconstruction	Free flap choice	Modality of compression	Flap failures	Other outcomes	Quality of Evidence
Early flap compression (POD 1 – 7)							
Hierner et al., 2008 ¹⁷	Case series	Lower extremity (n=50)	Gracilis flaps	Compression bandage wrapping on POD 5-7	None	-	High risk of bias
Knobloch et al., 2012 ¹⁸	Case series	Lower extremity (n=75)	LD flaps	Compression bandage wrapping on POD 7 followed by compression stocking on POD 13	4 cases (5.3%)	-	High risk of bias
Smith et al., 2012 ¹⁴	Case series	Lower extremity (n=3)	ALT flaps	2 and 3-inch Coban™ wrapping on POD 1	None	No significant difference in limb circumference when comparing operated with non-operated limb	Poor quality
Jokuszies et al., 2013 ¹⁵	RCT	Lower extremity (n=31)*	LD, ALT, lateral arm, rectus abdominis and parascapular flaps	Compression bandage wrapping on POD 3 (Cohort 1) and POD 7 (Cohort 2)	None	Hospital stay and time to weigh bearing were measured but no significant differences were reported	High risk of bias
Neubert et al., 2015 ¹⁶	RCT	Lower extremity (n=49)*	LD, ALT, upper arm, rectus abdominis, parascapular and gracilis flaps	Compression bandage wrapping on POD 3 (Cohort 1) and POD 7 (Cohort 2)	None	No statistical difference in micro-dialysis measurements (lactate and pyruvate) between groups	Some concerns
Suh et al., 2018 ⁸	Retrospective cohort	Lower extremity (n=46), upper extremity (n=2) and trunk (n=4)	SCIP, ALT, PAP, SIEA and regional propeller flaps	Cohesive elastic bandage on POD 3 followed by custom-made compression garment aimed at 30-40mmHg compression	None	No statistical difference on pedicle flow velocity and volume duplex ultrasound measurements	Good quality
Kolbenschlag et al., 2019 ⁹	Retrospective cohort	Lower extremity (n=30)	Parascapular, ALT and LD flaps	Elastic long stretch bandage targeted at 30mmHg of compression on POD 6	None	StO2 measured with infra-red spectroscopy was higher on wrapped limbs when dangling. Wrapped dangling was less painful for patients as per visual analogue scale measurements.	Good quality
Late flap compression (POD >7)							
Ridgway et al., 2010 ¹⁹	Case series	Lower extremity (n=1)	ALT and rectus abdominis flaps	3-inch Coban™ wrapping on POD 14	None	Near-infrared spectroscopy showed improved StO2 with wrapped limbs during dangling compared with the same limb unwrapped	Poor quality
Campione et al., 2011 ²⁰	Retrospective cohort	Lower extremity (n=3)	Not specified	Multi-layered short stretch compression bandaging on POD 28	None	10-17% reduction of limb oedema. Timing and modality of assessment for this outcome was not specified	Poor quality
Unal et al., 2012 ²¹	Retrospective cohort	Lower extremity (n=5)	ALT and one pedicled gastrocnemius flaps	Custom-made compression stocking with Velcro straps on POD 28	None	No difference in subjective comparison of oedema with contralateral limb	Poor quality

POD: Post-operative day / DVT: deep vein thrombosis / *: likely to be same cohort of patients at two points in time / ALT: anterolateral thigh / LD: latissimus dorsi / TDAP: thoracodorsal artery perforator / PAP: profunda artery perforator / SIEA: superficial inferior epigastric artery / SCIP: superficial circumflex iliac artery perforator / StO2: Tissue oxygenation / RCT: randomized controlled trial

Figure 1: PRISMA flow chart