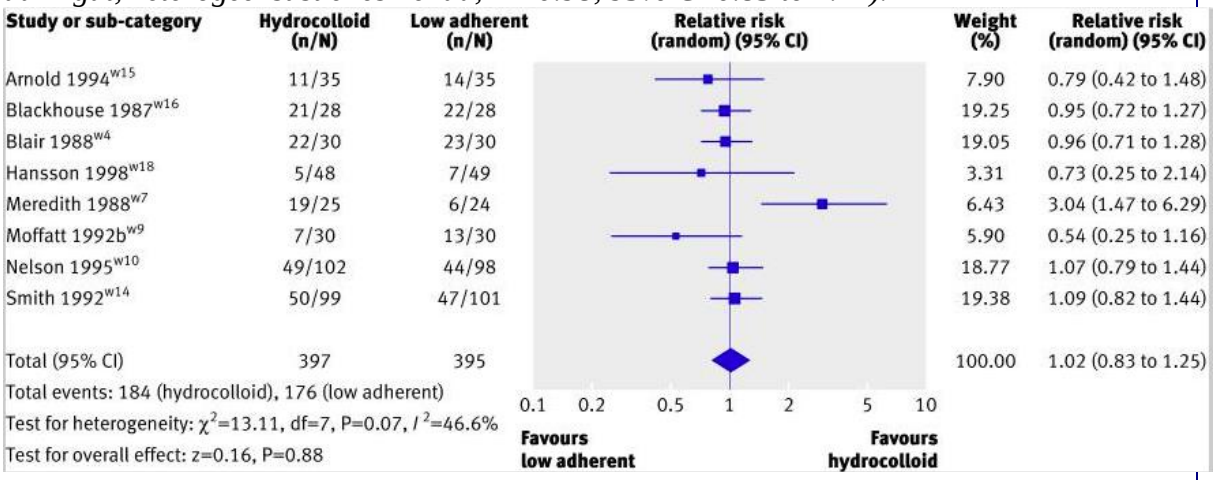
Kliiniline küsimus nr 16

Kas kõikidel kroonilise haavandiga patsientidel otsustada haavaravivahendite valik sõltuvalt haavandi faasist ja sügavusest vs mitte?

Kriitilised tulemusnäitajad: ravisoostumus, ravi tulemuslikkus, haavandi paranemine, haavandi retsidiivi teke, patsiendi elukvaliteet, patsiendi rahulolu, hospitaliseerimine, elulemus, üldsuremuse vähenemine

Süstemaatilised ülevaated

I *Palfreyman ja teised tegid 2007 aastal süstemaatilise ülevaate venoosse haavandi ja selle raviks kasutatavate plaastrite osas. Süstemaatiline ülevaade hõlmas 42 (enamik madala kvaliteediga) uuringut, kus kokku osales 3001 kroonilise venoosse haavandiga patsienti. Ülevaade leidis, et ükski haavaravi vahend ei ole teistest oluliselt parem. Uurijad leidsid, et kuna üksiki vahend ei näidanud olulist paremust võrreldes teistega peaks haavaravivahendite valimisel lähtuma mugavusest, võimalustest ning kuluefektiivsusest.*
Kokkuvõtvalt:
Hüdrokolloid plaastrid: kaasati uuringud, mis võrdlesid hüdrokolloidplaastreid madala adhesiivsusega plaastritega, vahtplaastritega, alginaat plaastritega ja teiste hüdrokolloidplaastritega
8 RCT uuringut (n=792) võrdles hüdrokolloid plaastreid madala adhesiivsusega plaastritega 4-12 nädala vältel. Täieliku paranemise osas erinevust ei täheldatud (8 uuringut, oluline uuringute erinevus; RR RR 1.02, 95% CI 0.83 to 1.25, p=0.88; 7 uuringut, heterogeensust ei esinenud, RR 0.98, 95% CI 0.85 to 1.12).



4 uuringut (n=311) võrdlesid hüdrokolloidplaastreid vahtplaastritega ning haavade paranemist 12 nädala jooksul. Statistiliselt olulist erinevust ei leitud (RR 0.98, 95% CI 0.79 to 1.22, p=0.87).

2 RCT uuringut võrdlesid hüdrokolloidplaastreid alginaatplaastritega (n=80). Ei leitud statiliselt olulist erinevust haavandite paranemises (RR 0.92, 95% CI 0.48 to 1.69).

2 RCT (n=69) uuringut võrdlesid erinevaid hüdrokolloidplaastreid omavahel. (RR 1.56, 95% CI 0.67 to 3.63). Statistiliselt olulist erinevust ei leitud.

Vahplaastrid: uuringud, mis võrdlesid vahtplaastreid madala adhesiivsusega plaastritega (2 uuringut, 203 osalejat, (RR 1.35, 95% CI 0.93 to 1.94)) alginaat plaastritega (1 uuring,

40 osalejat, RR 1.75, 95% CI 0.79 to 3.88)), silikoonplaastritega (1 uuring, 156 osalejat, RR 1.17; 95% CI 0.79 to 1.72) ning erinevaid vahtplaastreid omavahel (2 uuringut, 136 osalejat, RR 1.2, 95% CI 0.77 to 1.87)).

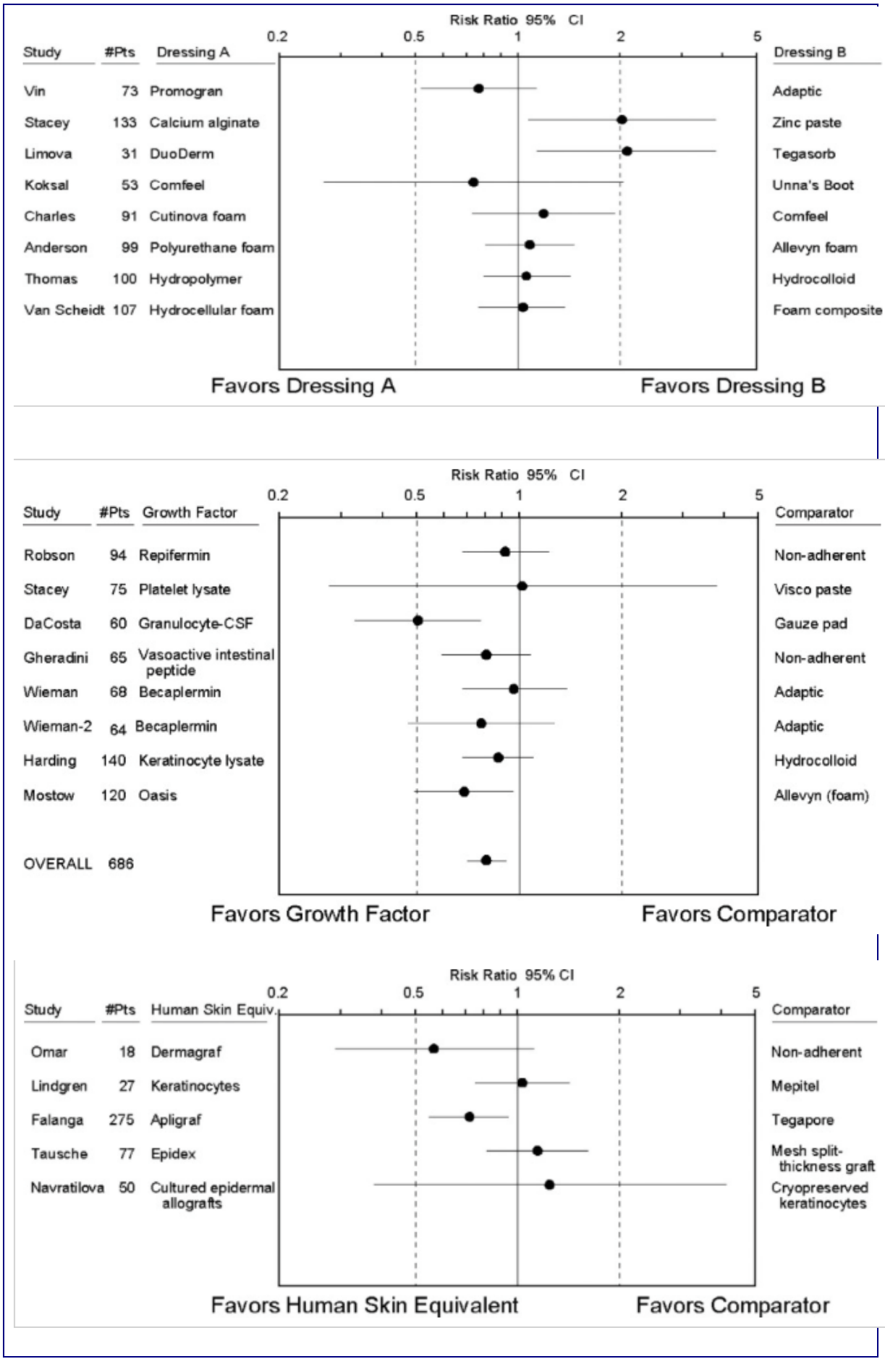
Hüdrogeel plaastrid: uuringud, mis võrdlesid hüdrogeel plaastreid madala adhesiivsusega plaastritega (2 uuringut; 151 osalejat, (RR 1.53, 95% CI 0.96 to 2.42)) , hüdrogeel plaastreid omavahel (2 uuringut, 175 osalejat. Meta-analüüs ei õnnestunud, kuna vaid 1 uuringutest tõi välja täielikult paranenud haavandite arvu. Statistiliselt olulist erinevust ei leitud) ja mitmesuguseid teisi plaastreid (statistilist erinevust ei esinenud).

Alginaat plaastrid: uuringud, mis võrdlesid alginaat plaastreid madala adhesiivsusega plaastritega (1 uuring, 60 osalejat, RR 1.08, 95% CI 0.86 to 1.36)) ja alginaat plaastreid omavahel (1 uuring, 20 osalejat, statistiliselt olulist erinevust ei leitud)
Teised uuringud: 1 uuring võrdles kadeksomeer iodiin puudrit standard raviga (otsustas arst). Esines 34% haavandi pindala vähenemine kadeksomeer iodiini grupis võrreldes 5% standard grupis.
1 RCT (n=24) võrdles hüaluronaan-derivaat fliisplaastreid parafiin sidemetega 8 nädala jooksul. Analüüs leidis statistiliselt olulise haavandi pindala vähenemise hüaluronaani grupis (p<0,002).
1 RCT (n=40) võrdles polüamiid aktiveeritud süsi plaastreid sidemetega, mis olid valitud haavandi faasile vastavalt. Ei leitud statistilist erinevust.

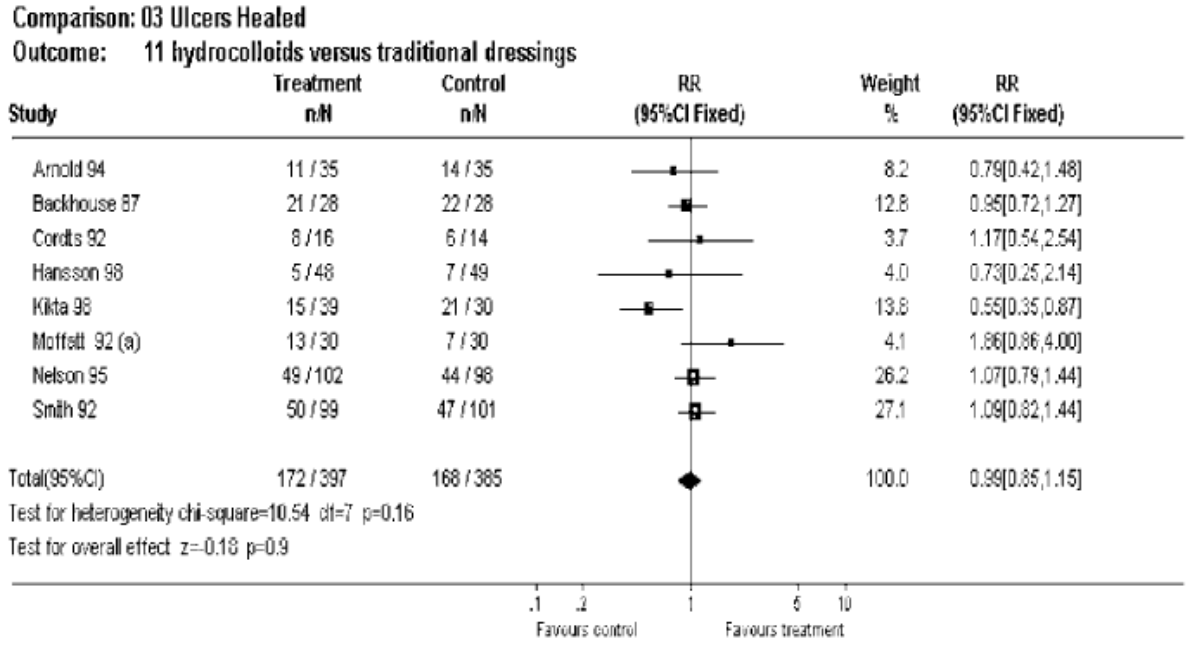
Kokkuvõtvalt: ei leitud olulist erinevust haavaraviks kasutatavatel toodetel. Kuna erinevatel plaastritel puudub oluline haavandi paranemist soodustav toime, siis peaks valikus mängima olulist rolli haavaravi toodete hind, mugavus ja kättesaadavus.

***II** 2006 aastal tehtud süstemaatiline ülevaade erinevatest haavaravi vahenditest hõlmab 20 RCT (enamikus madala kvaliteediga). 5 kaasatud uuringut näitasid statistiliselt olulist erinevust haavandite paranemises. 9 RCT uurisid semioklusiivseid plaastreid, kuid uuringud olid äärmiselt heterogeensed ja uuringuid oli raske kokkuvõtta (ei leitud statistiliselt olulist erinevust). 5 RCT uurisid human skin equivalent (HSE) tooteid (vaid 1 uuring näitas HSE paremat toimet; uuringud oli heterogeensed, mistõttu meta-analüüsi tegemine ei õnnestunud). 8 RCT uurisid kasvufaktoritega plaastreid, milledest vaid 2 näitasid statistiliselt olulist erinevust.*

Statistiline olulisus: Tsinkoksiid pasta sidemed (79% vs 56%) ja Tegasorb side (59% vs 15%) semioklusiivses/oklusiivses grupis. Kasvufaktori grupis näitasid statistilist olulisust granulotsüütide-makfrofaagide kolooniat-stimuleerivate faktorite perilesionaalne süstimine (57% vs 19%) ja sea peensoole submukoosast pärinev kollageen (Oasis; 55% vs 34%). Ainuke statistiliselt oluline RCT human skin equivalent grupis oli Apligraf (63%), mis näitas paremaid tulemusi kui Tegapore (48%).


Risk Ratio 95% CI
0.2
0.5
1
2
5
Study
#Pts
Dressing A
Dressing B
Vin 73 Promogran
Adaptic
Stacey 133 Calcium alginate
Zinc paste
Limova 31 DuoDerm
Tegasorb
Koksal 53 Comfeel
Unna's Boot
Charles 91 Cutinova foam
Comfeel
Anderson 99 Polyurethane foam
Allevyn foam
Thomas 100 Hydropolymer
Hydrocolloid
Van Scheidt 107 Hydrocellular foam
Foam composite
Favors Dressing A
Favors Dressing B
Risk Ratio 95% CI
0.2
0.5
1
2
5
Study
#Pts
Growth Factor
Comparator
Robson 94 Repifermin
Non-adherent
Stacey 75 Platelet lysate
Visco paste
DaCosta 60 Granulocyte-CSF
Gauze pad
Gheradini 65 Vasoactive intestinal peptide
Non-adherent
Wieman 68 Becaplermin
Adaptic
Wieman-2 64 Becaplermin
Adaptic
Harding 140 Keratinocyte lysate
Hydrocolloid
Mostow 120 Oasis
Allevyn (foam)
OVERALL 686
Favors Growth Factor
Favors Comparator
Risk Ratio 95% CI
0.2
0.5
1
2
5
Study
#Pts
Human Skin Equiv.
Comparator
Omar 18 Dermagraf
Non-adherent
Lindgren 27 Keratinocytes
Mepitel
Falanga 275 Apligraf
Tegapore
Tausche 77 Epidex
Mesh split-thickness graft
Navratilova 50 Cultured epidermal allografts
Cryopreserved keratinocytes
Favors Human Skin Equivalent
Favors Comparator

III *Bouza ja teised uurisid süstemaatilises ülevaates kaasaegseid haavaplaastreid. Uuringus oli 26 madala kvaliteediga RCT, paljud neist olid hõlmatud ka O'Donneli ja Lau poolt tehtud uuringus.*
8 RCT(n=397) võrdlesid hüdrokolloidplaastreid traditsiooniliste vahenditega 10 nädalat kuni 6 kuud. Kokkuvõtvalt ei leitud statistiliselt olulist erinevust (RR 0.99, 95% CI 0.85 to 1.15, p=0.90)



6 RCT võrdlesid 6-16 nädala vältel hüdrokolloidplaastreid polüuretaani, alginaadi või muu hüdrokolloidplaastriga. Kokkuvõtvalt ei leitud statistiliselt olulist erinevust haavandi paranemise osas (RR 1.13, 95% CI 0.86 to 1.47, p=0.40).
3 RCT (n= 238) võrdlesid 12 nädala kuni 12 kuu vältel polüurethaan plaastreid traditsiooniliste haavaravivahenditega (niiske marli, parafiinvõrk, mitte-adhesiivne kootud viskoos). Statistiliselt olulist erinevust paranemise osas ei täheldatud (RR 0.92, 95% CI 0.14 to 1.98, p=0.80).

IV *Cochrane 2013 aasta uuringus näidati, et hetkel ei ole tõenduspõhised uuringud suutnud näidata vahplaastrite paremaid tulemusi kroonilise venoosse haavandi ravis võrreldes teiste haavaravitoodetega. Kaasati 12 RCT (n=1023), millest enamus olid madala kvaliteediga. Hüdrotsellulaarsete vahtplaastrite ja polüuretaan vahtplaastrite võrdluses ei leitud statistiliselt olulist erinevust (3 RCT). 5 RCT (n=418; kestvusega 12-16 nädalat) ei leidnud statistiliselt olulist erinevust vahtplaastrite ja hüdrokolloidplaastrite vahel RR 1.00, 95% CI 0.81 to 1.22). Statistiliselt olulist gruppidevahelist erinevust ei leitud ka vahtplaastrite ja parafiinvõrkude (2 RCT); hüdrokapillaarse plaastri (1 RCT); kootud viskoosplaastri (1 RCT) ja proteaasi moduleeriva maatriksi vahel (1 RCT).*

V *2015 aasta Cochrane uuring võtab kokku alginaat plaastritega tehtud uuringud. Ülevaates on haaratud 5 RCT (n=295). 1 RCT võrdles alginaat plaastreid (n=20); 3 RCT võrdlesid alginaat ja hüdrokolloidplaastreid (n=215) ja 1 võrdles alginaati ning mitte-adhesiivseid plaastreid (n=60). Statistiliselt olulisi gruppide vahelisi erinevusi ei*

täheldatud. Meta-analüüsi sai teha vaid ühe võrdluse osas (alginaat ja hüdrokolloid plaastrid), andmed võeti 2 RCT (n=84) RR 0.42 (95% CI 0.14 to 1.21).

***VI** 2014 aastal tehtud süstemaatiline ülevaade kroonilise venoosse haavandi puhul kasutatavatest haavaravivahenditest võttis kokku 37 uuringut (38 publikatsiooni, n=3990), 36 uuringut 37'st olid RCT, 1 mitterandomiseeritud uuring nng üks retrospektiivne kohortuuring. 3 RCT (kestvusega 10-24 nädalat) uuringut näitasid, et hüdrokolloidplaastrid ei olnud efektiivsemad kui kompressioon üksinda. Paranemise protsent ja kiirus olid küll paremad hüdrokolloidgrupis, kuid tulemused ei olnud statistiliselt olulised. Võrdlevad uuringud hüdrokolloidtoodete ja teiste kaasaegsete haavaravitoodete vahel ei suutnud näidata erinevust. Üks nõrga tugevusega uuring suutis näidata sea peensoole submukoosa kollageen (Oasis Wound Matrix) andis haavandi paranemises paremaid tulemusi kui kompressioon üksinda (II süstematiline ülevaade andis samad tulemused O'Donnell et al). Uuringu tulemused, mis puudutasid human skin equivalente on toodud samuti O'Donnell et al uuringus .*

Viited

Kokkuvõtte (abstract või kokkuvõtlikum info)	**Viide kirjandusallikale**
I Results The search strategy identified 254 studies; 42 of these fulfilled the inclusion criteria. Hydrocolloids were no more effective than simple low adherent dressings used beneath compression (eight trials; relative risk for healing with hydrocolloid 1.02, 95% confidence interval 0.83 to 1.28). For other comparisons, insufficient evidence was available to allow firm conclusions to be drawn. None of the dressing comparisons showed evidence that a particular class of dressing healed more ulcers. Some differences existed between dressings in terms of subjective outcome measures and ulcer healing rates. The results were not affected by the size or quality of trials or the unit of randomisation. Insufficient data were available to allow conclusions to be drawn about the relative cost effectiveness of different dressings. Conclusions The type of dressing applied beneath compression was not shown to affect ulcer healing. The results of the meta-analysis showed that applying hydrocolloid dressings beneath compression produced no benefit in terms of ulcer healing compared with applying simple low adherent dressings. No conclusive recommendations can be made as to which type of dressing is most cost effective. Decisions on which dressing to apply should be based on the local costs of dressings and the preferences of the practitioner or patient.	Palfreyman S, Nelson EA & Michaels JA. Dressings for venous leg ulcers: systematic review and meta-analysis. British Medical Journal 2007; 335(7613):244–256. (URL= http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1939774/)
II RESULTS: Assessment of study design quality for the 20 RCTs showed a low percentage (<49%) of RCTs that incorporated at least 3 of 7 indicators of trial quality, but it seemed better in the 5 RCTs that showed significance for ulcer healing; 4 of the studies used at	O'Donnell TF & Lau J. A systematic review of randomized controlled trials of wound dressings for chronic venous ulcer.

least 6 of the 7 characteristics of adequate study design. Five (25%) of the 20 RCTs had a statistically significantly improved proportion of ulcers healed in the experimental dressing group over control values: zinc oxide paste bandage (79% vs 56%) and Tegasorb (59% vs 15%) in the semiocclusive/occlusive group and perilesional injection of granulocyte-macrophage colony-stimulating factor (57% vs 19%) and porcine collagen derived from small-intestine submucosa (Oasis; 55% vs 34%) in the growth factor group. In the sole significant RCT from the human skin equivalent group, Apligraf (63%) was superior to Tegapore (48%). Four of these five studies also showed an improved time to complete healing by Kaplan-Meier estimate. CONCLUSIONS: Certain wound dressings can improve both the proportion of ulcers healed and the time to healing over that achieved with adequate compression and a simple wound dressing. The selection of a specific dressing, however, will depend on the dressing characteristics for ease of application, patient comfort, wound drainage absorption, and expense.	Journal of Vascular Surgery 2006; 44(5):1118–25. (URL= http://www.jvascsurg.org/article/S0741-5214(06)01382-6/fulltext)
III Healing of leg ulcers constitutes a major clinical problem. Local methods for accelerating the healing process include modern wound dressings, but it is unclear what impact these dressings have on ulcer healing. This study examines the collective evidence on the effectiveness of modern dressings in the treatment of leg ulcers. To this end, a meta-analysis was conducted covering randomized clinical trials identified following a systematic review of the literature in different databases. Estimates of effect were calculated according to the fixed effects model. Thirty-one studies met the inclusion criteria (26 on ulcers of venous etiology, 5 on ulcers of mixed or poorly differentiated etiology). We found no study that exclusively addressed arterial ulcers. Although studies displayed considerable methodological limitations, analysis showed no significant differences in terms of the proportion of healed ulcers or reduction in wound size for both modern and conventional dressings. Similarly, no significant differences were observed between the different modern dressings compared in the studies. Thus, the current medical literature is poor in supporting the use of modern dressings to improve the healing rate of leg ulcers. There is insufficient evidence to determine whether the choice of any specific dressing type affects the healing course of these ulcers. Well-conducted trials are warranted to reliably address this question.	Bouza C, Munoz A & Amate JM. Efficacy of modern dressings in the treatment of leg ulcers: A systematic review Wound Repair and Regeneration 2005; 13(3):218–229 (URL= http://onlinelibrary.wiley.com/doi/10.1111/j.1067-1927.2005.130302.x/abstract)
IV MAIN RESULTS: Twelve RCTs (1023 participants) reporting 14 comparisons were included in this review. There was no difference in healing outcomes between hydrocellular foam dressings and polyurethane foam dressings (three RCTs). Pooled data across five RCTs (418 participants) showed no statistically significant difference between foam dressings and hydrocolloid dressings in the proportion of	O'Meara S1, Martyn-St James M. Foam dressings for venous leg ulcers. Cochrane Database Syst Rev. 2013 May 31;5:CD009907. doi: 10.1002/14651858.CD00

ulcers healed at 12 to 16 weeks (risk ratio (RR) 1.00, 95% confidence interval (CI) 0.81 to 1.22). No statistically significant between-group differences in healing outcomes were detected when foam dressings were compared with: paraffin gauze (two RCTs); hydrocapillary dressing (one RCT); knitted viscose dressing (one RCT); and protease modulating matrix (one RCT). No statistically significant between-group differences in the proportion of participants experiencing adverse events were detected when hydrocellular foam dressings were compared with polyurethane foam dressings, or when foam dressings were compared with hydrocapillary, hydrocolloid, or knitted viscose dressings (one RCT for each comparison). Six RCTs were considered as being at overall high risk of bias, and the remaining six RCTs were considered to be at overall unclear risk of bias. No included RCT had an overall low risk of bias. AUTHORS' CONCLUSIONS: The current evidence base does not suggest that foam dressings are more effective in the healing of venous leg ulcers than other wound dressing treatments. The evidence in this area is of low quality. Further evidence is required from well-designed and rigorously-conducted RCTs, that employ methods to minimise bias and report them clearly, before any definitive conclusions can be made regarding the efficacy of foam dressings in the management of venous leg ulcers.	9907.pub2. (URL= http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD009907.pub2/abstract)
V MAIN RESULTS: Five RCTs (295 participants) were included in this review. All were identified during the original review. The overall risk of bias was high for two RCTs and unclear for three. One RCT compared different proprietary alginate dressings (20 participants), three compared alginate and hydrocolloid dressings (215 participants), and one compared alginate and plain non-adherent dressings (60 participants). Follow-up periods were six weeks in three RCTs and 12 weeks in two. No statistically significant between-group differences were detected for any comparison, for any healing outcome. Meta-analysis was feasible for one comparison (alginate and hydrocolloid dressings), with data from two RCTs (84 participants) pooled for complete healing at six weeks: risk ratio 0.42 (95% confidence interval 0.14 to 1.21). Adverse event profiles were generally similar between groups (not assessed for alginate versus plain non-adherent dressings). AUTHORS' CONCLUSIONS: The current evidence base does not suggest that alginate dressings are more or less effective in the healing of venous leg ulcers than hydrocolloid or plain non-adherent dressings, and there is no evidence to indicate a difference between different proprietary alginate dressings. However, the RCTs in this area are considered to be of low or unclear methodological quality. Further, good quality evidence is required from well designed and rigorously	O'Meara S1, Martyn-St James M. Alginate dressings for venous leg ulcers. Cochrane Database Syst Rev. 2015 Aug 19;8:CD010182. doi: 10.1002/14651858.CD010182.pub3. (URL= http://www.ncbi.nlm.nih.gov/pubmed/26286189)

conducted RCTs that employ - and clearly report on - methods to minimise bias, prior to any definitive conclusions being made regarding the efficacy of alginate dressings in the management of venous leg ulcers.	
VI ABSTRACT The purpose of this study was to systematically review the literature on the benefits and harms of advanced wound dressings on wound healing, mortality, quality of life, pain, condition of the wound bed, and adverse events for patients with chronic venous leg ulcers as compared with treatment with compression alone. We searched for primary studies in the databases of MEDLINE, EMBASE, the Cochrane Central Register of Controlled Trials, and the Cumulative Index to Nursing and Allied Health Literature® from January 1980 through July 2012. Each study title, abstract, and full article was evaluated by two independent reviewers. Thirty-seven studies met our specific search criteria, although most evidence was of low or insufficient quality. Cellular dressings, collagen, and some antimicrobial dressings may improve healing rates of chronic venous leg ulcers vs. compression alone or other dressings. Limited data were available on other outcomes. The poor quality of the literature limits conclusions and necessitates future, well-conducted studies to evaluate the effectiveness of advanced wound dressings on chronic venous ulcers.	Valle MF, Maruthur NM. Comparative effectiveness of advanced wound dressings for patients with chronic venous leg ulcers: a systematic review. Wound Repair Regen. 2014 Mar-Apr;22(2):193-204. doi: 10.1111/wrr.12151. http://onlinelibrary.wiley.com/doi/10.1111/wrr.12151/full

Ravijuhendid

Kokkuvõte ravijuhendites leiduvast SVS ravijuhend: 1) Enzymatic Débridement We suggest enzymatic débridement of venous leg ulcers when no clinician trained in surgical débridement is available to débride the wound. [GRADE - 2; LEVEL OF EVIDENCE - C] We do not suggest enzymatic débridement over surgical débridement. [GRADE - 2; LEVEL OF EVIDENCE - C] 2) Topical Dressing Selection We suggest applying a topical dressing that will manage venous leg ulcer exudate and maintain a moist, warm wound bed. [GRADE - 2; LEVEL OF EVIDENCE - C] We suggest selection of a primary wound dressing that will absorb wound exudate produced by the ulcer (alginates, foams) and protect the periulcer skin. [GRADE - 2; LEVEL OF EVIDENCE - B] SIGN ravijuhend:

Simple non-adherent dressings are recommended in the management of venous leg ulcers. GRADE A

EDF ravijuhend_
There are indications that modern wound dressings are better than the traditional gauzes in the healing of wounds. Level 4.
The working group advises modern wound dressings for achieving a moist wound environment also because the dressings do not need frequent changing. The choice of a particular product depends mainly on the level of exudation.

RNAO ravijuhend

1) Dressings must be simple, low adherent, acceptable to the client and should be low cost. GRADE A

2) Choose a type of dressing depending on the amount of exudate and the phase of healing. GRADE C

3) No specific dressing has been demonstrated to encourage ulcer healing. GRADE A

AWMA ravijuhend:

No specific dressing product is superior for reducing healing time in VLUs. Select dressings based on clinical assessment of the ulcer, cost, access and patient/health professional preferences. (Grade B)

Otsingusõnad:
venous ulcer dressing, chronic ulcer dressing, chronic ulcer wound dressing, venous ulcer alginate, venous ulcer hydrocolloid, venous ulcer adhesive dressing, venous ulcer hydrogel dressing, venous ulcer healing, venous ulcer management, venous ulcer treatment.
Kasutatavaid allikaid leidus 6 + ravijuhendid 4 (SVS; AWMA; SIGN; RNAO)