Efficacy of modern dressings in the treatment of leg ulcers: A systematic review

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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. **(WOUND REP REG 2005;13:218–229)**

At present, leg ulcers constitute a serious clinical problem, not only because of their high prevalence,[1–4] refractory nature,[3–7] impact on patients' quality of life,[1,7–9] and morbidity and mortality,[1,6,7,10,11] but also because of their economic consequences on the health care system.[3,12–14] General management of leg ulcers includes control of the disease and associated risk factors as well as local treatment of the wound, whereby an attempt is made to foster the process of physiological healing and closure through the use of various procedures,[15] and of dressings in particular.[3,5,6,10,11]

RR Relative risk

Use of an occlusive or semi-occlusive dressing to maintain a moist microclimate in the wound bed was experimentally shown in the 1960s to achieve an improved epithelialization rate and to lead to faster wound healing compared with traditional healing methods.[16] These findings modified standard guidelines for local wound treatment and introduced a new concept of the dressing as being an active element capable of altering and enhancing the healing process,[17] a concept which in turn favored the development of large-scale industrial activity geared to the manufacture and marketing of technically advanced products in the form of so-called modern dressings[17,18] designed for moist-environment therapy.

The use of these dressings, of which there are now many sophisticated products composed of a wide range of materials,[17–20] has become generalized in health care practice, with the ensuing economic impact on the health care system. Indeed, half the cost of treating

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leg ulcers was recently reported as being attributable to the use of such products.[14] This widespread use has been based on the apparent capability of these dressings to alter the local environment, induce better and swifter epithelialization, and thus accelerate the process of tissue repair and healing of wounds. However, there seems to be no clear scientific evidence to support such a hypothesis,[6] nor has it been clearly established that the use of these kinds of dressings has an effect on the healing process which is in any way superior to that of simpler and cheaper conventional alternatives such as saline-gauze or nonadherent knitted viscose.[21]

Accordingly, this study sought to assess whether, on the basis of current scientific evidence, there was a real benefit, measured in terms of effectiveness, to be had in using modern vs. conventional dressings and, furthermore, whether there were significant differences between the different types of those modern dressings in the treatment of leg ulcers.

MATERIALS AND METHODS

This review confined itself to published randomized clinical trials comparing the effectiveness of one or more modern dressings (hydrocolloids, polyurethane, alginate, calcium alginate, activated charcoal, collagen)[17,18] to that of a conventional dressing or other modern dressing in the treatment of leg ulcers. We excluded other therapies used in this type of wound management, such as debriding agents; enzymes and other pharmacological agents, such as cadexomer iodine; skin substitutes; growth factors; laser; hyperbaric oxygen; electric stimulation; and application of continuous or intermittent subatmospheric pressure. The use of dressings on wounds of any other type was likewise excluded. Insofar as the studies themselves were concerned, we excluded all publications that failed to report relevant primary clinical data or present the results quantitatively.

Studies were identified by a systematic search of MEDLINE (WebSPIRS, SilverPlatter; 1966–January 2003), CINAHL (WebSPIRS) (1982–January 2003), and SWEESNET (1999–2002) electronic databases with no restriction on language and employing the following terms: Wound dressings/all subheadings; "Skin-Ulcer"/ all topical subheadings/all age subheadings; "Skin-Ulcer"/therapy/and ("dressings" or ("bandages"), Leg Ulcer/therapy and ("dressings" or ("bandages") and randomized-controlled-trial. Similarly, the Cochrane Controlled Trials Register was examined, and bibliographies of relevant articles were manually examined for additional studies.

Two reviewers evaluated and extracted the data independently. To extract data, we designed a specific form that included the following elements: study design and scope; duration of treatment and follow-up period; inclusion and exclusion criteria; sample size and method employed for calculation of same; interventions; type of randomization; baseline population characteristics and wounds studied; and clinical outcomes. Duplicate articles were removed. During the trial selection and data extraction, we were not masked to authors, institutions, journal, or interventions assessed.

Quality assessment

Methodological quality was evaluated for each selected paper using a validated scale.[22] This scale includes three items (adequate randomization, double blinding, and description of withdrawals), with a maximum possible score of five.

Data analysis

RevMan 4.1 software (Cochrane Collaboration 2000) was used to obtain a quantitative overall measure of the effect of modern dressings on the outcomes of interest. The studies were combined, by analogy, in terms of type of intervention, scope, treatment period, and outcomes. Only those studies in which the analysis and the form of presentation of results was comparable and showed no statistically significant heterogeneity were included. This was evaluated with the Q statistic ($p > 0.05$) and potential reasons for heterogeneity were explored. The meta-analysis was conducted using a fixed-effect model with dichotomous outcomes being analyzed by means of relative risk (RR; with 95% confidence interval). For analysis of the continuous variables, Weighted Mean Difference (with 95% confidence interval) was used. The data employed were reported by the authors quantitatively and explicitly; and thus, in the case of the continuous variables, in order for a study to be eligible for inclusion in the meta-analysis, the publication had to contain the results both for the mean and for the standard deviation. Scores obtained in the assessment of methodological quality allocated no weight to the meta-analysis. Results were deemed to be significant at a value of $p < 0.05$. In accordance with some recent literature we have not used funnel plots to examine the possibility of publication bias given the limitations and potential misleading results of these graphs.[23]

RESULTS

Figure 1 summarizes the search for relevant studies. After eliminating redundancies arising from the use of several databases, there were 37 potentially appropriate trials. Six studies were excluded from the analysis for the following reasons: study not obtainable;[24]

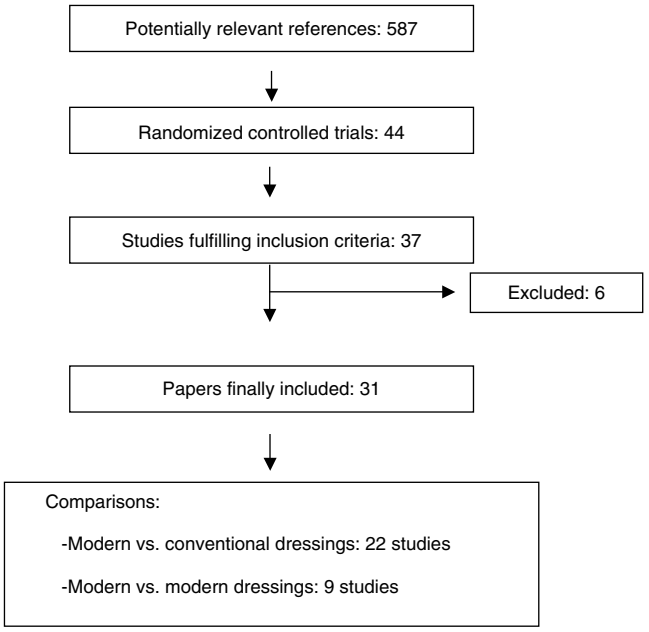

FIGURE 1. Flow diagram for study selection and comparisons performed.

failure to specify the type of chronic wound;[25] lack of description of results at the intercept in a cross-over design;[26] inclusion of several types of wounds coupled with the difficulty of identifying the data for each of the groups;[27] and no description of data on the healing variables.[28,29]

From those included, 22 studies[30–51] evaluated the use of modern vs. conventional dressings, and nine[52–60] were comparative studies of different modern dressings. Twenty-six studies[30–48,52–58] corresponded to ulcers of venous origin and five[49–51,59,60] to leg ulcers whose etiology was not clearly identified. No study that exclusively targeted arterial ulcers and met the inclusion criteria was identified.

All studies but one[37] were conducted on ambulatory patients, whether in primary or hospital care, yet, as shown in Tables 1 and 2, there were wide differences between them in terms of sample size, type of dressing employed (in both the intervention and comparator groups), baseline population characteristics and wounds studied, and duration of treatment. With respect to the outcome measures, 74% of the studies took complete healing as the primary outcome of interest. As these tables show, most of the studies displayed methodological limitations and only 10 trials scored greater than or equal to 3 on the Jadad scale, indicating good methodological quality.[22] Additionally, in some cases the description of the method and results was neither wholly clear nor complete. Five studies[36,37,52,54,59] made no reference to the size of the wound to be treated, and four failed to describe the baseline characteristics of the study population.[36,37,44,59] Seven studies made explicit mention of the fact that results were analyzed on an intention-to-treat basis[33,38,42,44,47,53,60] and only two[40,42] described the a priori calculation of the number of patients needed in order to be able to detect a clinical difference as statistically significant.

Efficacy

For analysis of efficacy, the proportion of healed ulcers within the study period was taken as the principal outcome measure, and two groups were established in line with the venous or mixed etiology of the wounds. Each group was in turn divided into two subgroups, with the comparisons between modern and conventional dressings being included in one and the results of the inter-comparisons between modern dressings being included in the other.

Ulcers of venous origin

Sixteen studies (Table 1) evaluated the complete healing of the wound and Figure 2 shows the variability in the percentage of healing obtained in the intervention and control groups in each such study by duration of treatment. Joint analysis of the eight studies (with 782 participants) that examined hydrocolloid dressings vis-à-vis gauze with paraffin or povidone iodine,[30] nonadherent knitted viscose,[31,40,42] paraffin-soaked gauze,[38,45] or Unna's boot (gauze mesh impregnated with zinc oxide, calamine, and gelatin; ConvaTec, Skillman, NJ)[35,39] revealed no statistically significant differences in healing rates between the respective hydrocolloid dressings and conventional treatment (Figure 3).

Of the studies that used polyurethane dressings, three failed to show statistical differences between said dressings and moist gauze,[43] paraffin-soaked gauze,[32] or nonadherent knitted viscose,[33] whereas Rubin[44] observed a healing rate, at 1 year of follow-up, that was significantly higher (94.7% vs. 41.2%, $p < 0.05$) for the Unna's boot group than for that treated with polyurethane (Synthaderm® Synthaderm Armour Pharmaceutical Co Ltd, East Sussex, England). In the three studies that were eligible for pooling,[32–34] the overall measure of the effect on the healing rate displayed a favorable trend in respect of the conventional group, although the difference was not significant (Table 3). Davis et al., on the other hand, observed that the polyurethane dressing achieved a significantly better mean reduction in wound area (39.26 ± 25.26 cm^2) than did conventional treatment with Unna's boot (7.11 ± 6.11 cm^2) (WMD [95% CI]:32.16 [9.56, 54,76], P = 0.005). Nevertheless, this study makes no reference to the initial size of the wound, thereby rendering these results difficult to assess.[36]

As shown in Table 3, no differences were observed in the outcome, "healing," in any of the studies that compared: an alginate against a conventional dressing[41] or zinc-impregnated gauze;[46] collagen against a

Table 1. Description of venous ulcer studies included in the analysis

Study	Inclusion and exclusion criteria	Length	Treatment	Outcome	Methodological quality
Modern vs. conventional					
Arnold et al. 1994[30]	Inclusion: venous ulcers Exclusion: arterial insufficiency, vasculitis, rheumatoid arthritis, deep dermal injury, muscle, bone, or tendon exposure	10 wk	I: hydrocolloid, n = 35 C: paraffin gauze in USA, gauze with povidone iodine in UK, n = 35 Compression bandage	Healing	Description of allocation method: no Blinded outcome assessment: no Description of withdrawals: yes
Backhouse et al. 1987[31]	Inclusion: wounds < 10 cm^2 Exclusion: Doppler-diagnosed arterial disease	12 wk	I: hydrocolloid (Granuflex®) n = 28 C: nonadherent knitted viscose, n = 28 Compression bandage	Healing	Description of allocation method: no Blinded outcome assessment: no Description of withdrawals: none
Banerjee et al. 1990[32]	Inclusion: venous ulcers in senior citizens Exclusion: (Doppler-evaluated) peripheral vascular disease	17 wk	I: polyurethane (Synthaderm®), n = 36. C: paraffin gauze (Paratull®), n = 35 Compression bandage	Healing	Description of allocation method: no Blinded outcome assessment: no Description of withdrawals: yes
Callam et al. 1992[33]	Inclusion: venous ulcers Exclusion: rheumatoid arthritis, diabetes mellitus, ABPI < 0.80	12 wk	I: knitted viscose (Tricotex®), n = 66 C: polyurethane (Allevyn®), n = 66 Compression bandage	Healing	Description of allocation method: no Blinded outcome assessment: no Description of withdrawals: yes
Capillas et al. 2000[34]	Inclusion: venous leg ulcers. One wound per patient Exclusion: infected wound	37 mo	I: Comfeel® range (hydrocolloid sheet with alginate, beads or paste, amorphous hydrogel and calcium alginate), n = 21 C: gauze dressing, n = 20	% healed surface/day Time to healing 1 cm^2	Description of allocation method: yes Blinded outcome assessment: yes Description of withdrawals: no
Cordts et al. 1992[35]	Inclusion: leg ulcers of confirmed venous etiology Exclusion: infected wound, arterial ulcers, area > 50 cm^2, uncontrolled diabetes mellitus, venous surgery in preceding month, ulcer with muscle, tendon or bone exposure, pregnancy, corticoids or chemotherapy, HIV positive	12 wk	I: hydrocolloid (Duoderm®), n = 16 C: Unna's boot*, n = 14	Healing	Description of allocation method: no Blinded outcome assessment: no Description of withdrawals: yes
Davis et al. 1992[36]	Inclusion: caused by venous insufficiency Exclusion: arterial disease	6 mo	I: polyurethane (Tegaderm/ Bioclusive®) and Unna's Boot, n = 5 C: Unna's boot, n = 7 Intermittent pneumatic compression	Reduction in area (cm^2/d) Reduction in area (cm^2)	Description of allocation method: no Blinded outcome assessment: no Description of withdrawals: no
Handfield-Jones et al. 1988[37]	Venous ulcers. No other inclusion or exclusion criteria stated	Two 3-wk periods	I: impermeable hydrocolloid (Granuflex®), n = 5 C: paraffin gauze (Jelonet®), n = 5 Compression bandage	Reduction rate/wk (%)	Description of allocation method: no Blinded outcome assessment: no Description of withdrawals: yes
Hansson 1998[38]	Inclusion: exudative wounds, area 1–100 cm^2 Exclusion: systolic ankle pressure <80 mmHg, local infection, diabetes, vasculitis, lupus, systemic sclerosis, rheumatoid arthritis, suspicion of thyroid disease, corticoids, antimicrobials, cytostatics in preceding 4 wks	12 wk	I: hydrocolloid (Duoderm E®, Granuflex E), n = 48 C: paraffin-soaked gauze (Jelonet®), n = 49 Compression bandage	Healing Reduction in area/wk (cm^2) Reduction in area (%)	Description of allocation method: no Blinded outcome assessment: no Description of withdrawals: yes
Kikta et al. 1988[39]	Inclusion: venous ulcers Exclusion: ABPI < 0.7, uncontrolled diabetes mellitus, systemic treatment with corticoids or cytostatics, recent venous surgery, infected ulcers, inability to comply with the treatment	6 mo	I: hydrocolloid (Duoderm®), n = 39 C: Unna's boot, n = 30	Healing	Description of allocation method: yes Blinded outcome assessment: no Description of withdrawals: yes

Table 1. (continued)

Study	Inclusion and exclusion criteria	Length	Treatment	Outcome	Methodological quality
Moffatt et al. 1992[40]	Inclusion: refractory ulcers Exclusion: known allergy or contraindication vis-à-vis any of the treatments	12 wk	I: hydrocolloid (Comfeel®), n = 30 C: knitted viscose, n = 30	Healing Cumulative healing rate	Description of allocation method: yes Blinded outcome assessment: no Description of withdrawals: yes
Moffatt et al. 1992[41]	Inclusion: venous ulcers, ABPI $\geq$ 0.80, area $<$ 10 cm^2 Exclusion: known allergy to any given dressing	12 wk	I: alginate (Tegagel®), n = 30 C: nonadherent porous dressing, n = 30	Healing	Description of allocation method: no Blinded outcome assessment: no Description of withdrawals: no
Nelson et al. 1995[42]	Inclusion: age >18 years, venous wounds of at least 8 weeks' duration and 1 cm in diameter. Doppler signs of venous insufficiency Exclusion: ABPI $<$ 0.80, serious disease, diabetes, rheumatoid arthritis, taking of warfarin, steroids, or vasoactive drugs	24 wk	I: hydrocolloid (Granuflex E®), n = 102 C: nonadherent knitted viscose dressing, n = 98	Healing	Description of allocation method: yes Blinded outcome assessment: no Description of withdrawals: no
Pessenhoffer, Stangl 1992[43]	Inclusion: venous ulcers Exclusion: none	281 days	I: polyurethane (Lyomousse®), n = 25. C: sterile gauze pads, n = 23 Fisher-method compression	% change in area	Description of allocation method: no Blinded outcome assessment: no Description of withdrawals: yes
Rubin et al. 1990[44]	Inclusion: chronic venous ulcers Exclusion: ABP $<$ 0.80, collagen disease, uncontrolled diabetes, chronic steroid therapy, other skin disease, lack of cooperation	1 year	I: polyurethane dressing (Synthaderm®), n = 17 C: Unna's boot, n = 19 Compression bandage	Healing Healing rate	Description of allocation method: yes Blinded outcome assessment: yes Description of withdrawals: yes
Smith et al. 1992[45]	Inclusion: Stage II wounds >2 cm in diameter Exclusions: diabetes, rheumatoid arthritis, infected ulcers, ABPI $<$ 0.75, iodine intolerance, neurological disorder, lymphoedema, malignancy in the ulcer, intolerance to compression	4 mo	I: hydrocolloid (Biofilm®), n = 99 ulcers C: paraffin gauze (Jelonet®), n = 101 Compression with bandages or stockings	Healing rate in 1st month (cm^2/d) Healing	Description of allocation method: yes Blinded outcome assessment: no Description of withdrawals: yes
Stacey et al. 1997[46]	Inclusion: venous ulcers of 0.5–10 cm diagnosed with plethysmography Exclusions: diabetes, rheumatoid arthritis, arterial disease, cellulitis	9 mo	I: alginate (Kaltostat®), n = 46 II: zinc-impregnated gauze (Viscopaste®), n = 43 III: zinc-impregnated stockinette (Acoband®), n = 44 Standard compression	Healing Time to healing	Description of allocation method: yes Blinded outcome assessment: no Description of withdrawals: yes
Vin et al. 2001[47]	Inclusion: stagnating venous ulcers, dimension $\geq$2 cm and $\leq$ 10 cm	12 wk	I: collagen (Promogran®), n = 37 C: nonadherent (Adaptic®), n = 36	Healing Surface reduction	Description of allocation method: yes Blinded outcome assessment: yes Description of withdrawals: yes
Wunderlich, Orfanos 1991[48]	Inclusion: venous ulcers Exclusion: diabetes mellitus, corticoids, drugs that might affect the healing process	6 wk	I: activated charcoal with silver (Actisorb®), n = 20 C: paraffin gauze, n = 20	Healing Mean reduction in area (%)	Description of allocation method: no Blinded outcome assessment: no Description of withdrawals: yes

Modern vs. modern					
Bale et al. 1998[52]	Inclusion: pressure ulcers, venous ulcers and ulcers due to other causes Exclusion: not stated	8 wk	I: polyurethane (Allevyn®), n: 16 venous ulcers C: improved hydrocolloid formulation (trade name not stated, ConvaTec), n = 14 venous ulcers	Healing	Description of allocation method: no Blinded outcome assessment: no Description of withdrawals: yes
Bowszyc et al. 1993[53]	Inclusion: venous, >18 years, ABPI $\geq$ 0.8 Exclusion: diabetes, heavy exudate, necrotic ulcers, clinical infection, poor state of health, corticoids immunodepression	16 wk	I: polyurethane dressing (Lyofoam®), n = 40 C: hydrocolloid dressing (Granuflex®), n = 40	Healing	Description of allocation method: yes Blinded outcome assessment: no Description of withdrawals: yes
Burgess 1993[54]	Inclusion: home patients with venous ulcers Exclusion: ABPI < 0.8	13 wk	I: Granuflex, n = 40 C: Comfeel, n = 40 III: improved Granuflex formulation, n = 41 Compression stockings	Reduction in area (mm^2/day)	Description of allocation method: no Blinded outcome assessment: no Description of withdrawals: no
Limova, Troyer-Caudle 2002[55]	Inclusion: > 21 years, venous ulcers > 1 month duration, size < 30 cm^2, length < 9 cm and depth < 1 cm, eschar < 50% of wound Exclusion: ABI < 0.8, vasculitis, uncontrolled diabetes, signs of infection, steroid or immunosupressive therapy, cutaneous disease, hypersensitivity to products to be studied	8 wk	I: hydrocolloid (Tegasorb®), n = 17 C: hydrocolloid (Duoderm CGF®), n = 14 Compression	Healing	Description of allocation method: no Blinded outcome assessment: no Description of withdrawals: yes
Smith 1994[56]	Inclusion: venous ulcers > 2.5 cm in diameter Exclusion: infection, malignancy, immunodeficiency, steroids	6 wk	I: Alginate (trade name not stated), n = 18 C: hydrocolloid (Granuflex®), n = 22 Compression bandage	Healing % change in area	Description of allocation method: no Blinded outcome assessment: no Description of withdrawals: yes
Thomas et al. 1997[57]	Inclusion: grade II–III venous or pressure ulcers, with a maximum diameter of 8 cm Exclusion: < 16 years, negligible cooperation, insulin-dependent diabetes, previous adverse reactions to study materials, infected wounds, moribund	13 wk	I: hydrocolloid (improved Granuflex formulation®), n = 50 C: polyurethane (Tielle®), n = 50 Compression bandage	Healing Change in area	Description of allocation method: yes Blinded outcome assessment: no Description of withdrawals: none
Zuccarelli 1992[58]	Inclusion: >18 years, venous ulcers of at least 4 wk, Doppler-confirmed venous disease Exclusion: ABPI < 0.80, pregnancy, myocardial infarction < 6 months, uncontrolled AHT, unstable diabetes, rheumatoid arthritis, necrotic, or infected wounds	12 wk	I: polyurethane (Allevyn®), n = 19 C: hydrocolloid (Granuflex®), n = 19 Compression bandage	Healing	Description of allocation method: no Blinded outcome assessment: no Description of withdrawals: yes

I = Intervention group; C= Control group; ABPI = ankle-brachial pressure index.
*Unna's boot = gauze mesh impregnated with zinc oxide, calamine, and gelatin convered with an elastic bandage.

Table 2. Description of leg ulcers of mixed or poorly differentiated etiology included in the analysis

Study	Inclusion and exclusion criteria	Length	Treatment	Outcomes	Methodological characteristics
Modern vs. conventional					
Mian et al. 1992[49]	Inclusion: patients with angiodermatitis in the legs Exclusion: not stated	Unclear	I: freeze-dried bovine collagen sponge (Condress®), n = 35 C: standard compression, n = 15	Area on termination of study-Reduction in area (%)	Description of allocation method: no Blinded outcome assessment: no Description of withdrawals: no
Nyfors et al. 1982[50]	Inclusion: arteriosclerotic, venous, or mixed ulcers Exclusion: infection, erysipelas	8 wk	I: polyurethane (Synthaderm®), n = 17 C: gauze soaked in saline, n = 17	Healing	Description of allocation method: no Blinded outcome assessment: no Description of withdrawals: no
Ohlsson et al. 1994[51]	Inclusion: leg ulcers of venous or mixed origin Exclusion: not stated	6 wk	I: hydrocolloid (Duoderm®), n = 15 C: gauze soaked in saline, n = 15	Healing % mean reduction in area	Description of allocation method: no Blinded outcome assessment: no Description of withdrawals: yes
Modern vs. modern					
Armstrong, Ruckley 1997[59]	Inclusion: > 18 years, ulcers with moderate-to-heavy exudate and < 7.5 cm in any dimension Exclusion: not stated	6 wk	I: hydrocolloid hydrofiber (Aquacel®), n = 21 C: hydrofiber alginate dressing (Kaltostat®), n = 23	Healing % mean reduction in area	Description of allocation method: yes Blinded outcome assessment: no Description of withdrawals: yes
Brandrup et al. 1990[60]	Inclusion: 1–100 cm^2 Exclusion: chemotherapy, corticoids, antibiotics, allergy to materials	8 wk	I: hydrocolloid (Duoderm®), n = 21 C: occlusive dressing with zinc (Mezinc®), n = 22	Healing % mean reduction in area	Description of allocation method: no Blinded outcome assessment: no Description of withdrawals: no

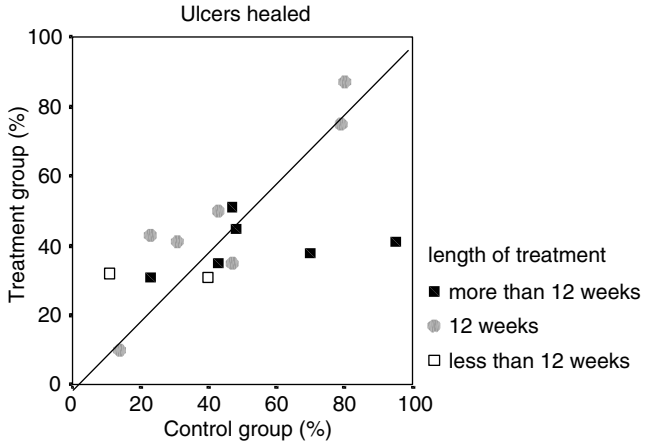

FIGURE 2. Percent of patients with healed leg ulcers in treatment (modern dressing) and control groups (conventional dressing) in relation to length of treatment.

nonadherent dressing;[47] or activated carbon against paraffin-soaked gauze.[48]

In a study in which various topical products and gauze dressings were compared with any given product in the Comfeel® (Coloplast, HumlebæK, Denmark) moist wound care range (hydrocolloid sheet with alginate, beads or paste, amorphous hydrogel and calcium alginate dressings), Capillas et al.[34] failed to observe significant differences in terms of percentage of healed surface/date of treatment, between the control (1.5%, range: 0.84–2.85) and intervention groups (1.75%, range: 0.98–2.7).

Withdrawals showed a great difference between studies, yet the pooled analysis of the 12 studies with 955 participants[30,32,33,35,38–40,44–48] that provided data failed to attain significant differences between the intervention group with modern dressings (22%) and the conventional group (17%; RR 95% CI: 1.20[0.76,1.89], P = 0.4).

A summarized description of the studies in which two different modern dressings were studied is provided in Table 1. All used hydrocolloid dressings for purposes of comparison, in three instances with polyurethane dressings[52,53,57,58] and in the remaining instances with another hydrocolloid[54,55] or an alginate dressing.[56] The overall effect estimator failed to show significant differences between groups (Figure 4).

Withdrawals showed a great variability between studies, yet the pooled analysis of the five[53,55–58] that furnished data nevertheless failed to reveal significant differences between the intervention group (10%) and the comparator (14%; RR 95% CI: 0.75[0.41,1.37], P = 0.4).

Ulcers of poorly differentiated etiology

As shown in Table 4, no significant differences were observed in the healing rate in any of the comparisons analyzed, whether between modern dressings and conventional treatment or between modern dressings and other modern dressings. Furthermore, in a small-sized study Mian et al.[49] failed to observe statistical differences in the percentage reduction in area, namely 39% in the intervention group vs. 24% in the comparator. Of the studies that used a conventional dressing, only Ohlsson et al.[51] described the withdrawal of one patient in each study group; and of those that conducted a comparative analysis of modern dressings, Armstrong and Ruckley[59] reported five cases in the hydrocolloid group and seven in the alginate comparator without specifying the cause. Brandrup et al.,[60] for their part, observed six cases in the hydrocolloid group and another six in the group treated with zinc dressing.

Safety

The adverse effect rate proved to be variable, ranging from 0[47] to 30%[33] of cases. Among the studies that compared modern dressings with conventional treatments in patients with ulcers of venous etiology, the most frequent adverse effects in both groups were clinical deterioration of the wound and presence of signs of local infection with or without cellulitis. In the case of modern dressings, special mention should

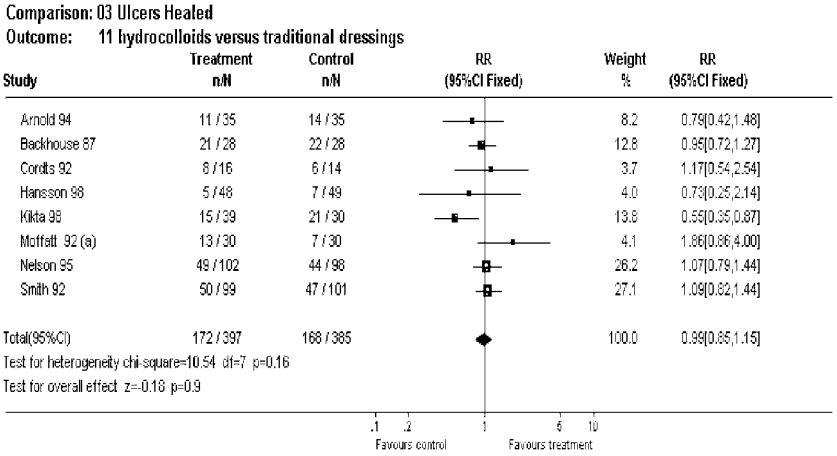

FIGURE 3. Results of the meta-analysis on ulcer healing using a fixed effects model—hydrocolloids vs. conventional dressings in venous ulcers. RR denotes relative risk. CI denotes confidence interval.

Table 3. Rate of healing comparing modern vs. conventional dressings in venous ulcers

Type of modern dressing	Studies that furnish data	Number of participants	RR (95% CI)	*p*-value
Polyurethane	3[32,33,44]	238	0.92 (0.14,1.98)	0.8
Alginate	2[41,46]	239	1.1 (0.86,1.43)	0.4
Collagen	1[47]	73	1.33 (0.71,2.49)	0.4
Activated charcoal	1[48]	38	3.00 (0.69,13.03)	0.1

also be made of the appearance of hypersensitivity and allergic reactions. Combined analysis of such studies failed to show significant differences between groups (RR [95% CI]: 1.21[0.75,1.96], P = 0.4).

Comparative studies targeting different modern dressings described similar adverse effects. Moreover, Thomas et al.[57] reported the presence of hypergranulation in three patients treated with hydrocolloid and two cases of dehydration of the wound and excessive adherence in the case of polyurethane. Overall, no significant differences were observed between groups (RR [95% CI]: 0.79[0.37,1.67], P = 0.5).[55–58]

With regard to ulcers of mixed etiology, Ohlsson et al.[51] described one case of erysipelas in the group treated with moist gauze. Brandrup et al.,[60] on the other hand, observed six adverse effects in the hydrocolloid group (two cutaneous irritations, one erysipelas and three deterioration of the wound) and four in the group treated with zinc dressing (two allergic reactions, one recurrent erysipelas, one pain).

DISCUSSION

The results of this analysis do not confirm the supposed benefits, in terms of greater effectiveness, of modern over conventional dressings in the healing of leg ulcers (whether of venous or mixed origin), in that no significant differences in healing rates are evident between the two types of dressings. Moreover, comparisons among modern dressings have similarly failed to show significant differences in said variable despite the different composition and properties of the materials employed.

The studies evince important methodologic limitations and could be affected by known causes of bias, such as little or no explanation of the procedure followed for random allocation of patients to treatment groups,[22,61] absence of blinded outcome assessment,[22,61] lack of description of inclusion/exclusion criteria or even the characteristics of the population and wound to be treated,[62] small sample size,[63] and poor quality in the description of results,[61] all of which enormously reduce the validity, both internal and external, of the information provided. Furthermore, the studies are marked by a considerable degree of heterogeneity in the types of intervention and duration of treatment. There is an evident imbalance between the study periods and the characteristics of the wounds, with a high percentage of studies having an excessively short duration given the chronicity, refractory nature, and recurrence of leg ulcers.[3–7,14] Insofar as the outcome measures are concerned, despite the fact that the different studies include variables such as visual evaluation of edema, erythema, granulation, ease of application and removal, etc., measurement of these parameters was made subjectively and was not validated, thereby rendering it difficult for decisions of effectiveness to be based on such measures. Consequently, this analysis took "complete healing" as the outcome measure of preference for comparing effectiveness from the clinical standpoint, due to the precision of the measure and its importance for clinicians and patients alike.[21,61,62] In addition, 74% of the studies took complete healing as the primary outcome of interest.

Despite these limitations, our results coincide with those of earlier studies[64] and indicate a similar effectiveness in terms of the proportion of healed ulcers or

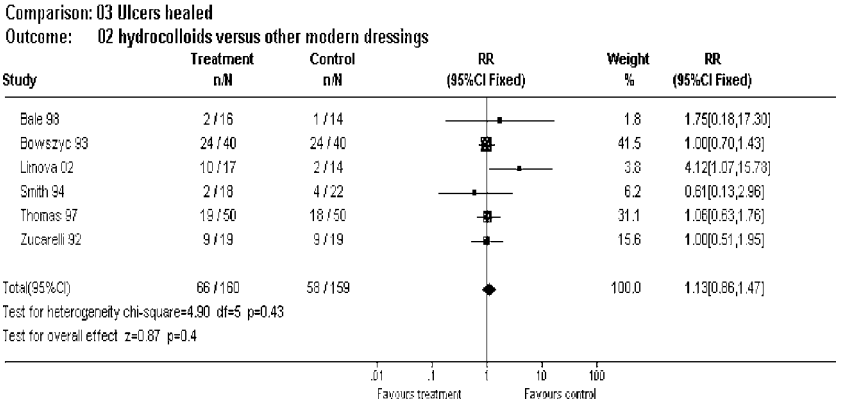

FIGURE 4. Results of the meta-analysis on ulcers healed. Fixed effects model—hydrocolloids vs. other modern dressings in venous ulcers. RR denotes relative risk. CI denotes confidence interval.

Table 4. Rate of healing comparing modern vs. conventional dressings in ulcers of mixed or poorly differentiated etiology

Study	Type of dressing	Comparator	RR (95% CI)	*p*-value
Nyfors[50]	Polyurethane	Gauze-saline	0.89 (0.45,1.75)	0.1
Ohlsson[51]	Hydrocolloid	Gauze-saline	0.29 (0.07,1.16)	0.1
Armstrong[59]	Hydrocolloid	Alginate	3.29 (0.74,14.54)	0.2
Brandrup[60]	Hydrocolloid	Occlusive-zinc	1.05 (0.30,3.68)	0.2

reduction in wound size for both modern and conventional dressings, raising doubts about the supposed benefit exerted by the former on the process of tissue repair in leg ulcers. Nevertheless, the strength of these results must be evaluated with caution, since, in addition to the above-mentioned methodological limitations, the influence of compression measures on the healing rate cannot be ruled out. Many of the studies included made use of compression in addition to dressings, a measure which has shown its effectiveness in the healing of venous leg ulcers regardless of the system employed[65] and which, it has been suggested, may foster the development of a greater degree of moisture in the wound bed and improve the effectiveness of conventional treatment.[66]

In line with what has been stated by different authors,[5,10,67] the variability observed in the healing rates reported by the individual studies suggests the existence of other factors that may be as or more important for the process of healing and closure than the degree of environmental moisture and type of dressing used. Indeed, while it has been shown experimentally that acute wounds, both animal and human, heal more quickly in a moist local environment,[16] the relevance of this fact to the healing process in chronic wounds is still not altogether clear.[68] A similar doubt is raised on considering the absence of data pointing to the greater efficacy of one or another type of modern dressing, despite the different characteristics and performance specifications attributed to the constituent materials of which these are made.[18,19,69]

Notwithstanding the enormous individual and public cost of chronic wounds, among which vascular leg ulcers are the most prevalent,[1,12–14] the best treatment for these lesions has not yet been successfully identified nor has an acceptable degree of agreement been reached by the majority of the scientific community. Perhaps for these same reasons, there is a unanimous conviction that the correct treatment of wounds demands scientifically valid data.[12,14,21,64,70,71] In this regard, the results obtained suggest that the use of modern dressings in the treatment of venous or mixed leg ulcers has become widespread in health care practice without there being any clear scientific evidence to support their superiority, in terms of effectiveness, over their conventional counterparts. Additionally, there is insufficient evidence to determine whether the choice of any specific dressing type affects the healing of leg ulcers. Well-conducted trials are warranted to reliably address all these questions. These data would be of critical importance in assessing the quality of the treatment offered to patients with leg ulcers and the suitability of the use of health care resources.

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