ORIGINAL ARTICLE

Use of oxidised regenerated cellulose/collagen dressings versus standard of care over multiple wound types: A systematic review and meta-analysis

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Abstract

Oxidised regenerated cellulose (ORC)/collagen dressings help maintain physiologically moist wound environments conducive to wound healing. While evidence supporting ORC/collagen dressing use exists, comprehensive assessment is needed. This systematic review/meta-analysis evaluated the performance of ORC/collagen dressings compared with standard dressings. A systematic literature search was performed using PUBMED, EMBASE, and QUOSA Virtual Library. Published studies and conference abstracts were assessed between 1 January 1996 and 27 July 2020. Comparative studies in English completed by 31 December 2019, with a study population ≥ 10 were included. Patient demographics, wound healing, and protease concentrations were extracted. A random-effect model was used to assess the effect of ORC/collagen dressings. Twenty studies were included following removal of duplicates and articles not meeting inclusion criteria. A statistically significant effect in favour of ORC/collagen dressings was found for wound closure ($P = 0.027$) and percent wound area reduction ($P = 0.006$). Inconclusive evidence or limited reporting prevented assessment of time to complete healing, days of therapy, number of dressing applications, pain, matrix metalloproteinase, elastase, plasmin, and gelatinase concentration. Statistically significant increase in wound closure rates and percent wound area reduction were observed in patients receiving ORC/collagen dressings compared with standard dressings in this systematic review/meta-analysis.

KEYWORDS

cellulose dressings, collagen dressings, matrix metalloproteinases, meta-analysis, wound healing

Key Messages
- oxidised regenerated cellulose (ORC)/collagen dressings help maintain physiologically moist wound environments conducive to wound healing, although a more thorough assessment of supporting literature is required
- this systematic review/meta-analysis of 20 studies evaluated the performance of ORC/collagen dressings compared with standard dressings across all wound types
- in these 20 studies, use of ORC/collagen dressings was associated with significantly increased rates of wound closure and percent wound area reduction

1 | INTRODUCTION

Rates of chronic and complex wounds have been increasing,[1] leading to the development of advanced wound dressings targeting the wound environment and helping remove potential barriers to healing, such as inadequate moisture and increased concentrations of proteases.[2,3] One such dressing family, oxidised regenerated cellulose (ORC)/collagen dressings, has a growing body of published literature to support its use. Increased wound healing rates and reduced protease activity in the wound bed have been reported in a wide variety of patients receiving ORC/collagen dressings.[4-9]

Although much of the available literature seems to be small case series without comparative dressing groups, there are a handful of comparative studies, including randomised controlled trials, that have been published. As such, a more comprehensive assessment of ORC/collagen dressing use in these comparative studies is needed. This systematic review/meta-analysis identified a set of comparative studies that evaluated the performance of ORC/collagen dressings compared with standard dressings in patients with all wound types. Differences in wound area reduction, percent area reduction, wound closure rates, and concentrations of matrix metalloproteainase-2 (MMP-2), elastase, plasmin, and gelatinase were assessed.

2 | METHODS

This systematic review/meta-analysis conformed to the statement and reporting check list of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses.[10] The systematic literature review and meta-analysis was conducted using an internal, unpublished protocol to evaluate the performance of ORC/collagen dressings (3M™ Promogran™ Matrix Wound Dressing, and 3M™ Promogran Prisma™ Matrix, Systagenix Wound Management Ltd, Gargrave, UK) versus standard dressings (ie, gauze, film dressings, hydrocolloid dressings, alginate dressings, or silicone dressings).

2.1 | Literature search

A systematic literature search using PubMed, EMBASE, and QUOSA Virtual Library was performed on 27 July 2020. Literature between 1 January 1996 and 27 July 2020 were assessed. The following search terms were used: "Promogran" OR "ORC/Collagen" OR "ORC/collagen/silver-ORC" OR ("oxidized regenerated cellulose AND Collagen"), OR ("kinetic concepts" OR "systagenix") AND ("ORC/Collagen" OR "ORC/collagen/silver-ORC" OR "oxidized regenerated cellulose" AND "Collagen."

Study inclusion criteria were published studies and conference abstracts written in English, comparison of ORC/dressings over any wound type to standard of care, and endpoint/outcomes of: healing rate, actual or percentage of wound area reduction, number and/or percentage of wounds healed, time to complete healing, MMP-2, elastase, plasmin, gelatinase concentration, wound scores, and pain scores. Studies conducted through 31 December 2019 and study populations ≥10 were also included in the analysis. Meta-analyses, reviews, protocols, pre-clinical studies, veterinary studies, and studies with <10 patients were excluded.

Studies were selected for inclusion following a review of titles and abstracts to identify studies for further review. Full text articles were assessed for eligibility by two independent reviewers. A third person reviewed the article when a disagreement occurred.

Data extraction was completed by one reviewer and was checked by a second independent reviewer. Disagreements were resolved by discussion between the two reviewers, or a third reviewer was brought in for review and discussion. Extracted data included funding source, evidence level, bias assessments, study date range, wound type, number of patients enrolled, number of patients analysed, standard of care treatment, patient characteristics and comorbidities, differences in baseline characteristics, healing rate, wound

area reduction, number and/or percentage of wounds healed or closed, time to complete healing, number of dressing changes/applications, total days of therapy, adverse events, haemostasis, wound scores, pain scores, and MMP-2, elastase, plasmin, and gelatinase concentration.

All studies included in the meta-analysis were assessed for bias in selection (randomisation and allocation concealment), performance (blinding of participants and personnel and outcome assessments), attrition (lost to follow-up or incomplete outcome data), and reporting (comparison of reported results to endpoints defined in the protocol). The Cochrane Collaboration tool for assessing risk of bias using the low risk, high risk, or unclear designations was used.

2.2 | Statistical analysis

The meta-analyses were performed by calculating standardised mean difference using random-effect models to assess the effect of ORC/collagen dressings versus the standard dressings on area reduction in cm^2. For percentage of wounds closed, odds ratios (ORs) were calculated using a random-effect model. Weighted standardised mean difference and 95% confidence intervals (CIs) were calculated to pool ORC/collagen and standard dressing groups in each publication for analysis. The outcomes were measured using a continuous variable. Treatment effects for each study were combined, and a random effects model was used for each analysis performed. The chi-square test of independence was used to assess heterogeneity. However, regardless of the heterogeneity assessment, the more conservative random effect models for sensitivity analyses were used. All analyses were performed using Comprehensive Meta-Analysis Version 3.3.070 software (Biostat Inc, Englewood, New Jersey).

Funnel plots were used to assess selection, identification, and publication bias displaying the OR by the standard error of each study. Descriptive graphs were created for MMP-2, elastase, plasmin, and gelatinase concentrations.

3 | RESULTS

3.1 | Literature search results

A total of 559 publications were identified during the literature search. After removal of duplicate publications (n = 134), 425 abstracts and titles were screened against the inclusion and exclusion criteria. Reasons for study exclusion are list in Figure 1. After the completion of the screening process, a total of 20 comparative studies

representing 2893 patients, of which 1867 (64.5%) received ORC collagen dressings and 1026 (35.5%) received standard dressings, were included in the meta-analysis (Figure 1).[11-30]

3.2 | Description of studies

Study characteristics of the included abstracts and articles are listed in Table 1. Eleven randomised controlled trials,[14,15,17-19,22-25,28,29] five prospective cohorts,[11,12,20,21,27] one case–control study,[30] and three retrospective cohorts[13,16,26] were included in the meta-analysis. The most common wound types reported were diabetic foot ulcers and venous leg ulcers. However, Snyder et al was not restricted to wound type and reported results on a wide variety of lower extremity wounds.[26] Eight studies reported patient risk factors for impaired wound healing including diabetes, peripheral vascular disease, and hypertension.[13,15,16,19,24,27,29] Dressings used in the control group included gauze, dermal templates, foam hydropolymer dressings, soft silicone contact layers, hydrocolloid dressings, film dressings, and non-adherent petrolatum-impregnated dressings. Length of treatment was reported for five studies with a treatment range from 8 to 56 days for both ORC/collagen and control dressing groups.[11,16,17,19,20] Limited reporting on time to complete healing, number of dressing changes and applications, total days of therapy, wound scores, and pain scores prevented further assessment of these outcomes.

3.3 | Risk of bias

The randomisation method was adequately explained in 11 studies (Table 2).[14,15,17-19,22-25,28,29] However, allocation masking was unclear in all 20 studies. Blinding of participants and personnel was considered high risk for all studies except Gottrup et al, where the participants and study personnel were blinded to treatment until the study had ended.[15] Blinded outcomes assessments were high risk for 13 studies and unclear in seven studies (Table 2). All 20 studies were at low risk for selective reporting bias.

Because of differences in reporting, not all of the studies reported on all the assessed outcomes. Thus, the outcome with the highest number of reporting studies was used to assess the potential for publication bias. The funnel plot of odds ratio from wound closure implies that there is little publication bias in our analysis (Figure 2). The markers that lie outside of the confidence interval depict the heterogeneity of the studies
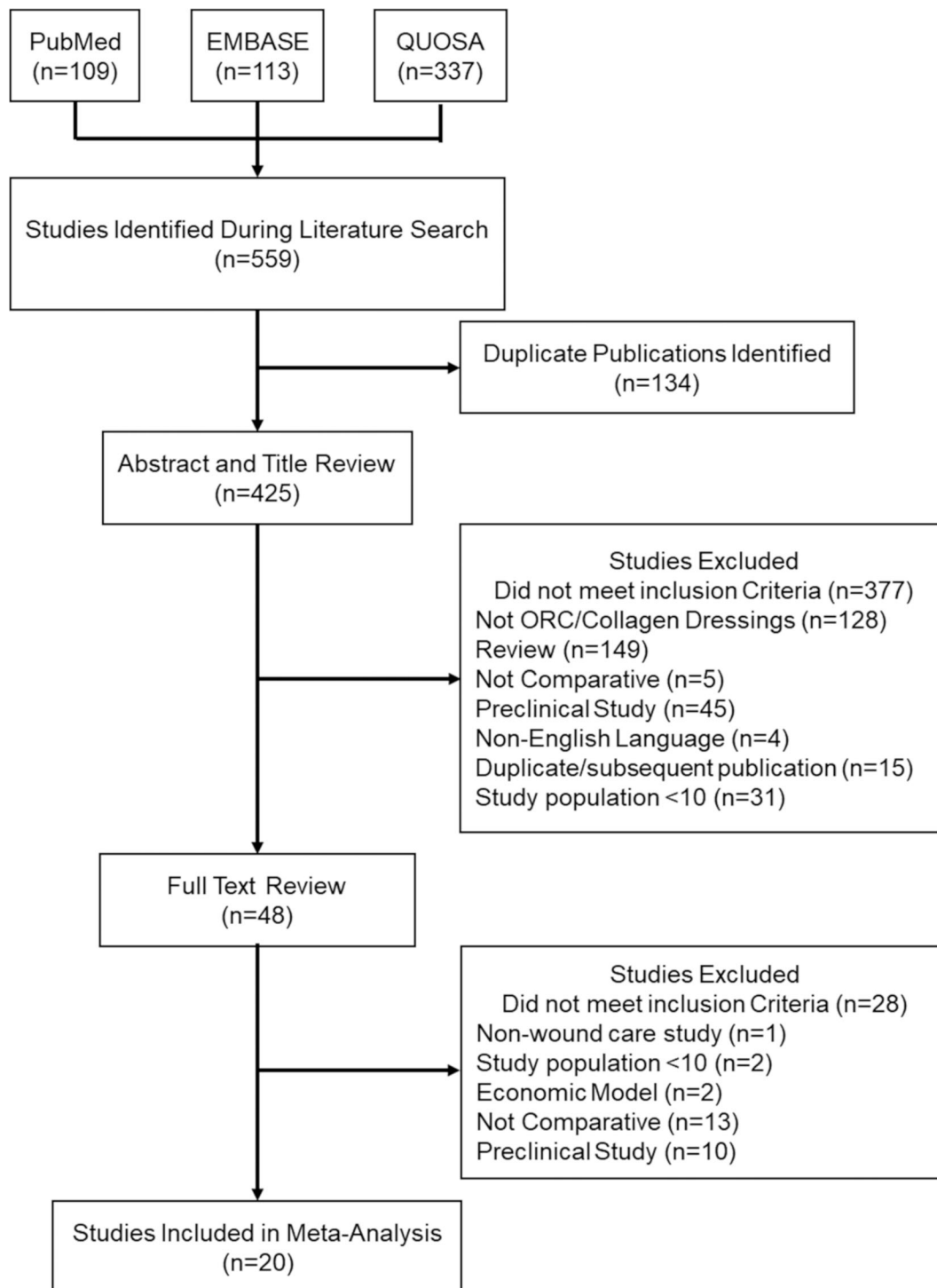
FIGURE 1 PRISMA flowchart showing the literature search process. ORC, Oxidised regenerated cellulose

in the analysis. This heterogeneity has been controlled in the meta-analyses by utilising a random effects model.

3.4 | Proportion of wounds closed

Wound healing was assessed during each study's follow-up time ranging from 2 weeks to 6 months.

Wounds receiving ORC/collagen dressings were 3.4 times more likely to close than wounds receiving control dressings (OR = 3.4, 95% CI [1.15, 10.1], $P = 0.027$; Figure 3). The Catalfamo et al study reported wound closures in all wounds for both treatment groups; therefore, an OR was unable to be calculated and the study could not be included in the analysis.

TABLE 1 Characteristics of studies included in the meta-analysis

Study	Study type	Wound type	Number of patients	Population risk factors	Therapy used Treatment	Therapy used Control	Length of therapy (days, SD) Treatment	Length of therapy (days, SD) Control
Ambrosch 2006[11]	PC	Chronic ulcers	25	Not reported	ORC/collagen	SOC	10-14	10-14
Catalfamo 2013[12]	PC	Oral cavity wounds	80	Not reported	ORC/collagen	Gauze, hydrogen peroxide, iodopovidone	NR	NR
Chowdhry 2019[13]	RC	Donor site wounds	59	HTN, hyperlipidaemia, PVD, Obesity, COPD, CHF, CAD, asthma, atrial fibrillation	ORC/Collagen/Ag-ORC	Film dressing	NR	NR
Cullen 2017[14]	RCT	VLU	49	Not reported	ORC/collagen/Ag-ORC	SOC	NR	NR
Gottrup 2013[15]	RCT	DFU	39	Diabetes	ORC/collagen/Ag-ORC	SOC	NR	NR
Griffin 2019[16]	RC	DFU	844	Arterial vascular disease, HTN, PVD, endovascular treatment	ORC/Collagen/Ag-ORC	ECM; endoform natural dermal template	21 (NR)	21 (NR)
Kakagia 2007[17]	RCT	DFU	34	Not reported	ORC/collagen	Gravitational platelet separation system	56 (NR)	56 (NR)
Kloeters 2015[18]	RCT	PI	33	Not reported	ORC/collagen	Foam hydropolymer dressing	NR	NR
Lazaro-Martinez 2007[19]	RCT	DFU	38	HTN, heart disease, PVD, amputation	ORC/collagen	SOC	14 (NR)	14 (NR)
Lobmann 2006[20]	PC	DFU	33	Not reported	ORC/collagen/Ag-ORC	SOC	8 (NR)	8 (NR)
Lüedemann 2009[21]	PC	DFU	21	Not reported	ORC/collagen	SOC	NR	NR
Motzkau 2011[22]	RCT	DFU	19	Diabetes	ORC/collagen	Silicone wound contact layer	NR	NR
Nisi 2005[23]	RCT	PI	80	Not reported	ORC/collagen	Daily disinfection of the wound, gauze soaked in white Vaseline, and hydropolymer patch	NR	NR
Schmutz 2008[24]	RCT	VLU	117	Diabetes, vein thrombosis	ORC/collagen	Nano-oligosaccharide factor	NR	NR
Smeets 2008[25]	RCT	VLU	27	Not reported	ORC/collagen	Hydrocolloid dressing	NR	NR
Snyder 2010[26]	RC	PI, DFU, surgical wounds, VLUs, infected wounds, trauma	974	Not reported	ORC/collagen	Gauze and saline	38.6 (4.62)	NR
Ulrich 2011[27]	PC	DFU	32	Diabetes	ORC/collagen	Hydrocolloid dressing	NR	NR
Veves 2002[28]	RCT	DFU	276	Not reported	ORC/collagen	Moistened gauze	NR	NR

(Continues)

TABLE 1 (Continued)

Study	Study type	Wound type	Number of patients	Population risk factors	Therapy used Treatment	Control	Length of therapy (days, SD) Treatment	Control
Vin 2002[29]	RCT	VLU	73	Hip arthrosis, knee arthrosis, diabetes, CHD, HTN	ORC/collagen	Non-adherent silicone dressing	65.9 (23.9)	63.8 (25.2)
Wollina 2005[30]	CC	VLU	40	Not reported	ORC/collagen	Hydropolymer and hydrocolloid dressings	NR	NR

Abbreviations: Ag, silver; CAD, coronary artery disease; CC, case–control study; CHD, coronary heart disease; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; DFU, diabetic foot ulcer; HTN, hypertension; NR, not reported; ORC, oxidised regenerated cellulose; PC, prospective cohort; PI, pressure injury; PVD, peripheral vascular disease; RC, retrospective cohort; RCT, randomised controlled trial; SD, standard deviation; VLU, venous leg ulcer.

3.5 | Percent area reduction

Using a random effects model, patients in the ORC/collagen group showed a greater percent area reduction compared with the control group (effect estimate of standard mean difference = 1.11, 95% CI [0.32, 1.90], $P = 0.006$; Figure 4). Studies that did not report standard deviations were not included in the analysis. An I^2 value of 0% was obtained indicating that the random effects model was successful in controlling for study variation.

3.6 | Area reduction

Area of reduction was only assessed in two studies because of lack of reporting in the remaining 18 studies. The random effects analysis indicated that patients receiving ORC/collagen showed increased area reduction compared with patients receiving control dressings (effect estimate of standard mean difference = 0.61, 95% CI [0.11, 1.11], $P = 0.017$; Figure 5). An I^2 value of 0% demonstrates that the random effects model was successful in controlling for study variation.

3.7 | MMP-2 concentrations

Four studies reported MMP-2 concentrations (Figure 6).[20,22,25,27] The studies assessed MMP-2 concentrations at different time points and reported different concentration units; therefore, a meta-analysis was unable to be performed. Lobmann et al, Motzkau et al, and Smeets et al did not find any statistically significant differences in MMP-2 concentrations at any time point between ORC/collagen and control groups.[20,22,25] However, Ulrich et al found significantly lower concentrations of MMP-2 at day 5 in the ORC/collagen group.[27]

3.8 | Elastase concentrations

Three studies reported average elastase levels (Figure 7).[18,25,27] Kloeters et al and Smeets et al observed a reduction in elastase concentrations in the ORC/collagen group compared across all time points.[18,25] Ulrich et al observed significant reduction in elastase concentration on day 5, 14, 28, 42, and 56 in the ORC/collagen group.[27] A meta-analysis could not be performed because of the elastase levels being estimated from graphical presentations.

TABLE 2 Risk of bias within studies

Study	Evidence level	Randomisation	Allocation masking	Blinding	Blinded outcomes assessments	Enrolled patients to number assessed	Results to defined endpoints
Ambrosch 2006	2	High risk	Unclear	High risk	High risk	Low risk	Low risk
Catalfamo 2013	2	High risk	Unclear	High risk	Unclear	Low risk	Low risk
Chowdhry 2019	3	High risk	Unclear	High risk	High risk	Low risk	Low risk
Cullen 2017	1	Low risk	Unclear	High risk	High risk	Low risk	Low risk
Gottrup 2013	1	Low risk	Low risk	High risk	High risk	Low risk	Low risk
Griffin 2019	3	High risk	Unclear	High risk	High risk	Low risk	Low risk
Kakagia 2007	1	Low risk	Unclear	High risk	High risk	Low risk	Low risk
Kloeters 2015	1	Low risk	Unclear	High risk	High risk	Low risk	Low risk
Lazaro-Martinez 2007	1	Low risk	Unclear	High risk	High risk	Low risk	Low risk
Lobmann 2006	2	High risk	Unclear	High risk	Unclear	Low risk	Low risk
Luedemann 2009	2	High risk	Unclear	High risk	Unclear	Low risk	Low risk
Motzkau 2011	1	Low risk	Unclear	High risk	Unclear	Low risk	Low risk
Nisi 2005	1	Low risk	Unclear	High risk	Unclear	Low risk	Low risk
Schmutz 2008	1	Low risk	Unclear	High risk	High risk	Low risk	Low risk
Smeets 2008	1	Low risk	Unclear	High risk	Unclear	Low risk	Low risk
Snyder 2010	3	High risk	Unclear	High risk	Unclear	Low risk	Low risk
Ulrich 2011	2	Unclear	Unclear	High risk	High risk	Low risk	Low risk
Veves 2002	1	Low risk	Unclear	High risk	High risk	Low risk	Low risk
Vin 2002	1	Low risk	Unclear	High risk	High risk	Low risk	Low risk
Wollina 2005	2	High risk	Unclear	High risk	High risk	Low risk	Low risk

3.9 | Plasmin concentrations

Three studies reported average elastase levels (Figure 8).[18,25,27] All three studies reported reduced levels of plasmin in ORC/collagen group compared with the control group, although it was only significant in Kloeters et al.[18,25,27] A meta-analysis could not be performed because of plasmin levels being estimated based on graphical presentations.

3.10 | Gelatinase concentrations

Two studies reported gelatinase concentrations between ORC/collagen and control groups (Figure 9).[25,27] Ulrich et al reported significantly reduced levels of gelatinase in the ORC/collagen group on day 5, 12, 28, and 42.[27] A meta-analysis could not be performed because of gelatinase levels being estimated based on graphical presentations.

3.11 | Adverse events

Eight studies reported adverse events.[12-15,24,26,28,29] Adverse events were reported in 87 (7.1%) ORC/collagen group patients and 79 (17.9%) control group patients. Adverse events included pain, infection, allergic reaction, and unspecified type (Table 3). Serious adverse events were reported in 25 (2.0%) ORC/collagen group patients and 35 (7.9%) control patients. Death was reported in two ORC/collagen patients and six control patients, although this was not related to treatment (Table 3).[28]

4 | DISCUSSION

Chronic and complex wounds can be difficult to heal and may require the use of advanced wound dressings. With the large number of advanced wound dressing options available, a comprehensive assessment of available published literature is warranted to evaluate the performance
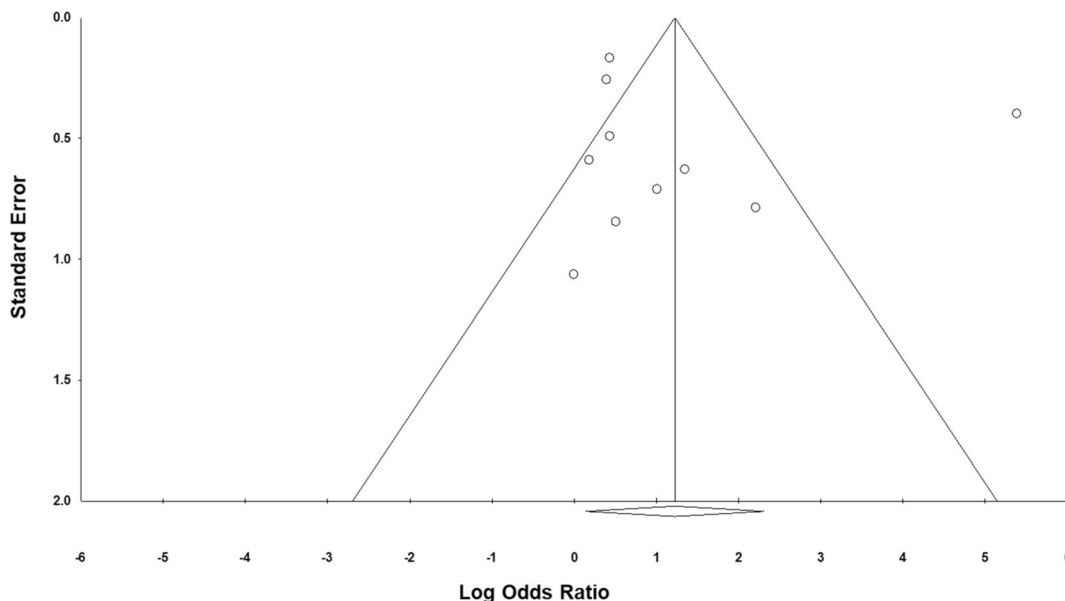
FIGURE 2 Funnel plot of studies included in the meta-analysis. Each circle indicates a single study; solid lines indicate the 95% confidence interval
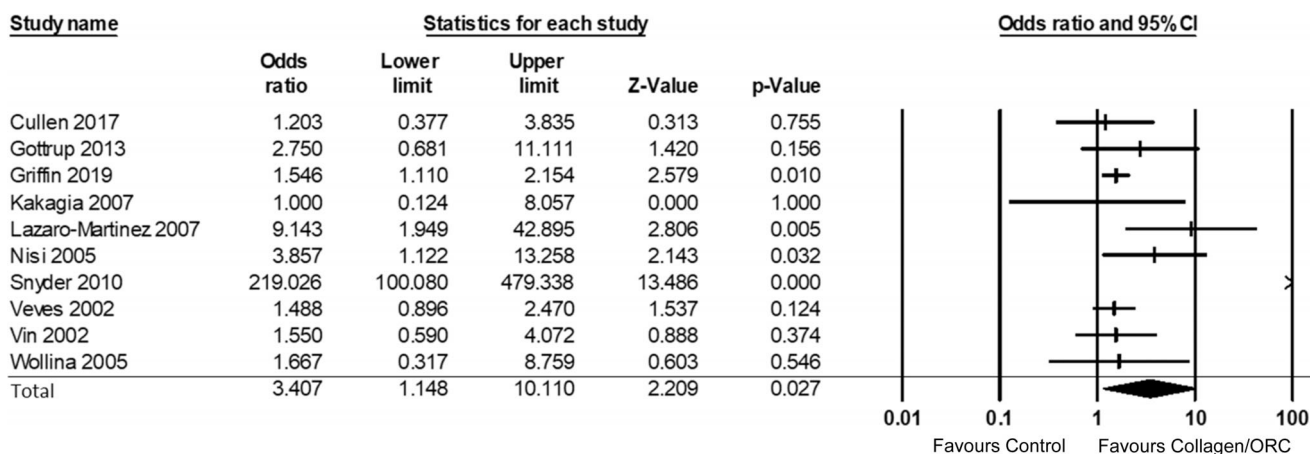

FIGURE 3 Forest plot of proportion of wounds closed comparing ORC/collagen dressings and standard dressing use. Each study is displayed with the standard difference of the means and standard error and 95% confidence interval
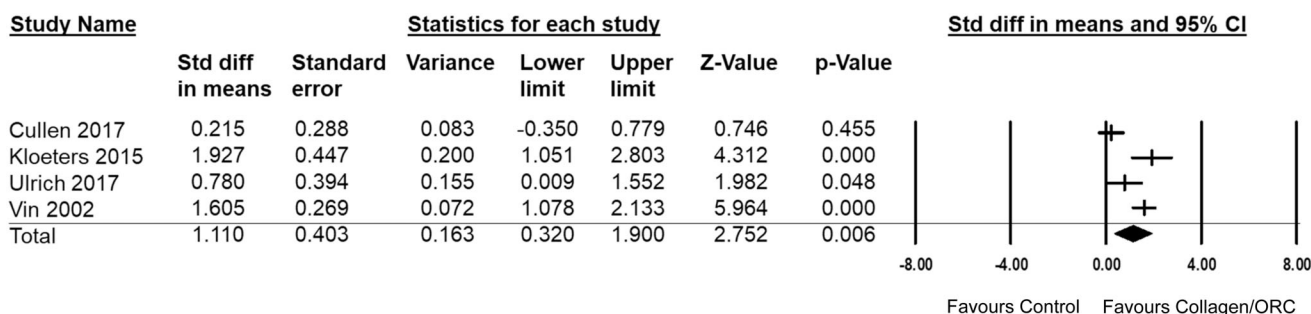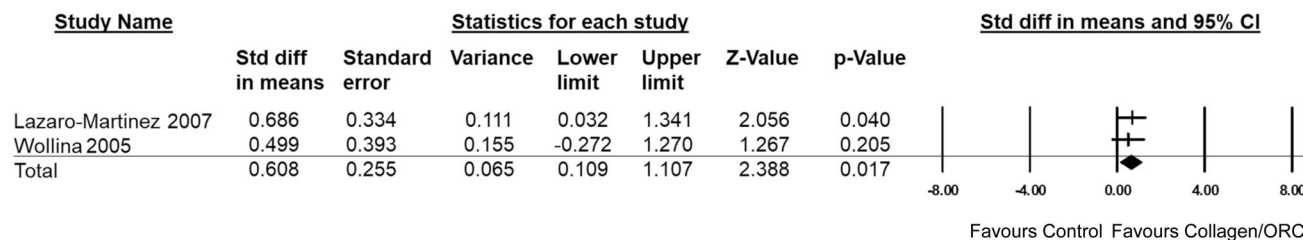

FIGURE 4 Forest plot of percent area reduction comparing oxidised regenerated cellulose (ORC)/collagen dressings and standard dressing use. Each study is displayed with the standard difference of the means and standard error, and 95% confidence interval

Study Name	Statistics for each study							Std diff in means and 95% CI
	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value	
Lazaro-Martinez 2007	0.686	0.334	0.111	0.032	1.341	2.056	0.040	
Wollina 2005	0.499	0.393	0.155	-0.272	1.270	1.267	0.205	
Total	0.608	0.255	0.065	0.109	1.107	2.388	0.017	

FIGURE 5 Forest plot of area reduction comparing ORC/collagen dressing and standard dressing use. Each study is displayed with the standard difference of the means and standard error
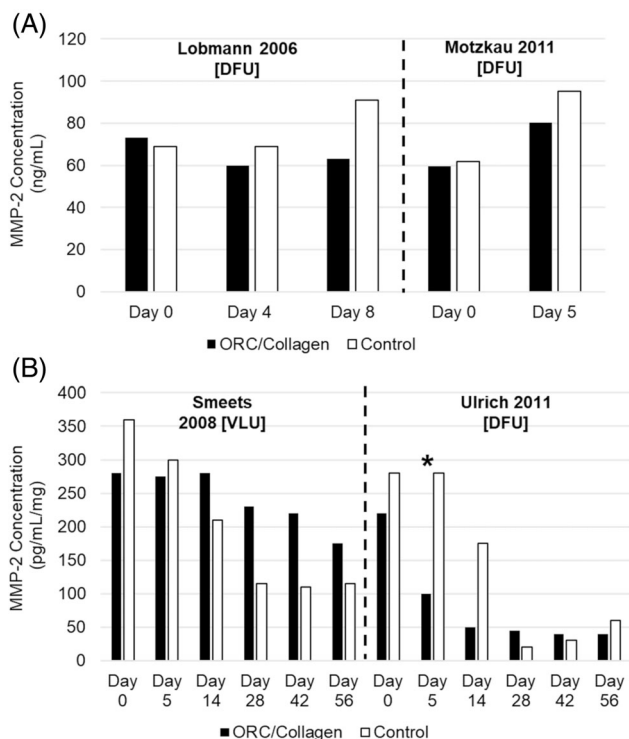
FIGURE 6 Estimated MMP-2 concentrations by study. MMP-2 concentrations reported as ng/mL (A) and pg/mL/mg (B) are shown. Oxidised regenerated cellulose (ORC)/collagen group is represented by black bars and the control group is represented by white bars. *P-value <0.05

of these dressings. This systematic literature review and meta-analysis evaluated wound area reduction, percent area reduction, wound closure rates, and concentrations of MMP-2, elastase, plasmin, and gelatinase in ORC/collagen dressings compared with standard dressings in patients with all wound types.

The literature review identified 20 comparative studies for analysis. The patient populations examined displayed patient risk factors for impaired wound healing, which was representative of the typical patient with chronic or complex wounds. Additionally, the most commonly reported wound types (diabetic foot ulcers and venous leg ulcers) are among the chronic wounds with

the highest incidence rates globally.[31] Thus, our results favouring ORC/collagen over standard dressings may be expected in similar, real-world patient populations.

Differences in wound closure rates and wound area reduction were examined between ORC/collagen and standard dressings. Individual studies reported significantly higher rates of wound closure and percentage of wound area reduction in wounds receiving ORC/collagen dressings.[16,18,19,23,26,27,29] These results were mirrored in the meta-analyses providing strong evidence for ORC/collagen dressing use resulting in improved wound closure and wound area reduction rates.

The effect of ORC/collagen dressings on wound bed protease concentrations was inconclusive. While several studies reported reductions in the concentrations of MMP-2, plasmin, elastase, and gelatinase in the wounds receiving ORC/collagen dressings,[18,20,22,25,27] concentration unit and time point differences made it difficult to accurately assess these outcomes. However, the Kloeters et al, Smeets et al, and Ulrich et al studies did report significantly reduced protease concentrations in wounds receiving ORC/collagen dressings indicating that these dressings may alter the wound environment to promote healing.[18,25,27]

Eight studies reported on adverse events with the most commonly reported being pain and infection for both the ORC/collagen dressing and standard dressing groups. A small number of patient deaths were reported for both groups but were deemed unrelated to treatment by study authors.[28] These results indicate that a similar safety profile exists between ORC/collagen and standard dressings.

Limited reporting prevented assessment of time to complete healing, days of therapy, number of dressing applications, and pain. As such, more data are needed to fully assess the clinical impact of ORC/collagen dressing use for these outcomes.

4.1 | Limitations

A majority of the available literature for ORC/collagen dressings are small, non-comparative studies. While larger,
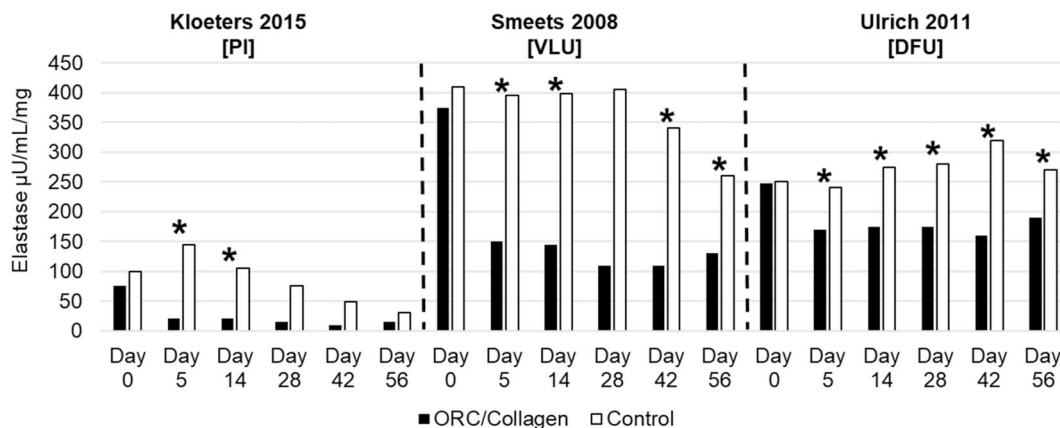
FIGURE 7 Estimated elastase concentrations by study. Oxidised regenerated cellulose (ORC)/collagen group is represented by black bars and the control group is represented by white bars. *P-value <0.05
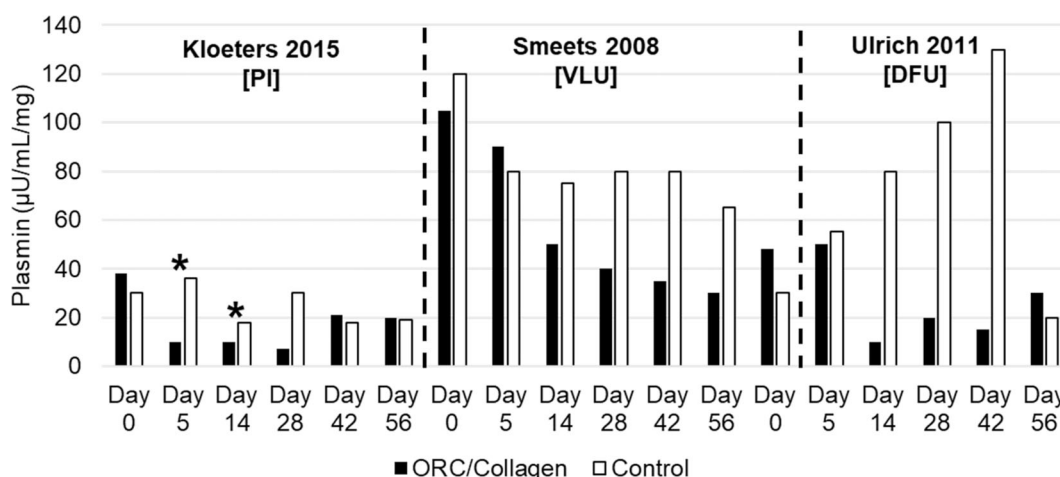

FIGURE 8 Estimated plasmin concentrations by study. Oxidised regenerated cellulose (ORC)/collagen group is represented by black bars and the control group is represented by white bars. *P-value <0.05
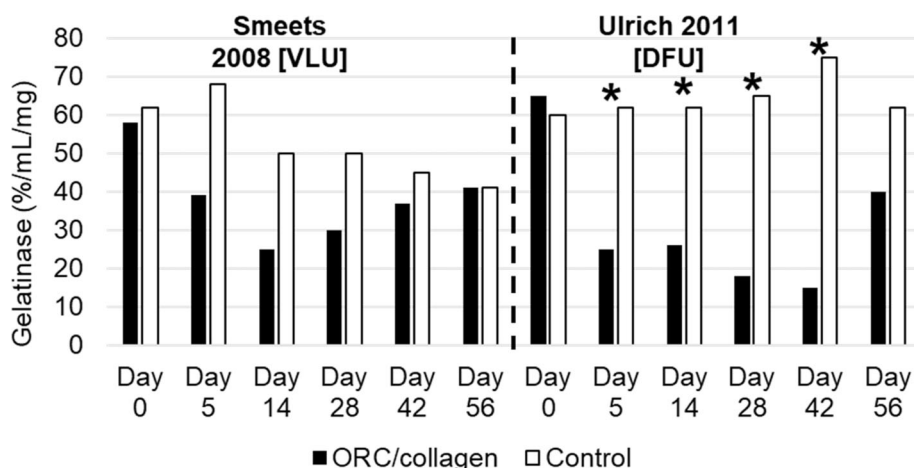

FIGURE 9 Estimated gelatinase concentrations by study. Oxidised regenerated cellulose (ORC)/collagen group is represented by black bars and the control group is represented by white bars. *P-value <0.05

randomised controlled studies will be needed to fully assess the potential clinical and health economic benefits of ORC/collagen dressings, this initial meta-analysis did find significant effects in favour of ORC/collagen dressing that should not be dismissed because of the mix of comparative studies included in the analysis.

TABLE 3 Adverse events reported from studies included in the meta-analysis

	Collagen/ORC N = 1224	Control N = 443
Number of subjects experiencing an AE	87 (7.1%)	79 (17.8%)
Number of AEs occurring by type[a]		
Allergic reaction	5 (0.4%)	5 (1.1%)
Erythema	2 (0.16%)	3 (0.68%)
Excessive exudate	3 (0.24%)	4 (0.90%)
Hyper granulation	1 (0.08%)	4 (0.90%)
Infection	14 (1.1%)	12 (2.7%)
Inflammation	2 (0.16%)	7 (1.6%)
Itching/pruritus	3 (0.24%)	0
Pain	18 (1.5%)	7 (1.6%)
Perilesional skin irritation	8 (0.65%)	7 (1.6%)
Unspecified AE type	44 (3.6%)	49 (11.1%)
Serious AE	25 (2.0%)	35 (7.9%)
Death[b]	2 (0.16%)	6 (1.4%)
Unspecified	23 (1.9%)	29 (6.5%)

Abbreviation: AE, adverse event; ORC, oxidised regenerated cellulose.
[a]Patients may experience more than one event.
[b]Death was not related to treatment.

Twelve studies did not report any patient risk factors for impaired wound healing. Thus, there is a potential for differences in patient populations between the included studies. However, heterogeneity was assessed and found to be 0%, indicating similar study populations across the included publications. To minimise any potential population heterogeneity, all meta-analyses were performed using the random effects model.

Differences in data reporting between the studies contributed to inconclusive results for time to complete healing, days of therapy, number of dressing applications, and patient reported pain. Additionally, several studies did not report standard deviations for percentage of area reduction, rendering the treatment effect of that outcome less precise.

There is always the risk for selection bias when a meta-analysis is performed. However, the authors followed a well-defined systematic literature search protocol to help minimise this potential bias. A funnel plot of the studies that reported wound closure odds ratios indicated a minimal risk of publication bias.

5 | CONCLUSIONS

In these meta-analyses, ORC/collagen dressing use was associated with increased wound closure rates and wound area reduction. More high evidence level studies are needed to fully assess the potential clinical and health economics benefits of ORC/collagen dressings.

CONFLICT OF INTEREST
S. A. Chowdhry is a consultant for 3M. Y. Nieves-Malloure, M. Camardo, J. M. Robertson, and J. Keys are employees of 3M.

DATA AVAILABILITY STATEMENT
The data that support the findings of this study are available from the corresponding author upon reasonable request.

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