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Original Research Article

EFFECT OF EPIDERMAL GROWTH FACTOR DRESSING IN COMPARISON TO COLLAGEN SHEET DRESSING FOR SKIN GRAFT DONOR SITE WOUND HEALING – A RANDOMIZED CONTROLLED TRIAL

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ABSTRACT

Background: Split-thickness skin-graft (STSG) donor sites are painful, exudative wounds, and the optimal dressing to balance rapid epithelialization, comfort, and safety remains uncertain. The objective is to compare the effectiveness of epidermal growth factor dressing and collagen sheet dressing for skin graft donor site wound healing. **Materials and Methods:** This single-centre, prospective, parallel, single-blind randomized controlled trial was conducted in the Department of General Surgery, Aarupadai Veedu Medical College & Hospital, Puducherry (July 2024–December 2025; CTRI: REF/2025/10/115713), enrolling adults (≥18 years) undergoing STSG. Participants were randomized 1:1 to EGF or collagen sheet donor-site dressings. Data were analysed using IBM SPSS Statistics v27. **Result:** Baseline profiles were well matched between groups: mean age 46.8±12.1 (EGF) vs 45.9±11.7 years (CS), male 73.3% vs 70.0%, BMI 24.1±3.1 vs 24.6±3.4 kg/m², and similar comorbidities, vitals, donor-site area (72.5±18.4 vs 73.9±19.2 cm²), and labs (all p≥0.05). Intraoperative variables were comparable, including graft thickness 0.40±0.05 vs 0.41±0.05 mm and operative time 63.2±12.4 vs 64.7±13.1 minutes. Postoperatively, pain favoured collagen sheets: POD2 3.8±1.2 vs 5.1±1.4; POD4 2.6±1.0 vs 4.0±1.3; POD6 1.6±0.8 vs 3.0±1.1 (all p<0.001). Healing favoured EGF: time to complete epithelialization 12.8±2.1 vs 15.3±2.6 days (p<0.001); complete by POD14 73.3% vs 33.3% (p=0.003); hospital stay 6.1±1.8 vs 7.2±2.1 days (p=0.022). Overall complications were lower with EGF (10.0% vs 33.3%; p=0.034). At POD14 and POD21, EGF showed less scab (40.0% vs 66.7%; p=0.036) and more normal pigmentation (66.7% vs 40.0%; p=0.036). **Conclusion:** EGF dressing accelerated epithelialization, reduced hospital stay and lowered overall morbidity compared with collagen sheets, while collagen provided superior early postoperative pain relief – supporting individualized donor-site dressing selection based on clinical priorities.

INTRODUCTION

Skin graft donor-site management remains a cornerstone of reconstructive surgery because split-thickness skin grafts (STSGs) are routinely harvested to resurface traumatic, burn, and chronic ulcer defects, yet donor sites themselves can be painful, exudative wounds with meaningful morbidity. Contemporary reviews emphasize that moist interactive dressings generally outperform dry contact layers for pain control and epithelial recovery, but comparative evidence across products is heterogeneous and high-quality trials remain limited, sustaining uncertainty about the optimal approach.[1, 2] Donor-site healing depends on rapid keratinocyte migration from adnexal structures and wound edges to restore barrier integrity, a process exquisitely regulated by growth factor signalling and the wound microenvironment.[3]

Epidermal growth factor (EGF) is a prototypical ligand for the EGFR (ErbB1) pathway that induces keratinocyte proliferation and directional migration, accelerates re-epithelialization, and modulates early inflammatory responses within acute wounds. Experimental and translational studies show that EGF triggers motogenic/mitogenic cascades (e.g., MAPK/ERK and PI3K/AKT), promotes front–rear polarity of migrating keratinocytes, and can dampen excessive inflammation – mechanisms directly relevant to donor-site closure.[4, 5] Topical delivery

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of EGF via dressings seeks to sustain bioactive concentrations in the protease-rich wound milieu, thereby enhancing resurfacing during the early postoperative phase when epithelial recovery predominates.[3] Collagen, by contrast, serves as a structural and bioactive matrix component that interacts with platelets, fibroblasts, and keratinocytes. As a dressing substrate, collagen can support haemostasis through platelet activation, provide a three-dimensional scaffold for cell adhesion and migration, and modulate inflammation, collectively fostering granulation and epithelial advancement at donor sites.[6] Modern collagen dressings are available as films, foams, and hydrogels; innovations in crosslinking and composite designs have aimed to improve exudate handling, biostability, and handling characteristics while preserving biocompatibility.[7]

Despite broad uptake of advanced dressings, practical challenges persist. Excess exudate can soak dressings and act as a medium for bacterial proliferation; displacement or shear at the interface impedes keratinocyte migration and heightens pain; and adherent contact layers may traumatize nascent epithelium upon removal.[8, 9] Large multicentre randomized data suggest that moist dressings (e.g., hydrocolloids) shorten donor-site healing time compared with other classes and that traditional gauze is associated with higher infection rates, but head-to-head evidence directly comparing bioactive strategies such as EGF-eluting platforms with collagen sheets is scarce.[10, 11] Given the complementary biological rationales – EGF as a targeted epithelial stimulant and collagen as a supportive, pro-haemostatic scaffold – a direct comparison is clinically pertinent for surgeons seeking to balance faster resurfacing, pain reduction, infection control, and cosmetic outcome after STSG harvest.[12] Against this background, the objective of the present study was to compare the effectiveness of epidermal growth factor dressing and collagen sheet dressing for skin graft donor site wound healing.

MATERIALS AND METHODS

This was a single-centre, hospital-based, prospective, parallel, single blinded, experimental study – randomized controlled trial – conducted in the outpatient department and/or inpatient wards of the Department of General Surgery, Aarupadai Veedu Medical College & Hospital, Puducherry over a period of 18 months (July 2024–December 2025; CTRI: REF/2025/10/115713). The study was approved by the Institutional Human Ethics Committee (IHEC) with reference number AV/IHEC/01/2024/056 dated 07/06/2024. The participants were given the Participant Information Sheet (PIS) in their native language, and its contents were verbally explained to ensure their understanding and satisfaction. Adult patients (≥18 years) of either sex with a healing ulcer scheduled for STSG and willing to provide written informed consent were included. Patients were excluded if they had known hypersensitivity to collagen, an infected donor-site wound, uncontrolled diabetes, severe anaemia or hypoproteinaemia, immunocompromised status, mental illness, malignancy with local irradiation, or collagen vascular disease.

The trial was powered for the continuous primary outcome (donor-site pain score) using a two-sample comparison of independent means with equal allocation in a superiority design (two-sided α=0.05; power=90%). Based on a prior similar study,[13] we assumed an expected between-group mean difference (Δ) of 2.0 points and a pooled SD of 2.3 (Cohen's d=0.87), which yielded a minimum sample size of 28 participants per arm; allowing for 5% attrition/non-response, this was increased to 30 per arm (total N=60; EGF n=30; collagen n=30). Participants were recruited using a non-probability approach (convenience/purposive sampling or complete enumeration). Each participant had undergone a detailed clinical evaluation, including medical/surgical history and a focused examination with documentation of vital signs and local wound status. Baseline investigations comprised complete blood count, urine routine and microscopy, serum urea, electrolytes, creatinine, and liver function tests. Intra-operative variables, including the duration of surgery (skin harvest to donor-site dressing application), were recorded prospectively by the operating team. Participants were randomized in a 1:1 ratio to receive either EGF dressing or collagen sheet dressing at the donor site. Randomization had been implemented using an allocation-concealment method with sequentially numbered, opaque, sealed envelopes prepared from a computer-generated sequence. The allocated donor-site dressing was applied intra-operatively per manufacturer recommendations and secured. Postoperative care was standardized across arms (analgesia, antibiotics if indicated, limb elevation, and routine nursing protocols). Donor-site dressings were not disturbed before postoperative day (POD) 14 unless clinically mandated (e.g., soakage or suspected infection). Participants were evaluated daily during admission for adverse events and predefined postoperative complications, including surgical-site infection (SSI, CDC criteria), seroma/hematoma, flap necrosis, graft rejection, graft necrosis, and any need for re-intervention. Length of hospital stay (admission to discharge) was recorded for all participants.

Pain at the donor site was assessed on POD 2, 4, and 6 using a 0–10 Numeric Rating Scale (0=no pain, 10=worst possible pain); for participants with low health literacy, the Wong–Baker FACES visual aid was used to facilitate scoring, and the corresponding 0–10 numeric value was documented. The primary healing outcome was time to complete epithelialization, defined as the number of days from surgery to the first date the donor site was fully epithelialized and no longer required a dressing.

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Outpatient follow-up visits were scheduled on POD 14 and POD 21. At each visit, the donor site was examined systematically, and the following parameters were recorded on a structured case-record form: (i) pigmentation (categorized as normal, hypopigmentation, or hyperpigmentation), (ii) presence/absence of scab formation, and (iii) evidence of infection. The first formal 'look' occurred on POD 14 (when the primary dressing was removed), and a second evaluation ('second look') was performed on POD 21 to capture interval healing and skin colour changes.

Statistical analysis: All analyses were two-tailed with α=0.05 and were performed using IBM SPSS Statistics v27. Baseline characteristics were summarized as mean ± SD or median (IQR) for continuous variables and as n (%) for categorical variables. Between-group differences at baseline were assessed using the independent-samples t-test (or Mann–Whitney U when Shapiro–Wilk indicated non-normality) and Chi-square/Fisher's exact tests for categorical variables. The analysis set was intention-to-treat (all randomized). No interim analyses were planned; all analyses followed a prespecified analysis plan aligned with CONSORT recommendations.

RESULTS

Of 74 individuals screened, 14 were excluded (9 ineligible, 5 declined), and 60 were randomized 1:1 to EGF (n=30) or collagen sheet (n=30); all received the allocated intervention, none were lost to follow-up, and all randomized participants were included in the final analysis. Baseline characteristics were comparable between the EGF and collagen sheet groups (n=30 each). The mean (SD) age was similar (46.8 [12.1] vs 45.9 [11.7] years; p=0.762), with most participants aged 31–50 years (53.3% vs 56.7%) and one-third aged >50 years in both groups (33.3%; p=0.793). Males predominated (73.3% vs 70.0%; p=0.787). Mean BMI was also comparable (24.1 [3.1] vs 24.6 [3.4] kg/m²; p=0.579), with overweight/obesity being common (overweight 36.7% vs 30.0%; obese 33.3% vs 46.7%; p=0.555). The prevalence of comorbidities did not differ significantly, including diabetes mellitus (30.0% vs 33.3%; p=0.790) and hypertension (26.7% vs 23.3%; p=0.774). Current smoking (20.0% vs 23.3%; p=0.754), current alcohol use (23.3% vs 20.0%; p=0.758), and prior surgery at the graft site (16.7% vs 13.3%; p=0.722) were likewise similar across groups.

Perioperative parameters were well balanced between the two groups (n=30 each). Baseline vitals were comparable, including temperature (36.9±0.4 vs 36.8±0.4 °C; p=0.498), pulse rate (82.4±10.6 vs 81.2±9.8 beats/min; p=0.620), systolic BP (122.6±11.3 vs 124.1±10.9 mmHg; p=0.541), and oxygen saturation (98.0±1.2 vs 97.8±1.3%; p=0.523). Donor sites were predominantly from the thigh in both arms (80.0% vs 76.7%; p=0.752), with similar donor-site area (72.5±18.4 vs 73.9±19.2 cm²; p=0.783) and low rates of local erythema (10.0% vs 13.3%; p=0.687) and edema (13.3% vs 16.7%; p=0.718). Laboratory values were also comparable, including haemoglobin (12.3±1.5 vs 12.1±1.6 g/dL; p=0.602), total leukocyte count (8.4±2.0 vs 8.6±2.1×10³/µL; p=0.672), platelet count (278±64 vs 271±68×10³/µL; p=0.642), renal function (creatinine 0.94±0.21 vs 0.96±0.22 mg/dL; p=0.628), and transaminases (ALT 28.4±9.7 vs 29.8±10.2 U/L; p=0.579). All participants received preoperative antibiotics (100% in both groups). Operative characteristics were similar, including time from harvest to dressing (18.7±4.6 vs 19.1±5.1 min; p=0.731), graft thickness (0.40±0.05 vs 0.41±0.05 mm; p=0.384), estimated blood loss (78±22 vs 82±24 mL; p=0.498), and duration of surgery (63.2±12.4 vs 64.7±13.1 min; p=0.640).

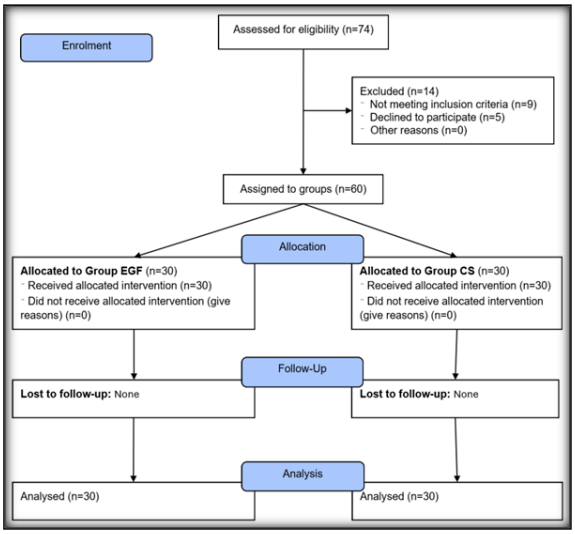

Figure 1: CONSORT flow diagram

Postoperative outcomes favoured the EGF group (n=30) compared with the collagen sheet (CS) group (n=30). Pain scores were consistently higher in the EGF arm at each assessment, including POD2 (5.1±1.4 vs 3.8±1.2), POD4 (4.0±1.3 vs 2.6±1.0), and POD6 (3.0±1.1 vs 1.6±0.8), with all differences statistically significant (p<0.001 for each). However, wound healing endpoints were significantly better with EGF: mean time to complete epithelialization was shorter (12.8±2.1 vs 15.3±2.6 days; p<0.001), and a higher proportion achieved complete epithelialization by POD14 (73.3% vs 33.3%; p=0.003). The EGF group also had a shorter hospital stay (6.1±1.8 vs 7.2±2.1 days; p=0.022) and more often maintained an undisturbed primary dressing until POD14 (96.7% vs 80.0%; p=0.042). Overall postoperative complications were less frequent with EGF (10.0% vs 33.3%; p=0.034), while individual events such as SSI (3.3% vs 16.7%), seroma/hematoma (3.3% vs 13.3%), graft necrosis (0% vs 6.7%), and re-intervention (0% vs 6.7%) were numerically lower but not statistically significant.

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On POD14, local infection was uncommon and did not differ significantly between groups (EGF 3.3% vs CS 16.7%; p=0.196). However, scab formation was significantly lower in the EGF group (40.0% vs 66.7%; p=0.036). Pigmentation also differed at POD14 (p=0.022), with a higher proportion showing normal pigmentation in the EGF arm (26.7% vs 13.3%), while hypopigmentation was more frequent in both groups (60.0% vs 73.3%) and hyperpigmentation was similar (13.3% in each). By POD21, infection remained rare (0% vs 6.7%; p=0.492) and scab presence was low overall (3.3% vs 16.7%; p=0.196). Pigmentation differences persisted and favoured the EGF group (p=0.036), with normal pigmentation observed in 66.7% of EGF participants compared with 40.0% in the CS group, and lower hypopigmentation in the EGF arm (30.0% vs 53.3%).

Table 1: Baseline demographic and clinical characteristics of participants by study group (EGF vs collagen sheet)

		Group EGF N = 30	Group CS N = 30	P value
		n (%)	n (%)	
Age (years), Mean (SD)		46.8 (12.1)	45.9 (11.7)	0.762
Age (years)	<30	4 (13.3)	3 (10.0)	0.793
	31–50	16 (53.3)	17 (56.7)	
	>50	10 (33.3)	10 (33.3)	
Gender	Male	22 (73.3)	21 (70.0)	0.787
	Female	8 (26.7)	9 (30.0)	
Body mass index (kg/m²), Mean (SD)		24.1 (3.1)	24.6 (3.4)	0.579
Body mass index (kg/m²)	Underweight (<18.5)	2 (6.7)	1 (3.3)	0.555
	Normal (18.5–22.9)	7 (23.3)	6 (20.0)	
	Overweight (23.0–24.9)	11 (36.7)	9 (30.0)	
	Obese (≥25.0)	10 (33.3)	14 (46.7)	
Comorbidities	Diabetes mellitus	9 (30.0)	10 (33.3)	0.790
	Hypertension	8 (26.7)	7 (23.3)	0.774
Current smoker	Yes	6 (20.0)	7 (23.3)	0.754
	No	24 (80.0)	23 (76.7)	
Alcohol use (current)	Yes	7 (23.3)	6 (20.0)	0.758
	No	23 (76.7)	24 (80.0)	
Prior surgery at graft site	Yes	5 (16.7)	4 (13.3)	0.722
	No	25 (83.3)	26 (86.7)	
*Statistically significant at p<0.05 SD, Standard deviation				

Table 2: Comparison of baseline vitals, donor-site characteristics, laboratory investigations, and perioperative parameters between EGF and collagen sheet groups

		Group EGF N = 30	Group CS N = 30	P value
		Mean (SD)	Mean (SD)	
Vitals				
Baseline temperature (°C)		36.9 (0.4)	36.8 (0.4)	0.498
Pulse rate (beats/min)		82.4 (10.6)	81.2 (9.8)	0.620
Systolic BP (mmHg)		122.6 (11.3)	124.1 (10.9)	0.541
Diastolic BP (mmHg)		78.4 (7.2)	79.0 (7.5)	0.741
Respiratory rate (/min)		18.4 (2.1)	18.7 (2.2)	0.598
Oxygen saturation (%)		98.0 (1.2)	97.8 (1.3)	0.523
Donor site and wound characteristics				
Donor site region, n (%)	Thigh	24 (80.0)	23 (76.7)	0.752
	Leg/Other	6 (20.0)	7 (23.3)	
Donor-site area (cm²)		72.5 (18.4)	73.9 (19.2)	0.783
Local wound erythema, n (%)	Yes	3 (10.0)	4 (13.3)	0.687
	No	27 (90.0)	26 (86.7)	
Local wound edema, n (%)	Yes	4 (13.3)	5 (16.7)	0.718
	No	26 (86.7)	25 (83.3)	
Laboratory investigations				
Haemoglobin (g/dL)		12.3 (1.5)	12.1 (1.6)	0.602
Total leukocyte count (×10³/µL)		8.4 (2.0)	8.6 (2.1)	0.672
Platelet count (×10³/µL)		278 (64)	271 (68)	0.642
Urea (mg/dL)		28.9 (7.8)	29.6 (8.2)	0.721
Serum creatinine (mg/dL)		0.94 (0.21)	0.96 (0.22)	0.628
Sodium (mmol/L)		138.6 (3.4)	138.2 (3.6)	0.642
Potassium (mmol/L)		4.1 (0.4)	4.1 (0.5)	0.874
ALT (U/L)		28.4 (9.7)	29.8 (10.2)	0.579
AST (U/L)		27.6 (8.9)	28.2 (9.1)	0.787
Urine microscopy – pus cells >5/hpf, n (%)		2 (6.7)	3 (10.0)	0.640
Preoperative and operative characteristics				
Preoperative antibiotic given, n (%)		30 (100.0)	30 (100.0)	_
Time from harvest to dressing (min)		18.7 (4.6)	19.1 (5.1)	0.731
Graft thickness (mm)		0.40 (0.05)	0.41 (0.05)	0.384
Estimated blood loss (mL)		78 (22)	82 (24)	0.498

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Duration of surgery (min)	63.2 (12.4)	64.7 (13.1)	0.640
*Statistically significant at p<0.05 SD, Standard deviation; BP, Blood pressure			

Table 3: Comparison of postoperative pain, donor-site healing outcomes, length of stay, and complications between EGF and collagen sheet groups

	Group EGF N = 30 Mean (SD)	Group CS N = 30 Mean (SD)	P value
Postoperative pain scores			
Pain score (0–10) POD 2	5.1 (1.4)	3.8 (1.2)	<0.001*
Pain score (0–10) POD 4	4.0 (1.3)	2.6 (1.0)	<0.001*
Pain score (0–10) POD 6	3.0 (1.1)	1.6 (0.8)	<0.001*
Time to epithelialization and length of stay			
Time to complete epithelialization (days), Mean (SD)	12.8 (2.1)	15.3 (2.6)	<0.001*
Complete epithelialization by POD 14, n (%)	22 (73.3)	10 (33.3)	0.003*
Length of hospital stay (days), Mean (SD)	6.1 (1.8)	7.2 (2.1)	0.022*
Primary dressing undisturbed to POD 14, n (%)	29 (96.7)	24 (80.0)	0.042*
Postoperative complications			
Any postoperative complication	3 (10.0)	10 (33.3)	0.034*
Surgical-site infection (SSI)	1 (3.3)	5 (16.7)	0.196
Seroma/hematoma	1 (3.3)	4 (13.3)	0.353
Graft necrosis (partial/any)	0 (0.0)	2 (6.7)	0.492
Flap necrosis	0 (0.0)	1 (3.3)	1.000
Re-intervention required	0 (0.0)	2 (6.7)	0.492
*Statistically significant at p<0.05 SD, Standard deviation			

Table 4: Comparison of donor-site wound appearance (infection, scab, and pigmentation) on POD14 and POD21 between EGF and collagen sheet groups

		Group EGF N = 30 n (%)	Group CS N = 30 n (%)	P value
POD 14				
Local infection present		1 (3.3)	5 (16.7)	0.196
Scab present		12 (40.0)	20 (66.7)	0.036*
Pigmentation	Normal	8 (26.7)	4 (13.3)	0.022*
	Hypopigmentation	18 (60.0)	22 (73.3)	
	Hyperpigmentation	4 (13.3)	4 (13.3)	
POD 21				
Local infection present		0 (0.0)	2 (6.7)	0.492
Scab present		1 (3.3)	5 (16.7)	0.196
Pigmentation	Normal	20 (66.7)	12 (40.0)	0.036*
	Hypopigmentation	9 (30.0)	16 (53.3)	
	Hyperpigmentation	1 (3.3)	2 (6.7)	
*Statistically significant at p<0.05				

DISCUSSION

The two randomized groups were well balanced at baseline across demographics, comorbidity burden, vitals, donor-site characteristics, and laboratory indices, minimizing the risk of confounding by indication and strengthening internal validity for causal interpretation of postoperative differences. In particular, the similarity in age, sex distribution, BMI categories, diabetes and hypertension prevalence, smoking and alcohol use, prior surgery at the graft site, harvest region (predominantly thigh), donor-site area, early local signs, hematologic and biochemical parameters, and peri-operative variables (antibiotic use, graft thickness, blood loss, surgical duration, and timing from harvest to dressing) indicates effective randomization and protocolized peri-operative care across arms. These conditions make it unlikely that systematic imbalances drove the divergent trajectories observed for pain, epithelialization kinetics, and short-term complications.

Pain trajectories favoured the collagen sheet group on every postoperative assessment (POD 2/4/6), with large and statistically robust mean differences. Several mechanisms plausibly account for this effect. First, collagen dressings form a conformable, moist interface that insulates exposed nerve endings in the partially denuded donor dermis, thereby reducing nociceptor stimulation compared with more bioactive but thinner contact layers; their intrinsic haemostatic properties can also diminish early inflammatory mediators associated with pain.[14] Collagen matrices engage platelets and provide a biocompatible scaffold for early cell adhesion, while modulating excessive inflammation—features associated with analgesic benefit as noted by Cheng et al. (2020), Maquart & Monboisse (2014), Rajavarman et al. (2025) and Sreekumar et al. (2015).[15-18] Second, moist occlusive environments are consistently associated with lower pain versus traditional contact gauze in donor-site RCTs and reviews including Shi et al. (2023) and Weber et al. (1995),[19,20] supporting the general principle that atraumatic, moisture-

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retentive interfaces lessen mechanical irritation during the early postoperative phase. Finally, ease of secondary dressing removal with collagen sheets reduces shear and microtrauma to nascent epithelium, an effect repeatedly implicated in lower procedural pain across modern donor-site platforms, as noted by Laurano et al. (2022)."[21]

"Despite higher early comfort with collagen sheets, biological time-to-closure metrics clearly favoured epidermal growth factor (EGF) dressings. EGF shortened mean time to complete epithelialization by approximately 2.5 days and tripled the probability of full epithelialization by POD 14 relative to collagen, with both differences statistically significant. This finding is highly consistent with the well-established role of EGF–EGFR signalling in coordinating keratinocyte migration ('restitution') and proliferation during the resurfacing phase of acute wounds. Binding of EGF to EGFR activates MAPK/ERK and PI3K/AKT cascades, enhances front–rear polarity and lamellipodial dynamics in keratinocytes, and supports survival of stromal cells—collectively accelerating restoration of epidermal continuity. These findings corroborate with that reported by Kobayashi et al. (2023) and Shin et al. (2023).[22,23] Topical or dressing-delivered EGF is specifically intended to sustain receptor-level stimulation in the protease-rich wound milieu where endogenous growth factors are rapidly degraded; this pharmacologic reinforcement of early epithelial events reasonably explains the faster closure observed here.[22]

The biological plausibility of EGF-accelerated donor-site closure also aligns with Berlanga-Acosta et al. (2024), Jain et al. (2017) and Khanbanha et al. (2014) in which interventions that optimize the microenvironment for keratinocyte migration tend to shorten epithelialization time.[5,14,24] Hydrocolloid platforms—another class that maintains a warm, moist milieu and protects against shear—achieved the shortest donor-site healing times in the largest randomized trial to date (REMBRANDT), while traditional gauze had higher infection rates, underscoring the importance of interface biology for epithelial kinetics.[10] Although hydrocolloids and EGF operate via distinct mechanisms (microclimate optimization vs receptor-targeted signalling), both reinforce the core pathophysiology of donor-site repair; rapid resurfacing from wound edges and adnexal remnants, as noted by Eskes et al. (2011).[25] Importantly, the EGF group's faster epithelialization translated into clinically meaningful secondary advantages. A shorter mean hospital stay and a higher likelihood of leaving the primary dressing undisturbed through POD 14. Earlier barrier restoration reduces exudate volume and the need for interim dressing manipulation, which in turn limits shear and the opportunity for bacterial ingress. These process improvements are consistent with the observed directionality of complications—lower overall postoperative morbidity in the EGF arm—even though individual event rates (SSI, seroma/hematoma, partial graft necrosis, flap necrosis, re-intervention) were low and not statistically different between groups. Reduced disturbance of the primary dressing also maps to contemporary best practices for skin graft donor sites, where stability of the interface is emphasized to avoid disrupting fragile neoepithelium.[21]

The pattern of surface findings at the first and second formal evaluations further supports these mechanisms. By POD 14, scab formation was significantly less frequent with EGF than with collagen, consistent with earlier and more complete epithelial cover reducing the need for desiccated fibrin crust formation; by POD 21, residual scab was uncommon in both arms but numerically lower with EGF. These findings echo the moist-healing paradigm. Interventions that hasten resurfacing tend to minimize crusting, which otherwise can adhere to immature epithelium and potentiate discomfort at dressing changes.[20] Pigment outcomes also favoured EGF, with higher rates of normal pigmentation and lower hypopigmentation by POD 21. Because repigmentation in donor sites depends on the timely return and viability of melanocytes from adnexal reservoirs and wound edges, faster, less inflamed re-epithelialization plausibly preserves melanocyte function and reduces post-inflammatory dyspigmentation. Shin et al. (2023) show that EGF can modulate inflammatory signalling in the wound bed and support keratinocyte–melanocyte crosstalk, offering a mechanistic basis for the observed cosmetic trend.[22]

Balancing these effects, the consistently lower early pain scores in the collagen group deserve emphasis for clinical decision-making, particularly in settings where patient-reported comfort is prioritized in the first postoperative week. Collagen's analgesic signal is congruent with Rajavarman et al. (2025), Shi et al. (2023) and Sreekumar et al. (2015) that occlusive, atraumatic interfaces decrease pain compared with drier, adherent materials, and with mechanistic reviews attributing collagen's benefits to inflammation modulation and a cushioning scaffold that shields terminal nerve endings.[17-19] Moreover, the absence of significant between-group differences in individual complications likely reflects both the low absolute incidence under modern protocols and adequate antimicrobial stewardship (universal preoperative antibiotics) and stable interface practices—factors repeatedly identified as important determinants of safe donor-site recovery alongside dressing choice.[26]

Contextualizing the present results within the broader evidence base clarifies their clinical relevance. Systematic assessments of donor-site dressings conclude that moist, occlusive platforms (films/hydrocolloids/foams/hydrofibers) generally outperform gauze in epithelialization time and pain, but head-to-head trials among advanced materials yield heterogeneous rankings and call for condition-specific comparisons.[27] The current comparison addresses an important gap by contrasting a receptor-

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targeted bioactive approach (EGF) with a biomaterial scaffold strategy (collagen). The trade-off identified—faster healing and better early pigment normalization with EGF versus lower early pain with collagen—is biologically coherent with their modes of action and provides a practical framework for individualized dressing selection. EGF-eluting dressings when rapid resurfacing and earlier discharge are paramount, and collagen sheets when pain minimization during the first postoperative days is the dominant priority.

This trial had several important limitations. It was a single-centre study with a modest sample size (N=60), which limits precision and external generalizability. Follow-up was short (formal assessments through POD 14 and POD 21), so longer-term outcomes—durable repigmentation, scar quality, pruritus, and patient-reported cosmesis—were not captured. The single-blind design introduces potential performance and detection bias, especially for subjective endpoints. Time to epithelialization and pigment categories were determined clinically without standardized objective measures (e.g., digital planimetry, transepidermal water loss, colorimetry) or blinded photographic adjudication, which may allow assessment bias. The study was powered for pain but not for relatively infrequent complications (e.g., SSI, necrosis, re-intervention), so null differences for these events may reflect limited power. Universal pre-operative antibiotics may also have attenuated between-group differences in infection. Finally, the evaluation compared one EGF dressing protocol with one collagen sheet protocol; results may not extrapolate to other formulations, dosing regimens, secondary cover strategies, or to alternative modern dressings (e.g., hydrofiber, film, or NPWT) not studied here.

CONCLUSION

In this randomized, single-blind comparison of epidermal growth factor (EGF) dressing versus collagen sheet for split-thickness skin-graft donor sites, baseline characteristics were well balanced, permitting valid inference on treatment effects. EGF significantly accelerated healing—shorter mean time to complete epithelialization (12.8 vs 15.3 days), a higher proportion fully epithelialized by POD 14 (73.3% vs 33.3%), fewer dressing disturbances to POD 14 (96.7% vs 80.0%), a shorter hospital stay (6.1 vs 7.2 days), and lower overall postoperative morbidity (10.0% vs 33.3%). Early surface findings also favoured EGF, with less scab formation at POD 14 and better pigment normalization by POD 21. Collagen sheets, however, provided superior early patient comfort, yielding significantly lower pain scores on POD 2, 4, and 6. Taken together, EGF offers greater healing efficiency and early cosmetic advantages, whereas collagen confers a clear analgesic benefit in the immediate postoperative period." These data support individualized dressing selection—prioritizing EGF when rapid epithelialization and earlier discharge are paramount and collagen when early pain control is the dominant clinical goal—while motivating larger, longer-term, and cost-effectiveness studies to refine donor-site protocols.

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