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Original Research Article

COMPARATIVE EFFICACY OF CYANOACRYLATE TISSUE ADHESIVE VERSUS CONVENTIONAL SUTURING FOR SPLIT-THICKNESS SKIN GRAFT FIXATION IN DIABETIC AND CHRONIC ULCERS: A RANDOMIZED CONTROLLED TRIAL

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ABSTRACT

Background: Secure fixation of split-thickness skin grafts (STSGs) is essential for graft survival. Cyanoacrylate tissue adhesives (CAs) have been proposed as an alternative to transcutaneous sutures and staples, with potential benefits including reduced operative time, decreased pain, and lower rates of seroma/hematoma. We performed a randomized controlled trial to compare CA fixation with conventional suturing for STSGs in patients with diabetic and chronic ulcers. **Materials and Methods:** Fifty patients with chronic or diabetic lower-extremity ulcers requiring STSG were randomized 1:1 to graft fixation with cyanoacrylate tissue adhesive (n = 25) or transcutaneous sutures (n = 25). Standard preoperative wound optimization and perioperative care were applied. Primary endpoints were operative time and graft uptake (clinically estimated percentage take) measured on postoperative days (POD) 3, 5, 7, and 9. Secondary endpoints included patient-reported pain (visual analog scale, VAS), seroma and hematoma formation, graft migration, dressing soakage, complications (infection, graft loss), and length of hospital stay. Statistical analyses used t-tests for continuous variables and chi-square/Fisher exact tests for categorical outcomes; significance threshold $p < 0.05$. **Results:** Mean age was 52.0 ± 10.9 years; gender distribution and baseline wound characteristics were balanced between groups. Mean operative time was significantly shorter with CA fixation (28 ± 4.2 min) versus suturing (37 ± 5.1 min), $p < 0.001$. Mean graft uptake was higher in the CA group at POD3 (76.3% vs 67.3%, p = 0.001), POD5 (87.7% vs 75.3%, p = 0.001), and POD7 (96.9% vs 84.7%, p = 0.001); by POD9 the difference was not significant (96.7% vs 94.4%, p = 0.539). The proportion of patients reporting VAS ≥ 6 was lower in the CA group (8% vs 36%, p = 0.02). Seroma formation was less frequent with CA (27% vs 73%, $p < 0.01$). Mean hospital stay was shorter in the CA group (7.4 ± 1.6 vs 9.7 ± 2.1 days, $p < 0.01$). No significant increase in infection or graft failure attributable to CA was observed. **Conclusions:** Cyanoacrylate tissue adhesive for STSG fixation demonstrated superior early graft adherence, reduced operative time and postoperative pain, and fewer seroma/hematoma events compared with transcutaneous sutures in this cohort. Benefits were most pronounced during the first postoperative week—critical for plasmatic imbibition and inosculation. Larger multicenter, blinded trials with objective graft-take measurements, long-term follow-up, and systematic safety assessments are warranted to confirm these findings and inform guideline development.

INTRODUCTION

Background and rationale

Split-thickness skin grafting (STSG) is a foundational reconstructive technique used to cover large wounds resulting from burns, trauma, chronic ulcers (including diabetic foot ulcers), and postinfectious or oncologic defects. Historically, the practice of skin grafting dates back millennia, with modern refinements over the 19th and 20th centuries

leading to current classifications of STSG and full-thickness grafts.[1-5] Unlike flaps, STSGs lack an intrinsic vascular supply; their survival depends on a sequence of biologic processes: plasmatic imbibition (initial fluid nutrition), inosculation (capillary alignment and connection), and neovascularization (angiogenesis and capillary ingrowth).[3,4] These early phases—particularly the first 3–7 days—are vulnerable to factors that disrupt graft–bed apposition, introduce shear forces, or permit fluid accumulation between graft and bed. Such disruptions predispose to seroma/hematoma formation, graft sloughing, and infection, collectively reducing graft take.[3,4,15]

Graft fixation techniques aim to maintain intimate contact between graft and recipient bed during the critical early period. Traditional methods include transcutaneous sutures, staples, quilting sutures, and use of pressure dressings with bolsters. Each has limitations: sutures and staples require time to place, can cause puncture-related trauma and pain, may permit micro-motion related to suture slippage or tension inequality, and can act as a nidus for infection.[5] Bolsters obscure direct graft visualization and may trap fluid. Tissue adhesives—most prominently cyanoacrylate-based adhesives—have emerged as potential alternatives that rapidly polymerize on contact with moisture to form a thin film, providing immediate adherence, sealing potential dead space, and creating a microbial barrier.[6,12-14]

Cyanoacrylates (e.g., n-butyl- and 2-octyl-cyanoacrylate) were first synthesized in the 1940s and, after overcoming initial issues with toxicity and brittleness, were developed into medical-grade formulations.[6] Their polymerization is exothermic and rapid, producing a strong adhesion that has been exploited in dermatologic closure, laceration repair, and more recently for STSG fixation. Proposed mechanistic advantages include reduction in micromotion at the graft–bed interface, sealing of lymphatic or small vessels that might otherwise contribute to seroma, elimination of transcutaneous points of trauma (and associated nociceptive input), and facilitation of early visualization without bulky bolsters.[6,12]

Prior studies and knowledge gap

Existing literature includes retrospective case series, small comparative studies, and animal experiments suggesting comparable or improved early graft take, reduced operative time, and decreased pain with CA fixation. However, studies vary in design, graft types (full- versus split-thickness), endpoints, and objective measurements. Limitations include small sample sizes, heterogeneity in adhesives used, lack of blinded outcome assessment, and few long-term cosmetic or functional outcome data. In diabetic and chronic ulcers—where wound bed quality, infection risk, and microvascular disease can complicate graft survival—robust data comparing CA and sutures are scarce.[12-14]

Objectives

We designed a single-center randomized controlled trial to compare cyanoacrylate tissue adhesive versus conventional transcutaneous sutures for STSG fixation in patients with diabetic and chronic ulcers. We focused on early graft uptake, operative efficiency, patient-reported pain, complication rates (including seroma and hematoma), and hospital stay, hypothesizing that CA fixation would improve early graft adherence and perioperative outcomes without increasing infectious or other adverse events.

MATERIALS AND METHODS

Study design and setting

This randomized controlled trial was conducted at the Department of General Surgery, Kanyakumari Medical Mission, Research Center,Medical Collage & Hospital, Muttom, between January 2025and December 2025. The institutional ethics committee approved the protocol, and all participants provided written informed consent. The trial adhered to CONSORT principles for randomized studies.

Participants

Inclusion Criteria

- Adults (≥18 years) with chronic non-healing ulcers or diabetic foot ulcers requiring STSG.
- Defects suitable for STSG on upper or lower extremities.
- Optimized wound bed (absence of active deep infection) confirmed by clinical assessment and negative or clinically acceptable microbiology as per protocol.

Exclusion Criteria

- Coagulopathy or deranged coagulation profile.
- Platelet disorders or thrombocytopenia.
- Large oncologic excisions or raw areas from malignancy resection.
- Known allergy to cyanoacrylate or components.
- Severe peripheral arterial disease not amenable to revascularization.
- Immunosuppression or systemic conditions precluding surgical intervention.

Randomization and allocation concealment

Patients were randomized 1:1 using computer-generated random numbers into either the cyanoacrylate adhesive group (CA) or the transcutaneous suturing group (SUT). Allocation was concealed in sealed opaque envelopes opened in the operating room after graft preparation.

Surgical technique and interventions

Preoperative care

All patients underwent standardized wound optimization: repeated debridement as indicated, topical/systemic antimicrobial therapy based on culture and sensitivity, glucose control for diabetic patients, and nutritional support. Perioperative prophylactic antibiotics were administered one hour before incision.

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Graft harvest: STSGs (thickness 0.3–0.45 mm) were harvested from standard donor sites (lateral thigh or trunk) using a powered dermatome. Grafts were meshed when necessary to cover larger defects and facilitate drainage.

Fixation techniques: CA group: After thorough hemostasis and lavage of the wound bed, cyanoacrylate tissue adhesive (medical-grade n-butyl or 2-octyl formulation as per institutional supply) was applied sparingly to the recipient bed in an even layer (approximately 0.5 ml per 50 cm^2 surface area). The graft was immediately laid onto the bed and gently smoothed to remove wrinkles and ensure contact. A non-adhesive dressing (Bactigras), betadine-soaked cotton if indicated, and a POP (plaster of Paris) or well-padded immobilization were applied. No transcutaneous fixation was used.

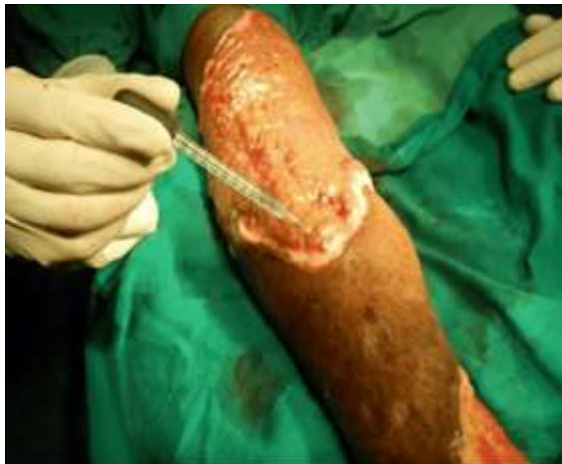

Figure 1: SSG FIXED WITH CYANOACRYLATE GLUE

SUT group: After graft placement, transcutaneous interrupted sutures (nylon 3-0 or equivalent) were placed at approximately 5–10 mm intervals to secure the graft margins. Non-adhesive dressing, padding, and immobilization were applied similarly.

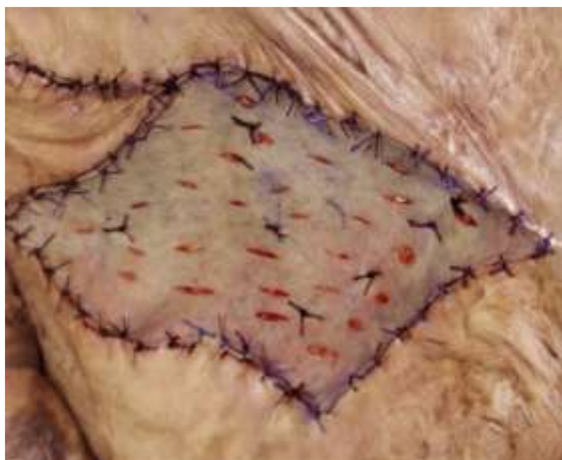

Figure 2: SSG FIXED WITH SUTURES

Postoperative care and assessment

Dressings were opened and assessed on POD 3, POD 5, POD 7, and POD 9. Wound assessments recorded percentage graft take (clinically estimated by the operating surgeon as percent of surface area adherent), presence of seroma/hematoma, dressing soakage, graft migration, and signs of infection. Pain at the recipient site was recorded using a standardized VAS at POD 3. Length of hospital stay was recorded from day of operation to discharge.

Outcome measures

Primary outcomes: Operative time (minutes from first incision to completion of fixation) and graft uptake percentage at POD 3, 5, 7, and 9.

Secondary Outcomes: Patient-reported VAS pain score, incidence of seroma/hematoma, graft migration, dressing soakage requiring intervention, infection rates, graft loss, and length of hospital stay.

Statistical Analysis: Continuous variables were summarized as mean ± standard deviation, categorical variables as counts and percentages. Between-group comparisons used t-tests for continuous variables and chi-square or Fisher's exact tests for categorical variables. P-values <0.05 were considered statistically significant. Statistical analyses were performed using standard statistical software.

RESULTS

Participant flow and baseline characteristics

Fifty patients were enrolled and randomized equally (25 CA, 25 SUT). All randomized patients completed follow-up through POD 9 and were included in the analysis. Baseline demographics were comparable: mean age 52.03 ± 10.89 years; sex distribution balanced between groups; ulcer etiology and size ranges were similar. [Table 1]

Operative time

Mean operative time was significantly reduced in the CA group (28.0 ± 4.2 minutes) compared with the SUT group (37.0 ± 5.1 minutes), $p < 0.001$. Time savings were attributed primarily to elimination of suturing steps and faster fixation.

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Table 1: Showing the distribution of gender among the study participants

Gender	Frequency		Percent	
	Study group	Control	Study group	Control
Female	7	9	14	18
Male	18	16	36	32
Total	25	25	50	50

Table 2: Operating time in cases and controls

Operating Time	Study Group	Control
25–28 minutes	8 (15 %)	2 (4%)
28–31 minutes	27 (54 %)	10 (20%)
32–35 minutes	15 (30%)	12 (24%)
35–38 minutes	00 (0%)	26 (52%)

Graft uptake

Mean clinically estimated graft take (%) at each postoperative time point:

- POD3: CA 76.3 ± 8.1% vs SUT 67.3 ± 7.8% ($p = 0.001$)
- POD5: CA 87.7 ± 8.6% vs SUT 75.3 ± 7.3% ($p = 0.001$)
- POD7: CA 96.9 ± 6.8% vs SUT 84.7 ± 7.8% ($p = 0.001$)
- POD9: CA 96.7 ± 8.2% vs SUT 94.4 ± 7.9% ($p = 0.539$)

By POD 9, most grafts in both groups achieved near-complete take, with the early advantage of CA narrowing over time.

Table 3: Comparison of the graft uptake between the two groups

Graft uptake (>90%)	Study group		Control		t-test (p-value)
	Mean	SD	Frequency (n)	Mean	
POD3	76.3	8.1	19	67.3	7.8
POD5	87.7	8.6	22	75.3	7.3
POD7	96.9	6.8	24	84.7	7.8
POD9	96.7	8.2	24	94.4	7.9

*****SIGNIFICANT (p value less than 0.05 is significant)***

Pain

Postoperative VAS distribution at POD 3 showed fewer patients in the CA group reporting moderate-to-severe pain (VAS ≥ 6): CA 2/25 (8%) versus SUT 9/25 (36%), $p = 0.02$. Median VAS was lower in the CA group (median 0–2 range) compared with the SUT group.

Table 4: Assessment of postoperative pain in cases and controls

VAS	STUDY GROUP %		CONTROL %	
	Frequency	Percentage	Frequency	Percentage
0	15	60	3	12
2	3	12	5	20
4	5	20	8	32
6	2	8	8	32
8	0	0	1	4
10	0	0	0	0

Complications

Seroma formation on POD 3 occurred in 7/25 (27%) CA patients versus 18/25 (73%) SUT patients ($p < 0.01$). Hematoma rates and combinations of seroma with hematoma followed the same trend, with fewer occurrences in the CA group. Graft migration occurred less frequently with CA. No significant differences in overt graft infection rates were observed between groups, and there were no systemic adverse events attributable to CA in this cohort. No cases of clinically significant thermal injury, allergic contact dermatitis, or delayed graft loss directly attributable to CA were recorded within the observation period.

Length of hospital stay

Mean hospital stay was shorter in the CA group (7.4 ± 1.6 days) compared with the SUT group (9.7 ± 2.1 days), $p < 0.01$.

Supplementary outcomes

Dressing soakage requiring unplanned dressing changes was less frequent in the CA group. No patient required early reoperation for graft failure within the first 9 days. Cosmetic/scar assessments and long-term functional outcomes were not part of the primary protocol.

DISCUSSION

Principal findings

In this randomized controlled study of STSG fixation for diabetic and chronic ulcers, cyanoacrylate tissue adhesive resulted in significantly reduced operative time, improved early graft uptake during the critical first week, lower early postoperative pain, fewer seroma/hematoma events, and shorter hospital stays compared with conventional transcutaneous suturing. Differences in graft take were most pronounced at POD 3–7—

periods corresponding to plasmatic imbibition and early inosculation—suggesting mechanistic effects of CA on early graft–bed interactions.[3,4]

Mechanistic Interpretation

Cyanoacrylate adhesives polymerize rapidly upon contact with surface moisture to form a continuous film that bonds the graft to the recipient bed. This film likely confers several biomechanical and biologic advantages:

- Reduction in micromotion: By distributing fixation forces across the graft surface rather than localized suture points, CA reduces localized shear and micro-movement that can separate nascent capillary buds from graft vessels.
- Dead-space obliteration: CA can seal small interstices and lymphatic channels, preventing accumulation of serous fluid or blood that otherwise creates a barrier to revascularization.
- Reduced tissue trauma and inflammation: Avoidance of transcutaneous needle punctures eliminates focal trauma and decreases nociceptive input, which may reduce local inflammatory cytokine production detrimental to graft take.
- Barrier and antimicrobial effect: The polymer film may offer a partial barrier to bacterial ingress; some in vitro data suggests cyanoacrylates exert bacteriostatic properties, though clinical significance remains to be fully established.

Together, these factors plausibly explain improved early take, reduced seromas, and less pain.[9,10]

Comparison with prior literature

Our findings align with several prior reports indicating time-savings, reduced pain, and comparable or improved graft take with CA fixation.[12-14] Reddy et al. and others have reported reduced pain, and shorter hospital stays with adhesives versus staples or sutures.[14] Chandrashekhar described rapid fixation of STSGs using cyanoacrylate with favorable uptake.[12] However, heterogeneity in adhesives (n-butyl vs 2-octyl), surgical contexts, and outcome measures has limited generalizability. Our trial adds randomized data in a diabetic/chronic ulcer population, a group at higher baseline risk of graft complications.

Clinical implications

For reconstructive surgeons managing STSGs, particularly in patients with comorbidities such as diabetes, CA fixation offers a practical alternative to sutures and staples. The reduced operative time can improve operating room efficiency and resource utilization; decreased pain and shorter hospitalization may translate to better patient satisfaction and lower healthcare costs. Moreover, CA fixation simplifies postoperative care by eliminating suture removal and enabling early visual inspection of the graft.

Safety profile

Medical-grade cyanoacrylates (n-butyl, 2-octyl) have acceptable biocompatibility with low incidence of contact dermatitis and minimal exothermic damage when applied in thin layers.[6] We observed no CA-related adverse effects in the early postoperative window. Occupational exposure risks for staff and potential for allergic reactions warrant standard precautions (avoid skin contact, adequate ventilation) and surveillance.[7] Appropriate application technique—thin, even layers and avoidance of excess adhesive—reduces thermal and cytotoxic risks.

Limitations

This study has several limitations. It is single center with a modest sample size, which limits power to detect infrequent adverse events and may limit generalizability. Outcome assessment of graft take was clinical and not blinded, introducing potential observer bias. We did not use objective imaging (e.g., laser Doppler flowmetry, indocyanine green angiography) or standardized photographic volumetric analysis, which would provide quantitative measures of perfusion and graft adherence. Long-term outcomes including scar quality, contracture, and functional recovery were not assessed. Finally, the study did not stratify by adhesive formulation; different cyanoacrylates may differ in flexibility, strength, and tissue response.

Future research

Larger multicenter randomized trials with blinded outcome assessment are required to validate these findings. Incorporation of objective graft perfusion metrics (e.g., laser speckle contrast imaging, indocyanine green fluorescence) and standardized photographic analysis will strengthen evidence. Comparative cost-effectiveness analyses considering adhesive cost, operative time savings, analgesic requirements, and length of stay would inform resource allocation. Long-term follow-up to assess scarring, contracture, and patient-reported outcomes is necessary. Mechanistic laboratory studies evaluating cyanoacrylate effects on microvascular inosculation, local cytokine milieu, and bacterial colonization would further elucidate the biologic basis of clinical observations.

CONCLUSION

In this randomized controlled trial involving patients with diabetic and chronic ulcers undergoing STSG, cyanoacrylate tissue adhesive fixation improved early graft uptake, reduced operative time and postoperative pain, decreased seroma/hematoma formation, and shortened hospital stay compared with conventional transcutaneous suturing. The adhesive's benefits were most evident during the first postoperative week, a critical window for graft revascularization. While results are promising, larger, blinded, and methodologically rigorous trials with objective outcome measures and longer follow-

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up are recommended to confirm efficacy, fully characterize safety, and inform clinical practice guidelines.

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