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Randomized Clinical Trial

Tissue adhesive, adhesive tape, and sutures for skin closure of paediatric surgical wounds: prospective randomized clinical trial

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Abstract

Background: Tissue adhesive, adhesive tape, and sutures are used to close surgical incisions. However, it is unclear which produces the best results in children, and whether combination wound closure is better than sutures alone.

Methods: In this parallel randomised controlled trial (ANZCTR: ACTRN12617000158369), children (aged 18 years or less) undergoing elective general surgical or urological procedures were randomized to skin closure with sutures alone, sutures and adhesive tape, or sutures and tissue adhesive. Participants were assessed 2 weeks, 6 weeks, and more than 6 months after operation. Outcomes included wound cosmesis (clinician- and parent-rated) assessed using four validated scales, parental satisfaction, and wound complication rates.

Results: 295 patients (333 wounds) were recruited and 277 patients (314 wounds) were included in the analysis. Tissue adhesive wounds had poorer cosmesis at 6 weeks: median 10-point VAS score 7.7 with sutures alone, 7.5 with adhesive tape, and 7.0 with tissue adhesive ($P = 0.014$). Respective median scores on a 100-point VAS were 80.0, 77.2, and 73.8 ($P = 0.010$). This difference was not sustained at over 6 months. There was no difference in parent-rated wound cosmesis at 6 weeks ($P = 0.690$) and more than 6 months ($P = 0.167$): median score 9.0 with sutures alone, 10.0 with adhesive tape, and 10.0 with tissue adhesive at both stages. Parental satisfaction was similar at all points, with a median score of 5 (very satisfied) for all groups. There was one instance of wound dehiscence in the tissue adhesive group and no wound infections.

Conclusion: Short-term wound cosmesis was poorer with tissue adhesive although it is unclear whether this difference is sustained in the long-term. There were no differences between techniques for the study outcomes.

Registration number: ACTRN12617000158369 (ANZCTR) (https://anzctr.org.au/Trial/Registration/TrialReview.aspx?id=372177&isReview=true).

Introduction

Skin closure of surgical wounds has traditionally been achieved using sutures. Tissue adhesive and adhesive tape are frequently used alternatives for skin closure in paediatric surgical and emergency settings because of their ease of application and rapid wound closure[1,2]. Tissue adhesives, or adhesive glue, comprise a liquid cyanoacrylate compound that polymerizes on contact with moisture to form a flexible, haemostatic, and waterproof film, which seals the wound edges together[3]. Adhesive tape can be used to approximate wound edges, traditionally in low-tension wounds. Although both tissue adhesive and adhesive tape are used for primary skin closure, they are often applied as an adjunct to subcuticular or dermal sutures, reinforcing the wound and acting as a dressing[3,4]. Whilst tissue adhesive and adhesive tape are viable and established alternatives to sutures for wound closure in children[5,6], a recent systematic review and meta-analysis demonstrated that there is a paucity of evidence comparing tissue adhesive with adhesive tape, and these techniques have not been directly compared with sutures. Furthermore, the use of tissue adhesive and adhesive tape as an adjunct to sutures in children is supported by limited evidence, and this combination closure has not been compared directly with suturing alone[7].

The aim of this study was to compare three common skin closure techniques in children undergoing elective surgical procedures in a prospective RCT. These included sutures with tissue adhesive, sutures with adhesive tape, and sutures alone. It was hypothesized that there would be no difference between the three intervention arms for evaluated endpoints.

Methods

Registration and ethics approval

The trial was registered prospectively with the Australian and New Zealand Clinical Trials Registry (ACTRN12617000158369)

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Table 1 Summary of outcome measures

Method of assessment	Outcome measure	Timing of assessment
Primary outcome		
Clinician-rated wound cosmesis		6 weeks
Hollander Wound Evaluation Scale	0, poor outcome 6, optimal wound cosmesis	
Stony Brook Scar Evaluation Scale	0, poor wound cosmesis 5, optimal wound cosmesis	
10-point and 100-point VAS	0, worst possible scar 10/100, best possible scar	
Secondary outcomes		
Clinician-rated wound cosmesis		≥ 6 months
Hollander Wound Evaluation Scale	0, poor outcome 6, optimal wound cosmesis	
Stony Brook Scar Evaluation Scale	0, poor wound cosmesis 5, optimal wound cosmesis	
10-point and 100-point VAS	0, worst possible scar 10/100, best possible scar	
Parent-rated wound cosmesis		
10-point VAS	0, worst possible scar 10, best possible scar	2 weeks, 6 weeks, ≥ 6 months
Parental satisfaction with technique		
5-point Likert scale	5, very satisfied 4, satisfied 3, neutral 2, dissatisfied 1, very dissatisfied	2 weeks, 6 weeks, ≥ 6 months
Wound infection—parent-reported	Presence of ≥ 3 of wound erythema, wound oedema, purulent discharge, *or* fever *or* positive wound swab culture	2 weeks
Wound dehiscence—parent-reported	Reopening of wound incision along line of sutures/skin closure reported by parents *and* confirmed by a medical practitioner	2 weeks
Requirement to see healthcare practitioner for wound review		2 weeks
Time taken for wound closure		During surgery

VAS, visual analogue scale.

and study approval was obtained from the clinical and educational institutional ethics committees.

Patient selection

Children presenting to two campuses of Monash Children's Hospital between March 2017 and November 2018 for an elective general surgical or urological procedure were recruited. Patients were eligible if they were aged 18 years or less, undergoing an elective general surgical or urological procedure, and had surgical wound(s) amenable to closure with all three skin closure techniques. Exclusion criteria were: face, head, scrotal or penile incisions, emergency surgery, repeat surgical procedures, and wounds that were not amenable to primary wound closure with all three techniques. Patients receiving chemotherapy, immunosuppression, systemic corticosteroids, or with known malignancy were excluded owing to impaired wound healing. Recruitment occurred in either the outpatient clinic when surgery was booked or before operation on the day of admission. Written informed consent was obtained from parents of all participants and additionally from patients who were mature minors.

Randomization and blinding

Patients were randomized in a 1 : 1 : 1 ratio for wound closure using subcuticular sutures with tissue adhesive, subcuticular sutures with adhesive tape, or subcuticular sutures alone which served as the control arm. Randomization was performed using sequential, identical sealed opaque envelopes to maintain allocation concealment, as described previously[8]. A computer-generated, non-stratified block randomization sequence was used for the envelopes, which were prepared and sealed by non-study personnel before the start of the trial. Randomization envelopes were removed sequentially at the start of each operation and opened in the operating theatre once skin closure with subcuticular sutures had been achieved to advise the operating surgeon of the allocation. Where patients had multiple wounds, all eligible wounds were closed using the allocated technique. However, for laparoscopic procedures only, the umbilical wound was included; the remaining port sites were closed using a technique chosen by the operating surgeon. Blinding of participants, parents, and surgeons was not feasible given the visually apparent differences between techniques. However, clinicians were blinded when evaluating the photographs for assessment of wound cosmesis.

Outcome measures

The primary and secondary outcome measures are summarized in *Table 1*. Clinician-rated wound cosmesis at 6 weeks was the primary outcome measure. This was evaluated by paediatric surgeons blinded to the wound closure technique who assessed

wound cosmesis using four validated wound scales: the Hollander Wound Evaluation Scale (HWES), the Stony Brook Scar Evaluation Scale (SBSES), 10-point visual analogue scale (VAS), and 100-point VAS.

Follow-up

Follow-up was conducted at 2 weeks, 6 weeks, and at least 6 months after operation. Parents were contacted by telephone 2 weeks after surgery to assess wound complications, requirement to see a healthcare practitioner, and their overall satisfaction with the skin closure technique using a five-point Likert scale. Parents were also e-mailed a deidentified questionnaire with a 10-point VAS to rate wound cosmesis. Where it was not possible to contact parents by telephone, the electronic version of the follow-up questionnaire was also e-mailed to them.

Follow-up at 6 weeks was conducted in the paediatric surgical outpatient clinic. Parents were asked to complete a survey rating wound cosmesis (VAS) and their overall satisfaction with the skin closure technique (Likert scale). A deidentified close-up clinical photograph of the wound(s) was also taken. Patients who missed the 6-week follow-up appointment were rebooked to the next available appointment. If they failed to attend again, they were considered lost to follow-up.

Follow-up at 6 months or more was included as a protocol amendment following an interim analysis of data in 2017. The interim analysis was undertaken as this study was conducted as part of a research degree for a study author. Parents who consented to long-term follow-up were e-mailed a deidentified questionnaire in which they rated wound cosmesis (VAS) and their overall satisfaction with the skin closure technique (Likert scale). Parents were asked to submit a deidentified clinical photograph of the wound(s) via the online questionnaire. Parents could also request a review in the paediatric surgical outpatient clinic at this point. Parents taking a clinical photograph of the wound were instructed to take a close-up image of the scar only in a well-lit room to ensure adequate image quality. Where parents did not respond to the initial e-mail, an attempt to contact them was made twice more via e-mail and then SMS message. If a response was not obtained after the third attempt, participants were considered lost to follow-up. All wound photos were reviewed by three independent consultant paediatric surgeons blinded to skin closure technique, who assessed wound cosmesis using validated wound assessment scales: HWES, SBSES, and 10- and 100-point VAS. For each wound assessment scale, scores from each assessor were averaged (mean) for analysis.

Study interventions

There was no alteration to the standard operative technique, although the wound closure technique was standardized. VICRYL® (polyglactin 910; Ethicon, Somerville, NJ, USA), or Polysorb® (Covidien, Minneapolis, MN, USA), or PDS® II (polydioxanone; Ethicon) was used for fascial closure depending on hospital supply and/or surgeon preference. All subcuticular sutures were Coated VICRYL RAPIDE™ (polyglactin 910; Ethicon, Somerville, NJ, USA) placed in a running fashion along the length of the wound and secured with a single buried Aberdeen knot. After randomization, either tissue adhesive, adhesive tape, or an occlusive film wound dressing was applied. For the tissue adhesive group, High Viscosity DERMABOND® Topical Skin Adhesive (2-octylcyanoacrylate; Ethicon, Somerville, NJ, USA) was applied over the sutured wound in two or more layers with time allowed between each layer in accordance with the manufacturer's instructions. For the adhesive tape group, Steri-Strip™ Reinforced Skin Closures 12 mm × 100 m (3 M Health Care, St Paul, MN, USA) adhesive tape was cut to size and applied over the sutured wound in a non-overlapping fashion perpendicular to the wound. For the sutures-alone group, Tegaderm™ Transparent Film Dressing Frame Style (3 M Health Care, St Paul, MN, USA) was applied over the sutured wound. In line with clinical practice in this department, wounds in the adhesive tape group were similarly covered with the same occlusive film dressing applied over the adhesive tape to create a waterproof barrier to prevent wound soiling and to prevent children from picking at the easily removed adhesive tape. To assess for differences in wound closure time, the time taken to close 10 inguinal skin incisions from each group was recorded from commencement of closure of Scarpa's fascia to dressing application. Before discharge, participants were informed about the skin closure technique used and provided a handout containing standardized wound care instructions.

Statistical analysis

The initial, *a priori* non-inferiority (10 per cent) power calculation for this study, based on a 20 per cent difference in optimal clinician-rated wound cosmesis measured with the HWES at 6 weeks between tissue adhesive and sutures alone[9], using a two-sided Z test with 80 per cent power and a 5 per cent significance level, determined that a sample size of 508 patients (254 in each treatment arm, equivalent to 363 in each arm allowing for attrition) was needed. A power calculation for three groups was not considered feasible because of a lack of paediatric studies comparing all three techniques and based on studies that did not assess entirely similar interventions. It was therefore decided arbitrarily to recruit 1089 patients (363 in each of the 3 treatment arms). It became apparent during an interim analysis 1 year after commencement of recruitment that this large-scale trial was not feasible within the 3-year interval at a single centre during which time research personnel were available. The authors therefore opted for an overall sample size of 300 patients as this was feasible within a 3-year interval, with this study serving as a pilot to power future trials.

Statistical analysis was conducted using Prism® 9 for macOS® (GraphPad Software, CA, USA). To account for multiple eligible wounds in some surgical procedures, the analysis used the number of wounds in each group as the statistical unit. A per-protocol analysis was used for this trial. Patients for whom a protocol breach occurred were excluded from subsequent analysis, and results were analysed only for those who completed each stage of follow-up. In the instance of missing data, results were analysed only for patients who had available data. Data were tested for normality, and presented as mean (s.d.) or median (i.q.r.), as appropriate. Data were analysed using the χ^2, Kruskal–Wallis or Mann–Whitney U test, as appropriate. Two-sided $P < 0.050$ was considered statistically significant.

Results

Patient demographics

295 patients with 333 eligible wounds were recruited. Five randomization envelopes were misplaced across the two participating sites. Of the recruited participants, 18 patients with 19 wounds were excluded (*Fig. 1*). Therefore, a total of 277 patients with 314 wounds were included in the final analysis. Baseline participant and wound characteristics are summarized in *Table 2*.

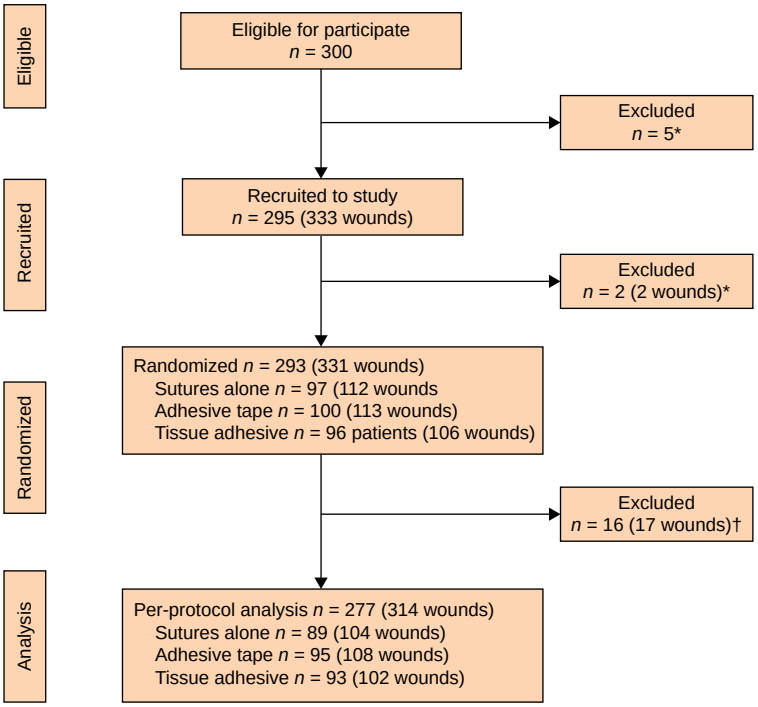

Fig. 1 Study flow chart

*Lost randomization envelopes. †Previous surgery (1 patient), clinical decision to use alternative technique after randomization (5), incorrect application of allocated technique (7), incorrect technique used after randomization (3).

Table 2 Baseline demographics of participants

	Sutures alone	Adhesive tape	Tissue adhesive
No. of patients	89	95	93
No. of wounds	104	108	102
Age (years), median (i.q.r.)	2.2 (0.3–5.9)	2.3 (0.2–7.6)	3.3 (1.0–7.4)
Sex			
M	65 (73.0)	82 (86.3)	72 (77.4)
F	24 (27.0)	13 (13.7)	21 (22.6)
Wound type			
Incision	100 (96.2)	106 (98.1)	97 (95.1)
Excision	4 (3.8)	2 (1.9)	5 (4.9)
Wound site			
Neck, thorax or limb	4 (3.8)	3 (2.8)	7 (6.9)
Inguinal	68 (65.4)	72 (66.7)	63 (61.8)
Laparoscopic (umbilical)	21 (20.2)	24 (22.2)	17 (16.7)
Abdominal	11 (10.6)	9 (8.3)	15 (14.7)
Wound contamination			
Clean	89 (85.6)	98 (90.7)	91 (89.2)
Clean-contaminated	15 (14.4)	10 (9.3)	11 (10.8)
Contaminated	0 (0)	0 (0)	0 (0)
Dirty	0 (0)	0 (0)	0 (0)
Suture used for fascia			
VICRYL®	60 (56.6)	64 (59.3)	67 (65.0)
Polysorb®	30 (28.3)*	30 (27.8)	28 (27.2)*
PDS® II	14 (13.2)*	10 (9.2)	6 (5.8)*
Not documented/not used	2 (1.9)	4 (3.7)	2 (1.9)

Values are *n* (%) unless otherwise indicated. *Two wounds in sutures-alone group group and one in tissue adhesive group had fascial closure with both Polysorb® and PDS® II.

Follow-up

The response rate at 2 weeks was 87.9 per cent for the parental telephone survey and 69.4 per cent for parent-rated wound cosmesis sent by e-mail. 79.0 per cent of parents completed the 6-week parental survey and wound photographs were available for clinician-rated wound cosmesis for 75.2 per cent of participants. There was significant attrition for the follow-up of at least 6 months; 35.4 per cent completed the e-mailed parent survey and 34.7 per cent of participants had an available wound photograph for clinician-rated wound cosmesis. There was no significant difference in follow-up rates between the three groups for 2-week, 6-week, and 6-month follow-up.

Clinician-rated wound cosmesis

Clinician-rated wound cosmesis at 6 weeks and 6 months or more is summarized in *Fig. 2* and *Table S1*. Wounds in the tissue adhesive group had poorer cosmesis scores on all four assessment scales at short-term follow-up; this difference attained statistical significance on the 10- and 100-point VAS, with the difference lying between the sutures-alone and tissue adhesive groups. This difference was not sustained at long-term follow-up. Pairwise comparisons between the three groups using the Mann–Whitney *U* test revealed that wounds in the tissue adhesive group had significantly poorer cosmetic outcome at 6 weeks compared with those closed with sutures alone using all four wound evaluation scales (*Table S2*).

A subgroup analysis was undertaken for clinician-rated wound cosmesis at 6 weeks given that this was the primary outcome measure. Subgroup analysis was performed based on patient age (less than 1 year *versus* 1–5 years *versus* 5 years or more), incision type (open *versus* minimally invasive/laparoscopic), and wound type (incisional *versus* excisional). There was a significant difference in results between groups (*Table 3*). In the minimally invasive (laparoscopic) wound subgroup, wounds closed with tissue adhesive had a significantly poorer cosmetic outcome at

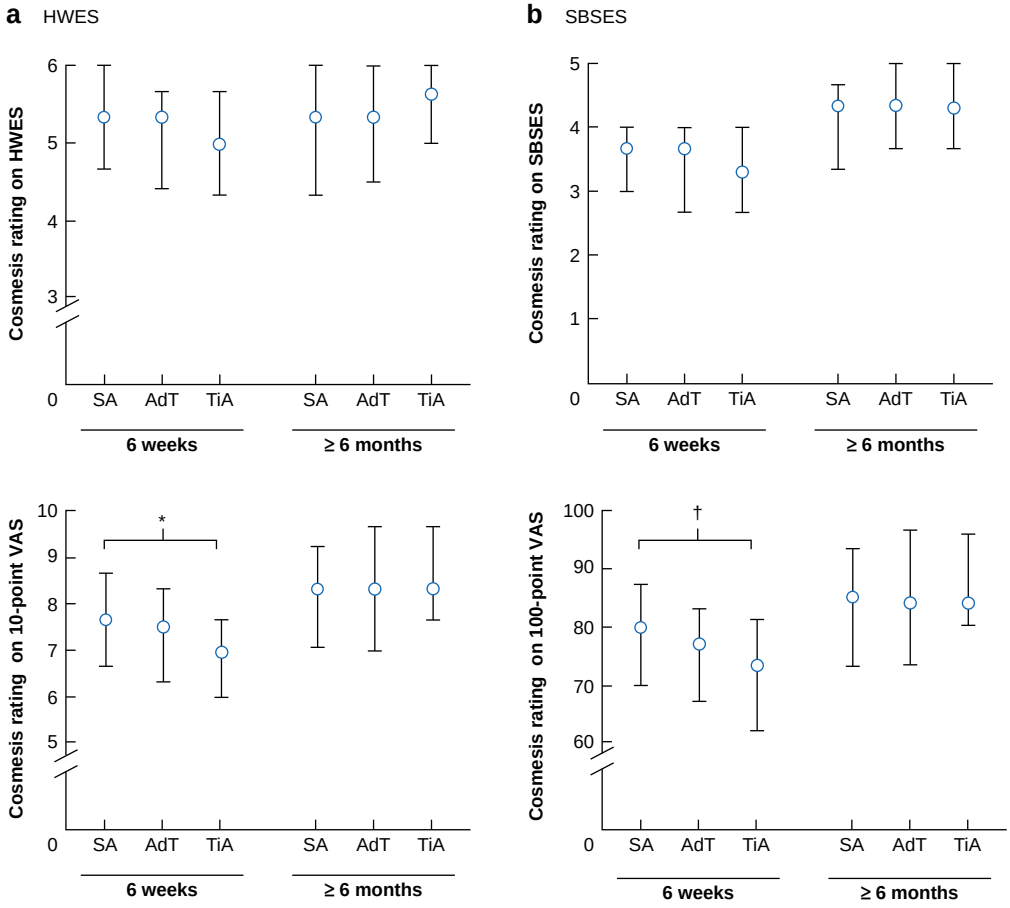

Fig. 2 Clinician-rated cosmesis at 6 weeks and after 6 months or more

Values are median (i.q.r.) scores on **a** Hollander Wound Evaluation Scale (HWES), **b** Stony Brook Scar Evaluation Scale (SBSES), **c** 10-point visual analogue scale (VAS), and **d** 100-point VAS. SA, sutures alone; AdT, adhesive tape; TiA, tissue adhesive. *P = 0.014, †P = 0.010 (Kruskal–Wallis test).

6 weeks than wounds closed with sutures alone as assessed using the SBSES, and 10- and 100-point VAS. Similarly, in the incisional wound subgroup, wounds closed with tissue adhesive had significantly poorer cosmesis at 6 weeks than those closed with sutures alone as assessed using the 10- and 100-point VAS.

Parental satisfaction

Parental satisfaction with the technique used was not significantly different between the three groups at 2 weeks (P = 0.187, Kruskal–Wallis test), 6 weeks (P = 0.848), and 6 months or more (P = 0.868), with a median score of 5 (very satisfied) for each group at each follow-up interval.

Parent-rated wound cosmesis

Results for parent-rated wound cosmesis at 2 weeks were not analysed because a large proportion of results were gathered retrospectively at the 6-week follow-up owing to poor participant response to the 2-week e-mail. Furthermore, cosmesis ratings were provided for some wounds even though the dressing was still applied. There was no difference in parent-rated wound cosmesis between groups at 6 weeks (P = 0.690, Kruskal–Wallis test) and at 6 months or more (P = 0.167) (*Fig. 3* and *Table S1*).

Wound complications

There were no confirmed cases of wound infection. There was one superficial wound dehiscence in the tissue adhesive group for an excisional arm wound.

Requirement for healthcare practitioner for wound review

Twenty-one patients with 22 wounds saw a healthcare practitioner for wound review after the operation: 6 patients (6 wounds) in the sutures-alone group, 8 patients (9 wounds) in the adhesive tape group, and 7 patients (7 wounds) in the tissue adhesive group. It was unclear whether a patient in the adhesive tape group saw the healthcare practitioner for one or both included wounds so both wounds were included in the analysis. There was no significant difference in the frequency of requirement to see a healthcare practitioner (P = 0.715, χ^2 test).

Time taken for wound closure

Median time to wound closure was longer in the tissue adhesive group (361 s) compared with the sutures-alone group (196 s), and adhesive tape group (262 s). However, this difference was not significant (P = 0.163, Kruskal–Wallis test).

Cost of materials

At this centre, the current cost of each of the evaluated materials in 2021 Euros is €19.23 for each vial of High Viscosity

Table 3 Subgroup analysis of clinician-rated wound cosmesis at 6 weeks

	Clinician-rated wound cosmesis score, median i.q.r.			*P**
	Sutures alone	Adhesive tape	Tissue adhesive	
Age < 1 year (*n* = 75)	*n* = 28	*n* = 26	*n* = 21	
HWES	5.7 (5.1–6.0)	5.3 (4.7–5.7)	5.3 (4.0–5.5)	0.056
SBSES	3.8 (3.3–4.3)	3.7 (3.0–4.1)	3.7 (2.8–4.0)	0.197
10-point VAS	8.2 (7.0–9.0)	7.7 (6.6–8.4)	7.3 (6.0–8.0)	0.060
100-point VAS	83.5 (72.6–90.3)	79.2 (68.2–84.6)	76.0 (61.2–81.8)	0.059
Age 1–5 years (*n* = 79)	*n* = 19	*n* = 23	*n* = 37	
HWES	6.0 (4.0–6.0)	5.3 (4.3–5.7)	5.3 (4.7–5.7)	0.363
SBSES	3.7 (3.0–4.0)	3.7 (2.7–4.0)	3.3 (3.0–4.0)	0.787
10-point VAS	7.7 (7.0–8.7)	7.3 (6.3–8.0)	7.3 (6.7–7.8)	0.387
100-point VAS	79.0 (73.3–86.0)	73.3 (67.0–80.3)	76.0 (68.8–81.5)	0.293
Age ≥ 5 years (*n* = 82)	*n* = 26	*n* = 31	*n* = 25	
HWES	5.2 (4.0–5.8)	5.3 (4.3–6.0)	5.0 (3.5–5.5)	0.336
SBSES	3.3 (2.3–4.0)	3.7 (2.7–4.0)	3.0 (1.5–3.8)	0.143
10-point VAS	7.3 (5.7–8.3)	7.3 (6.3–8.3)	7.0 (5.0–7.5)	0.116
100-point VAS	77.0 (59.8–84.2)	74.7 (66.7–84.3)	68.3 (50.8–78.8)	0.103
Minimally invasive (laparoscopic) wounds (*n* = 48)	*n* = 15	*n* = 18	*n* = 15	
HWES	5.7 (5.0–6.0)	5.3 (3.7–5.7)	4.7 (4.0–5.7)	0.167
SBSES	4.0 (3.3–4.0)	3.7 (2.9–4.1)	3.3 (2.7–3.7)	0.038†
10-point VAS	8.0 (7.0–8.7)	7.5 (5.9–8.3)	6.7 (5.7–7.3)	0.026†
100-point VAS	83.7 (72.3–89.3)	76.2 (60.1–84.3)	68.0 (57.3–76.7)	0.024†
Open wounds (*n* = 188)	*n* = 58	*n* = 62	*n* = 68	
HWES	5.3 (4.7–6.0)	5.3 (4.7–5.8)	5.3 (4.7–5.7)	0.313
SBSES	3.5 (2.9–4.0)	3.7 (2.7–4.0)	3.3 (2.7–4.0)	0.306
10-point VAS	7.7 (6.5–8.7)	7.5 (6.6–8.0)	7.3 (6.1–7.9)	0.173
100-point VAS	79.3 (67.8–87.3)	77.2 (67.7–82.4)	76.0 (63.0–81.7)	0.147
Incision (*n* = 225)	*n* = 69	*n* = 78	*n* = 78	
HWES	5.7 (4.8–6.0)	5.3 (4.6–5.7)	5.0 (4.3–5.7)	0.060
SBSES	3.7 (3.0–4.0)	3.7 (2.7–4.0)	3.3 (2.7–4.0)	0.055
10-point VAS	8.0 (6.8–8.7)	7.7 (6.3–8.3)	7.2 (6.0–7.7)	0.009†
100-point VAS	81.3 (70.0–87.8)	78.2 (67.6–83.4)	73.8 (62.8–81.4)	0.006†
Excision (*n* = 11)	*n* = 4	*n* = 2	*n* = 5	
HWES	4.3 (3.3–5.3)	4.3 (4.0–4.7)	5.0 (1.7–5.6)	0.969
SBSES	3.3 (1.5–3.7)	2.8 (1.7–4.0)	3.0 (1.0–4.0)	0.865
10-point VAS	6.3 (4.3–7.6)	6.5 (6.3–6.7)	6.3 (2.7–8.3)	0.991
100-point VAS	62.8 (44.1–76.6)	69.0 (66.7–71.3)	66.3 (25.8–83.2)	0.979

HWES, Hollander Wound Evaluation Scale; SBSES, Stony Brook Scar Evaluation Scale; VAS, visual analogue scale. †Significance due to a statistically significant difference between sutures-alone and tissue adhesive groups.

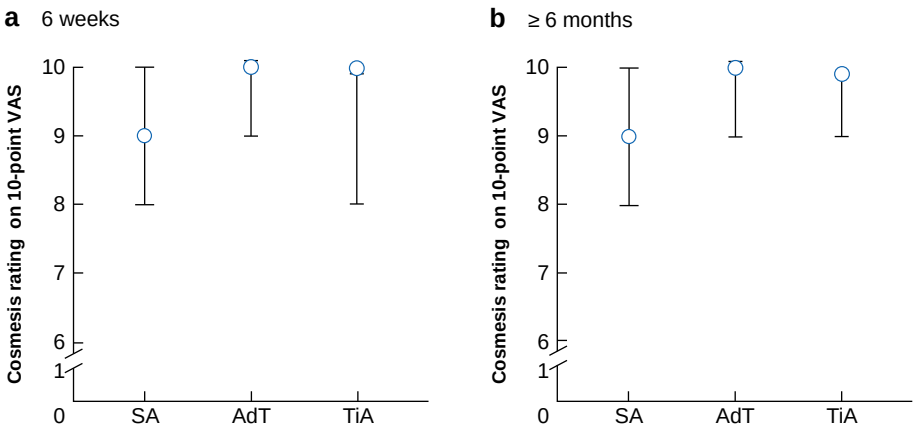

Fig. 3 Parent-rated wound cosmesis at 6 weeks and after after 6 months or more

Values are median (i.q.r.) scores on a 10-point visual analogue scale (VAS) at **a** 6 weeks and **b** 6 months or more. SA, sutures alone; AdT, adhesive tape; TiA, tissue adhesive. **a** $P = 0.690$, **b** $P = 0.167$ (Kruskal–Wallis test).

DERMABOND® Topical Skin Adhesive, €0.05 per packet of Steri-Strip™ Reinforced Skin Closures (12 mm × 100 mm), and €0.15 for each Tegaderm™ Transparent Film Dressing. The fascial suture cost was €3.79 per suture for VICRYL®, €2.47 per suture for Polysorb®, and €4.62 per suture for PDS® II. There was no significant difference in the frequency with each suture type was used for fascial closure between the three groups ($P = 0.598$) (*Table 1*).

Interim analysis

The interim analysis was conducted in 2017 with 82 patients and 95 wounds: 24 patients (26 wounds) in the tissue adhesive group, 28 patients (34 wounds) in the adhesive tape group, and 30 patients (35 wounds) in the sutures-alone group. There was no significant difference between groups for all evaluated outcomes.

Discussion

Clinician-rated wound cosmesis assessed using four validated wound evaluation scales demonstrated that wounds closed with tissue adhesive had poorer cosmesis at 6 weeks than those closed with sutures alone or adhesive tape. This difference was significant between the sutures-alone and tissue adhesive groups. However, the difference was not sustained at long-term follow-up (at least 6 months). Wound cosmesis was assessed independently by three paediatric surgeons blinded to the skin closure technique, with their averaged scores used for analysis, which was a strength of the study. Although previous paediatric studies have tended to use the VAS and HWES, the SBSES was included here as it has been validated for long-term cosmesis assessment[10], whereas the HWES has been validated for evaluation of short-term cosmesis[11]. In interpreting the present findings, it is important to consider the high attrition rate to follow-up at 6 months or more, which may have masked a potential difference in long-term cosmetic outcomes.

The finding of inferior clinician-rated wound cosmesis with tissue adhesive is concordant with the results of Romero *et al.*[5], who also evaluated the use of tissue adhesive/adhesive tape as an adjunct to subcuticular sutures, similar to the present trial methodology. In paediatric surgical studies comparing sutures and tissue adhesive, in the short term (12 weeks or less), there is less clear evidence, with studies assessing excisional[9] and elective[12] surgical wounds demonstrating better results with sutures. However, studies[13,14] assessing hernia incisions showed no difference. In the paediatric emergency setting, there was no cosmetic difference between lacerations repaired with sutures or tissue adhesive[6,15,16]. The authors' meta-analysis[7] similarly demonstrated no cosmetic difference in wounds closed with tissue adhesive and sutures. However, wounds closed with adhesive tape had better cosmesis than those closed with tissue adhesive, although this difference was largely powered by the 2011 study of Romero *et al.*, and two small studies with significant heterogeneity in wound type and time of cosmesis assessment.

Parent-rated wound cosmesis and satisfaction was high at 6 weeks and 6 months or more in this study, irrespective of technique. This may have been driven by a lack of parental experience with surgical wounds and the relative paucity of wound complications, which predispose to poorer cosmetic outcomes. The finding is somewhat concordant with the existing literature; comparing tissue adhesive with adhesive tape, parents and patients found wound cosmesis to be equivalent between techniques for laceration repair[6] and surgical wound closure[5,17]. However, comparing tissue adhesive with sutured surgical wounds, sutured wounds demonstrated better parent-rated wound cosmesis[12,14]. The high parental wound cosmesis and satisfaction with all wound closures in this trial is reassuring as parental satisfaction has not previously assessed been extensively[5,17]. In keeping with the present findings, existing studies demonstrated no significant difference in parental satisfaction with wound cosmesis when comparing tissue adhesive with adhesive tape[5] and tissue adhesive with sutures[17]. However, these previous studiesfocused on wound cosmesis only, whereas the aim here was to better evaluate parents' satisfaction with caring for individual wounds.

Wound complications were infrequent in this study, consistent with existing paediatric studies[13,17]. However, van den Ende *et al.*[12] demonstrated a significantly increased risk of dehiscence when tissue adhesive was used for skin closure of surgical wounds: 13 of 50 glued wounds (26 per cent) dehisced compared with no dehiscence in the suture group. This may potentially be related to the study's evaluation of *n*-butylcyanoacrylate, an older adhesive glue with lower tensile strength than octylcyanoacrylate, which was used in this trial and other studies[1]. A systematic review[18] comparing tissue adhesive with sutures demonstrated an increased risk of wound dehiscence with tissue adhesive, although the wound infection rate remained similar among pooled adult and paediatric cohorts. Although the present trial did not demonstrate a difference in wound complication rate between techniques, it is likely that the study was underpowered to detect this outcome. Wound infections are infrequent in paediatric surgery, with an estimated incidence of 1.2–6.7 per cent, and increased risk with greater wound contamination and emergency surgery[19,20]. Wound dehiscence is similarly uncommon, occurring in 0.4–1.2 per cent of patients, and is more commonly encountered in infected wounds and emergency surgery[21]. The inclusion of elective surgical wounds which were all clean or clean-contaminated, coupled with the infrequent nature of these complications in children, means that the study was probably underpowered to detect any differences.

Although no formal cost analysis was undertaken, the cost of materials is an important consideration, particularly in the setting of techniques yielding otherwise identical outcomes except for short-term wound cosmesis. All wounds were closed in an identical fashion with the same materials. However, it is apparent that the difference in cost of materials was significant, with tissue adhesive being 128-fold more expensive than a simple occlusive film dressing in this trial. Fascial sutures used were standardized to VICRYL®, Polysorb®, and/or PDS® II for each wound; however, individual choice was dependent on the operation and surgeon preference. PDS® II was substantially more expensive that the other two sutures; however, the frequency with which each suture was used was similar in the three groups. Previous cost analyses comparing tissue adhesive with sutures demonstrated either a significant overall reduction in cost with tissue adhesive used for closure of paediatric facial lacerations[22], or no difference in overall cost when used in paediatric hernia repairs after factoring in more rapid wound closure and shorter operating time with glue[13]. However, in the present study, there was no significant difference in wound closure times between techniques, factoring in that all wounds had subcuticular sutures placed, whereas existing studies evaluated skin closure with tissue adhesive alone.

This study has some limitations. First, although short-term wound cosmesis was shown to be poorer with tissue adhesive, the significant loss to long-term follow-up limits any conclusions. Second, the study was underpowered to detect differences in wound complications (such as infection and dehiscence) between techniques, which is an important clinical endpoint when assessing skin closure. Given that wound infection and dehiscence are relatively infrequent complications in the paediatric surgical cohort, the sample size may have been limited in ability to detect potential differences between groups. Based on the present findings, a power calculation for a three-arm superiority RCT comparing sutures alone, adhesive tape, and tissue adhesive ($\alpha = 0.05$, $1 - \beta = 0.80$) would require a total of 1053 (10-point VAS at 6 months) or 927 (100-point VAS) patients,

which may be difficult for a single centre to achieve. Third, although one of the study aims was to compare skin closure with sutures alone with combination skin closure, wound closure with tissue adhesive or adhesive tape alone was not evaluated. This was borne out of the existing literature demonstrating a potentially higher rate of wound complications, in particular wound dehiscence, with use of adhesive glue alone compared with sutures in both paediatric[12] and adult[18] studies. Additionally, owing to its low tensile strength and the resulting risk of dehiscence, adhesive tape is typically used in combination with sutures. There is limited evidence for its use as a primary wound closure method outside of the emergency setting[1]. Future studies should consider the assessment of tissue adhesive or adhesive tape alone for wound closure in appropriate, low-tension wounds to evaluate whether they can be used safely for surgical skin closure in children as an alternative to sutures. The present study used sealed envelopes prepared by non-study personnel to randomize recruited patients. This method is not as reliable as a computer-based electronic randomization system. In this trial, five randomization envelopes were lost before patient recruitment. However, selection and allocation bias were minimized as the envelopes were opaque and the randomization sequence was computer-generated, with envelopes prepared by non-study personnel before the start of the study. Finally, a per-protocol analysis was used in this study as opposed to an intention-to-treat analysis. Similar numbers of patients were lost to follow-up in each of the three groups, with most exclusions of randomized patients due to surgical factors (such as use of a non-evaluated wound closure technique or materials leading to a protocol breach). As these were different techniques, a per-protocol analysis was adopted for this study rather than an intention-to-treat analysis. Furthermore, this meant that excluded participants did not have to attend all the required trial follow-up clinic appointments. The authors acknowledge that, although a per-protocol analysis does have advantages, including providing a true reflection of the technique evaluated, not using an intention-to-treat analysis may have introduced bias owing to attrition and potentially undermine the randomization process. Given that patients who were excluded did not have complete follow-up data, the authors believe that analysing these few patients would have potentially introduced further bias.

This RCT demonstrated that wounds closed with sutures alone did not differ significantly in terms of evaluated outcomes from those closed with sutures and adjunctive tissue adhesive or adhesive tape. Although use of tissue adhesive as an adjunct to sutures was associated with poorer short-term wound cosmesis, this difference did not appear to be sustained in the long term. There was no significant difference between techniques for all other outcomes evaluated. Given that adjunctive skin closure appears to yield similar outcomes to use of sutures alone, and the substantially higher cost of materials and poorer short-term wound cosmesis associated with tissue adhesives, it may be preferable to use sutures alone or sutures with adhesive tape in preference to sutures with tissue adhesive.

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Disclosure

The authors declare no conflict of interest.

Supplementary material

Supplementary material is available at *BJS* online.

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Glucagonoma syndrome

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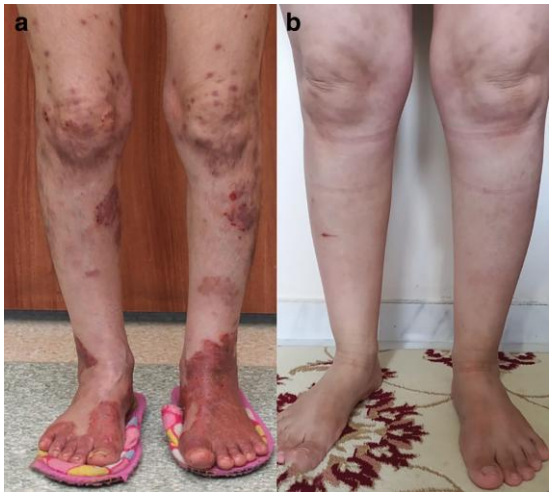
Surgical Snapshots

A 37-year-old female patient was referred with a widespread itchy rash, weight loss, and new-onset diabetes mellitus. Blood glucagon hormone measurement was >500 pg/ml. Laparoscopic distal pancreatectomy and splenectomy was performed. Her complaints disappeared afterwards. Surgery is the mainstay of treatment for glucagonoma disease and associated symptoms.



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