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A 4-arm randomized controlled pilot trial of innovative solutions for jugular central venous access device securement in 221 cardiac surgical patients

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ABSTRACT

Purpose: To improve jugular central venous access device (CVAD) securement, prevent CVAD failure (composite: dislodgement, occlusion, breakage, local or bloodstream infection), and assess subsequent trial feasibility.
Materials and Methods: Study design was a 4-arm, parallel, randomized, controlled, nonblinded, pilot trial. Patients received CVAD securement with (i) suture + bordered polyurethane (suture + BPU; control), (ii) suture + absorbent dressing (suture + AD), (iii) sutureless securement device + simple polyurethane (SSD + SPU), or (iv) tissue adhesive + simple polyurethane (TA + SPU). Midtrial, due to safety, the TA + SPU intervention was replaced with a suture + TA + SPU group.
Results: A total of 221 patients were randomized with 2 postrandomization exclusions. Central venous access device failure was as follows: suture + BPU controls, 2 (4%) of 55 (0.52/1000 hours); suture + AD, 1 (2%) of 56 (0.26/1000 hours, $P = .560$); SSD + SPU, 4 (7%) of 55 (1.04/1000 hours, $P = .417$); TA + SPU, 4 (17%) of 23 (2.53/1000 hours, $P = .049$); and suture + TA + SPU, 0 (0%) of 30 ($P = .263$; intention-to-treat, log-rank tests). Central venous access device failure was predicted ($P < .05$) by baseline poor/fair skin integrity (hazard ratio, 9.8; 95% confidence interval, 1.2-79.9) or impaired mental state at CVAD removal (hazard ratio, 14.2; 95% confidence interval, 3.0-68.4).
Conclusions: Jugular CVAD securement is challenging in postcardiac surgical patients who are coagulopathic and mobilized early. TA + SPU was ineffective for CVAD securement and is not recommended. Suture + TA + SPU appeared promising, with zero CVAD failure observed. Future trials should resolve uncertainty about the comparative effect of suture + TA + SPU, suture + AD, and SSD + SPU vs suture + BPU.

1. Introduction

Central venous access devices (CVADs) are placed in the large veins of intensive care patients to deliver critical treatment and monitor central venous pressures. Central venous access devices are commonly used medical devices in hospitals, with 3 million used in the United States and 250 000 in the UK each year alone [1,2]. In total, 25% to 30% of CVADs are reported to fail via dislodgement, blockage, breakage, thrombosis, or infection, resulting in premature device removal [3,4]. This adversely impacts patients' care through interrupted treatment

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(eg, interruption of vasopressors, or sedatives) and requires additional CVAD insertion with inherent associated risks and procedural pain. Failure may involve localized or catheter-associated bloodstream infections (CABSIs) which lengthen stay by ~10 days, increase absolute risk of death by 1%, and increase costs by AUD$14 886 (2010) [5]. The placement of CVADs in the jugular vein increases this risk of CABSI and ultimately CVAD failure, when compared with subclavian vein placement [6]. All forms of CVAD failure significantly increase hospital costs and workloads.

Central venous access device securement is key to minimizing complications, yet CVAD failure rates suggest that current approaches do not adequately prevent dislodgement or the catheter micromotion which precipitates endothelial damage and occlusion, and facilitates the entry of skin microorganisms through the catheter insertion site [7,8]. Traditionally, sutures with either gauze and tape, or nonbordered, polyurethane dressings have been used for CVAD securement [9]. Clinical practice guidelines now recommend *against* the use of sutures due to needle-stick injury risks and significantly increased CABSI in one randomized controlled trial (RCT) [8,10]. Instead, sutureless securement devices (SSDs) are recommended [8,11]. These have a strong adhesive footplate affixed to the skin, with a plastic clip or velcro fabric clasp to secure the CVAD. Sutureless securement devices are designed to reduce movement, kinking, and flow impedance, yet to date, there has been no published RCT in short-term CVADs, and our experience is that uptake of SSDs in Australian intensive care units (ICU) is limited.

More recently, reinforced bordered polyurethane (BPU) dressings have emerged and are now used in many ICUs in place of traditional transparent dressings, but still in combination with sutures. No published RCT has yet reported on the effectiveness of BPU to prevent CVAD failure. Another alternative is absorbent dressings (ADs), some of which retain a degree of visibility of the site [12]. Developed for postsurgical wounds, these dressings may be beneficial, particularly in postcardiac surgical or other patients whose CVAD sites ooze hemoserous discharge; however, they are untested for CVAD securement.

In a novel approach to various vascular device securement, we have previously investigated in vitro use of tissue adhesive (TA; ie, medical grade "superglue"), finding it potentially beneficial to avoid dislodgment and microbial growth [13]. In short peripheral arterial and venous lines, TA securement led to absolute reductions in catheter failure ranging from 11% to 24% compared with traditional non-BPU films [14-16]. We hypothesized that TA could also improve CVAD securement, although only case series have to date reported its use for this indication with mixed results [17-20].

A lack of rigorous data on effective interventions for CVAD dressing and securement has seen practice change little for decades [21]. Given the large number of CVADs used globally each year and frequent CVAD complications, this is a high priority area for research. With this in mind and in preparation for a large multisite study, we undertook a pilot RCT to consider the feasibility, safety, and acceptability of a study protocol [22], and to prioritize products for a planned large-scale RCT.

2. Materials and methods

2.1. Study design and participants

After hospital and university ethical approval (HREC/11/QRCH/152; NRS/10/14/HREC), this randomized controlled pilot trial was commenced. Written informed consent was obtained before scheduled cardiac surgery. The study design was a 4-arm, parallel trial. The single-center setting was in the operating theaters and a 21-bed ICU at The Prince Charles Hospital—a tertiary referral hospital in Queensland, Australia, with a large cardiac surgical cohort. The target sample size was 220, 50 per group, plus 10% for potential attrition, determined by recommendations for pilot trial sample sizes [22]. The study was registered with the Australian Clinical Trials Registry: ACTRN12613001103752.

From 2nd September 2013 to 8th April 2014, Monday to Friday, clinical research nurses (CRNs) screened elective cardiac surgical patients preoperatively. Only 1 CVAD per patient was studied. Inclusion criteria were as follows: written informed consent, aged ≥18 years, and a CVAD expected to be in use for at least 24 hours. Patients were excluded if they had an existing bloodstream infection (<48 hours), were non–English-speaking without an interpreter, had burned or diseased skin at the entry site, had extreme diaphoresis at enrollment, had existing skin tears or "papery" poor quality skin, or had a known allergy to any study product.

2.2. Randomization and masking

The CRN performed randomization using an independent Web-based service (https://www151.griffith.edu.au/) to ensure allocation concealment until study entry. Patients were randomly assigned in a 1:1:1:1 ratio with computer-generated and randomly varied block sizes of 4 and 8 to prevent prediction of allocation. Urn randomization was not used and the groups could potentially have more than 55 patients allocated to them, with recruitment to be continued until a minimum of 55 per group were enrolled. Dressing and securement interventions could not be blinded because clinical staff needed to be able to continuously monitor that they were clean, dry, and intact for purposes of patient safety, and research staff needed to check the adherence of the study products and inflammation/discharge. All infection and microbiological end points were blinded through the use of blinded scientists.

2.3. Study interventions

Central venous access devices (quadruple-lumen 8.5F 8-in./20-cm, or triple-lumen 7F 6-in./16-cm chlorhexidine impregnated ARROWg^{+}ard Blue Plus CVC, Teleflex, Research Triangle Park, NC) were inserted into the internal jugular vein using landmark/ultrasound technique by anesthetic registrars or anesthetists, at the inserter's discretion. Preinsertion, skin preparation was with chlorhexidine 0.5% in 70% alcohol (PharmAust, Welshpool, Western Australia), or Riodine Povidone Iodine 10% (PharmAust), at the inserter's discretion.

Group 1. Suture + BPU (controls): CVADs were sutured with an Ethicon 3-0 Prolene 30-in. (75-cm) SH needle 26-mm 1/2c Taper (Johnson & Johnson, North Ryde, NSW, Australia), and the catheter entry site was secured with a BPU (Tegaderm I.V. 1650 Dressing 10 × 15.5 cm; 3M, St Paul, Minn). This is a polyurethane adhesive film with a reinforced fabric border Fig. 1A.

Group 2. Suture + AD: CVADs were sutured as for group 1 and the catheter entry site was secured with an AD (OpSite Post-Op Visible 10 × 8 cm; Smith & Nephew, Hull, United Kingdom). This has a low adherent wound contact layer, a "criss-cross" lattice-shaped absorbent pad, and a waterproof, bacteria-resistant polyurethane film with adhesive coating Fig. 1B.

Group 3. SSD + SPU: CVADs were not sutured. Instead, an SSD (Grip-Lok CVC 3601 Securement Device; TIDI, Neenah, Wis) was used to anchor the hub near the catheter entry site, with the "tails" anchored to the skin with a second Grip-Lok. A simple polyurethane (SPU) borderless dressing (IV3000™ 10 × 14 cm; Smith & Nephew) was used to cover the catheter entry site Fig. 1C.

Group 4. TA + SPU: CVADs were not sutured. Instead, Histoacryl Blue TA (BBraun #1050044, Ann Arbor, Mich) was applied at the insertion site, and under each CVAD wing (see Fig. 2). Approximately a half to three quarters of a 0.5 ml vial was used to secure the CVAD. After allowing the TA to dry, an SPU (as in group 3) was used to cover the catheter entry site. This combination was used for 24 patients. After CVAD dislodgement in 3 of these patients, we ceased randomization to this arm midtrial, and instead created a fifth intervention group for the remaining 30 patients Fig. 1D.

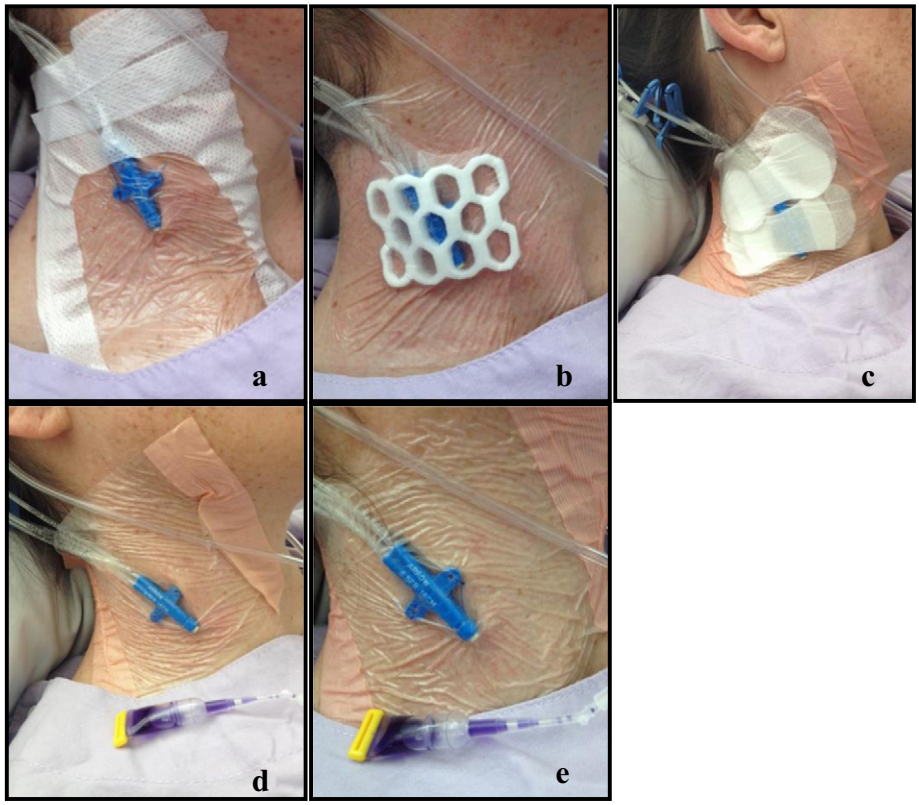

Fig. 1. Central venous access device securement methods. A, Suture + BPU (control). B, Suture + AD. C, SSD + SPU. D, TA + SPU dressing. E, TA + suture + SPU dressing.

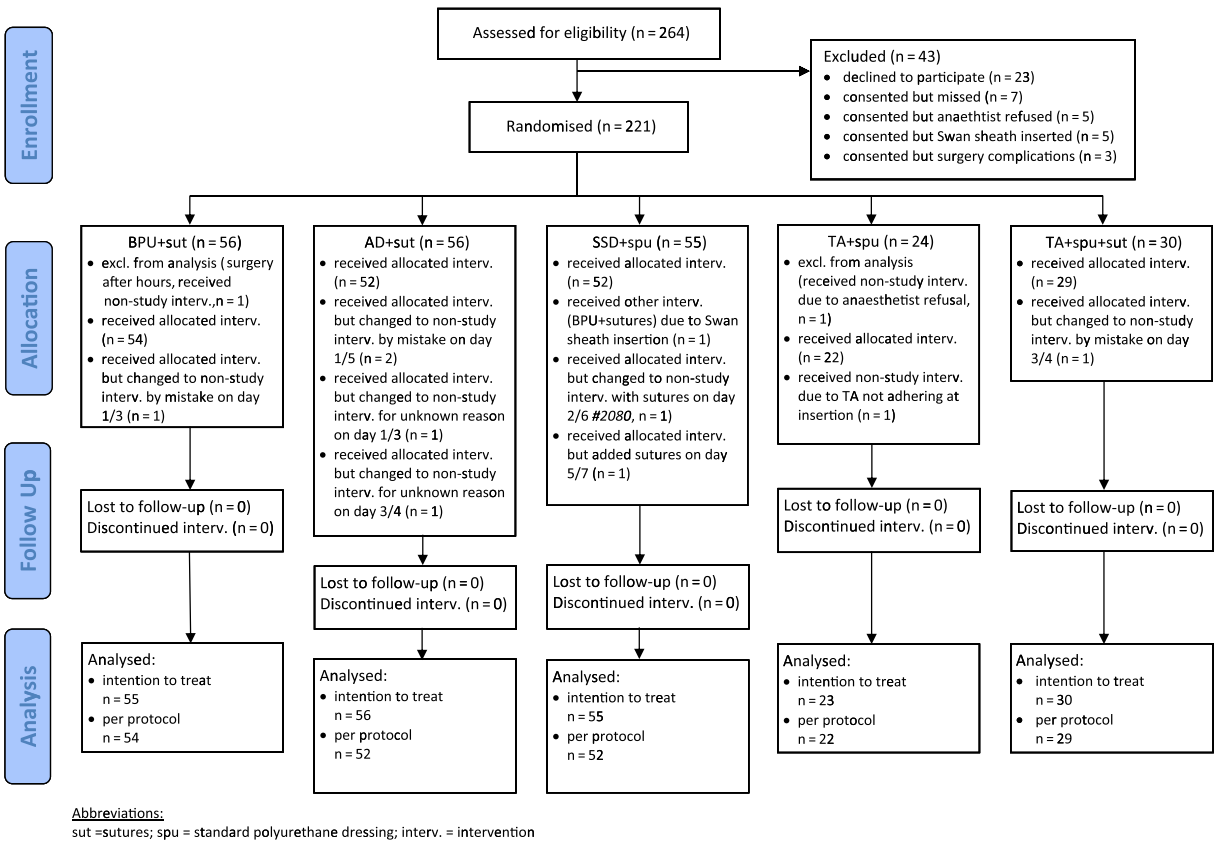

Fig. 2. CONSORT flowchart.

Group 5. Suture + TA + SPU: a suture (as for group 1) was used to secure the CVAD hub. TA and SPU were applied as for group 4 Fig. 1E.

2.4. Study end points

The primary end point was a composite of complications causing catheter failure (premature CVAD removal before completion of therapy). This included (i) dislodgement (total); dislodgement (partial) as evidenced either by change in length from skin site to hub, CVAD no longer in superior vena cava (diagnosed radiologically), intravenous fluids leaking from skin entry site when injected/infused; (ii) occlusion (monitor failure, inability to infuse or aspirate fluids); (iii) local infection (purulent discharge or redness extending 1 cm beyond the site, in conjunction with clinician-initiated CVAD removal with antimicrobial therapy commencement); (iv) CVAD-associated bloodstream infection (CABSI, a laboratory confirmed bloodstream infection in a patient with the CVAD in place within 48 hours that is not related to an infection at another site [23]; or (v) CVAD breakage (visible split in CVAD material diagnosed by treating clinician).

Secondary end points included (i) individual components of CVAD failure—dislodgement, occlusion, local infection, or CABSI; (ii) CVAD-associated bloodstream infection (CABSI, laboratory-confirmed bloodstream infection in a patient who had a CVAD within 48 hours, not related to an infection at another site. The CABSI must meet one of the following: recognized pathogen from one or more blood cultures, not related to an infection at another site, or common skin contaminant from 2 or more blood cultures drawn on separate occasions and if patient has fever (>38°C), chills, or hypotension, not related to an infection at another site; (iii) CVAD colonization (>15 colony-forming units [CFU] isolated from CVAD tip) [8]; (iv) CVAD dwell time (hours); (v) dressing failure (replacement required for soiled, loose, or missing dressing); (vi) dressing life (time in hours from application until removal), (vii) patient-reported satisfaction (11-point numerical rating scale from 0 [very dissatisfied] to 10 [very satisfied]), collected just after removal of the study dressing and securement; (viii) patient-reported pain (11-point numerical rating scale from 0 [no pain] to 10 [worst imaginable pain]), collected just after removal of the study dressing and securement, with a rating of 2 or more of 10 considered clinically significant pain (dichotomized yes/no); (ix) bedside nurse–reported ease of application and removal of the study dressing and securement (11-point numerical rating scale from 0 [very difficult] to 10 [very easy]) collected just after removal; and (x) costs from the hospital perspective (purchase prices for dressing/securements and consumables used for dressing/securement replacement procedures).

2.5. CVAD insertion and care

Extensive prestudy education was undertaken by CRNs to all clinicians involved with care of CVADs and allocated study products. All other aspects of CVAD care were as per routine practice within the ICU and postoperative cardiac surgical ward. The randomized dressing intervention was applied by the CVAD inserter in the operating theater immediately after insertion. The CRN was in attendance to collect relevant data and maintain protocol adherence. Prepacks of study products were left at the patient bedside and were used by the bedside nurses or CRNs to replace dressings that were loose, soiled, or moist. Central venous access devices were used until the treating medical team decided they were no longer required. The CRN and investigators had no involvement in the decision to remove the CVAD. Central venous access device tip and blood cultures were not taken routinely, but only if the treating clinician suspected infection.

2.6. Data collection

At CVAD insertion, CRNs collected data on demographic and clinical conditions. Daily checks were carried out by the CRNs for protocol adherence on week days, with a simple bedside form completed by bedside clinical nurses on weekends. All dressing changes had the date, time, and reason for the dressing change recorded. Additional products or tape reinforcements added by clinical staff to the allocated dressing were recorded, as well as intravenous fluids and drugs infused through the CVAD. Clinical research nurses and clinical nurses assessed patients and recorded outcome data daily. Adverse events were monitored (rash, pruritus, bruising, adhesive residue, skin tears, erythema).

On removal of the CVAD, patients were asked to rate their satisfaction with the dressing products and score pain associated with removal. Bedside nurses were asked to document the ease with which the study products were removed. At CVAD removal, data were also collected on altered mental state (yes/no for any of confusion/agitation/drowsy), continued tracheal intubation (yes/no), and altered mobility (yes/no). Patients were followed up at 48 hours after CVAD removal, for CVAD-related blood stream infection (yes/no) and mortality (yes/no).

2.7. Statistical analysis

Data were exported to Stata 13.1 (Stata-Corp, College Station, Tex) for cleaning and analysis. Patients were the unit of measurement (only 1 CVAD per patient studied). The number of catheter failures between intervention and control groups was compared using Fisher exact test. Failure incidence rates (per 1000 catheter-hours) and incident rate ratios were calculated. Results were further analyzed as time-to-event data with a Kaplan-Meier survival curve and log-rank tests. Hazard ratios were calculated with Cox proportional hazards models. The 10% change-in-estimate rule [24] was used to select covariates for the multivariable model (a covariate was included in the multivariable model if it changed the univariable coefficient of a study group dummy variable by at least 10%). The adjusted effects of the selected covariates were checked again in the multivariable model, and covariates were dropped if their adjusted change-in-estimate was less than 10%, following the manual backward stepwise method. Rules of thumb limiting the number of covariates based on the sample size [25] and the number of outcome events [26] were also considered. The proportional hazards assumption and correlation between covariates in multivariable models were checked. Both intention-to-treat (ITT) and per-protocol analyses were performed to assess the effect of protocol deviations (ITT results presented and discussed throughout, unless otherwise specified). Statistical significance was considered at $P < .05$. Costs were calculated using Queensland Health purchase prices for dressing/securements in Australian dollars (2014; Appendix A) multiplied by the number of dressing/securement replacements required during the CVAD dwell. Patient and staff satisfaction scores, ease of product application, and difficulty of product removal scores were reported descriptively.

3. Results

3.1. Sample

Of 264 potentially eligible patients, 23 declined consent, 7 gave consent but were missed due to surgery occurring after hours, and 13 were excluded due to anesthetist refusal or other reasons (see Fig. 2). Of 221 patients randomized, there were 2 postrandomization exclusions due to surgery being scheduled after hours (n = 1, control group) and anesthetist refusal (n = 1, TA + SPU group). No further data were collected on these 2 patients. Of the 219 patients analyzed by ITT, 209 (95%) received the allocated intervention at all times and were included in the per-protocol analysis. Of the remaining 10 patients, 8 received the allocated intervention for some, but not all, of their CVAD dwell time, and 2 patients received the incorrect intervention for the entire dwell time (see Fig. 2). One patient (SSD + SPU group) developed a hematoma requiring CVAD removal within 6 hours of insertion. This patient was deemed a nonfailure because hematoma was not included in our

prestudy definition of failure. Recruitment was ceased when the planned sample size was achieved. In total, 15 479 catheter-hours were studied, and 100% follow-up was achieved. Patient and device characteristics are displayed in Table 1.

3.2. CVAD failure (composite)

Across the study, CVAD failure incidence was 11 (5%) of 219 (or 9/209 [4%] per protocol), with all failure cases involving dislodgement (see Table 2). Central venous access device failures by group (lowest to highest) were as follows: suture + TA + SPU, 0 (0%) of 30 (incidence rate/1000 CVAD-hours [IR], 0); suture + AD, 1 (2%) of 56 (IR, 0.26); suture + BPU, 2 (4%) of 55 (IR, 0.52); SSD + SPU, 4 (7%) of 55 (IR, 1.04); and TA + SPU, 4 (17%) of 23 (IR, 2.53). These between-group differences were significant ($P = .038$, Fisher exact test) and confirmed on survival analysis ($P = .043$, log-rank test). However, all pairwise comparisons for each intervention group compared with control were not significant ($P > .05$; Table 2). Per-protocol analyses were consistent with the ITT results (Fig. 3A and B). Multivariable Cox regression found CVAD failure significantly associated with fair/poor skin integrity ($P = .033$) and altered mental state ($P = .001$) at the time of CVAD removal (see Table 3).

3.3. Secondary outcomes

There were no local or CABSI infections, and no CVAD occlusion or breakage in any group. One patient had a colonized (>15 CFU) CVAD tip (control group). The overall median CVAD dwell time was 69.5 hours, and not significant difference between the intervention groups and control (Table 2). Most patients required only the initial study product application, with the exception of the TA + SPU group whose average dressing stayed in place only half as long as for controls (25 vs 46 hours, $P < .05$), resulting in more dressing changes in the TA + SPU group. Median patient satisfaction in the control group was 10 of 10 indicating high satisfaction, and this differed significantly only for TA + SPU patients, who provided an average rating of 7.5. Similarly, only TA + SPU patients reported pain on dressing removal (≥2/10) significantly more often than controls (40% vs 12%). Nurses rated the ease of product application significantly better for suture + AD, and significantly worse for SSD + SPU and TA + SPU, compared with the control approach. In contrast, only the 2 TA groups were reported by nurses as significantly worse for ease of removal than for controls. Average costs for product use per patient were as follows: suture + BPU (controls), $78.15; suture + AD, $82.80; SSD + SPU, $81.25; TA + SPU, $113.20; and suture + TA + SPU, $102.60.

3.4. Adverse events and mortality

Minor adverse events occurred in all groups (suture + BPU: rash n = 1, bruising n = 1; suture + AD: pruritus n = 1, bruising n = 5; SSD + SPU: skin tear n = 1; TA + SPU: pruritus n = 1). A dressing was applied to the skin tear which completely resolved within a few days. Study product residue was observed on the skin after study product removal in the suture + AD (n = 2), TA + SPU (n = 10), and suture + TA + SPU (n = 4) groups. One suture + BPU patient had a serious adverse event not considered to be related to the study product. All patients were alive at 48 hours after CVAD removal.

4. Discussion

In this pilot study, TA + SPU had significantly more CVAD failure over time than controls (suture + BPU) on absolute comparisons, although this difference was no longer detectable in the multivariable model. Compared with controls, TA + SPU saw double the number of product applications required, the lowest patient satisfaction, and the highest pain rating, worse for both ease of application and removal, and was the most expensive option. The clinical implication of these results is that TA + SPU should not be used for jugular CVAD dressing and

Table 1
Participant and device characteristics at baseline (n = 221 randomized patients)

	Suture + BPU (ctrl)		Suture + AD		SSD + SPU		TA + SPU		Suture + TA + SPU		Total	
	n	%	n	%	n	%	n	%	n	%	n	%
Group size	56	25	56	25	55	25	24	11	30	14	221	100
Age (y), median (IQR)	69	17	69	19	68	21	73	14	66	12	69	17
Sex: male	39	70	45	80	42	76	15	63	25	83	166	75
APACHE II, mean (SD)	14.1	3.6	14.3	4.5	13.0	4.0	15.9	4.0	14.2	3.1	14.1	4.0
APACHE III, mean (SD)	48	14.1	50	15.1	47	11.4	54	13.2	51	9.8	49	13.2
BMI (kg/m^2), mean (SD)	28.6	5.9	27.6	3.8	29.4	6.2	29.6	6.0	30.8	4.9	29.0	5.4
Overweight or obese	37	73	36	75	38	78	18	82	27	96	156	79
Leucocytes <1000/μL absolute	0	0	0	0	1	2	0	0	1	3	2	1
Any infection at recruitment[a]	1	2	0	0	1	2	1	4	0	0	3	1
Wound (preexisting, not cardiac)	3	6	0	0	0	0	1	4	0	0	4	2
Comorbidities: ≥3	33	60	28	50	30	55	18	75	16	53	125	57
Skin integrity: good	32	58	28	50	29	53	9	38	21	70	119	54
Skin-type color: pale/white (Fitzpatrick scale)	35	64	39	70	34	62	16	67	17	57	141	64
Antibiotic therapy (during study period)	2	4	0	0	0	0	1	4	0	0	3	1
Regular CVAD flushes (documented)	0	0	3	5	4	7	0	0	0	0	7	3
CVAD insertion side: dominant side	53	96	54	96	51	93	22	92	28	93	208	95
Inserted by: anesthetist registrar	35	64	25	45	33	60	19	79	13	43	125	57
Number of CVAD lumens: 4	49	91	52	93	53	96	22	92	27	90	203	93
CVAD insertion attempts: single	47	86	49	88	46	84	24	100	24	80	190	86
Skin prep: chlorhexidine 0.5% in alcohol	41	75	43	77	42	76	21	88	21	70	168	76
Extension tubing excluding administration set	2	4	1	2	3	6	1	4	3	10	10	5
3-way tap attached	36	66	34	61	35	64	13	54	19	63	137	62
5-way tap attached	7	13	8	14	8	15	7	29	0	0	30	14
Hair unclipped at CVAD site	1	2	4	7	3	5	1	4	2	7	11	5
Reduced mobility at CVAD removal	13	24	10	18	11	20	7	29	10	33	51	23
Altered mental state at CVAD removal	3	5	4	7	1	2	4	17	0	0	12	5
Tracheal intubation at CVAD removal	1	2	0	0	2	4	1	4	0	0	4	2

n and % presented unless indicated otherwise; frequencies and proportions may not add up to the group size and 100% due to missing data or rounding. ctrl indicates control; IQR, interquartile range.

[a] Includes, for example, wound or respiratory but not bloodstream infections.

Table 2
Study outcomes by treatment group (n = 219)

	Suture + BPU (ctrl)		Suture + AD		SSD + SPU		TA + SPU		Suture + TA + SPU		*P*
	n	%	n	%	n	%	n	%	n	%	
Group size	55	25	56	26	55	25	23	11	30	14	
CVAD failure (composite indicator)	2	4	1	2	4	7	4	17	0	0	
Fisher exact test (*P* value)	Referent		.618		.679		.059		.538		.038
CVAD dwell time (h)[a]	69.0	29.4	68.2	28.2	67.8	32.4	69.0	49.3	72.2	7.6	
CVAD-hours (sum)	3855		3909		3858		1579		2278		
IR (per 1000 CVAD-hours, 95% CI)	0.52 (0.13-2.07)		0.26 (0.04-1.82)		1.04 (0.39-2.76)		2.53 (0.95-6.75)		0.00[b]		
IRR (95% CI)	referent		0.5 (0.1–9.5)		2.0 (0.3–22.1)		4.9 (0.7–54.0)		0.0 (0.0–9.0)		
Log-rank test (*P* value)	Referent		.560		.416		.049		.263		.033
Per protocol analysis (n = 209)											
- Group size	54	26	52	25	52	25	22	11	29	14	
- CVAD failure (composite indicator)	2	4	0	0	4	8	3	14	0	0	
- Fisher exact test (*P* value)	Referent		.495		.433		.142		.540		.028
- IR (per 1000 CVAD-hours, 95% CI)	0.52 (0.13-2.10)		0.00[b]		1.15 (0.43-3.06)		2.00 (0.64-6.16)		0.0[b]		
- Log-rank test (*P* value)	Referent		.170		.369		.127		.270		.043
CVAD dislodgement	2	4	1	2	4	7	4	17	0	0	
CVAD tip colonization (CFU > 15)	1	2	0	0	0	0	0	0	0	0	
Dressing/securement applications[c]	1.0	1.51	1.0	1.73	1.0	1.64	2.0*	2.26	1.0	1.60	
Product duration (h)[a]	46.2	36.9	46.5	28.5	48.3	42.9	25.1*	25.8	49.4	37.5	
Time for application (s)[a]	20	17	10	10	60*	45	60*	80	[b]	[b]	
Ease of product application[a,d]	10.0	1.0	10.0*	0.0[e]	8.0*	2.0	8.5*	1.0	10.0	1.0	
Ease of product removal[a,d]	9.0	1.0	10.0	1.0	9.0	2.0	8.5*	5.0	8.0*	5.0	
Patient satisfaction[a,d]	10.0	2.0	10.0	2.0	9.0	2.0	7.5*	5.0	10.0	2.0	
Pain (≥2/10)[d]	6	12	11	20	9	18	9*	40	5	17	

Intention-to-treat analysis unless otherwise stated; n and % presented unless indicated otherwise. ctrl indicates control group; IRR = incidence rate ratio; CI = confidence interval.
[a] Median and interquartile range shown.
[b] Cannot be calculated.
[c] Median and mean shown.
[d] 0 = minimum, 10 = maximum.
[e] Greater than 75% had a score of 10.
* $P < .05$ compared with SPU using rank-sum or *t* tests.

securement. The TA + SPU combination likely lost adherence because our postcardiac surgery patients were often coagulopathic and diaphoretic. In addition, the "drag" of multiple infusion tubings, particularly during early patient mobilization, seemed to overcome the adhesive strength of TA + SPU. Central venous access device failure appeared to be exacerbated by male beard growth, which grew "against" and "into" the TA. Tissue adhesive was painful on removal from beard hair for some males, despite the use of adhesive remover wipes. Because of the feasibility design, we pragmatically modified this study group after 4 of 24 patients experienced CVAD dislodgement, creating an alternative TA + suture + SPU group. There were zero CVAD failures (n = 30) with this approach, and although product removal was somewhat harder than for controls, this approach is worthy of exploration in future trials and clinical care. It does not avoid the need for sutures, but there may be benefits in reduced dislodgement and infection risk, and overall cost-effectiveness may negate higher purchase costs.

The 3 other approaches tested for CVAD dressing and securement—suture + AD, SSD + SPU, and suture + TA + SPU—appeared feasible, safe, and acceptable, with comparable (±4%) CVAD failure rates compared with controls, and generally positive feedback from both patients and nurses. This pilot trial found high consent rates, no loss to follow-up, and high (95%) protocol compliance, all of which support the feasibility

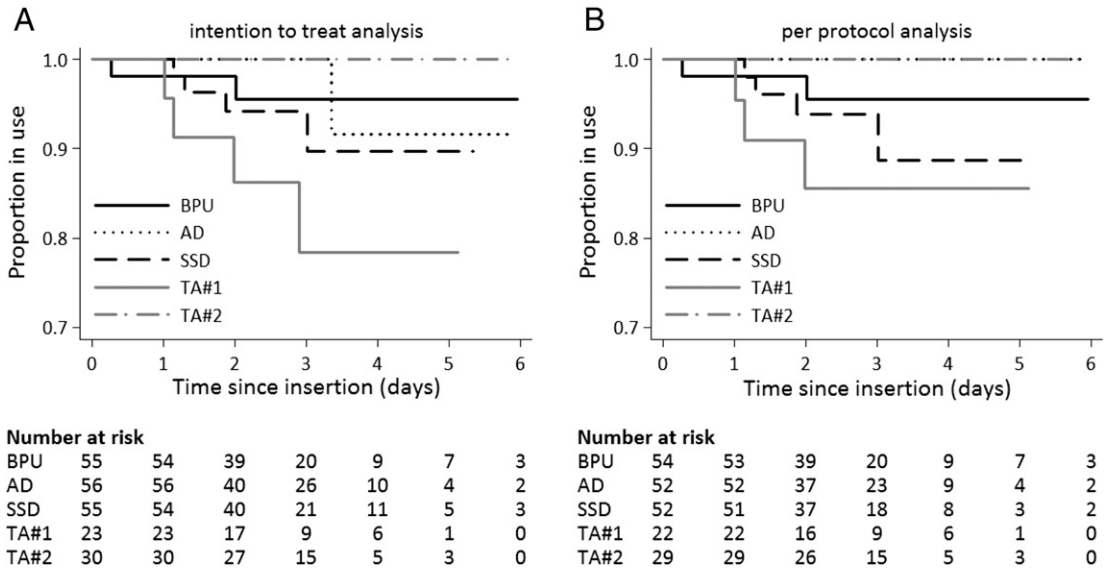

Fig. 3. A and B, Kaplan-Meier curves of catheter failure for ITT (a) and per-protocol (B) analyses. A, Log-rank test, $^*P = .033$. B, Log-rank test, $^*P = .043$.

Table 3
Cox regression for predictors of CVAD failure (ITT analysis, n = 219)

	Univariable, HR (95% CI)	Multivariable, HR (95% CI)
Group		
- Suture + AD vs suture + BPU	0.50 (0.05-5.48)	0.17 (0.01-2.16)
- SSD + SPU vs suture + BPU	1.99 (0.37-10.89)	2.42 (0.42-13.96)
- TA + SPU vs suture + BPU	4.70 (0.86-25.67)*	1.73 (0.29-10.50)
- Suture + TA + SPU vs suture + BPU	[a]	[a]
Older age[b]	1.04 (0.97-1.10)	–
Female sex (ref. "male")	1.65 (0.48-5.66)	–
Obese/overweight BMI (ref. "other")	1.08 (0.23-5.09)	–
≥3 comorbidities (ref. 0-2)	1.14 (0.33-3.92)	–
APACHE II	1.12 (0.97-1.29)	–
APACHE III	1.04 (1.00-1.08)*	–
Fair/poor skin integrity (ref. "good")	10.79 (1.38-84.57)**	9.80 (1.20-79.91)**
Brown skin color (ref. "white")	0.44 (0.09-2.03)	–
Insertion on dominant side (ref. "yes")	[a]	–
Inserted by (ref. "anaesth. registrar")	0.50 (0.13-1.87)	–
Betadine skin prep (ref. "chlorhex.")	0.82 (0.18-3.81)	–
Multiple insertion attempts (ref. "no")	[a]	–
Hair not clipped/remained (ref. "no")	2.10 (0.27-16.4)	–
Altered mobility(ref. "independent")	3.82 (1.16-12.55)**	–
Altered mental state[c] (ref. "no")	11.13 (3.24-38.22)***	14.22 (2.96-68.37)**
Intubated[c] (ref. "no")	7.78 (0.99-61.30)*	–

Chlorhex indicates chlorhexidine; HR, hazard ratio; BMI, body mass index; APACHE, Acute Physiology and Chronic Health Evaluation; ref., Referent category; anaesth, anesthetic.
[a] Unable to be calculated.
[b] Centered over the mean; for example, HR of 1.04 signifies relative increased risk for each 1 year older than the mean age.
[c] At CVAD removal.
* $P < .1$.
** $P < .05$.
*** $P < .001$.

of a larger definitive trial. Future work should add severe hematoma to the composite measure of CVAD failure because we saw one patient develop this complication, and this could theoretically be avoided by improved dressing and securement.

Tissue adhesive use has been favorably assessed for CVADs in case studies [19,20] and even implemented as routine in at least one hospital [18]. Ours is the first RCT to assess TA for CVAD securement, and we found that it was ineffective with SPU alone but was effective when combined with suturing and an SPU. Sutureless securement devices are currently recommended instead of sutures, based on one peripherally inserted central catheter study that showed significantly reduced bloodstream infections [8,10]. There has been no similar RCT in CVADs and we observed no bloodstream infections. Although not statistically significant, the rate of CVAD failure with SSD + SPU was twice that of suture + BPU (1.04 vs 0.52 per 1000 CVAD-hours, $P = .45$), and most failures in the SSD + SPU group were partial dislodgement, which is concerning because the primary purpose of SSDs is securement. There are several styles of SSD available, and some attach better than others for particular CVADs or insertion sites. We plan in the future to trial a different SSD style for this particular patient and CVAD cohort.

The suture + AD group had half the incidence rate of CVAD failure as controls, although this was not statistically significant (0.26 vs 0.52 per 1000-hours, $P = .62$). Thus, AD appears potentially beneficial for postcardiac surgical patients, who are typically diaphoretic and/or oozing from the CVAD. Absorbent dressings limit visualization of the CVAD site; however, a systematic review of RCTs found no difference in the incidence of bloodstream infections when sterile gauze was used, compared with transparent dressings [27]. The AD used in this study had a relatively narrow SPU-style border around the absorbent zone—future trials should assess ADs with more strongly reinforced adhesive borders for CVAD use.

Limitations of this pilot study include the small sample size, although the study was not designed to have adequate statistical power to compare outcomes between groups. The need to modify one of the treatment groups for safety reasons was a limitation; however, given that one of the pilot trial objectives was to assess the feasibility of the study procedures, modification of this treatment group was within the study's scope [22]. Furthermore, the study was unable to be blinded because the study products must, for safety reasons, be visible to clinical and research staff. However, there is no suggestion in the literature that staff have a preference for one of the study products or would intentionally sabotage them to bias the study. Blinding was possible for microbiology results for those patients who had blood/CVAD tip cultures ordered with analysis performed by blinded scientists. Finally, the results are likely specific to the particular products and the study cohort chosen, and generalization to other products and patient groups must be cautious.

Strengths of this study included the concurrent control group, randomization, concealment until allocation, 95% protocol adherence, and no loss to follow-up. Randomization led to groups being generally comparable considering the pilot trial design, with exceptions for comorbidities, sex, overweight/obese, poor skin integrity, and inserter, for which at least one group had a more than 10% absolute difference compared with at least one other group. These differences were mostly not statistically significant and would be likely to disappear in a larger trial, but could be considered in future studies as potential stratification factors at randomization.

Despite ubiquitous use and importance to patients, limited research to date has focused on dressing and securement products that prevent CVAD failure, with the only comprehensive work undertaken with chlorhexidine-impregnated dressings [28,29]. Clinicians should be aware that the products they are currently using are unlikely to have been tested for effectiveness in randomized trials. We observed CVAD failure in 5% of CVADs despite their relatively short dwell time of 3 days and 1:1 nursing ratios. Because many CVADs are used for longer, it would be expected that overall failure incidence is actually far higher. Central venous access device failure has important economic and clinical consequences and future studies are urgently needed to provide reliable strategies for improved dressing and securement. Almost half (46%) of our participants had fair or poor skin quality at enrollment, and this characteristic significantly predicted CVAD failure. This suggests that our cohort is a high-risk group to target in future trials. Furthermore, our data identify that postoperative cardiac patients who remain significantly compromised on day 3 with an altered mental state (drowsy, confused, or agitated) are at higher risk for catheter failure, and CVAD maintenance strategies should therefore be of high priority in these patients.

5. Conclusions

Central venous access devices are crucial for critically ill patients, yet failure is common and likely relates to inadequate securement. The ideal CVAD dressing should (1) prevent accidental removal, micromotion, and pistoning; (2) block bacteria entering the wound; (3) have antimicrobial properties; (4) be comfortable for the patient; (5) be easy to use for health staff; and (6) be cost-effective. Care of jugular CVADs is additionally challenging in postcardiac surgical patients who are coagulopathic and mobilized early with multiple infusions. TA + SPU was significantly inferior to suture + BPU and should not be used. Future trials are needed to resolve uncertainty about the comparative effect of suture + TA + SPU, suture + AD, and SSD + SPU compared with suture + BPU for CVAD securement in various insertion sites and patient populations. The innovative approach of suture + TA + SPU was particularly promising, with no CVAD failure occurring in this pilot trial.

Competing interests

C.M.R.'s employer has received on her behalf: unrestricted research, educational grants, and consultancy payments for lectures based on her research from 3M and BBraun. 3M and BBraun manufacture products used in this trial, however, had no involvement in the study design,

execution, analysis, or preparation of this manuscript and provided no funding or products. No competing interests for the other authors.

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Appendix A. Product purchase and labor costs (Queensland Health 2014)

Item	Cost
Histoacryl (TA)	$13.17
Grip-Lok (SSD)	$5.80
IV3000 (required in TA#1, TA#2, and SSD groups)	$0.92
Post-Op Visible (AD)	$3.02
Tegaderm I.V.1650 (BPU)	$2.20
Suture kit (required in AD and TA#2 groups)	$6.13
Dressing pack (required 1× for every dressing application)	$0.43
BD Persist skin preparation (required 1× for every dressing application)	$1.58
Sterile glove (each, required 2× for every dressing application)	$0.24
Plastic gown (required 1× for every dressing application)	$0.07

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