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

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Footnote regarding abbreviations

CVAD – central venous access device

BPU - bordered polyurethane

AD - absorbent dressing

SSD - sutureless securement device

SPU - simple polyurethane dressing

TA- tissue adhesive

BSI – bloodstream infection

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Abstract (200)

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 four-arm, parallel, randomised, controlled, non-blinded, 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). Mid-trial, due to safety, the TA+SPU intervention was replaced with a Suture+TA+SPU group.

Results: 221 patients were randomised with two post-randomisation exclusions. CVAD failure was Suture+BPU controls: 2/55 (4%, 0.52/1000 hours); Suture+AD: 1/56 (2%, 0.26/1000 hours, $p=0.560$); SSD+SPU: 4/55 (7%, 1.04/1000 hours, $p=0.417$); TA+SPU: 4/23 (17%, 2.53/1000 hours, $p=0.049$); and Suture+TA+SPU: 0/30 (0%, $p=0.263$) (intention-to-treat, log-rank tests). CVAD failure was predicted ($p<0.05$) by: baseline poor/fair skin integrity (hazard ratio [HR] 9.8, 95%CI 1.2-79.9), or impaired mental state at CVAD removal (HR 14.2, 95%CI 3.0-68.4).

Conclusions: Jugular CVAD securement is challenging in post-cardiac surgical patients who are coagulopathic and mobilised 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 versus Suture+BPU.

Keywords: Vascular access devices, Occlusive dressings, Randomised controlled trial, Securement device, Tissue adhesives

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. CVADs are commonly used medical devices in hospitals, with three million used in the United States of America (USA), and 250,000 in the UK each year alone [1, 2]. In total, 25-30% 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 (e.g. interruption of vasopressors, or sedatives) and requires additional CVAD insertion with inherent associated risks and procedural pain. Failure may involve localised or catheter-associated bloodstream infections (CABSI) which lengthen stay by ~10 days, increase absolute risk of death by 1% increase, 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 to subclavian vein placement [6]. All forms of CVAD failure significantly increase hospital costs, and workloads.

CVAD securement is key to minimising complications, yet CVAD failure rates suggest current approaches do not adequately prevent dislodgement, nor the catheter micro-motion which precipitates endothelial damage, occlusion, and facilitates the entry of skin microorganisms through the catheter insertion site [7, 8]. Traditionally, sutures with either gauze and tape, or non-bordered, polyurethane dressings have been used for CVAD securement [9]. Clinical practice guidelines now recommend *against* the use of sutures due to needlestick injury risks, and significantly increased CABSI in one randomised controlled trial (RCT) [8, 10]. Instead, sutureless securement devices (SSD) 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. SSDs 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 (AD), some of which retain a degree of visibility of the site [12]. Developed for post-surgical wounds, these dressings may be beneficial - particularly in post-cardiac surgical or other patients whose CVAD sites ooze haemoserous 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) (i.e. 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 to traditional non-bordered polyurethane films [14-16]. We hypothesised 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 multi-site study, we undertook a pilot RCT to consider the feasibility, safety, acceptability of a study protocol [22], and to prioritise products for a planned large-scale RCT.

Materials and Methods

Study design and participants

After hospital and university ethical approval (HREC/11/QRCH/152; NRS/10/14/HREC), this randomised controlled pilot trial was commenced. Written informed consent was obtained prior to

scheduled cardiac surgery. The study design was a four-arm, parallel trial. The single centre setting was in the operating theatres 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 pre-operatively. Only one CVAD per patient was studied. Inclusion criteria were: 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; extreme diaphoresis at enrolment; had existing skin tears or “papery” poor quality skin; or had a known allergy to any study product.

Randomisation and masking

The CRN performed randomisation 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 randomisation 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, since 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 endpoints were blinded through the use of blinded scientists.

Study interventions

CVADs (quadruple lumen 8.5Fr 8 inch/20cm, or triple lumen 7Fr 6 inch/16cm chlorhexidine impregnated ARROWgard Blue Plus® CVC, Teleflex, Research Triangle Park, NC, USA) were inserted into the internal jugular vein using landmark/ultrasound technique by anaesthetic registrars or anaesthetists. Pre-insertion skin preparation was with chlorhexidine 0.5% in 70% alcohol (PharmAust, Welshpool, Western Australia), or Riodine Povidone Iodine 10% (PharmAust, Welshpool, Western Australia), at the inserter's discretion.

See Figure 1 for illustration of dressings.

Group 1. Suture+BPU (controls): CVADs were sutured with an Ethicon™ 3-0 Prolene 30 inch (75cm) SH needle 26mm 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 x 15.5cm, 3M, St Paul, USA). This is a polyurethane adhesive film with a reinforced fabric border. Figure 1a.

Group 2. Suture+AD: CVADs were sutured as for Group 1 and the catheter entry site was secured with an Absorbent Dressing (AD, OpSite™ Post-Op Visible® 10 x 8cm, 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. Figure 1b.

Group 3: SSD+SPU: CVADs were not sutured. Instead, a sutureless securement device (Grip-Lok® CVC 3601 Securement Device, TIDI, Neenah, USA) 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 x 14cm, Smith & Nephew, Hull, United Kingdom) was used to cover the catheter entry site. Figure 1c.

Group 4: TA+SPU: CVADs were not sutured. Instead, Histoacryl™ Blue tissue adhesive (BBraun #1050044, Ann Arbor, USA) was applied at the insertion site, and under each CVAD wing (see Figure 2). Approximately a half to three quarters of a 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 randomisation to this arm mid-trial, and instead created a 5th intervention group for the remaining 30 patients. Figure 1d.

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. Figure 1e.

Study endpoints

The primary endpoint was a composite of complications causing catheter failure (premature CVAD removal prior to 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 (IV) 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 1cm 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 endpoints 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: recognised

pathogen from one or more blood cultures, not related to an infection at another site; or common skin contaminant from two or more blood cultures drawn on separate occasions and patient has fever ($>38^{\circ}\text{C}$), chills, or hypotension, not related to an infection at another site; (iii) CVAD colonisation ($>15\text{cfu}$ 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 out of 10 considered clinically significant pain (dichotomised yes/no); (ix) bedside nurse-reported ease of application, and removal, of the study dressing & 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).

CVAD insertion and care

Extensive pre-study 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 randomised dressing intervention was applied by the CVAD inserter in the operating theatre immediately after insertion. The CRN was in attendance to collect relevant data and maintain protocol adherence. Pre-packs 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. CVADs 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. CVAD tip and blood cultures were not taken routinely, but only if the treating clinician suspected infection.

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 IV fluids and drugs infused through the CVAD. CRNs 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).

Statistical analysis

Data were exported to Stata 13.1 (Stata-Corp, College Station, USA) for cleaning and analysis. Patients were the unit of measurement (only one CVAD per patient studied). The number of catheter failures between intervention and control groups was compared using Fisher's exact test. Failure incidence rates (per 1000 catheter-hours) and incident rate ratios were calculated. Results were further analysed 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 <10%, following the

manual backwards 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 $p < 0.05$. Costs were calculated using Queensland Health purchase prices for dressing/securements in Australian dollars (2014; Appendix As) 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.

Results

Sample

Of 264 potentially eligible patients, 23 declined consent, seven gave consent but were missed due to surgery occurring after hours, and 13 were excluded due to anaesthetist refusal or other reasons (see Figure 2). Of 221 patients randomised, there were two post-randomisation exclusions due to surgery being scheduled after hours ($n=1$, control group) and anaesthetist refusal ($n=1$, TA+SPU group). No further data were collected on these two patients. Of the 219 patients analysed by ITT, 209 (95%) received the allocated intervention at all times and were included in the per protocol analysis. Of the remaining 10 patients, eight received the allocated intervention for some, but not all, of their CVAD dwell time, and two patients received the incorrect intervention for the entire dwell time (see Figure 2). One patient (SSD+SPU group) developed a haematoma requiring CVAD removal within six hours of insertion. This patient was deemed a non-failure, since haematoma was not included in our pre-study 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.

CVAD failure (composite)

Across the study, CVAD failure incidence was 11/219 (5%, or 9/209 [4%] per protocol), with all failure cases involving dislodgement (see Table 2). CVAD failures by group (lowest to highest) were: Suture+TA+SPU 0/30 (0%, incidence rate/1000 CVAD-hours [IR] 0), Suture+AD 1/56 (2%, IR 0.26), Suture+BPU 2/55 (4%, IR 0.52), SSD+SPU 4/55 (7%, IR 1.04), and TA+SPU 4/23 (17%, IR 2.53). These between group differences were significant ($p=0.038$, Fisher's exact test) and confirmed on survival analysis ($p=0.043$, log-rank test). However, all pairwise comparisons for each intervention group compared to control, were not significant ($p>0.05$, Table 2). Per protocol analyses were consistent with the ITT results (Figures 3a and 3b). Multivariable Cox regression found CVAD failure significantly associated with fair/poor skin integrity ($p=0.033$), and altered mental state ($p=0.001$) at the time of CVAD removal (see Table 3).

Secondary Outcomes

There were no local, or CABSIs infections, and no CVAD occlusion or breakage, in any group. One patient had a colonised ($>15\text{cfu}$) CVAD tip (control group). The overall median CVAD dwell time was 69.5 hours, and not significantly different 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, $p<0.05$) resulting in more dressing changes in the TA+SPU group. Median patient satisfaction in the control group was 10 out 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 out of 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 to the control

approach. In contrast, only the two TA groups were reported by nurses as significantly worse for ease of removal, than for controls. Average costs for product use per patient were: Suture+BPU (controls) \$78.15, Suture+AD \$82.80, SSD+SPU \$81.25, TA+SPU \$113.20, and Suture+TA+SPU \$102.60.

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.

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 to controls, TA+SPU saw double the number of product applications required, the lowest patient satisfaction, 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 securement. The TA+SPU combination likely lost adherence since our post-cardiac surgery patients were often coagulopathic and diaphoretic. In addition, the 'drag' of multiple infusion-tubings, particularly during early patient mobilisation, seemed to overcome the adhesive strength of TA+SPU. CVAD failure appeared to be exacerbated by male beard growth, which grew 'against' and 'into' the TA. TA was painful on removal from beard hair for some males, despite the use of adhesive remover

wipes. Due to 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, infection risk and overall cost-effectiveness may negate higher purchase costs.

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

TA use has been favourably 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 it was ineffective with SPU alone, but was effective when combined with suturing and an SPU. SSDs are currently recommended instead of sutures, based on one peripherally inserted central catheter study which 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, $p=0.45$), and most failures in the SSD+SPU group were partial dislodgement, which is concerning since 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 future to trial a different SSD style for this particular patient and CVAD cohort.

The Suture+Absorbent dressing (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, $p=0.62$). Thus, AD appears potentially beneficial for post-cardiac surgical patients, who are typically diaphoretic and/or oozing from the CVAD. ADs limit visualisation 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 to 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]. Further, the study was unable to be blinded since the study products must, for safety reasons, be visible to clinical as well as 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 generalisation to other products and patient groups must be cautious.

Strengths of this study included the concurrent control group, randomisation, concealment until allocation, 95% protocol adherence and no loss to follow up. Randomisation led to groups being generally comparable considering the pilot trial design with exceptions for comorbidities, gender, overweight/obese, poor skin integrity, and inserter, for which at least one group had a >10% absolute difference compared to 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 randomisation.

Despite ubiquitous use, and importance to patients, limited research to date has focussed 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. We observed CVAD failure in 5% of CVADs despite their relatively short dwell time of three days and 1:1 nursing ratios. Since many CVADs are used for longer, it would be expected that overall failure incidence is actually far higher. CVAD 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 enrolment, and this characteristic significantly predicted CVAD failure. This suggests our cohort is a high risk group to target in future trials. Further, our data identify that post-operative cardiac patients who remain significantly compromised on Day 3 with an altered mental state (drowsy, confused or agitated) are at higher risk of catheter failure, and CVAD maintenance strategies should therefore be of high priority in these patients.

Conclusions

CVADs 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, micro-motion 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 post-cardiac surgical patients who are coagulopathic and mobilised 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, SSD+SPU compared to 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.

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Competing interests**Claire M Rickard**

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Figure 1. CVAD securement methods. Fig 2a. Suture+ Bordered Polyurethane (control); Fig 2b. Suture +Absorbent Dressing; Fig 2c Sutureless Securement Device + Simple Polyurethane dressing; Fig 2d. Tissue Adhesive + Simple Polyurethane dressing; Fig 2e. Tissue Adhesive+Suture+Simple Polyurethane dressing.

Figure 2. CONSORT flowchart

Figure 3a and 3b. Kaplan-Meier curves of catheter failure for Intention to Treat (3a) and Per Protocol (3b) analyses. *Fig 3a log rank test $p=0.033$, Fig 3b log rank test $p=0.043$

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

Item	Cost
Histoacryl (TA)	\$ 13.17
StatLock (SSD)	\$ 5.80
IV3000 (required in TA#1, TA#2 and SSD groups)	\$ 0.92
Post-Op Visible (AD)	\$ 3.02
IV1650 (BPU)	\$ 2.20
Suture kit (required in AD and TA#2 groups)	\$ 6.13
Dressing pack (required 1x for every dressing application)	\$ 0.43
BD Persist skin preparation (required 1x for every dressing application)	\$ 1.58
Sterile glove (each, required 2x for every dressing application)	\$ 0.24
Plastic gown (required 1x for every dressing application)	\$ 0.07

Figure 1. CVAD treatment and control group securement methods. Fig 1a. Suture+ Bordered Polyurethane (control); Fig 1b. Suture +Absorbent Dressing; Fig 1c Sutureless Securement Device + Simple Polyurethane dressing; Fig 1d. Tissue Adhesive + Simple Polyurethane dressing; Fig 1e. Tissue Adhesive+Suture+Simple Polyurethane dressing.

Figure 2. CONSORT flowchart

Figure 3a and 3b. Kaplan-Meier curves of catheter failure for Intention to Treat (3a) and Per Protocol (3b) analyses

*Fig 3a log rank test $p=0.033$, Fig 3b log rank test $p=0.043$

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

	Suture+ BPU (ctrl)		Suture+ AD		SSD+S PU		TA+SP U		Suture + TA+SP U		total	
	n	%	n	%	n	%	n	%	n	%	n	%
Group size	56	25%	56	25%	55	25%	24	11%	30	14%	22	100%
Age (median, IQR)	69	17	69	19	68	21	73	14	66	12	69	17
				80		76		63		83	16	75
Gender: male	39	70%	45	%	42	%	15	%	25	%	6	%
	14.		14.		13		15		14		14	
APACHE II (mean, SD)	1	3.6	3	4.5	.0	4.0	.9	4.0	.2	3.1	.1	4.0
				15.		11.		13.				13.
APACHE III (mean, SD)	48	14.1	50	1	47	4	54	2	51	9.8	49	2
	28.		27.		29		29		30		29	
BMI (mean, SD)	6	5.9	6	3.8	.4	6.2	.6	6.0	.8	4.9	.0	5.4
				75		78		82		96	15	79
Overweight or obese	37	73%	36	%	38	%	18	%	27	%	6	%
						2		3				
Leucocytes <1000 / µl absolute	0	0%	0	0%	1	%	0	0%	1	%	2	1%
						2		0				
Any infection at recruitment ^a	1	2%	0	0%	1	%	1	4%	0	%	3	1%
Wound (pre-existing, not cardiac)	3	6%	0	0%	0	%	1	4%	0	%	4	2%
				50		55		75		53	12	57
Co-morbidities: three or more	33	60%	28	%	30	%	18	%	16	%	5	%
				50		53		38		70	11	54
Skin integrity: good	32	58%	28	%	29	%	9	%	21	%	9	%
Skin type/colour: pale/white (Fitzpatrick scale)	35	64%	39	%	34	%	16	%	17	%	1	%
Antibiotic therapy (during study period)	2	4%	0	0%	0	%	1	4%	0	%	3	1%
Regular CVAD flushes (documented)	0	0%	3	5%	4	%	0	0%	0	%	7	3%
				96		93		92		93	20	95
CVAD insertion side: dominant side	53	96%	54	%	51	%	22	%	28	%	8	%
Inserted by: anaesthetist				45		60		79		43	12	57
registrar	35	64%	25	%	33	%	19	%	13	%	5	%
				93		96		92		90	20	93
Number of CVAD lumens: four	49	91%	52	%	53	%	22	%	27	%	3	%
CVAD insertion attempts: single	47	86%	49	%	46	%	24	%	24	%	0	%
Skin prep: chlorhexidine 0.5% in alcohol	41	75%	43	%	42	%	21	%	21	%	8	%
Extension tubing excl. Administration Set	2	4%	1	2%	3	%	1	%	3	%	10	5%
				61		64		54		63	13	62
3 way tap attached	36	66%	34	%	35	%	13	%	19	%	7	%
5 way tap attached	7	13%	8	14	8	15	7	29	0	0	30	14

				%		%		%		%		%
						5				7		
Hair unclipped at CVAD site	1	2%	4	7%	3	%	1	4%	2	%	11	5%
Reduced mobility at CVAD				18		20		29		33		23
removal	13	24%	10	%	11	%	7	%	10	%	51	%
Altered mental state at CVAD						2		17		0		
removal	3	5%	4	7%	1	%	4	%	0	%	12	5%
Tracheal intubation at CVAD						4				0		
removal	1	2%	0	0%	2	%	1	4%	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 = control; GCS = Glasgow Coma

Scale; μ l = microlitre; ^a Includes e.g. wound or respiratory but not bloodstream infections.

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

	Suture+BP U (ctrl)		Suture+A D		SSD+SPU		TA+SPU		Suture+ TA+SP U		P- valu e
	n	%	n	%	n	%	n	%	n	%	
Group size	55	25%	56	26%	55	25%	23	11	30	14	0.03 8
CVAD failure (composite indicator)	2	4%	1	2%	4	7%	4	17	0	0%	
Fisher's exact test (p-value)	referent		0.618		0.679		0.059		0.538		
CVAD dwell time (hours) ^a	69.0	29.4	68.2	28.2	67.8	32.4	69.0	49.3	72.2	7.6	
CVAD-hours (sum)	3,855		3,909		3,858		1,579		2,278		
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 (^)		
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		0.560		0.416		0.049		0.263		
Per protocol analysis (n=209):											
- group size	54	26%	52	25%	52	25%	22	11	29	14	0.02 8
- CVAD failure (composite indicator)	2	4%	0	0%	4	8%	3	14	0	0%	
- Fisher's exact test (p-value)	referent		0.495		0.433		0.142		0.540		
- IR (per 1000 CVAD-hours, 95% CI)	0.52 (0.13-2.10)		0.00 (^)		1.15 (0.43-3.06)		2.00 (0.64-6.16)		0.0 (^)		
- log-rank test (p-value)	referent		0.170		0.369		0.127		0.270		
CVAD dislodgement	2	4%	1	2%	4	7%	4	17	0	0%	
CVAD tip colonisation (CFU>15)	1	2%	0	0%	0	0%	0	0%	0	0%	
Dressing/securement applications ^b	1.0	1.51	1.0	1.73	1.0	1.64	2.0*	2.26	1.0	1.60	
Product duration (hours) ^a	46.2	36.9	46.5	28.5	48.3	42.9	25.1*	25.8	49.4	37.5	
Time for application (sec) ^a	20	17	10	10	60*	45	60*	80	^	^	
Ease of product application ^{a,c}	10.0	1.0	10.0*	0.0 ^c	8.0*	2.0	8.5*	1.0	10.0	1.0	
Ease of product removal ^{a,c}	9.0	1.0	10.0	1.0	9.0	2.0	8.5*	5.0	8.0*	5.0	
Patient satisfaction ^{a,c}	10.0	2.0	10.0	2.0	9.0	2.0	7.5*	5.0	10.0	2.0	
Pain (2 or more out of 10) ^c	6	12%	11	20%	9	18%	9*	40	5	17	
								%		%	

intention to treat analysis unless otherwise stated; n and % presented unless indicated otherwise;

ctrl = control group; IR = incidence rate; IRR = incidence rate ratio; CI = confidence interval;

CFU = colony-forming units; ^ cannot be calculated; # not calculated; ^a median and inter-quartile

*range shown; ^b median and mean shown; ^c 0=min, 10=max; ^d >75% had score of 10; * $p < 0.05$*

compared to SPU using rank-sum or t tests.

Table 3. Cox regression for predictors of CVAD failure (intention to treat 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	^	^
Older age ^a	1.04 (0.97,1.10)	-
Female gender (ref. 'male')	1.65 (0.48,5.66)	-
Obese/overweight BMI (ref. 'other')	1.08 (0.23,5.09)	-
3 or more 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 colour (ref. 'white')	0.44 (0.09,2.03)	-
Insertion on dominant side (ref. 'yes')	^	-
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')	^	-
Hair not clipped/remained (ref. 'no')	2.10 (0.27,16.4)	-
Altered mobility ^b (ref. 'independent')	3.82 (1.16,12.55)**	-
Altered mental state ^b (ref. 'no')	11.13 (3.24,38.22)***	14.22 (2.96-68.37)**
Intubated ^b (ref. 'no')	7.78 (0.99,61.30)*	-

^a centred over the mean, for example HR of 1.04 signifies relative increased risk for each 1yr older

than the mean age; ^b at CVAD removal; ^ unable to be calculated; chlorhex = chlorhexidine; *

$p < 0.1$; ** $p < 0.05$; *** $p < 0.001$; HR = hazard ratio; AD = absorbent dressing; BPU = bordered

polyurethane dressing; SSD = sutureless securement device; SPU = simple polyurethane dressing;

TA = tissue adhesive; BMI = body mass index; APACHE = acute physiology and chronic health

evaluation; ref = referent category; anaesth = anaesthetic.