

Evaluation of Skin Colonisation And Placement of vascular access device Exit sites (ESCAPE Study)

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Abstract

Background: Skin microorganisms may contribute to the development of vascular access device (VAD) infections. Baseline skin microorganism type and quantity vary between body sites, yet there is little evidence to inform choice of VAD site selection.

Objective: To compare microorganisms present at different body sites used for VAD insertions and understand the effect of transparent dressings on skin microflora.

Methods: The ESCAPE observational study consisted of three phases: (1) skin swabs of four sites (mid-neck, base neck, chest, upper arm) from 48 hospital patients; (2) skin swabs of five body sites (mid-neck, base neck, chest, upper arm, lower arm) from 10 healthy volunteers; and (3) paired skin swabs (n = 72) under and outside of transparent dressings from 36 hospital patients (16 mid/base neck, 10 chest, upper arm). Specimens were cultured for 72 h, species identified and colony-forming units (CFU) counted. Ordinal logistic regression compared CFU categories between variables of interest.

Results: The chest and upper arm were significantly associated with fewer microorganisms compared to neck or forearm (odds ratio [OR] = 0.40, 95% confidence interval [CI] = 0.25-0.65, P < 0.05). CFU levels under transparent dressings were not significantly different from outside (OR = 0.57, 95% CI = 0.22-1.45). *Staphylococci* were predominant at all sites. Other significant (P < 0.05) predictors of higher CFU count included prolonged hospitalisation and medical/surgical patient status.

Discussion: Skin microorganism load was significantly lower at the upper arm or chest, compared to the mid- or base neck. This may impact VAD site selection and subsequent infection risk.

Keywords

Infection, vascular access device, central venous, intravenous catheter, skin microorganisms, colonisation, site selection, risk

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Introduction

More than seven million central venous vascular access devices (VADs) and 330 million peripheral intravenous VADs are purchased each year in the USA alone (iData Research, 2014). These intravenous devices allow access to the bloodstream to deliver important treatments associated with the majority of illnesses managed in acute care medicine. Bloodstream infections are the most serious complication associated with the use of peripheral and central VADs.

The Centers for Disease Control (CDC) guidelines for the prevention of VAD-related infection indicate, in addition to other factors, that insertion site and quantity of skin microorganisms play a significant role in both infection and IPICC Excellence, Inc., Alliance for Vascular Access Teaching and Research (AVATAR) Group, Menzies Health Institute Queensland (MHIQ), Griffith University, Brisbane, Australia
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thrombophlebitis risk (O'Grady et al., 2011). Although skin is cleansed with antiseptic before VAD insertion, the skin is never sterile; some microorganisms remain on the skin and in the subdermal layers and immediately begin to regrow to baseline levels. Without adequate knowledge of skin flora or microorganisms at common VAD insertion sites, clinicians cannot make informed decisions for selection of devices and in evaluation of patient risk. Clinicians appraise criteria to determine the best insertion location and preferred exit site, which should include knowledge of the quantity and type of microorganisms present in a given insertion location. VAD insertion procedures require consideration of the risk/benefit ratio associated with the insertion location, and choice of a device with the lowest risk of infection and other potential complications, that will meet the patient's vascular access needs (Moureau et al., 2012).

VAD-related bloodstream infections account for approximately 11% of all healthcare-acquired infections in the USA, with cost estimates at \$4000–56,000 per episode (Abad and Safdar, 2011). A recent meta-analysis of ten prospective studies from acute care patients found chest placement to be associated with fewer VAD-associated infections than either the neck (incidence density ratio [IDR] = 0.46, 95% confidence interval [CI] = 0.30–0.70) or groin site (IDR = 0.27, 95% CI = 0.15–0.48); the authors noted that skin microbial load may have been a contributing factor, although this was not measured (Parienti et al., 2012).

The association between skin microbiome, infection and disease has been studied in the literature without specific attention to VAD infections. Studies have characterised the human microbiome in healthy individuals (Costello et al., 2009; Rosenthal et al., 2011). The skin of hospitalised patients is exposed to environmental microorganisms that affect the type and load distribution, and the longer the period of hospitalisation the more skin microorganism make-up may change. Variation in the microbiome for certain diseases such as 'Crohn's and ulcerative colitis' (Rehman et al., 2010) and 'Clostridium difficile colitis' (Chang et al., 2008) has been established compared to healthy individuals. Investigation into the skin microbiome to date has not clearly demonstrated the connection between microbial communities and disease (Rosenthal et al., 2011). Little exploration has been undertaken on the study of risk of VAD-related infection in relation to skin microbial load.

Transmission of microorganisms, including multi-drug resistant organisms, occurs through direct skin contact (Rosenthal et al., 2011). In one study, microorganism colonisation was heaviest in the proximal section of the VAD, the portion closest to the skin of the insertion site (Koh, 2011; Koh et al., 2012). Early VAD colonisation and infection suggests that the majority of VADs developing infections within the first two weeks after insertion are due to skin organisms and extraluminal sources; however, when VAD use exceeds 64 days the source of infection is intraluminal (Mermel, 2011; Prielipp and Sherertz, 2003). Environmental factors in hospitals include inconsistent hand washing, glove use, cleaning of surfaces, patient bathing practices and application of lotions, all of which impact the transmission and microbial load on the skin (Kaplowitz et al., 1988; Larson, 1985, 1999; Veien, 1998). Patient characteristics of chronic illness, acute disease or trauma, genetics and even gender play a part in concentration of microorganisms on the skin. Microorganisms are both beneficial and pathogenic, with a careful balance maintained in healthy individuals (Chiller et al., 2001). Medication administered to patients, including antibiotics, steroids and other treatments, disrupt the careful balance of skin organisms thereby increasing risk for infection with VADs (Schein et al., 1996).

VADs are inserted through the skin at different body sites which likely present with different baseline bacterial quantity. The limitation of current evidence is that no studies thus far have specifically studied VAD insertion sites. Microbial load on skin at the insertion site of a central venous VAD promotes intralumenal contamination of the VAD and entrance of bacteria into the bloodstream. The density of skin flora at the VAD insertion site is a significant risk factor for VAD-related bloodstream infections, and yet data are limited (Garland et al., 2008; Lorente et al., 2005, 2007; Moro et al., 1994; O'Grady et al., 2011; Ponnusamy et al., 2014; Safdar and Maki, 2004).

While Grice and others have performed topography of the skin biome and microbial distributions, few have quantitatively measured microorganisms in patients at the specific sites of both peripheral and central VAD locations (Findley and Grice, 2014; Grice and Segre, 2011; Grice and Segre, 2012; Li, 2011; Ruocco et al., 2007). Comparative data on quantity and microorganism type at VAD insertion sites of acute care patients provides information to guide VAD selection based on level of risk from the microbial load. Baseline information on skin microorganisms of hospitalised patients also aids in VAD site and VAD dressing selection that may also reduce infection risk. Concentration of microorganisms on the skin at VAD insertion sites may contribute to patient morbidity and mortality (Garland et al., 2008). More research is needed for healthy people versus acute care patients with manifested illness so as to establish skin microorganism counts typical at specific sites commonly used for peripheral and central VAD insertion.

Methods

The study aim was to measure baseline microorganisms on the skin at various body sites, in order to inform VAD site selection with the least risk of infection. A secondary aim was to understand the effect of transparent dressings, commonly used for VADs, on skin microorganisms. The study questions were:

- 1. What skin microorganisms are present on intact skin, at sites commonly used for VADs?
- 2. Does skin microbial load differ significantly at body sites commonly used for VADs?
- 3. Is skin microbial load significantly different for intensive care patients, medical/surgical patients and healthy volunteers, at body sites commonly used for VADs?
- 4. Does skin microbial load differ significantly under standard transparent VAD dressings versus intact skin?

Study design and participants

This was an observational study in Australia with three phases: (1) skin swabs of four sites (mid-neck, base neck, chest, upper arm) from 48 hospital patients (24 medical/ surgical, 24 intensive care unit [ICU]); (2) skin swabs of five body sites (four sites and lower arm) from 10 healthy volunteers; and (3) paired skin swabs (n = 72) under and outside dressings (26 ICU, 16 internal jugular mid-/base neck, 10 subclavian chest, 10 medical/surgical upper arm) from 36 hospital patients. Specimens were cultured for 72 h, species identified and colony-forming units (CFU) counted. Ordinal logistic regression compared CFU categories between variables of interest.

Phase 1. This phase studied 48 hospitalised patients. Patients aged > 18 years and able to provide written informed consent were conveniently sampled from the medical and surgical wards (n = 24) of the Royal Brisbane and Women's Hospital (RBWH) in December 2015, and the intensive care unit (ICU) (n = 24) of The Prince Charles Hospital (TPCH) between May 2016 and June 2016. Skin swabs were collected at one time point from each patient at four body sites that are commonly used for VADs: (1) mid-neck; (2) base of neck; (3) chest; and (4) upper arm. Samples were taken from intact skin (no VAD present), without use of antiseptic decontamination.

Phase 2. Ten healthy volunteers (academic staff) aged > 18 years and able to provide written informed consent (including consent provided by proxy) were invited to participate. Skin swabs were collected from five body sites (the same sites as for Phase 1, with the addition of swabs from the mid-forearm). No skin disinfection was performed before sampling. This phase was performed at Griffith University.

Phase 3. Paired skin swabs were taken from 36 hospital patients (26 intensive care at the TPCH site and 10 medical/surgical patients at the RBWH site). Skin disinfection with alcoholic chlorhexidine was standard for insertion and dressing changes; however, no skin disinfection was performed before sampling. Each patient had one swab taken from underneath a transparent dressing at a central venous catheter insertion site (immediately after dressing removal), as well as a paired skin swab immediately outside the site where there had been no dressing (total 72 samples). We initially planned to also study swabs taken from under antimicrobial sponges at VAD sites, but insufficient patients had these in place to make analysis meaningful.

Ethics and approvals

Ethics committee approval for Phase 1 and Phase 3 was obtained from the Royal Brisbane and Women's Hospital (HREC/15/QRBW/237) and Griffith University (NRS/26/15/HREC) and Phase 2 from Griffith University (NRS/23/15/HREC). Participants or representatives provided written informed consent. This study incorporated substitute decision-maker consent for those patients who were unable to consent for themselves. This minimised the risk of researchers being restricted to a specific cohort of patients who could provide consent for themselves and resulted in a more representative sample of the ICU patient cohort.

Sample collection

All skin swab samples were collected using a DrySwabTM (Medical Wire & Equipment, Wiltshire, UK), moistened with 0.9% Saline from a 10-mL ampoule (Pfizer Ltd.), by the research nurse (ReN) who had received specific training regarding collection technique. Samples were taken from the skin without use of antiseptic decontamination. Each site was swabbed using a brisk back/forth and rotating motion for 10 s. This swab was then placed into a sterile container containing glycerol medium labelled with study number and swab site. All samples were transferred (within 1 h) to a 4 °C fridge and subsequently (within 24 h) transferred and stored in a -20 °C freezer until processing.

Microbiology testing

The swabs were then streaked onto blood agar plates and incubated at 37 °C. After 24 h of incubation, all plates were examined for colony counts and organism identification. The plates were then re-incubated for 48 h to enable growth of slow-growing species. Identification of species was determined morphologically, and biochemically for representative colonies.

Data analysis

Microbial species were identified morphologically and biochemically, and predominant species described per participant group, per body site and under/outside of transparent dressings. Microbial load was measured as CFUs. CFUs were categorised as nil/any and as 0, 1–29, 30–299

	Phases I and 2 (body site)	Phase 3 (dressing)
Participants by recruitment sites		
Medical/surgical ward patient	24 (41)	10 (28)
Intensive care patient	24 (41)	26 (72)
Healthy volunteer	10 (17)	-
Total	58 (100)	36 (100)
Samples by body parts		
Base of neck	58 (24)	-
Chest	58 (24)	-
Mid-neck	58 (24)	-
Upper arm	58 (24)	-
Lower arm	9 (4)	-
Around dressing	-	36 (50)
Under dressing	-	36 (50)
Total	241 (100)	72 (100)
CFU count	5 (0–93)*	0 (0–12)*
0	61 (25)	37 (51)
I–29	98 (41)	25 (35)
30–299	39 (16)	4 (6)
≥ 300	43 (18)	6 (8)
Total	241 (100)	72 (100)
Length of hospital stay (days) ^{†‡}	10 (7–17)*	9.5 (7.5–16.5)
Length of device dwell (days) [‡]	-	6 (5–7.5)

Table 1. Participant and sample characteristics for all study phases.

Values are presented as n (%) unless otherwise noted. *Median (25th and 75th percentiles). †Intensive care and hospital ward participants only.

CFU, colony-forming unit.

and \geq 300 (includes growth too numerous to count). These categories were selected since < 30 CFUs are considered clinically unreliable to consider 'colonised', and \geq 300 colonies impacts the formation of individual colonies due to overcrowding, leading to inaccurate counts (Engelkirk et al., 2011). Odds ratio (ORs) with 95% CIs were calculated, and univariable ordinal logistic regression was used to compare CFUs between body locations, participant groups, under/outside of transparent dressings and lengths of hospital stay or device dwell. Presence of *S. aureus* (yes/no) was compared between mid-neck and other body sites using chi-square test. *P* values < 0.05 were considered significant. Stata 15 was used. Missing values were not imputed.

Results

Participant characteristics, sample location and colony counts are presented in Table 1. Results are based on CFU

analysis as a categorical variable with distribution of results in Tables 1–4.

Organism type

Staphylococci were the dominant organisms isolated from all body sites in hospital patients and healthy volunteers, with *S. epidermidis* being the most abundant species (Table 2). Table 2 indicates body site locations within each specific group with designation of predominant organisms. *S. aureus* was present in 21% medical/surgical, 18% intensive care and 16% of volunteer specimens. Organisms from the *Escherichia* and *Streptococcal* families were also identified in volunteers. CFU distribution was not significantly different (P > 0.05) for medical/surgical patients (OR = 0.92, 95% CI = 0.50– 1.68) or ICU (OR = 0.66, 95% CI = 0.41–1.06) compared to healthy volunteers; however, higher counts were present in medical/surgical compared to ICU patients (OR = 4.80, 95% CI = 1.51–15.3, P < 0.05, Table 4).

[‡]Per participant analysis.

Body site and participants		Predominant microorganisms
Base neck (n = 58)	Intensive care Medical/surgical Healthy volunteers	S. epidermidis* S. epidermidis and S. haemolyticus S. epidermidis
Mid-neck (n = 58)	Intensive care Medical/surgical Healthy volunteers	S. haemolyticus S. epidermidis S. epidermidis and S. aureus
Chest (n = 58)	Intensive care Medical/surgical Healthy volunteers	S. epidermidis, S. haemolyticus and S. aureus S. epidermidis, S. haemolyticus and S. aureus S. epidermidis and S. aureus
Upper arm (n = 58)	Intensive care Medical/surgical Healthy volunteers	S. haemolyticus S. aureus S. epidermidis and S. haemolyticus
Mid-forearm (n = 9)	Intensive care Medical/surgical Healthy volunteers	n.a. n.a. S. epidermidis
Dressing and participants		Predominant microorganisms
Transparent dressing	Intensive care Medical/surgical	S. haemolyticus S spp., S. haemolyticus, Escherichia coli
Intact skin	Intensive care Medical/surgical	S. haemolyticus S. epidermidis. Enterobacteriaceae (NLF)

Table 2. Culture results from body site locations by participant group.

*Staphylococcus has been abbreviated as S. NLF, non-lactose fermenting.

Organisms by site

Patient specimens most commonly returned \geq 30 CFUs from the mid-neck (22/48, 45.8%), base of neck (21/48, 43.8%) and chest (15/48, 31.3%) compared to the upper arm (7/48, 14.6%) (Table 3). Similar distribution between these sites was seen for the volunteer specimens (Table 3). In addition, volunteers' lower forearms rarely colonised \geq 30 CFUs (Table 3). Table 3 denotes all CFU load within each hospital and volunteer group including location, sample size and results in frequencies and row percentages. The regression model (Table 4) confirmed that the chest or upper arm sites were significantly (P < 0.05) associated with lower CFU levels (OR = 0.40, 95% CI = 0.25-0.64) compared to the neck (either mid or base) or lower arm. In addition, higher CFU was predicted by greater hospital length of stay (OR = 1.02, 95% CI = 1.00-1.03, P < 0.05,Table 4). There was one isolation from the Enterobacteriaceae family, taken from the upper arm of a medical/surgical patient.

Effect of dressing

There was some difference in CFU counts in relation to the dressing, with 1/36 (2.8%) outside-dressing specimens returning \geq 300 CFUs compared to 5/36 (13.9%) underdressing samples (Tables 3 and 4). However, if specimens returning \geq 30 CFUs were considered, the two locations were identical with 5/36 (13.9%) effected (Table 2). CFU count differences were not significant in the regression model (dressing OR = 0.57, 95% CI = 0.22–1.45, P > 0.05) (Table 4).

Discussion

Our normal skin flora is our primary defence from infection; however, in patients with VADs, 60% of bloodstream infections are caused by microorganisms originating from normal skin flora (Gahlot et al., 2014). In the ESCAPE study we observed microbial flora on skin to be dominated by *S. aureus* and coagulase-negative

	Medical/surgical			Intensive care			Healthy volunteers					
	0	l- 29	30– 299	≥ 300	0	l- 29	30– 299	≫ 300	0	l- 29	30– 299	≥ 300
Base neck	6 (25)	9 (38)	2 (8)	7 (29)	3 (12)	9 (38)	5 (21)	7 (29)	0 (0)	6 (60)	3 (30)	l (10)
Chest	8 (33)	6 (25)	4 (17)	6 (25)	 (46)	8 (33)	4 (17)	l (4)	0 (0)	8 (80)	l (10)	l (10)
Mid-neck	6 (25)	7 (29)	4 (17)	7 (29)	7 (29)	6 (25)	5 (21)	6 (25)	0 (0)	2 (20)	5 (50)	3 (30)
Upper arm	5 (21)	15 (62)	l (4)	3 (12)	 (46)	10 (42)	3 (12)	0 (0)	3 (30)	5 (50)	l (10)	l (10)
Lower arm	-	-	-	-	-	-	-	-	 (11)	7 (78)	 (11)	0 (0)
Around dressing	0 (0)	8 (80)	2 (20)	0 (0)	l 6 (62)	7 (27)	2 (8)	l (4)	-	-	-	-
Under dressing	5 (50)	4 (40)	0 (0)	l (10)	16 (62)	6 (23)	0 (0)	4 (15)	-	-	-	-

Table 3. Microorganism load (CFU) by participant group and sampling site.

Values are presented as n (%).

Table 4. Logistic regression of CFU category.*

	Location Crude OR (95% CI)	Dressing Crude OR (95% CI)
Recruitment site	n = 241	n = 72
Healthy volunteer	Referent	-
Intensive care	0.66 (0.41–1.06)	Referent
Medical/surgical	0.92 (0.50–1.68)	4.80 (I.5I–I5.3) [†]
Sample location [‡]	n = 241	n = 72
Neck or lower arm	Referent	-
Chest or upper arm	0.40 (0.25-0.64)†	-
Around dressing	-	Referent
Under dressing	-	0.57 (0.22–1.45)
Length of stay§	1.02 (1.00–1.03)†	1.03 (0.99–1.08)
Length of device dwell [§]	-	1.13 (0.98–1.29)

*Dependent variable (CFU count) set up as ordinal (0/1–29/30–299/ \geq 300) variable for 'Location', and dichotomous (nil/any) for 'Dressing' analysis. †Statistically significant at P < 0.05.

[‡]Categories with similar effect sizes and directions were combined.

[§]One-day increment.

OR, odds ratio; CI, confidence interval.

Staphylococci (CoNS), namely *S. epidermidis* and *S. haemolyticus*, the two most isolated CoNS microorganisms. The results are consistent with existing literature that colonisation occurs predominantly by Staphylococcus, in particular the *epidermidis* species, and *S. aureus* around the neck and chest region (Gahlot et al., 2014). *S. aureus* colonises approximately 20% of the population, and 30% transiently. *S. aureus* predominately colonises

the nose but is also isolated from the pharynx, perineum, axillae and on the skin (predominantly on the hands, chest and abdomen) (Otto, 2010). Of the CoNS group, *S. epidermidis* colonises all the body whereas *S. haemolyticus* colonises more around the glands, legs and arms (Becker et al., 2014). Microorganisms from the Enterobacteriaceae family were also isolated, including an organism associated with the normal gut flora (Murray et al., 2005); however, it is known to be an indwelling device pathogen in 8% of cases (Gahlot et al., 2014).

Site selection appears to have an important role in preventing VAD microbial colonisation and potential harmful infections. While site and device selection include other factors contributing to the role of both infection and thrombosis, microbial load on the skin impacts risk during insertion of VADs and during long-term dwell of the device. Certain microflora colonise various locations due to differences in local skin temperature, moistness and exposure to the environment (Grice et al., 2009). Our results were not consistent with the assumption that warmer temperatures of the chest were associated with higher quantity of microorganisms (Grice and Segre, 2011). We found microbial load to be significantly higher at the base of the neck, mid-neck and lower arm than the chest and upper arm. These results suggest the chest and upper arm are preferential central VAD sites, compared to the neck. The lower arm contributed little to this analysis due to the smaller sample size (n = 10) but may provide a point of comparison for future research.

Our findings appear to explain the results of studies where chest-placed VADs were observed to have lower bloodstream infection outcomes (Parienti et al., 2012). Recent suggestions to use the base of the neck rather than the mid-neck to reduce infection risk were not supported by our results, which found little difference in microbial load at these two sites, but both higher than the chest. This higher bacterial load may be related to increased humidity from the nose and mouth in this region. Post insertional positioning of internal jugular catheters, inserted at the base of the neck, can allow the dressing and external catheter position to reside on the chest instead of the neck taking greater advantage of lower bacterial load on the skin of the chest. When access to the internal jugular is needed, consideration may also be given to tunnelling to position the exit site in an optimal region with lower bacterial counts.

We observed non-significant differences in microbial loads of hospital patients compared to healthy volunteers. This failure to achieve significance between groups may have been due to the sample size, and future larger studies may confirm the trends we saw in the reduced CFU counts in hospitalised patients, particularly ICU patients, compared to healthy volunteers. However, to our knowledge, no studies have been performed on ICU, medical/surgical and volunteers. In a study of ICU patients that compared outpatients to those in the medical ICU, a twofold increase in high skin colony counts (> 600CFUs) were represented in the medical ICU versus the outpatients (Larson et al., 2000). Literature of skin colonisation in association with chlorhexidine bathing have examined differences of skin micro-organisms specific to the presence of drug-resistant organisms in hospitalised patients in ICU versus medical/surgical units, but none on normal skin flora in these patient populations (Kaiser et al., 1988; Vernon et al., 2006). Our dressing analysis observed medical/surgical patients to have significantly higher CFU counts than ICU patients. Such

differences could be potentially explained by air-conditioned temperatures, more frequent or thorough bathing of patients in ICU, or different length of stay (Kaplowitz et al., 1988; Larson, 1985, 1999; Veien, 1998).

Bacterial counts under transparent dressings were (lower but) not statistically different to skin outside of the dressing. It may be assumed that skin antiseptic decontamination performed with dressing changes is applied to an entire skin area where swab samples were affected by both under dressing and outside transparent dressings. Alcoholic chlorhexidine was used as the standard disinfecting agent on skin performed with CVAD insertion and dressing changes for the skin samples where a catheter was present. Chlorhexidine could remain on skin for 5-7 days (Macias et al., 2013). However, research by Macias and associates with 2% chlorhexidine in 70% isopropyl alcohol on skin proved an added substantive effect for up to 24 h, with regrowth of bacteria after that time period (Macias et al., 2013). Therefore, significant bacterial regrowth, if not all, should be observed from the skin swabs taken from three or more day-dressings. Our results are suggestive that the regrowth approached baseline levels after 24 h compared to the skin outside the dressing. Ideally, skin disinfection before catheter placement should substantially reduce the numbers of skin bacteria and inhibit their regrowth for the first few days. While the substantive effect of chlorhexidine skin disinfection has limits, the current use of antimicrobial sponges/dressings on central catheter insertion sites, supported in the literature, inhibits bacterial regrowth up to seven days and prevents catheter-related infection (Timsit et al., 2009, 2012).

Since no statistical significance was found between under dressing and skin samples outside dressing, the evidence is not consistent with our original expectations of higher levels under polyurethane dressings. Prior Cochrane research has reported wide confidence intervals and a fourfold increased risk of catheter-related bloodstream infections when polyurethane dressings were used versus gauze dressings (Webster et al., 2011). Later research with chlorhexidine dressings indicated reduction of infection in comparison with standard polyurethane dressings (Ullman et al., 2015). The results of this study suggest skin treated with antiseptic and then protected from environmental contamination by the sterile polyurethane dressing may have less bacteria than noted in previous studies. While not statistically significant, skin antiseptics could have affected the quantity of bacteria on the samples; a larger sample size may have detected a significant difference. Currently, the results suggest that the clinical significance of using such dressings is that they may reduce, but certainly do not increase, the number of bacteria present and thus the risk of infection to the patient. The strength of this study is that it provides quantitative data for the normal microflora of patients and healthy volunteers at specific sites commonly used for vascular device insertion (Findley and Grice, 2014; Grice and Segre, 2011, 2012; Li, 2011; Ruocco et al., 2007).

Limitations

The study was limited by the sample size, which may have contributed to the non-significant findings for some analyses. In particular, the healthy volunteer cohort was small, but we felt this was important to include to have some understanding of baseline risk in patients who have not already spent time in the hospital environment. Not all sites were sampled in both healthy volunteers and hospital patients due to funding limitations. In addition, as we took specimens at one time point only, without follow-up swabbing, we cannot extrapolate changes in skin colonisation over time. Skin disinfection, performed before insertion or dressing change with ICU patient CVADs, could have affected the quantity of bacteria in the samples collected from the insertion site of these patients. And while the substantive effect of chlorhexidine on the skin is limited there could be an impact on the samples. The use of just four numerical categories (0, 1–29, 30–299 and \geq 300) for enumeration was a limiting factor.

Conclusion

Potential VAD insertion sites at the chest and upper arm were associated with lower microbial loads than the neck or forearm and this finding establishes foundational evidence for designing interventions to reduce risk of skin colonisation and VAD infection. All patients are at risk of infection from skin microorganisms, via VAD insertion; however, choice of the chest or upper arm site, where possible, would appear to reduce infection risk for central VADs. Future studies should include skin colonisation outcomes when testing the relative effectiveness and cost-effectiveness of skin antiseptics, antimicrobial dressings and antimicrobial devices for infection prevention.

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References

- Abad CL and Safdar N. (2011) Catheter-related bloodstream infections. Infectious Disease Special Edition 14: 84–98.
- Becker K, Heilmann C and Peters G. (2014) Coagulase-negative Staphylococci. *Clinical Microbiology Reviews* 27: 870–926.
- Chang JY, Antonopoulos DA, Kalra A, Tonelli A, Khalife WT, Schmidt TM and Young VB. (2008) Decreased diversity of the fecal microbiome in recurrent clostridium difficile—associated diarrhea. *Journal* of Infectious Diseases 197: 435–438.
- Chiller K, Selkin BA and Murakawa GJ. (2001) Skin microflora and bacterial infections of the skin. *Journal of Investigative Dermatology*. *Symposium Proceedings* 6: 170–174.
- Costello EK, Lauber CL, Hamady M, Fierer N, Gordon JI and Knight R. (2009) Bacterial community variation in human body habitats across space and time. *Science* 326: 1694–1697.
- Engelkirk PG, Duben-Engelkirk JL and Wilson Burton GR. (2011) Burton's Microbiology for the Health Sciences. Philadelphia, USA: Lippincott Williams & Wilkins.
- Findley K and Grice EA. (2014) The skin microbiome: a focus on pathogens and their association with skin disease. *PLoS Pathogens* 10: e1004436.
- Gahlot R, Nigam C, Kumar V, Yadav G and Anupurba S. (2014) Catheterrelated bloodstream infections. *International Journal Critical Illness* and Injury Science 4: 162–167.

- Garland JS, Alex CP, Sevallius JM, Murphy DM, Good MJ, Volberding AM, Hofer LL, Gordon BJ and Maki DG. (2008) Cohort study of the pathogenesis and molecular epidemiology of catheter-related bloodstream infection in neonates with peripherally inserted central venous catheters. *Infection Control* 29: 243–249.
- Grice EA, Kong HH, Conlan S, Deming CB, Davis J, Young AC, NISC Comparative Sequencing Program, Bouffard GG, Blakesley RW, Murray PR, Green ED, Turner ML and Segre JA. (2009) Topographical and temporal diversity of the human skin microbiome. *Science* 324: 1190–1192.
- Grice EA and Segre JA. (2011) The skin microbiome. Nature Reviews Microbiology 9: 244–253.
- Grice EA and Segre JA. (2012) The human microbiome: our second genome. Annual Review of Genomics and Human Genetics 13: 151.
- iData Research I. (2014) iData Research Inc (2014) Report: US Market on Vascular Access Devices and Accessories, Vancouver BC Canada. Burnaby, BC: iData Research.
- Kaiser AB, Kemodle DS, Barg NL and Petracek MR. (1988) Influence of preoperative showers on staphylococcal skin colonization: a comparative trial of antiseptic skin cleansers. *Annals of Thoracic Surgery* 45: 35–38.
- Kaplowitz L, Comstock J, Landwehr D, Dalton HP and Mayhall CG. (1988) Prospective study of microbial colonization of the nose and skin and infection of the vascular access site in hemodialysis patients. *Journal of Clinical Microbiology* 26: 1257–1262.
- Koh D. (2011) Exploration of the patterns of microbial colonization of intravascular devices in severely ill patients. University of Tasmania. Available at: https://eprints.utas.edu.au/12482/2/Whole_excluding_ Chs._3-5-FINALTHESIS-David_Koh%5B271708%5D_290811.pdf (accessed 1 October 2018).
- Koh DBC, Robertson IK, Watts M and Davies AN. (2012) Density of microbial colonization on external and internal surfaces of concurrently placed intravascular devices. *American Journal of Critical Care* 21: 162–171.
- Larson E. (1985) Handwashing and skin physiologic and bacteriologic aspects. *Infection Control* 6: 14–23.
- Larson E. (1999) Skin hygiene and infection prevention: more of the same or different approaches? *Clinical Infectious Diseases* 29: 1287–1294.
- Larson EL, Cronquist AB, Whittier S, Lai L, Lyle CT and Della Latta P. (2000) Differences in skin flora between inpatients and chronically ill outpatients. *Heart & Lung: The Journal of Acute and Critical Care* 29: 298–305.
- Li H. (2011) The Human Skin Microbiome in Health and Skin Diseases. In: Metagenomics of the Human Body. New York: Springer, pp. 145–163.
- Lorente L, Henry C, Martín MM, Jimenez A and Mora ML. (2005) Central venous catheter-related infection in a prospective and observational study of 2,595 catheters. *Critical Care* 9: R631.
- Lorente L, Jiménez A, Santana M, Iribarren JL, Jimenez JJ, Martin MM and Mora ML. (2007) Microorganisms responsible for intravascular catheter-related bloodstream infection according to the catheter site*. *Critical Care Medicine* 35: 2424–2427.
- Macias JH, Arreguin V, Munoz JM, Alvarez JA, Mosqueda, JL and Macias AE. (2013) Chlorhexidine is a better antiseptic than povidone iodine and sodium hypochlorite because of its substantive effect. *American Journal of Infection Control* 41: 634–637.
- Mermel LA. (2011) What is the predominant source of intravascular catheter infections? *Clinical Infectious Diseases* 52: 211–212.
- Moro ML, Vigano EF and Cozzi Lepri A. (1994) Risk factors for central venous catheter-related infections in surgical and intensive care units. The Central Venous Catheter-Related Infections Study Group. *Infection Control and Hospital Epidemiology* 15: 253–264.
- Moureau N, Trick N, Nifong T, Perry C, Kelley C, Carrico R, Leavitt M, Gordon SM, Wallace J, Harvill M, Biggar C, Doll M, Papke L, Benton L and Phelan DA. (2012) Vessel health and preservation (Part 1): a new evidence-based approach to vascular access selection and management. *Journal of Vascular Access* 13: 351–356.
- Murray PR, Rosenthal KS and Pfaller MA. (2005) *Medical Microbiology*. Maryland Heights, USA: Elsevier Health Sciences.

- O'Grady N, Alexander M, Burns L, Dellinger EP, Garland J, Heard SO, Lipsett PA, Masur H, Mermel LA, Pearson ML, Raad II, Randolph AG, Rupp ME, Saint S and Healthcare Infection Control Practices Advisory Committee (HICPAC). (2011) *Guidelines for the Prevention* of Intravascular Catheter-Related Infections, 2011. Atlanta, GA: Centers for Disease Control.
- Otto M. (2010) Staphylococcus colonization of the skin and antimicrobial peptides. *Expert Review of Dermatology* 5: 183–195.
- Parienti JJ, du Cheyron D, Timsit JF, Traore O, Kalfon P, Mimoz O and Mermel LA. (2012) Meta-analysis of subclavian insertion and nontunneled CVC-associated infection risk reduction in critically ill patients. *Critical Care Medicine* 40: 1627–1634.
- Ponnusamy V, Perperoglou A, Venkatesh V, Curley A, Brown N, Tremlett C and Clarke P. (2014) Skin colonisation at the catheter exit site is strongly associated with catheter colonisation and catheter-related sepsis. *Acta Paediatrica* 103: 1233–1238.
- Prielipp RC and Sherertz RJ. (2003) Skin: the first battlefield. Anesthesia & Analgesia 97: 933–935.
- Rehman A, Lepage P, Nolte A, Hellmig S, Schreiber S and Ott SJ. (2010) Transcriptional activity of the dominant gut mucosal microbiota in chronic inflammatory bowel disease patients. *Journal of medical microbiology* 59: 1114–1122.
- Rosenthal M, Goldberg D, Aiello A, Larson E and Foxman B. (2011) Skin microbiota: microbial community structure and its potential association with health and disease. *Infection, Genetics and Evolution* 11: 839–848.
- Ruocco E, Cuomo A, Salerno R, Ruocco V, Romano M and Baroni A. (2007) Crohn's disease and its mucocutaneous involvement. *SKINmed: Dermatology for the Clinician* 6: 179–185.
- Safdar N and Maki D. (2004) The pathogenesis of catheter-related bloodstream infection with noncuffed short-term central venous catheters. *Intensive Care Med* 30: 62–67.
- Schein M, Wittmann DH and Lorenz W. (1996) Duration of antibiotic treatment in surgical infections of the abdomen. *European Journal of Surgery* 576: 1–70.
- Timsit J, Mimoz O, Mourvillier B, Souweine B, Garrouste-Orgeas M, Alfandari S, Plantefeve G, Bronchard R, Troche G, Gauzit R, Antona M, Canet E, Bohe J, Lepape A, Vesin A, Arrault X, Schwebel C, Adrie C, Zahar JR, Ruckly S, Tournegros C and Lucet JC. (2012) Randomized controlled trial of chlorhexidine dressing and highly adhesive dressing for preventing catheter-related infections in critically ill adults. *American Journal of Respiratory Critical Care Medicine* 186: 1272–1278.
- Timsit J, Schwebel C, Bouadma L, Geffroy A, Garrouste-Orgeas M, Pease S, Herault MC, Haouache H, Calvino-Gunther S, Gestin B, Armand-Lefevre L, Leflon V, Chaplain C, Benali A, Francais A, Adrie C, Zahar JR, Thuong M, Arrault X, Croize J, Lucet JC and Dressing Study Group. (2009) Chlorhexidine-impregnated sponges and less frequent dressing changes for prevention of catheter-related infections in critically ill adults: a randomized controlled trial. *Journal of the American Medical Association* 301: 1231–1241.
- Ullman A, Cooke M, Mitchell M, Lin F, New K, Long DA, Mihala G and Rickard CM. (2015) Dressings and securement devices for central venous catheters (CVC). *Cochrane Database of Systematic Reviews* 9: CD10367.
- Veien N. (1998) The clinician's choice of antibiotics in the treatment of bacterial skin infection. *British Journal of Dermatology* 139 (Suppl. 5): 30–36.
- Vernon MO, Hayden MK, Trick WE, Hayes RA, Blom DW, Weinstein RA and Chicago Antimicrobial Resistance Project (CARP). (2006) Chlorhexidine gluconate to cleanse patients in a medical intensive care unit: the effectiveness of source control to reduce the bioburden of vancomycin-resistant enterococci. *Archives of Internal Medicine* 166: 306–312.
- Webster J, Gillies D, O'Riordan E, Sherriff KL and Rickard CM. (2011) Gauze and tape and transparent polyurethane dressings for central venous catheters. *Cochrane Database of Systematic Reviews* 11: CD003827.