Skin Complications Associated With Pediatric Central Venous Access Devices: Prevalence, Incidence, and Risk

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Abstract

Central venous access devices (CVADs) are vital to enable treatment for children with cancer and other complex health conditions. However, complications effecting the CVAD wound are commonly reported. This study aimed to identify the incidence and prevalence of CVAD-associated skin complications current management, and characteristics associated with complication development, in pediatrics. A prospective observational study performed across medical, oncology, and hematology departments at a tertiary pediatric hospital in Australia, between April and July 2017. Children admitted with CVADs were assessed twice weekly for CVAD-associated skin complications and associated signs and symptoms. The data were analyzed using descriptive statistics (i.e., proportions, frequency) and time-to-event multivariable regression (i.e., hazard ratios [HRs]). Two hundred and seventy-one CVADs were reviewed over 43,787 catheter days, with over one eighth of participants (14%; n = 37) having a CVAD-associated skin complication during their admission (0.95 per 1,000 catheter days, 95% confidence interval [CI; 0.61, 1.17]), most commonly contact dermatitis (11%; n = 29; 0.72 per 1,000 catheter days 95% CI [0.50, 1.04]). Within biweekly checks the median point prevalence of complications varied between 0.4% and 11% and clinical management was wide-ranging. A primary diagnosis of oncology (HR 2.89, 95% CI [1.10, 7.62]) or medical/surgical (HR 2.55, 95% CI [1.04, 6.22]) conditions; plain, nonbordered polyurethane dressings (HR 4.92, 95% CI [2.00, 12.13]); and poor dressing integrity (HR 2.64, 95% CI [1.18, 5.92]) were significantly associated with contact dermatitis. In conclusion, substantial numbers of pediatric patients experience CVAD-associated skin complications, and innovations are necessary to identify, prevent, and treat these health care–associated injuries.

Keywords

vascular access, oncology, hematology, pediatrics, wound care, skin, evidence-based nursing

Introduction

Central venous access devices (CVADs) provide a stable route for the administration of supportive and interventional treatments for children with oncolgical and hematological malignancy and other chronic and complex medical conditions. A variety of CVADs are used, ranging from peripherally inserted central catheters (PICCs) for short- to medium-term therapy administration, to totally implanted venous devices (e.g., port-a-cath) for long-term therapy (Chopra et al., 2015). CVADs are more than a simple tool of the trade—there is growing recognition that
careful selection, insertion, and management of these devices plays a major role in successful treatment administration and thereby in long-term survival and recovery (Athale, Siciliano, Cheng, Thabane, & Chan, 2012; Ullman, Marsh, Mihala, Cooke, & Rickard, 2015). However, complications effecting the CVAD wound created by its insertion can become a significant cause of harm and potential adverse sequelae for many patients.

Systemic skin complications, including infections and graft versus host disorder, are a known consequence of many anticancer therapies and stem cell transplantation (Gandhi, Brieva, & Lacouture, 2014). Young age, poor nutritional status, preexisting skin conditions (e.g., eczema), and underlying comorbidities also reduces skin health and places patients at risk for further skin complications (Curley et al., 2018; McNichol, Lund, Rosen, & Gray, 2013). These are frequently present in children relying on CVADs for administration of treatments.

The insertion of the CVADs into sometimes fragile skin results in localized trauma, often with associated bruising, which may be extensive for children with coagulopathies. After successful insertion, the CVAD wound and surrounding tissue are repeatedly exposed to multiple stressors, including the vigorous application of decontaminants (e.g., chlorhexidine gluconate [CHG] in alcohol), adhesive products (e.g., polyurethane dressings), and combinations of the two (e.g., CHG-impregnated dressing products).

Together, these treatment-, patient- and device-related risks are likely to result in significant skin complications surrounding CVAD sites. These CVAD-associated skin complications include bruising, contact dermatitis, mechanical skin injuries (e.g., skin tears and blisters), pressure injuries, and local site infections (Broadhurst, Moureaux, & Ullman, 2017; McNichol et al., 2013).

While clinically evident, and reported in case studies (Wall, Divito, & Talbot, 2014; Weitz et al., 2013), a robust description of the prevalence, incidence, and risks associated with the development of CVAD-associated skin complications is absent from the literature. This is especially relevant for patients undergoing treatment for oncological and hematological malignancies, due to their reliance on CVADs for time-sensitive treatments and potential underlying increased risk for skin complications and infections. A comprehensive description of CVAD-associated skin complications is necessary to focus innovation, interventional trials, and health care resources toward the prevention and treatment of these conditions.

**Method**

**Design**

A prospective, observational study was undertaken, aiming to describe the prevalence and incidence of skin complications surrounding pediatric CVADs, the current management of skin surrounding pediatric CVADs, and the treatment-, patient-, and device-associated risk factors associated with the development of these complications. Approval from Children’s Health Queensland Hospital and Health Service and Griffith University’s Human Research Ethics Committee was obtained prior to study commencement (HREC/16/QRCH/310; 2016/835).

**Setting and Sample**

The study was undertaken within the hematology/oncology and respiratory departments at Queensland Children’s Hospital, a large tertiary referral pediatric hospital in Brisbane, Australia, between April and July 2017 (3 months). All children admitted to the hematology/oncology and general medical wards, with any type of CVAD in situ (e.g., PICC, hemodialysis catheter, non-tunneled percutaneous CVAD, tunneled, cuffed CVAD [e.g., Hickman], totally implantable CVAD [e.g., port-a-cath]) were included. Data were collected twice weekly. The hematology, oncology, and respiratory departments were chosen as patients with these conditions are frequent and long-term users of CVADs, within pediatrics (Ullman, Kleidon, Cooke, & Rickard, 2017).

**Process**

Twice per week, each child admitted to the two clinical areas with a CVAD was assessed by trained research nurses (ReNs). All changes to the skin surrounding the CVAD site were prospectively documented into a secure, web-based database (REDCap: https://www151.griffith.edu.au/redcap/) at the bedside. The original data collection tool was designed and trialed by Ullman, Kleidon, Cooke, and Rickard (2017), with additional variables added to document potential treatment, patient and device risk factors for CVAD-associated skin complications, suitable to the pediatric hematology, oncology, and general medical populations. ReNs are clinicians with at least 5 years of pediatric and vascular access experience and at least 3 years research experience. ReNs were given one-on-one training by the project managers and investigators, regarding the CVAD site assessment using previous clinical practice guidelines, involving photographic examples (Broadhurst et al., 2017; McNichol et al., 2013; National Pressure Ulcer Advisory Panel, European Pressure Ulcer Advisory Panel, & Pan Pacific Pressure Injury Alliance, 2014).

The data collection tools were piloted for interrater reliability and feasibility prior to use, achieving consistency between ReNs, with a maximum of 10 minutes per patient assessment. Education and familiarization with the data collection tool by the ReNs were assured prior to the
study. This included a training session to clarify process and to ensure consistency of approach to patient assessment. The CVAD site complications identified were reported to the patient’s bedside nurse and the nursing shift coordinator. A coded screening log was used by the RNs for participant tracking; however, no identifying patient information was collected within the database.

Outcomes

CVAD-associated skin complications were defined in accordance with best practice literature:

- **Contact dermatitis**: Either irritant or allergic contact dermatitis occurring as a result of exposure to a chemical (e.g., CHG) or allergic irritant (Broadhurst et al., 2017; McNichol et al., 2013)
- **Mechanical skin injury**: Skin stripping, skin tears, and tension blisters occurring following exposure to an adhesive product (Broadhurst et al., 2017; McNichol et al., 2013)
- **Pressure injuries**: Graded as per the National Pressure Ulcer Advisory Panel, European Pressure Ulcer Advisory Panel, Pan Pacific Pressure Injury Alliance (National Pressure Ulcer Advisory Panel, 2014)
- **Local site infection**: Two or more symptoms of localized erythema, swelling, warmth, or purulence surrounding the CVAD insertion site

Signs and symptoms of skin complications were also collected, to report accurately all clinical symptomatology surrounding the CVAD sites, even when they did not meet the a priori skin complication definitions. These signs and symptoms included rash, raised skin, lesion, irritation, erythema, bruising, itch, swelling (generalized and localized), vesicles, oozing/weeping, and localized warmth.

Variables

Risk factors were developed a priori after a systematic review of the literature and consultation with interdisciplinary, international key opinion leaders within the fields of oncology, hematology, pediatrics, wound management, parenteral nutrition, dermatology, and vascular access. The characteristics include primary diagnosis, skin integrity overall (good, fair, poor), skin type (Fitzpatrick scale; Fitzpatrick, 1998), chemotherapy agents with known skin effects, recent bone marrow transplant, underlying comorbidities (e.g., renal impairment, diabetes), age, nutrition status, immunosuppression, and previous history of sensitive skin and skin allergies. Data were also collected regarding the CVAD characteristics (i.e., CVAD type) and management (including frequency and type of dressings, securement, decontaminants, skin protectants, adhesive removers, dressing change procedure and dressing integrity upon assessments). Details on the presence of CVAD-associated complications unrelated to the skin were collected in accordance with best practice literature, and included CVAD-associated bloodstream infection (Centers for Disease Control and Prevention, 2014), dislodgement (Fratino et al., 2005), occlusion (Fratino et al., 2005), thrombosis (Fratino et al., 2005), and CVAD breakage (Fratino et al., 2005).

Data Analysis

The demographic and clinical characteristics of the participants and their CVAD management were descriptively reported, using categorical and continuous descriptors appropriate to their distribution. The incidences of skin complication development per patient are reported proportionally and using incidence rates (with 95% confidence intervals [CIs]) per 1,000 catheter days. The point prevalence of CVAD-associated skin complications is reported descriptively using rates (proportions) across weekly periods, and an overall mean (with standard deviation [SD]). CVADs still in place at study completion were censored from that date. As skin complication development for each participant were time dependent, Cox proportional hazards regression model were used for time-to-event analysis with shared frailty model to account for the random effects, and survival data/hazard rates reported with 95% CI. In order to include failures that occurred on Day 0 (i.e., complication on first assessment), +1 day was added for all participants.

Variables significant at $p < .20$ on univariable analysis were subjected to multivariable regression. Correlation between variables were checked ($R^2$ value for continuous/categorical or continuous/continuous variables). Correlations were considered significant if $r > 0.5$. Covariate interactions were explored, and effects at $p < .05$ noted. Baseline covariates were explored initially for multivariable model building with manual stepwise removal at $p < .05$. Treatment covariates were then explored with manual stepwise removal at $p < .05$. A combination of the significant covariates from baseline and treatment covariates (including the clinically significant variables) was then explored by manual stepwise removal at $p < .05$. The variables that were dropped during the previous steps were then explored by manual stepwise addition and removal and interactions were tested. Final model was selected by assessing the Akaike’s information criterion and Bayesian information criterion and was checked for global proportional hazards assumption test. The analysis was undertaken using Stata (Version 13; StataCorp, College Station, TX).
Results

Participant and Device Characteristics

Over a 3-month period 271 patients with 271 CVADs (2 nontunneled CVAD, 84 PICC, 92 totally implanted CVAD, 93 tunneled CVAD) were reviewed over 43,787 catheter days, between the two clinical areas. These devices remained in situ for varying durations, relevant to the device type (median and interquartile range [IQR] nontunneled 2.5 days [1-4], PICC 36 days [12-61], totally implanted CVAD 294 days [253-316.5], and tunneled CVAD 193 days [90-272]). Many remained in situ at study end (101, 37%) or were removed due to completion of treatment (75, 28%) with 38 CVADs (14%) removed due to complication (e.g., infection, occlusion, thrombosis).

Participant characteristics are reported in Table 1. Median participant age was 9 years (IQR 4-14 years), with the majority of participants undergoing treatment for hematological (137, 50%) or oncological (78, 29%) conditions. Comorbidities and a priori skin complication risk factors were common, and 26% of children (n = 69) were having fair to poor skin integrity on admission to hospital.

Incidence and Prevalence of CVAD-Associated Skin Complications

As displayed in Table 2, overall, 14% of participants (n = 37) had a CVAD-associated skin complication, or signs and symptoms of a skin complication, during their admission, at a rate of 0.95 per 1,000 catheter days (95% CI [0.69, 1.31]). Examples demonstrating the complications identified in the study can be seen in Figure 1. The most common CVAD-associated skin complication was contact dermatitis, presenting in 11% of participants (n = 29) at a rate of 0.72 per 1,000 catheter days (95% CI [0.50, 1.04]). Nine participants (4%) developed multiple skin complications, and no CVAD-associated pressure injuries were evident in the study. As displayed in Figure 2, these complications developed at any stage during the participant’s admission, with dermatitis being persistently the predominant skin complication across number of assessments, with a small increase evident over the assessment periods.

On biweekly observation, the prevalence of CVAD-associated skin complications, signs, or symptoms varied considerably within the clinical areas audited, as displayed in Figure 3. Between 0.4% and 11% of children assessed had a CVAD-associated skin complication, sign, or symptom at each assessment point, with a mean prevalence of 2.2% (95% CI [0.8%, 4.8%]).
Current Management of Patients With CVAD-Associated Skin Complications

A variety of CVAD procedures and products were used to manage the patients who developed CVAD-associated skin complications, as evident in Table 3. This was especially apparent in the range of dressing and securement products used, with nine different primary dressings in use. This variability was still evident for participants who developed contact dermatitis. Overall, there was a high use of adhesive removal wipes (72%) and low use of skin protectant products (12.5%), during dressing change procedures, with or without contact dermatitis present.

Risk Factors for the Development of CVAD-Associated Contact Dermatitis During Hospital Admission

Multivariate regression to explore the association between demographic and clinical characteristics of participants and the development of CVAD-associated contact dermatitis is presented in Table 4. A primary diagnosis of oncology (hazard ratio [HR] = 2.89; 95% CI [1.10, 7.62]) or medical/surgical (HR = 2.55, 95% CI [1.04, 6.22]) conditions, in comparison to hematological conditions; the use of plain, nonbordered polyurethane dressings (HR = 4.92; 95% CI [2.00, 12.13]); and poor
dressing integrity (HR = 2.64; 95% CI [1.18, 5.92]) were significantly associated with contact dermatitis.

**Discussion**

This is the first systematic, prospective description of CVAD-associated skin complications in pediatrics, internationally. This phenomenon represents a significant health care–associated complication, at the same or higher incidence as pediatric pressure injuries (Curley et al., 2018), yet it has not been previously described in the literature. Fourteen percent of children admitted to hospital within the oncology, hematology, or medical departments requiring a CVAD for treatment experienced a CVAD-associated skin complication, sign, or symptom, with 11% developing CVAD-associated contact dermatitis. These complications are uncomfortable, are disfiguring, and can have potential systemic effects, including progression into bloodstream infection or catheter failure.
Table 4. Cox Proportional Hazards Regression Model for the Development of CVAD-Associated Contact Dermatitis Within 619 Assessments.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Univariate</th>
<th>Multivariate</th>
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<tbody>
<tr>
<td></td>
<td>HR 95% CI p</td>
<td>HR 95% CI p</td>
</tr>
<tr>
<td>Age (years)</td>
<td>0.06 [0.99, 1.14] .11</td>
<td>1.06 [0.98, 1.14] .14</td>
</tr>
<tr>
<td>Poor or fair skin integrity</td>
<td>0.71 [0.29, 1.73] .45</td>
<td>0.47 [0.17, 1.26] .13</td>
</tr>
<tr>
<td>Primary diagnosis: Oncologya</td>
<td>1.86 [0.78, 4.45] .16</td>
<td>2.89 [1.10, 7.62] .03</td>
</tr>
<tr>
<td>Primary diagnosis: Medical/surgicala</td>
<td>1.82 [0.78, 4.20] .16</td>
<td>2.55 [1.04, 6.22] .04</td>
</tr>
<tr>
<td>Dressing does not meet the criteria of clean, dry and intact</td>
<td>3.00 [1.36, 6.62] &lt;.01</td>
<td>2.64 [1.18, 5.92] .02</td>
</tr>
<tr>
<td>Dressing changed since last assessment</td>
<td>0.41 [0.19, 0.92] .03</td>
<td>0.28 [0.11, 0.70] &lt;.01</td>
</tr>
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Note. CVAD = central venous access device; CI = confidence interval; HR = hazard ratio. Preexisting skin allergy was not included due to violation of global proportional hazards assumption test.

aReference = hematology.

(Thayer, 2015; Wall et al., 2014). Overall, skin complications in patients with cancer are associated with reduced health-related quality of life (Rosen et al., 2013).

From a health services perspective, CVAD skin complication prevalence in the assessed clinical departments ranged up to 11%, representing a significant problem across all types of CVADs. These results build upon the recent Australian point prevalence study (Ullman, Kleidon, Cooke, & Rickard, 2017), which demonstrated that 10% of pediatric CVADs in tertiary, acute care facilities were associated with a localized skin complication, such as dermatitis or bruising. Many of the improvements in pressure injuries have been driven by internationally benchmarked clinical audits, using high-quality assessment tools. Researchers and clinicians should consider including the skin health of CVAD sites within a regular audit schedule, to enable benchmarking, improvements, and innovation. Further systematic exploration of the prevalence and incidence of CVAD-associated skin complications in other settings (e.g., neonates, adults) and countries is urgently needed. It is also important to demonstrate the financial burden associated with the management of these complex conditions, in terms of products, personnel time, and the systemic sequelae.

In the multivariate models, the risk for developing contact dermatitis was significantly affected by underlying diagnosis and the management of the CVADs. Children with onco logical, medical, and surgical conditions, in comparison to hematological conditions, were associated with a significantly increased risk for the development of contact dermatitis. The reasons for this are unclear but are likely to be related to underlying skin condition (e.g., excessive salt excretion by children with cystic fibrosis) and treatment characteristics (e.g., chemotherapy characteristics). Other clinical and treatment characteristics previously considered to increase the risk of skin complications, such as bone marrow transplantation and malnutrition, were not significantly associated with increased risk of contact dermatitis within the current study; however, this may be due to sample size, and requires further exploration. Overall, it is difficult to give context to these results within the wider literature, due to the scarcity of previous research.

The relationship between dressings (e.g., plain, unbordered polyurethane dressings), poor dressing integrity, and contact dermatitis development is likely to be bidirectional, where patients who develop contact dermatitis have more challenges with the CVAD dressing adherence. Previous point prevalence studies in Australia have demonstrated that up to 25% of CVADs in oncology and hematological settings have poor dressing integrity (New, Webster, Marsh, & Hewer, 2014; Russell, Chan, Marsh, & New, 2014). The use of high-quality CVAD dressing products is likely to prevent poor dressing integrity, and potentially CVAD skin complications. However, research in this area is scarce, despite an Australian pilot randomized controlled trial of tunneled CVAD dressing highlighting feasibility and significance (Ullman, Kleidon, Gibson, et al., 2017).

The study also demonstrated the wide variety of dressing, securement, decontamination, and skin protectant practices used to manage these conditions in a single center, despite standardized hospital policy. This variation is likely to have occurred because of the lack of high-quality evidence to support practice (Gavin, Webster, Chan, & Rickard, 2016; Ullman, Cooke, et al., 2015). Over the past 10 years, clinical practice guidelines have been developed to identify and treat specific elements of CVAD-associated skin complications, including skin tears (LeBlanc & Baranoski, 2011), medical adhesive–related skin injury (McNichol et al., 2013), and pressure injuries (National Pressure Ulcer Advisory Panel, 2014). In 2017, Broadhurst et al. (2017) published an evidence-based algorithm to assist in the identification, prevention, and treatment of CVAD-associated skin injuries, and they provide a useful summary to inform practice in this area. However, throughout these clinical practice guidelines, the recommendations are frequently based on low-quality...
evidence, relying on expert opinion and observational studies, especially with regard to dressing selection and skin protective technologies. These guidelines consistently recommend early referral to wound care specialists, in order to optimize complex wound management, but this is inconsistently applied in clinical settings. With growing evidence demonstrating the prevalence, incidence, and sequelae associated with these sometimes preventable health care–associated injuries, it is time for a systematic and coordinated approach to build evidence to support clinical practice.

This study has limitations. The data are based out of a single Australian tertiary pediatric hospital, so they may not be reflective of current contemporary practice outside of Australia, or even that single institution. Due to the limited scope of study population, we also could not undertake multivariate regression for other skin complications due to small case numbers. We encourage researchers to replicate and build upon this study, to ensure external validity. The ReNs assessing the participants were experienced pediatric clinicians and were provided training and resources regarding skin assessments; however, they were not wound experts. Nevertheless, this study provides a systematic description of a previously underreported phenomenon and is useful to inform future research and practice innovation.

The clinical and research implications for this research are far-reaching. CVAD-associated skin complications are evident in a significant proportion of pediatric patients with hematological, oncological, and respiratory conditions. Research has yet to establish what is effective to prevent and treat these conditions; however, consensus- and evidence-based clinical practice guidelines are available to inform practice (Broadhurst et al., 2017). An international, systematic program of research to identify products and practices that are effective to prevent and treat these health care–associated injuries is essential.

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