Title

The safety and efficacy of midlines compared to Peripherally Inserted Central Catheters for adult cystic fibrosis patients: a retrospective, observational study.

Rebecca Sharp [a],*, Adrian Esterman [a], Helen McCutcheon [b], Neville Hearse [c], Melita Cummings [c]

a School of Nursing and Midwifery, University of South Australia, Adelaide, Australia

b Florence Nightingale School of Nursing & Midwifery, King's College London, United Kingdom

c Department of Radiology, Royal Adelaide Hospital, Adelaide, Australia

Abstract

Background: intravenous antibiotics are the cornerstone of treatment for patients with cystic fibrosis (CF). Midlines are a type of vascular access device (VAD) used exclusively in one treatment facility within Australia, most other centres use peripherally inserted central catheters (PICCs).
Objective: To ascertain the safety and efficacy of midlines for CF patients receiving intravenous antibiotics.
Design: Retrospective observational.
Setting: A large, major metropolitan teaching hospital in Adelaide, South Australia.
Participants: Adult patients with a diagnosis of CF, who had a PICC or midline inserted for the commencement of antibiotic therapy during the period 2004 – 2010 to treat a respiratory exacerbation.
Methods: Medical records and hospital reports were used to record rates of adverse events and unexpected removal of VADs. The primary outcome was a composite measure of adverse events (catheter-related blood stream infection, deep vein thrombosis, occlusion, pain, infiltration, bleeding, phlebitis, catheter leakage and dislodgement) and whether the VAD was removed before planned.
Results: There were 231 midlines and 97 PICCs inserted into 64 patients (39 male and 25 female; age range 18-47 years old). Presented as per 1000 VAD days, patients with PICCs and midlines had similar rates of adverse events (14 and 11 adverse events per 1000 VAD days respectively). Unexpected removal was higher for patients with midlines (6.90 per 1000 VAD days) than for PICCs (2.89 per 1000 VAD days). Incident rate ratios (IRRs) showed that patients with midlines and PICCs had similar rates of adverse events (IRR 1.18, P=0.617, CI 0.62-2.22) although the removal rate of patients with midlines was

twice that of patients with PICCs (IRR 2.24, P=0.079, CI 0.91-5.56). As an absolute risk there were only 4.09 more cases of removal for patients with midlines per 1000 VAD days than those with PICCs.
Conclusions: Midlines may be an alternative to PICCs for adult CF patients although further research is required with a larger sample size to enable definitive conclusions.

Key words

Catheters vascular; Catheterisation-Adverse Effects; Cystic Fibrosis; Midlines;

Peripherally Inserted Central Catheters; Retrospective; Observational.

What is already known about the topic?

Several large studies in other populations have shown that midlines are appropriate for medium-term intravenous antibiotics.

What this paper adds

Midlines may be a safe and effective alternative to PICCs in adult CF patients but further research with a larger sample size is needed.

Introduction

Cystic Fibrosis (CF) is a life-limiting, congenital disorder that affects approximately 1 in 2,500 births in Australia, the European Union and United States (World Health Organisation 2012).Life expectancy of people with CF in Australia has improved greatly in the last 30 years. Where once mortality was likely in infancy, average age of mortality is now around thirty years of age and is projected to increase to over 50 years of age in the next decade (Cystic Fibrosis Data Registry 2008; Fernandes, Plummer & Wildman 2008).

The aggressive treatment of acute respiratory infections (exacerbations) including the use of intravenous antibiotics has been a major factor in this decreased mortality making reliable vascular access imperative for these patients (Dobbin & Bye 2003; Fernandes, Plummer & Wildman 2008).

Peripherally inserted central catheters (PICCs) and midlines are non-permanent vascular access devices (VADs) that are advocated for CF patients internationally (Cystic Fibrosis Trust 2007; Cystic Fibrosis Standards of Care 2008; Cystic Fibrosis Foundation 2010). These devices are both inserted above the ante cubital fossa area; the place of termination and recommended dwell time differ. A PICC terminates in the superior vena cava (SVC), a large vein leading into the right atrium to give access to the central circulation whilst a midline terminates in a large peripheral vein in the axillary region (Gorski & Czaplewski 2004).The tip termination location determines the type of solution that can be safely infused. The Infusion Nurses Society standards of practice (2011) state that a PICC is classed as central access, indicated for caustic and irritating medications such as chemotherapy and some antibiotics due to greater haemodilution in the SVC. Whereas a midline is a peripheral device, appropriate for non-irritating medications including the antibiotics used to treat exacerbations in CF patients (Cystic Fibrosis Standards of Care 2008; Monthly Index of Medical Specialties 2010).

The acceptable dwell time of PICCs and midlines also differ. PICCs are considered a long-term VAD and are able to remain in place for months whereas a midline is indicated for up to a month (Gorski & Czaplewski 2004; Infusion Nurses Society, 2011). Regardless, in

CF patients, both devices are considered temporary and are removed after the course of intravenous antibiotics is completed, which is on average 10-14 days (Bilton 2008; Cystic Fibrosis Standards of Care 2008).

The hospital where the study was conducted introduced midlines to replace PICCs for some CF patients in 2004. This was due to an increase in venous abnormalities such as superior vena cava occlusions from repeated PICC insertions, which led to problems accessing the central circulation (Cummings et al. 2011). These abnormalities resulted in increased time and difficulty inserting the devices, causing much distress for the patient and in some cases hospital avoidance. Yet, most other CF treatment centres in Australia use PICCs rather than midlines when a non-permanent VAD is needed (Cummings et al. 2011).

Existing research in CF patients

There has been no research to date that has compared rates of adverse events for PICCS and midlines in CF patients. Limited research has examined the devices individually but tends to focus on PICCs in paediatric populations which make generalising to adult populations problematic (Bui et al. 2009; Jones & Kaslowsky 2000; Morin et al. 2007; Tolomeo & Mackey 2003).

Only one study was identified that examined adverse events in adult CF patients with PICCs (Nash et al. 2009). This centred on deep vein thrombosis (DVT) rates and found a relatively high rate of symptomatic DVT (8%). They surmised that the risk for DVTs in the CF population is heightened due to an inflammatory response involved with lung

infection as well as an increased risk of an inherited thrombotic abnormality (Balfour-Lynn et al. 2005; Nash et al. 2009).

Conversely, research in midlines in the adult CF population demonstrated low rates of adverse events including DVT (Cummings et al. 2011). This study, which was based in the same hospital as the present study, found no examples of either DVT or catheter-related blood stream infection (CR-BSI) during the study period and a rate of 2% and 1% respectively in the following year (Cummings et al. 2011).

Research in other populations has shown similar numbers of adverse events associated with the two devices. Several large studies in homecare and older adult populations have found low rates of adverse events and the unexpected need for removal with both devices (Anderson 2004; Leone & Dillon 2008; Moureau et al. 2002).

2. Methods

The aim of the study was to compare rates of adverse events and unexpected removal in patients with midlines versus those with PICCs in adult CF patients. The setting of the study was a large, urban teaching hospital in Adelaide, South Australia which operates a specialist CF service. This includes an outpatient intravenous service (OPIVS) which offers support to patients with CF so that they can administer intravenous antibiotics at home.

PICCs and midlines were inserted in the Radiology department predominantly by specially trained Registered Nurses. These devices were 4 French single lumen PICCs and midlines, inserted using strict protocols which follow international guidelines. The

majority of the PICCs and midlines were distal valved silicone devices, a small number were polyurethane VADs. These were inserted utilising ultrasound technology (Sonosite Inc. Bothell, WA, USA). All adult patients (aged 18 or older) with a diagnosis of CF, who had a PICC or midline inserted during the period 2004-2010 for the commencement of antibiotic therapy to treat a respiratory exacerbation were selected. The observational, retrospective design of this study was necessary as midlines were routinely used for CF patients since 2007 and few PICCs were inserted after this time for this patient group.

Primary outcome measures

The primary outcome measure consisted of a composite of adverse events, namely if a patient had one or more of the following: catheter-related blood stream infection (CR-BSI), deep vein thrombosis (DVT), occlusion, pain, bleeding, infiltration, phlebitis, catheter fracture, leakage or dislodgement. This study used a diagnostic definition of CR-BSI, which aims to identify the VAD as the specific source of infection as recommended by the Centres for Disease Control and Prevention (CDC 2011). DVT was included where diagnosed by a Radiologist using ultrasound. Occlusion, pain, bleeding, infiltration, phlebitis, catheter fracture, leakage and dislodgementwere included when documented in the medical record by a healthcare professional, whether medical or nursing staff.

The composite measure was defined as the number of adverse events per VAD days (the time period that either the midline or PICC was in place). A composite rate was used to show a total complication rate so as to give both patients and clinicians an overall understanding of the safety and efficacy of each device. Additionally, whether these

complications resulted in the VAD requiring removal was recorded.These composite measures were presented as per 1000 VAD days. This is advocated in the literature to enable a meaningful measure of risk to compare VADs with different dwell times and provide a standardised measure that allows different studies to be compared (Moureau et al. 2002; Maki, Kluger & Crnich 2006).

Other variables measured

The variables age, gender, co-morbid conditions, whether the patients were inpatients, outpatients (or a combination) and severity of exacerbation (as evidenced by lung function scores) were also recorded. Lung function was measured using the value percentage-predicted FEV_1 (forced air expiration in 1 second). This value already incorporates the variables which may cause differences in lung function (that are not disease related), that is, age, gender and body size and such allows for a more meaningful comparison between the participants (Burton 2010; Pellegrino et al. 2005). Co-morbidities were measured using a Charlson index, a disease burden scoring system with 17 disease categories that are weighted based on their association with mortality at one year (Khan et al. 2010). Although not validated in a CF population it is a commonly used measure of co-morbidity in many patient groups (Smith et al. 2005).

Data collection

An existing database was used to recall VAD insertions of patients that met the sampling inclusion criteria. Unit record numbers (UR) were used to cross match to the Department of Radiology and the Infection Prevention and Control Unit (IPCU) reports for instances of

DVT and CR-BSI respectively. Medical records were hand searched for instances of other adverse events and VAD insertion/removal dates. Other Health Department information systems were used to gather information regarding co-morbidities and lung function scores. Co-morbidities were measured using International classification of disease (ICD) codes as defined by the World Health Organisation (2011). These were translated into a Charlson index using an algorithm.

Sample size and statistical analysis

A power analysis was conducted using average adverse event frequencies from the literature and a two group chi-squared test with a 0.05 two-sided significance level. This found that a sample of 151 PICCs and 268 midlines was needed to have 80% power to detect the difference between an expected adverse event rate of 20% with PICCs and 10% with midlines respectively. Many patients were included in the study more than once, however, due to the lack of previous research in this area we could not estimate a likely intra-class correlation (ICC), and hence we made no adjustment for clustering in sample size calculations. A 2:1 ratio of midlines to PICCs in the sample size calculation was used due to change in practice at the hospital where the study which resulted in far more midline insertions than PICCs within the time frame studied.

The statistical package SPSS (Version 18.0, 2009) was used to generate simple incidence rates and perform Chi square and Mann-Whitney testing to test for associations between the variables measured. A p-value was set at ≤0.05 for statistical significance. A composite rate per 1000 VAD days was generated by dividing the composite rate of

adverse events by the number of days the VAD was inserted and then multiplied by 1000. Log binomial generalized linear and robust Poisson models were used to generate incident rate ratios (IRR) of adverse events and removal using Stata (Release 11, 2009).Clustering was adjusted for as each patient could have had more than one VAD inserted over the time period of the study. A comparison of unadjusted rates was modelled followed by an analysis adjusting for age, gender, Charlson Index, whether the patient had intravenous antibiotics as part of the outpatient service (OPIVS) and lung function.

Ethics

Ethical approval was obtained from the hospital where the study was based –protocol number 110109.

3. Results

The sample

There were 64 patients (39 male and 25 female) who had 328 VADs inserted over the time period (231 midline catheters and 97 PICCs). The age range of the patients was 18-47 years old (mean 29 years). There was a similar distribution for age, gender, FEV_1 and those who received treatment as part of the outpatient programme (Table 1). Although the difference in the distribution of the Charlson Index was statistically significant (p=0.021), the pattern of results was not consistent as there was no obvious linear relationship. Further analysis that treated the data as a continuous variable found that

the median Charlson index score was one for both groups and there was no statistically significant difference between the groups (p=0.538 using a Mann-Whitney test).

Table 1: Demographic information

Variable	PICC		Midline		Total		
	N	%	N	%	N	%	Sig.*
Age							0.204
18-26	50	52	98	43	148	45	
27-35	33	34	97	42	130	40	
36+	14	14	36	15	50	15	
Total	97	100	231	100	328	100	
Gender							0.423
Male	59	61	130	56	189	58	
Female	38	39	101	44	139	42	
Total	97	100	231	100	328	100	
FEV_1							0.078
< 30%	25	26	42	18	67	20	
31-40%	16	17	53	23	69	21	
41-70%	41	42	112	49	153	47	
>70%	15	15	24	10	39	12	
Total	97	100	231	100	328	100	
Charlson index							0.021
0	17	20	23	13	40	15	
1	47	56	139	76	186	69	
2+	20	24	22	11	42	16	
Total	84	100	184	100	268	100	
OPIVS							0.532
Yes	44	45	114	49	158	48	
No	53	55	117	51	170	52	
Total	97	100	231	100	328	100	

* Based on Chi squared test - not adjusted for clustering. Clustering would have the effect of making each comparison less significant.VAD= vascular access device; PICC= peripherally inserted central catheter; FEV1 =% predicted lungfunction; OPIVS=outpatient intravenous service.

Adverse events

Mean days in situ were 14 days for PICCs (range 5-41 days) and 22 days for midlines (range 1-59 days). There were a total of 66 adverse events in 57 different VADs within 32 patients (51 adverse events with midlines and 15 with PICCs). Individual adverse events experienced by patients with midlines and PICCs are shown in Table 2.

Table 2: Individual adverse events

Adverse event	PICC		Midline		Total	
	n	%	n	%	n	%
DVT	0	0.0	3	5.9	3	4.5
Occlusion	1	6.7	8	15.7	9	13.7
Bleeding	3	20.0	4	7.8	7	10.7
Leakage	1	6.7	18	35.3	19	28.8
Pain	6	40.0	9	17.6	15	22.7
Dislodgment	3	20.0	5	9.8	8	12.1
Fracture/ broken	1	6.7	2	3.9	3	4.5
Phlebitis	0	0.0	2	3.9	2	3.0
Total	15	100	51	100	66	100

PICC= peripherally inserted central catheter; DVT= deep vein thrombosis; CR-BSI=catheter related blood stream infection

There were no examples of CR-BSI or infiltration found in patients with midlines or PICCs.

A composite rate of all adverse events showed that patients with PICCs and midlines had similar rates of complications. There was a complication rate of 11 adverse events per 1000 VAD days for PICCs compared to 14 adverse events per 1000 VAD days for midlines. Table 3 shows the results of univariate analysis of predictors of a composite adverse event. Notably, the adverse event rates for PICCs and midlines were similar (15.5% versus 18.2% or IRR 1.18 CI 0.62-2.22). Of the other variables considered, only gender appeared to be related to the probability of an adverse event, females had a higher rate (21.6%) than males (14.3%). But when gender and the other covariates were added to the model comparing VADs, it made little difference to the result (p=0.541).

Table 3: Variables associated with Adverse Events

Variable	Adverse Event				IRR	95% CI	Sig.*
	Yes		No				
	N	%	N	%			
VAD							
PICC	15	15.5	82	84.5	1.00		
Midline	42	18.2	189	81.8	1.18	0.62 – 2.22	0.617
Age							
18-26	20	13.6	127	86.4	1.00		
27-35	26	20	104	80	1.54	0.88-2.69	0.129
36+	11	21.6	40	78.4	1.33	0.72-2.47	0.368
Gender							
Female	30	21.6	109	78.4	1.00		
Male	27	14.3	162	85.7	0.60	0.36-0.99	0.048
Charlson Index[#]							
0	6	15	34	85	1.00		
1-2	41	18.4	182	81.6	1.24	0.59-2.56	0.570
3+	1	25	3	75	1.16	0.67-4.60	0.247
FEV_1							
<30%	14	20.6	54	79.4	1.00		
31-40%	9	13	60	87	0.44	0.12-1.64	0.478
41-70%	29	19.1	123	80.9	0.90	0.36-2.28	0.828
> 70%	5	12.8	34	87.2	0.60	0.13-2.75	0.514
OPIVS							
Yes	22	14	135	86	1.00		
No	35	20.5	136	79.5	1.57	0.91–2.73	0.107

* Based on univariate clustered log binomial generalised linear and robust Poisson models using VAD days as an exposure variable.

[#] Missing values due to outpatient care which did not generate ICD codes and thus Charlson indices. VAD = vascular access device; PICC = peripherally inserted central catheter; OPIVS = outpatient intravenous service; FEV1 = % predicted lung function; IRR = incident rate ratio.

Unexpected removal

Most complications were able to be managed without the VAD requiring removal or replacement. Less than half of the 57 VADs which had adverse events associated with them were removed (44%; n=25). Patients with midlines required unexpected removal of their device more than twice that of patients with PICCs, however this was not statistically significant and instances of removal were infrequent for both devices (Table

4). Notably presented as an absolute risk, the difference was small, with only 4.03 more removals per 1000 VAD days for patients with a midline (90% CI 0.56 - 8.63). Those who had a Charlson index of 3 or more (i.e. three or more co-morbidities) were more likely to have an adverse event requiring removal of their VAD (IRR 3.63 90% CI 1.47-9.02 p=0.005), although this was only one patient (table 4).

There were no instances of CR-BSI in reports generated by IPCU for the sample. However, there were three VADs (two PICCs and one midline catheter) removed on suspicion of CR-BSI. These VADs removed did not meet the definition of CR-BSI used in this study. In one case, blood samples were not taken and the other two instances involved the same patient who had persistent temperatures (above 38.5 degrees Celsius) but negative blood cultures. The VADs in these cases were already in the analysis as they were removed due to other adverse events (namely leaking and pain).

Discussion

The present study suggests that patients with midlines and PICCs had similar, low rates of adverse events. It would seem that midlines may be an appropriate alternative to PICCs for adult patients with CF requiring intravenous antibiotics. Although removal rates were higher for patients with midlines using a ratio measure, the actual number of cases of removal in both groups was small. It must be noted that this study was underpowered, further research with a larger sample size is required to make conclusive statements.

However these results are supported by research in other populations that have compared patients with PICCs and midlines. In an outpatient setting, patients with PICCs and midlines had similar rates of adverse events and removal, indicating that midlines are an appropriate alternative to PICCs when a central device is not indicated (Moureau et al. 2002; Leone & Dillon 2008). But these previous studies did demonstrate much lower complication and removal rates than the present study. Moureau et al. (2002) found an adverse event rate of 2.02 per 1000 VAD days for patients with PICCs and 4.50 per 1000 VAD days for those with midlines. This compares to the present study which found a complication rate of 11 and 14 per 1000 VAD days in patients with PICCs and midlines respectively. Yet the previous studies did not include pain and bleeding in the composite rate which may account for the lower figures. Together, these adverse events made up the second most common complication in midlines and the most common complication for PICCs in the present study. Therefore, the inclusion of these adverse events increased the overall rate in the present study and the clinical importance of these complications is debateable. Although unpleasant for the patient, these are not unanticipated events and were able to be rectified quickly by nursing staff.

Unexpected removal rates for patients with midlines and PICCs were also similar in previous research (Leone & Dillon 2008). This supports the present study, which although the removal rate for midlines was higher, was not statistically significant. Nonetheless, the removal rate in the previous research was much lower than the present study. Leone & Dillon (2008), found a removal rate of 0.67 and 0.06 per 1000 VAD days for patients with PICCs and midlines respectively, compared to the present study rate of 2.9 and 6.9

per 1000 VAD days for PICCs and midlines. This indicates that adult patients with CF may have intrinsic factors that inflate their risk for complications that require removal of their VAD. But, comparison with these studies is problematic as the management of VADs and the samples themselves are different.

Although the adverse event/removal rate of patients with midlines was not statistically significant more than those with PICCs, patients with midlines did have more adverse events and VADs that required removal. This is clinically important as treatment is often interrupted and can result in discomfort to the patient due to the adverse event itself or because of re-insertion. This indicates that further attention must be paid to these complications in order to improve patient care.

Notably, patients with midlines did have more instances of thrombotic type complications namely; leakage, DVT and occlusion. Leakage is thought to originate after a thrombus develops in the vein at the catheter tip causing the infusate to build up within the catheter and leak out of the insertion site (Leick-Rude & Haney 2006). Leakage was the most common adverse event for patients with midlines (n=18). This may be due to the location of the tip which terminates in a much smaller vein than a PICC and would increase the risk of leakage if a thrombus develops at this location. This adverse event may be accentuated in the CF patient population due to the multiple vascular access insertions they undertake for treatment from infancy onwards which often leads to scarring and sclerosis of the vessels (Lacy et al. 1996). In 2011, a protocol was introduced at the hospital where the study was set to perform venograms on CF patients once the

inserters experienced difficulty inserting midlines. This allows the identification of vessels with stenosis and collaterals so that the most appropriate vein can be identified which may reduce the risk of thrombotic events (pers. Comm. Cummings 2012).

Yet it would be assumed that the damage to the vasculature of many of the CF patients after repeated insertions would also increase the risk of DVT, but there were only 3 cases associated with patients that had a midline inserted (and none with PICCS). Nonetheless it is a complication that warrants further attention due to the serious consequences and the ongoing management required. The DVT rate in the present study is much lower than that found by Nash et al. (2009) who found an 8% DVT rate in adult CF patients with a PICC. This led to the suggestion that CF patients have an increased risk for DVT due to genetic clotting abnormalities and systemic infection (Nash et al. 2009). It was outside the realm of this study to measure for the genetic abnormalities that increase risk. It should be noted that two of the three patients who developed a thrombus had further risk factors for DVT. One patient was pregnant and a current intravenous drug user, both of which are associated with increased risk for DVT (Sprizza & Witko 2003; Syed & Beeching 2005). The remaining patient's respiratory system was colonised with *Burkholderia cepacia*, a bacterium that is thought to be associated with increased risk due to stimulation of inflammation (Raffini et al. 2006; Morin et al. 2007).

There is debate about whether high risk individuals need to be prescribed prophylactic anti-coagulant medication when they have a VAD inserted. It has been suggested that all adult CF patients with a VAD be given prophylaxis treatment (Hogan et al. 1998).

Moreover, this risk may increase as the life expectancy of people with CF improves (Cystic Fibrosis Data Registry 2008; Veiraiah, Shetty & Routledge 2008). It is unknown what effect predicted co-morbidities such as coronary artery disease and vascular changes from CF related Diabetes Mellitus will have (Parkins et al. 2011).

However, the use of prophylactic anticoagulants is problematic, as low molecular weight heparins are injected subcutaneously, making this option unpopular with patients (Geerts et al. 2008).Furthermore, other factors need to be considered, for example there may be an increased risk of haemoptysis (Raffini et al. 2006). It is important for clinicians to assess each individual CF patient taking into account their co-morbidities as well as lifestyle so as to plan an appropriate treatment plan.

Occlusion may also be a result of a thrombotic type event, the build-up of blood components within the catheter (Gorski & Czaplewski 2004). Research in non-CF populations also indicates that occlusion is a common complication in patients with midlines and PICCs (Anderson 2004; Moureau et al. 2002). Often this complication can be reduced by nursing staff using correct flushing techniques (Gorski & Czaplewski 2005; Hadaway 2006).Flushing of a VAD is designed to expel medications and blood products out of the line to reduce the risk of occlusion and is reliant on nursing staff using correct flushing techniques(Gorski & Czaplewski 2005; Hadaway 2006). However nursing staff are not always compliant with VAD management protocols (Smith et al. 2011). Flushing protocols differ according to the design of the VAD inserted. The onus is therefore on

nursing staff to identify the VAD type and use the correct flushing protocol, as was the case in the present study where two types of devices were used (Moureau 2006). Specialised education was provided for the Registered Nurses managing patients at the hospital where the study was set, which has been advocated to decrease this complication; yet, education is only one element of change in nursing practice (Holt et al. 2010; Ngo & Murphy 2005). Clinical knowledge and experience has been shown to be associated with decreased compliance with VAD protocols (Smith et al. 2011). There is a need for the individual nurse to have a positive attitude towards the use of evidence and be motivated to incorporate change (Estabrooks et al. 2003). Ngo and Murphy (2005) found education incorporating principles to promote self-efficacy and proactive management of VADs decreased occlusion rates considerably (from 29% to 8.5%). Self-efficacy or the belief that an individual's actions can influence an event has been shown to motivate nurses to change practice which indicates that education needs to be designed to promote this.

Occlusions can often be rectified with anti-thrombolytic solutions for patients with PICCs (Moureau 2002). Commonly; tissue-type plasminogen activator (t-PA) is injected into the catheter and left for up to 2 hours which breaks fibrin proteins, dissolving the clot (Gabriel 2011). A large clinical trial demonstrated that approximately 90% of occluded central catheters achieving patency after the use of this solution (Deitcher et al. 2002). Yet the use of this solution is currently only indicated for patients with central devices, further research needs to be conducted in patients with midlines to determine the safety and efficacy of this technique to treat this adverse event (Infusion Nurses Society 2011).

Another adverse event that is commonly measured in VAD research and which has potentially serious consequences is CR-BSI. The current study planned to use surveillance reports from the Infection control unit at the hospital to identify possible CR-BSI that would be verified with clinical signs so as to use a more stringent diagnostic definition as suggested by the CDC (2011).There were no cases of CR-BSI identified in reports from this department for the sample. Perhaps the absence of cases of CR-BSI in the present study can be explained by the use of a procedure room in the radiology department staffed by specialised PICC insertion nurses that concentrate on inserting VADs. This team follow international best practice standards espoused by the CDC (2011). Some suggest strict adherence to evidence based guidelines for insertion of VADS to be the most important factor in the prevention of CR- BSI (McKenny, Fitzgerald & Scully 2010).Unfortunately, VADs were removed in this study on the basis of suspicion of CR-BSI. It is accepted practice at the hospital where the study was carried out and in many health care facilities to remove a VAD if a patient has a systemic infection and no other cause is apparent (Raad, Hanna & Maki 2007). This method leaves the patient with a febrile illness and no vascular access which compromises patient care and is costly to the health care organisation (McKenny, Fitzgerald & Scully 2010; Raad, Hanna & Maki 2007). Furthermore, this method is unreliable as it is difficult to diagnose a CR-BSI as symptoms are non-specific, such as fever (Chen et al. 2009). In this study, all of the patients who had their VADs removed due to a suspected CR-BSI had negative blood cultures, indicating that the VAD was not the source of the febrile illness.

Further research is required to determine conclusively the appropriateness of midlines for adult CF patients but if efficacy and safety is established, several factors support their use. Central access (and thus a PICC) is not required for the intravenous antibiotics used in the treatment of respiratory exacerbations in CF patients. Further midlines are less invasive and cost effective alternatives to PICCs.

It is recommended by the CDC (2011) and the Infusion Nurses Society (2011) that the least invasive device should be used for the intravenous therapy that is to be given. This is especially relevant in this population as a device that accesses the central circulation is not necessary for the treatment they require and the more invasive PICC is associated with central venous abnormalities (Bui et al. 2009; Cummings et al. 2011). Also, as a PICC terminates in the central circulation, x-ray confirmation of the tip position is required (Turner, Unsworth & David 2002). This is problematic as increasingly; more women with CF are becoming pregnant which presents unique management challenges including VAD choice. Midlines provide a benefit for these women as they do not require x-ray confirmation of the tip unlike PICCs which means they avoid exposing their unborn children to radiation (Turner, Unsworth & David 2002).

Cost is an important consideration in today's health care environment. Australian healthcare expenditure is expected to increase $161 billion by 2033 to a total spend of $246 billion, making prudent health care choices important (Goss 2008). It is difficult to get an exact cost of these VADs as there are many variables involved (e.g. procedure room and staff costs) and manufacturers are often reluctant to divulge the cost of each

device due to commercial reasons. But if only one element of insertion is analysed, the x-ray required for PICC tip confirmation, midlines do offer health care organisations a substantial cost saving. X-ray confirmation is not required for patients who have a midline, a cost saving of AUD$50 (USD$48.73) per insertion (Cummings et al. 2011).Currently 10 Midlines are inserted per week for CF patients saving the organisation approximately AUD$26,000 per year.

Limitations

The present study was underpowered; the aim was to have a sample of at least 151 PICCs and 268 midlines. Due to time-constraints and difficulties accessing some medical records, information regarding 97 PICCs and 237 midlines was able to be collected. Further, a post-hoc calculation of the Intraclass correlation coefficient (ICC) to account for clustering in the power analysis using a variance components model gave an ICC for adverse events of 0.05. On average, each patient entered into the database 5 times, hence the design effect (the amount the sample size needs to be inflated by to account for clustering) was calculated to be 1.2. In other words, we needed to include 181 PICCs and 322 midlines in the study. Clearly the study was underpowered, limiting the ability of the study to demonstrate a clinical difference or draw definitive conclusions.

A further limitation, as with all retrospective studies is the reliance on existing data which in this study was evident in problems with missing and incomplete documentation and difficulties physically accessing large numbers of medical records that covered the time period studied. Furthermore, the organisation of the outpatient programme meant that

there was missing data needed to generate a Charlson Index. This is because participants that had all of their treatment as outpatients did not generate ICD codes (as these are only generated for inpatients). In these cases the Charlson index was left blank. Of the 328 VAD episodes, there were 267 Charlson indexes generated (81%).

Conclusion and further research

Midlines may be an effective alternative to PICCs for the administration of antibiotics in the CF population but further research with a larger sample size is needed to make conclusive claims. Further research in other populations is also indicated to investigate the appropriateness of midlines for groups who receive a PICC where central access is not required. Currently, some patients undergo PICC insertion when there are difficulties inserting and maintaining the patency of short-term cannulas e.g. the frail elderly or morbidly obese patients (Cummings et al. 2011). In these cases midlines may be appropriate and result in a cost saving to the health care organisation without negatively impacting on patient outcomes.

References

Anderson, N., 2004. Midline catheters: the middle ground of intravenous therapy administration.Journal of Infusion Nursing27 (5), 313-321.
Balfour-Lynn, I., Malbon, K., Burman, J., Davidson, S., 2005. Thrombophilia in children with cystic fibrosis.Pediatric Pulmonology 39 (4), 306-310.
Bilton, D., 2008. Cystic fibrosis.Medicine 36(5), 273-278.
Bui, S., Babre, F., Hauchecorne, S., Christoflour, N., Ceccato, F., Boisserie-Lacroix, V., Clouzeau, H., Fayon, M., 2009. Intravenous peripherally-inserted central catheters for antibiotic therapy in children with cystic fibrosis. Journal of Cystic Fibrosis 8(5), 326-331.
Burton, D., 2010. Spirometry Tests. Australian Pharmacist 29(8), 682-685.
Centers for Disease Control and Prevention 2011. Guidelines for the prevention of intravascular catheter-related infections.<http://www.cdc.gov/hicpac/pdf/guidelines/bsi-guidelines-2011.pdf>.
Chen, W., Liu, T., Wu, S., Tan, T., Tseng, H., Shih, C., 2009. Improving diagnosis of central venous catheter-related bloodstream infection by using differential time to positivity as a hospital-wide approach at a cancer hospital. Journal of Infection 59 (5), 317-323.
Cummings, M., Hearse, N., McCutcheon, H.,Deuter, K., 2011. Improving antibitoic treatment outcomes through the implementation of a midline: Piloting a change in practice for cystic fibrosis patients. Journal of Vascular Nursing 24(1), 11-15.
Cystic Fibrosis Trust 2007. Home intravenous therapy and Cystic Fibrosis. Cystic Fibrosis trust, London. <http://www.cftrust.org.uk/aboutcf/publications/factsheets/Home_IVs-may07-latest.pdf>.
Cystic Fibrosis Data Registry 2008, Cystic Fibrosis Association Australia. <http://www.cysticfibrosis.org.au/pdf/Cystic_Fibrosis_in_Australia_2008.pdf>.
Cystic Fibrosis Standards of Care 2008, Cystic Fibrosis Association Australia. <http://www.cysticfibrosis.org.au/pdf/CFA_Standards_of_Care_journal_31_Mar_08.pdf>
Cystic Fibrosis Foundation 2010, Cystic Fibrosis Care Guidelines. <http://www.cff.org/treatments/CFCareGuidelines/Respiratory/>.
Deitcher, S., Fesen, M., Kiproff, P., Hill, P., Li, X., McCluskey, E., Semba, C., 2002. Safety and efficacy of alteplase for restoring function in occluded central venous catheters: Results of the Cardiovascular Thrombolytic to Open Occluded Lines Trial. Journal of Clinical Oncology 20(1), 317–324.
Dobbin, C., Bye, P., 2003. Adults with cystic fibrosis: meeting the challenge! Internal Medicine Journal 33 (12), 593-597.
Estabrooks, C., Floyd, J., Scott-Findlay, S., O'Leary, K., Gushta, M., 2003. Individual determinants of research utilization: a systematic review. Journal of Advanced Nursing 43 (5), 506-520.
Fernandes, B., Plummer, A., Wildman, M., 2008. Duration of intravenous antibiotic therapy in people with cystic fibrosis.Cochrane Database of Systematic Reviews, no. 2.<http://onlinelibrary.wiley.com.ezlibproxy.unisa.edu.au/doi/10.1002/14651858.CD006682.pub3/full >.
Gabriel, J., 2011. Vascular device occlusion: causes, prevention and management.

Nursing Standard. 25 (44), 49-55.
Geerts, W., Bergqvist, D., Pineo, G., Heit, J., Samama, C., Lassen, M., Colwell, C., 2008. Prevention of Venous Thromboembolism. Chest133 (suppl. 6) 381S-453S.
Gorski, L., Czaplewski, L., 2004. Peripherally inserted central catheters & midline catheters for the home care nurse. Home Healthcare Nurse 22(11), 758-773.
Goss, J., 2008. Projection of Australian health care expenditure by disease, 2003 to 2033. Australian Institute of Health and Welfare.
<http://www.aihw.gov.au/publicationdetail/?id=6442468187&tab=2>.
Hadaway, L., 2006. Technology of flushing vascular access devices. Journal of Infusion Nursing 29(3), 137-145.
Hogan, M., Coley, B., Shiels, W., Allen, E., McCoy, K., 1998. Recurrent deep venous thrombosis complicating PICC line placement in two patients with cystic fibrosis and activated protein C-resistance. Pediatric Radiology28(7), 552-553.
Holt, D., Lewis, C., Klimpel, K., Sloan, C., Aguda, C., 2010. The Effects of Focused Nursing Education on 3F Groshong(TM) PICC Occlusion Rates: The Experience of One Tertiary Pediatric Care Facility. Journal of the Association for Vascular Access15(4), 213 - 221.
Infusion Nurses Society, 2011.Infusion Nursing Standard of Practice.Infusion Nurses Society. Norwood, MA.
Jones, S., Kaslowsky, R., 2000. Successful utilization of peripherally inserted central catheters (PICC) for IV antibiotic therapy in pediatric patients with cystic fibrosis. Pediatric Pulmonology30(suppl.20), S535.
Khan, N., Perera, R., Harper, S., Rose, P., 2010. Adaptation and validation of the Charlson Index for Read/OXMIS coded databases. BMC Family Practice 11(1), 1.
Lacy, D., Spencer, D., Venkataraman, M., Ruiz, G., Weller, P., 1996. Comparison of two percutaneous intravenous "midline" catheters in cystic fibrosis. Journal of Intravenous Nursing. 19(1), 28-31.
Leick-Rude, M., Haney, B., 2006. Midline catheter use in the intensive care nursery.Neonatal Network25(3), 189-99.
Leone, M., Dillon, L., 2008. Catheter Outcomes in Home Infusion. Journal of Infusion Nursing31(2), 84-91.
Maki, D., Kluger, D., Crnich, C., 2006. The risk of bloodstream infection in adults with different intravascular devices: a systematic review of 200 published prospective studies. Mayo Clinic Proceedings81(9), 1159-1171.
McKenny, M., Fitzgerald, M., Scully, M., 2010. How do I diagnose and manage catheter-related blood stream infections?Evidence-Based Practice of Critical Care263-270.
Monthly Index of Medical Specialties 2010.MIMS Annual. UBM Medica, Sydney.
Morin, S., Gifford, A., Parker, H., Whittaker, L., Lahiri, T., Cornell, A., Hertzig, J., Stokes, D., Zuckerman, J., 2007. Complications of intermediate and long-term central venous catheters in CF patients. Pediatric Pulmonology 42 (suppl.30), 411.
Moureau, N., 2006. Vascular safety: it's all about PICCs. Nursing Management37(5), 22-27.
Moureau, N., Poole, S., Murdock, M., Gray, S., Semba, C., 2002. Central venous catheters in home infusion care: outcomes analysis in 50,470 patients. Journal of Vascular and Interventional Radiology13 (10), 1009-1016.

Nash, E., Helm, E., Stephenson, A., Tullis, E., 2009. Incidence of deep vein thrombosis associated with peripherally inserted central catheters in adults with cystic fibrosis. Journal of Vascular and Interventional Radiology20 (3), 347-351.
Ngo, A., Murphy, S., 2005. A theory-based intervention to improve nurses' knowledge, self-efficacy, and skills to reduce PICC occlusion. Journal of infusion nursing28 (3), 173 - 181.
Parkins, M., Parkins, V., Rendall, J., Elborn, S., 2011. Changing epidemiology and clinical issues arising in an ageing cystic fibrosis population.Therapeutic Advances in Respiratory Disease 5(2), 105-119.
Pellegrino, R., Viegi, G., Brusasco, V., Crapo, R., Burgos, F., Casaburi, R., Coates, A., van der Grinten, C., Gustafsson, P., Hankinson, J., Jensen, R., Johnson, D.,MacIntyre, N., McKay, R., Miller,M., Navajas, D., Pedersen, O., Wanger, J., 2005. Interpretative strategies for lung function tests. European Respiratory Journal26, (5), 948-968.
Raad, I., Hanna, H., Maki, D., 2007. Intravascular catheter-related infections: advances in diagnosis, prevention, and management. The Lancet Infectious Diseases 7(10) 645-657.
Raffini, L., Raybagkar, D., Blumenstein, M., Rubenstein, R., Manno, C., 2006. Cystic fibrosis as a risk factor for recurrent venous thrombosis at a pediatric tertiary care hospital. Journal of paediatrics 148 (5), 659-64.
Smith, J., Kirksey, K., Becker, H., Brown, A., 2011. Autonomy and Self-efficacy as Influencing Factors in Nurses' Behavioral Intention to Disinfect Needleless Intravenous Systems. Journal of Infusion Nursing34 (3), 193-200.
SPSS, 2009.PASW Statistics for Windows, Version 18.0.SPSS Inc. Chicago.
Smith S., Sinclair, D., Raine, R., Reeves, B., 2005. Understanding public health.Health Care Evaluation.<http://site.ebrary.com/lib/unisaau/docDetail.action?docID=10175202>.
Sprizza, L., Witko, A., 2003. The ABCs of DVT. Medsurg Nursing 12 (6), 403-5.
Stata, 2009. Stata Statistical Software: Release 11. StataCorp LP. Texas.
Syed, F., Beeching, N., 2005. Lower-limb deep-vein thrombosis in a general hospital: risk factors, outcomes and the contribution of intravenous drug use. Quarterly Journal of Medicine 98 (2), 139-145.
Tolomeo, C., Mackey, W., 2003. Peripherally inserted central catheters (PICCs) in the CF population: one center's experience. Pediatric Nursing 29 (5), 355-359.
Turner, M., Unsworth, V., David, T., 2002. Intravenous long-lines in children with cystic fibrosis: a multidisciplinary approach. Journal of the Royal Society of Medicine 95 (Suppl.41), 11-21.
Veiraiah, A., Shetty, H., Routledge, P., 2008. Prevention and treatment of venous thromboembolism in older people. Reviews in Clinical Gerontology 18 (3) 219-228.
World Health Organisation 2011. International Classification of Diseases. <http://www.who.int/classifications/icd/en/>.
World Health Organisation 2012.Genes and human disease.
< http://www.who.int/genomics/public/geneticdiseases/en/index2.html#CF >.