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Original article

Catheter-related infections in patients with acute type II intestinal failure admitted to a national centre: Incidence and outcomes

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SUMMARY

Introduction: The management of intestinal failure (IF) requires safe and sustained delivery of parenteral nutrition (PN). The long-term maintenance of central venous catheter (CVC) access is therefore vital, with meticulous catheter care and salvage of infected CVCs being of prime importance. CVC-related infection and loss of intravenous access are important causes of morbidity and mortality in IF. Avoidance, prompt recognition and appropriate management of CVC-related infections are crucial components of IF care. However, there are few, if any, data on the occurrence of CVC-related infections in patients with acute, type 2, IF managed on a dedicated IF unit and no data on the salvage outcomes of infected CVCs in this group of patients.

Methods: This is a retrospective observational study conducted between January 2011 and July 2017. All patients with acute, type 2 IF newly admitted to a national U.K. IF unit (IFU) during these dates were included. All patients admitted to the unit with a CVC in place underwent immediate 'screening' paired central and peripheral blood cultures on arrival before the CVC was used for any infusate. A prospectively maintained database was used to record all confirmed catheter-related blood stream infections (BSI)/colonisations, demographic and clinical data. Diagnosis of catheter-related BSI/colonisation was based on quantitative and qualitative analysis of paired central and peripheral blood cultures. A standardized 10–14-day catheter salvage treatment protocol involving antibiotic and urokinase CVC locks and systemic antibiotic administration was used to salvage any infected or colonised CVCs, as appropriate. The CVC was not used for PN until successful salvage had been confirmed by negative blood cultures drawn 48 h after antibiotic completion. The development of a subsequent catheter-related BSI was recorded for all patients, both during the remaining in-patient stay on the IFU and after discharge home on PN.

Results: Of the 509 patients with type 2 IF admitted to the IFU during the study period, 341 (54% female; mean age 54.6 (range 16–86 years)) had an indwelling CVC that had been placed in the referring hospital. Surgical complications and mesenteric ischaemia were the most common underlying disease aetiologies. Sixty-five of 341 (19.1%) patients had an infected/colonised CVC on the initial screening set of blood cultures. A successful CVC salvage rate of 91% was achieved in this cohort after antibiotic therapy. The subsequent in-patient catheter-related BSI rate for those admitted with a CVC ($n = 341$) on the IFU was 0.042 per 1000 catheter days, over a total of 23,548 in-patient catheter days. Two hundred and seventy nine of 341 patients were discharged on home PN (HPN); with a subsequent catheter-related BSI rate on HPN of 0.22 per 1000 catheter days (mean duration of HPN = 778 catheter days (range:)) over a follow-up period of 216,944 out-patient catheter days. There was no increased risk of HPN-related catheter-related BSI ($p = 0.09$) or mortality ($p = 0.4$) in those admitted with an infected CVC.

Conclusion: This is the first study to report catheter-related BSI/colonisation rates and salvage outcomes in patients with type 2 IF newly admitted to a dedicated IF Unit. We report that nearly one-fifth of all patients were referred with evidence of a catheter related BSI/colonisation; despite this, successful catheter salvage is possible and, with stringent CVC care, an extremely low subsequent catheter related

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BSI rates can be achieved and maintained during in-patient stay on a dedicated IF Unit and after discharge on HPN. These data provide novel evidence to support ESPEN recommendations that patients with type 2 IF are managed on a dedicated IF Unit.

1. Introduction

Type 2 intestinal failure (IF) is defined as a prolonged acute condition, in metabolically unstable patients, requiring multidisciplinary care and intravenous supplementation over periods of weeks or months [1,2]. Safe and sustained delivery of parenteral nutrition (PN) via a dedicated central venous catheter (CVC) are key to the successful management of this complex condition [2], both while the patient remains an in-patient and following subsequent discharge on home PN (HPN) [1,3]. CVCs are at risk of infection, with reported incidences of catheter-related blood stream infections (BSI) in the Home PN (HPN) setting ranging from 0.31 to 11.5 per 1000 catheter days [1,4–6].

Reports of the incidence of catheter-related BSI in-patients receiving PN in hospital have also provided highly variable results. Catheter-related BSIs are common in patients receiving and not receiving PN and account for 10%–20% of hospital-acquired infections in the U.K.; such infections are, of course, a concern since they are associated with both increased Intensive Care Unit (ICU) stay and mortality [7]. Notably, in-patient catheter-related BSI rates vary internationally, between institutions and even between different departments of the same institution. For example a national assessment of catheter-related BSI from the U.S.A. showed the median rate of catheter-related BSIs in ICUs of all types ranged from 1.8 to 5.2 per 1000 catheter days [8]. Further studies have reported rates (per 1000 catheter days) of 5.1 for medical-surgical ICUs, 5.8 for trauma ICUs and 30.2 for burn units [7,9]. In the general surgical and medical ward setting, catheter-related BSI rates have also been shown to vary, with some studies reporting rates as high as 20.5 per 1000 catheter days [10–12].

ESPEN guidance on the management of chronic IF suggests that the incidence of catheter-related BSI can be used as a quality indicator of care for the patient dependent on home PN (HPN) [3]. Furthermore, guidelines for the management of acute, type 2 IF recommend that patients are managed on a dedicated IFU unit (IFU), suggesting that this may lead to a lower catheter-related BSI rate in these metabolically-vulnerable patients [1]. However, it is noteworthy that there are no data on the incidence of catheter-related BSIs on a dedicated IFU to-date to support these guidelines.

Once infected, current guidelines suggest that CVC salvage is paramount for preserving long term venous access in patients with chronic, type 3, IF [3]. However, CVC salvage is also relevant to patients with type 2 IF, not least because around 70% of such patients will be discharged home with type 3 IF and require PN via a CVC for months or years, and sometimes lifelong [2]. Recent publications have demonstrated that successful salvage rates between 67 and 72.5% can be achieved for patients with type 3 when managed with systematic protocols involving systemic antibiotics and antibiotic CVC locks [4,5,13]. However, there are, as yet, no published data on the epidemiology and salvage outcomes of infected CVCs in patients purely with type 2 IF.

With this study, we aimed to evaluate the occurrence of CVC-related infection or colonisation in new patients with type 2 IF referred to a national unit as well as the CVC salvage success rate of these infected or colonised CVCs. We also aimed to determine the subsequent catheter-related BSI rates of these patients, both during their in-patient stay on the IFU and after discharge home on PN.

2. Methods

2.1. Study cohort

This is a retrospective observational study conducted between January 2011 and July 2017. All new patients with type 2 IF admitted to the IFU during these dates were eligible for inclusion. A prospectively maintained database was used to record microbiological, demographic and clinic data.

2.2. Study protocol

Because of our historical experience of high catheter-related BSI/colonisation rates in patients referred from other hospitals, the standard protocol relating to CVCs at admission to our IFU dictates that paired central and peripheral blood cultures are taken and results obtained confirming the absence of CVC infection or colonisation before the CVC is used for any infusate; this includes all patients with an indwelling CVC, even without systemic signs of infection. Diagnosis of catheter-related BSI/colonisation (see below) on admission, or any subsequent CRBSI after admission on the IFU or after discharge on HPN, was based on quantitative and qualitative analysis of paired central and peripheral blood cultures [14,15]; specifically, a confirmatory positive diagnosis required greater than 4-fold higher colony count in the central vs. peripheral pour plates.

A standardized 10–14-day catheter salvage treatment protocol involving antibiotic and urokinase CVC locks and systemic antibiotic administration was used to salvage any colonised/infected catheters, as appropriate [5]. The 10-day protocol was used exclusively for coagulase negative *Staphylococcus*, with the 14 day protocol being used for all other pathogens [4]. The CVC was not used for systemic therapy for the duration of the salvage protocol. Repeated sets of peripheral and central blood cultures were taken 48 h after completion of antimicrobial therapy to confirm salvage success or failure; in the case of the latter, the CVC was removed and replaced. Failed salvage was defined as recurrent positive blood cultures identified from a catheter lumen at the end of the salvage therapy [4,5]. Salvage was not performed in any patient with a fungal or methicillin-resistant *Staphylococcus aureus* (MRSA) pathogen identified, or any patient with a mal-positioned CVC position; in these instances, the CVC was removed and replaced.

2.3. Definition of catheter-related BSI/colonisation on 'screening' cultures on admission to the IFU

Since all indwelling CVCs were immediately screened on admission to the IFU using paired central and peripheral blood cultures, patients were not assessed for the development of clinical symptoms on CVC infusion. Thus, a CVC with positive results identified on screening central/peripheral blood cultures on admission may have represented an infected CVC or a CVC colonised with micro-organisms. Therefore, the term 'catheter-related

BSI/colonisation' was used to denote a CVC demonstrated to have greater than 4-fold higher colony count in the central vs. peripheral pour plates on screening admission blood cultures.

2.4. Definition of CRBSI during subsequent in-patient stay or after discharge on HPN

Following any salvage of any infected or colonised CVC on admission, the subsequent diagnosis of a catheter-related BSI was made in any patient presenting with clinical signs of sepsis during their subsequent in-patient stay or after discharge home, in tandem with quantitative and qualitative analysis of paired central and peripheral blood cultures.

2.5. Data collection and statistical analysis

Data collected included age, gender and type of CVC at admission. ESPEN classifications were used to categorise pathophysiology and underlying aetiology leading to IF [16]. For patients with a catheter-related BSI/colonisation diagnosed on admission, the isolated microorganism/s and salvage success were recorded. Categorical variables have been summarised as frequency (%) and continuous variables as mean and/or median. Univariate analysis was performed by Student's *t*-test, Fisher's exact test and χ^2 test. A p value of <0.05 was considered as statistically significant.

3. Results

3.1. Patient demographics and CVC types

Between the 1st January 2011 and 30th June 2017, 509 (mean age 55.1 years (range 16–87 years); 57.5% female) patients with type 2 IF were admitted to the IFU. Of these, 341 (66.9%) already had indwelling CVC which had been placed at the referring hospital. The type of existing CVC at admission can be seen in Table 1.

3.2. IF pathophysiology and underlying disease aetiology

Of the 341 patients admitted with an indwelling CVC, 149 (43.7%) had underlying short bowel syndrome responsible for their IF (SBS-IF), with the presence of a jejunostomy (SBS-J) being the most common SBS-IF pathophysiological category (Table 2). Surgical complications, mesenteric ischaemia and Crohn's disease were the principal underlying diseases in this patient cohort (Table 3). Sixty-five of the 341 (19.1%) patients admitted with an indwelling CVC had a diagnosis of catheter-related BSI/colonisation on the initial screening set of blood cultures. The relationships between IF pathophysiology, underlying disease aetiology and catheter-related BSI/colonisation rates are summarised in Tables 2 and 3

3.3. Causative pathogens and CVC salvage

CVC salvage was attempted in 24 of the 63 patients found to have catheter-related BSI/colonisation, with 22/24 (91%) deemed to have been successful on the basis of negative paired central and peripheral blood cultures 48 h after antibiotic completion. Details of the causative pathogens, salvage attempts and their success are summarised in Table 4. Thirty-one patients admitted with a catheter-related BSI/colonisation did not undergo salvage attempt because of causative pathogen/s and/or poor CVC tip position; in all such patients, the infected CVC was removed and replaced. Of those patients with successful salvage, 2 went on to develop future catheter-related BSI. One patient developed catheter-related BSI during their subsequent HPN management, 491 days after the salvage. The second occurred whilst an inpatient prior to discharge, 134 days after the initial CVC salvage; notably, this catheter-related BSI occurred as a result of a different pathogen from the initial causative organism on admission. Both these salvage attempts were considered sustained successful salvage because the subsequent catheter-related BSI occurred greater than 90 days after the initial catheter-related BSI/colonisation on admission [4].

Table 1
Type and number of indwelling CVC in situ for the patients at the point of admission to the IF unit. Other CVCs included portacaths and quad lumen catheters.

Type of CVC on admission	Number (%)
PICC	145 (42.5)
Tunnelled (Broviac or Hickman CVC)	133 (39)
Subclavian	51 (14.9)
Other	12 (3.5)

Table 2
Pathophysiological diagnoses of the 341 patients admitted with an indwelling CVC, along with the number of catheter-related BSI/colonisations on admission in each group.

Pathophysiology	Number (%)	Number with catheter-related BSI/colonisation on admission (%)
SBS-J	109 (31.9)	20 (19.3)
SBS-I	23 (6.7)	5 (21.7)
SBS-JC	14 (4.1)	1 (7.1)
SBS-JIC	3 (0.8)	1 (33.3)
Obstruction	26 (7.6)	3 (11.5)
Fistula	126 (36.8)	27 (22.2)
Motility	33 (9.7)	5 (15.2)
Mucosal disease	9 (2.6)	1 (11.1)

Table 3
Underlying aetiology for the 341 patients admitted with an indwelling CVC, along with the number of catheter-related BSI/colonisations on admission in each group.

Underlying aetiology	Number (%)	Number with catheter-related BSI/colonisation on admission (%)
Surgical complications	133 (38.9)	30 (23.3)
Mesenteric ischaemia	57 (16.7)	9 (17.5)
Crohn's disease	47 (13.7)	10 (21.2)
Cancer	32 (9.4)	5 (15.6)
CIPO primary	24 (7.0)	4 (16.6)
CIPO secondary	10 (2.9)	1 (10)
Radiation enteritis	9 (2.6)	1 (11.1)
Diverticular	6 (1.7)	1 (16.6)
Bariatric surgery	5 (1.4)	1 (20)
Collagenous vascular	3 (0.8)	0
NET	3 (0.8)	0
Trauma	3 (0.8)	1 (33.3)
Adhesions	2 (0.5)	0
Volvulus	2 (0.5)	0
Other	2 (0.5)	0
Desmoid	1 (0.2)	0
Neurological	1 (0.2)	0
Ulcerative colitis	1 (0.2)	0

3.4. Predictors of catheter-related BSI/colonisation at admission

None of the measured variables were identified as predictors of catheter-related BSI/colonisation at index admission. This included SBS-IF vs. non-SBS-IF ($p = 0.8$) as the underlying disease aetiology, pathophysiological classifications ($p = 0.6$), underlying aetiology ($p = 0.7$), type of CVC at admission ($p = 0.1$) and gender ($p = 0.4$).

Table 4
Summary of the pathogens isolated, salvage attempts and their success.

Isolated pathogen	Number	Number with attempted salvage	Number with successful Salvage
Coagulase negative staphylococcus (CNS)	22	11	10
Gram positive (other than *Staphylococcus* sp.)	13	7	6
Polymicrobial	8	2	2
Gram negative	7	4	4
Fungus	6	0	NA
Staphylococcus aureus (MSSA)	3	0	NA
Klebsiella sp	2	0	NA
Methicillin resistant *Staphylococcus aureus* (MRSA)	1	0	NA
Unknown	1	0	NA

3.5. Follow-up: in-patient

Of the 341 patients admitted to the IFU with an indwelling CVC placed at the referring hospital, including the 65 identified to have a catheter-related BSI/colonisation at admission on screening cultures, only 1 (0.3%) patient suffered from a subsequent inpatient catheter-related BSI during the in-patient stay on the IFU; this equates to an IFU catheter-related BSI rate of 0.04 per 1000 catheter days for a total of 23 548 in-patient catheter days. There were no inpatient deaths attributable to catheter-related BSI in any patient.

3.6. Follow-up: outpatient on HPN

279 of the 341 patients were discharged on HPN with an indwelling CVC; these patients remained on HPN for a mean of 777.5 (range 28–2452) catheter days during the follow-up period. Following discharge on HPN, 42 patients developed a subsequent HPN-related catheter-related BSI after discharge, equating to an out-patient (HPN) catheter-related BSI rate 0.22 per 1000 catheter days, with no increased likelihood for those patients with a catheter-related BSI/colonisation at their index admission, $p = 0.09$. There was also no difference in patient survival when comparing those with and without index admission CRI, $p = 0.4$, Fig. 1. There were no reported deaths directly attributed to catheter-related BSI in the HPN cohort.

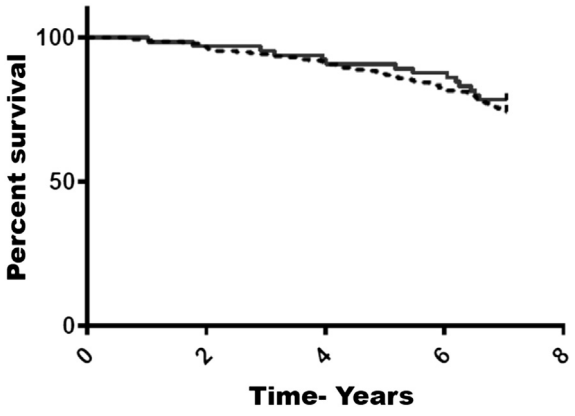

Fig. 1. Kaplan Meier curve demonstrating survival for those with and without CRI at index admission. *Dotted line represents those admitted to IFU without* catheter-related BSI/colonisation, *solid line those with* catheter-related BSI/colonisation *on initial cultures.*

4. Discussion

This study is the first to report catheter-related BSI/colonisation rates and salvage outcomes in patients with type 2 IF admitted to a dedicated IFU. We report that nearly one-fifth of all patients had contracted a catheter-related BSI/colonisation in the referring hospital that was identified on screening blood cultures on admission to the IFU; despite this, successful catheter salvage is possible and stringent CVC care with aseptic strategies can achieve a very low catheter-related BSI rate of 0.04 per 1000 catheter days during the subsequent in-patient stay on a dedicated IF Unit. Furthermore, once treated, by CVC salvage or replacement, the presence of a catheter-related BSI/colonisation on admission did not influence future risk of catheter-related BSI occurrence.

Although current guidelines do not recommend screening blood cultures to detect CVC colonisation in the HPN setting, our long-term experience had suggested that in-patients with indwelling CVCs admitted from other hospitals to the IFU had a high incidence of catheter-related BSI or colonised CVCs. Indeed, we were able to confirm this experience in the present paper, demonstrating that almost one fifth of patients admitted to our unit had evidence of a catheter-related BSI/colonisation on screening cultures. It is noteworthy that the catheter-related BSI/colonisation had not been recognised by the referring team prior to admission to our unit, despite the continued infusion of PN in the referring hospital. Since screening blood cultures are taken routinely on admission in all patients admitted with an indwelling CVC to our IFU, we are unable to report the symptoms on PN infusion through any infected catheter after admission or whilst awaiting culture results. The apparent failure to recognise CVC-related infection in referring hospitals may be because the diagnosis of a catheter-related BSI can be difficult as patients often do not present with classical symptoms of pyrexia or elevated WCC whilst feeding [17]. Alternatively, and as outlined above, the positive culture results may have simply reflected the fact that the CVC was colonised with microbes in asymptomatic individuals. Nonetheless, since there is a risk that continued PN infusion may serve as an infective milieu, identification of CVC colonisation is clearly important to attempt to reduce the risk of the associated morbidity resultant from subsequent catheter-related BSI development.

Sepsis remains the principle cause of death in patients with type 2 IF [1,2]. While much of this results from intra-abdominal sepsis, related to the underlying disease aetiology of type 2 IF [18], the need to avoid the morbidity and mortality resultant from any concomitant catheter-related BSI in these already metabolically unstable individuals should not be under-emphasised. Indeed, the risk to life of an acquired catheter-related BSI is significant; overall, catheter-related BSI s have a reported attributable mortality rate of between 12% and 25% [19], with a study published last year including 546 cases of catheter-related BSIs, reporting a 13.9% 30-day mortality rate across a number of different clinical specialities [19]. Therefore, early identification and management of any source of sepsis – CVC-related, intra-abdominal, or elsewhere – is vital in these vulnerable patients, as reflected in the algorithmic management strategies of type 2 IF advocated by international authorities [1], including the 'Sepsis-Nutrition-Anatomy-Plan' (SNAP) and 'Sepsis-Optimisation of Nutritional Status-Wound Care-Anatomy-Surgical Timing and Strategy' (SOWATS) approaches. Furthermore, and as demonstrated in this study, since 80% of patients with type 2 IF needed long term HPN, continued attempts to reduce the risk of subsequent catheter-related BSIs are also vital to sustain safe long term CVC access; indeed, the HPN catheter-related BSI rate of 0.2 per 1000 catheter days of this patient cohort is amongst the lowest catheter-related BSI rate published to-date in type 3 IF [4,20].

It may be worth highlighting that the in-patient IFU catheter-related BSI rate of 0.04 per 1000 catheter days on the IFU is – to our knowledge – the lowest published in-patient catheter-related BSI rate in any patient cohort. Given the complexity of the condition, ESPEN guidance on the management of type 2 IF states that to 'improve the outcome of acute IF, it is recommended that the treatment is provided by dedicated, experienced and multidisciplinary teams, in units with adequate diagnostic, therapeutic and financial resources' [1]. These ESPEN guidelines state 'catheter-related BSI rates in experienced referral centres can be expected to range from 0.14 to 1.09 episodes per catheter year' (this equates to 0.38 to 2.9 per 1000 catheter days); these guidelines use Pironi et al. [3] and Dreesen et al. [20] to support this statement. However, it is noteworthy that both of the latter two papers refer to catheter-related BSI rates in patients with type 3 IF on long term HPN, not those with type 2 IF managed in a dedicated IFU [1,20–25]. Furthermore, while quality improvement measures may be able to reduce the catheter-related BSI rates in patients receiving PN on the general hospital ward to around 0.7 per 1000 [11] the latter figure is still greater than 17-fold higher than the 0.04 in-patient catheter-related BSI rate reported in this study. Thus, the very low in-patient catheter-related BSI rate in patients with type 2 IF presented in this paper provides novel data to strongly support ESPEN Guidelines on the role of the dedicated IFU in managing patients with type 2 IF. In the future, we propose that all dedicated IFUs aim to class catheter-related BSI as a 'never event', which have been defined as serious incidents that are entirely preventable because guidance or safety recommendations providing strong systemic protective barriers are available [26].

5. Conclusion

Meticulous catheter care in type II and type III IF can allow for ultra-low rates of catheter-related BSI. Patients with catheter-related BSI/colonisation can achieve high levels of CVC salvage preventing unnecessary CVC removal and reducing the risk of secondary septic complications. Future work is required to disseminate best practise and reduce the occurrence of catheter complications in all IFUs and general wards managing patients requiring PN.

Conflict of interest

None declared.

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