Central Venous Catheter Associated Bloodstream Infections and Thrombosis in Patients Treated for Gastroschisis and Intestinal Atresia: a Retrospective Cohort Study of 238 Patients

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Abstract

Background: Central venous catheter related complications, mainly central line associated bloodstream infections (CLABSI) and thrombosis, can complicate treatment of intestinal atresia or gastroschisis. Incidences and risk factors, e.g., location (central versus peripheral inserted) or mode of insertion (tunnelled versus non-tunnelled), of these complications are widely unknown. Therefore, we aim to identify the incidence of and risk factors for CLABSI and thrombosis in these patients.

Methods: Children treated for intestinal atresia or gastroschisis between 1998-2021 at our tertiary referral center were retrospectively included. Risk factors for CLABSI were identified using logistic regression and the correlation between thrombosis and location/mode of insertion was evaluated using chi^2-tests.

Results: In 238 patients, 35% developed CLABSI and 7% thrombosis. Treatment by enterostomy (OR:3.1;95%-CI:1.5–6.4) and non-tunnelled catheters (OR:2.0;95%-CI:1.3–4.6) significantly increased the CLABSI-risk whilst patient's sex, catheter placement directly into central vein, preterm birth, trisomy 21, experiencing a major postoperative complication (Clavien-Dindo grade ≥III) and birthweight didn't. Catheter dwell time was shorter ($p<0.01$) and CLABSIs developed faster ($p=0.02$) in non-tunnelled compared to tunnelled catheters. Catheter related thrombosis occurred more often in non-tunnelled catheters ($p=0.03$), whilst no correlation ($p=0.34$) was found between location of insertion.

Conclusion: CLABSI occurs in approximately one third of the children treated for intestinal atresia or gastroschisis and a catheter related thrombosis occurs in one in fourteen. When in doubt which catheter to use in these patients, a tunnelled catheter is preferred over a non-tunnelled, specifically in case of enterostomy formation, since a tunnelled catheter is comparatively less at risk of catheter related infections and thrombosis.

What Is Currently Known About This Topic?

Central venous catheter related complications can complicate treatment of intestinal atresia or gastroschisis.

What New Information Is Contained In This Article?

CLABSI occurs in approximately one-third and catheter related thrombosis in one in fourteen. When in doubt which catheter to use in these patients, a tunnelled catheter is preferred over a non-tunnelled, specifically in case of enterostomy formation.

Introduction

Total parenteral nutrition (TPN) via a central venous catheter is essential in the treatment of children with an intestinal atresia or gastroschisis. Without TPN, patients would experience severe malnutrition

because of impaired intestinal function. The duration of TPN feeding is a median of 26 days in gastroschisis patients and 20 days in intestinal atresia patients [1, 2].

The central venous catheters used to administer parenteral nutrition differ in the mode of insertion, either tunnelled subcutaneously before entering a vein or non-tunnelled, and the anatomical location of the vein used for insertion, either a large central vein or a smaller peripheral vein. The choice between these types of central venous catheters is a trade-off between the advantages and disadvantages. For instance, tunnelling the catheter subcutaneously before entering the vein supposedly results in less central venous catheter associated bloodstream infections (CLABSIs) [3]. Moreover, a cuffed segment of a tunnelled catheter adheres to the body, limiting the risk of dislocation which can be a problem when using non-tunnelled catheters [3]. However, tunnelled central venous catheters have to be placed surgically, necessitating operation room capacity and general anaesthesia. A non-tunnelled central venous catheter can often be placed in the ward under local anaesthesia. Inserting a central venous catheter in a peripheral vein can also be done in the ward and is supposed to have less risks of iatrogenic damage, such as pneumothorax, which can occur during direct insertion into a central vein. Furthermore, peripherally inserted central venous catheters seem to have a slightly lower risk of CLABSI compared to centrally inserted catheters in pediatric intensive care patients in general [4]. However, it is assumed that catheters inserted in a peripheral vein have an increased risk of thrombosis, through a number of mechanisms, including injury of the vessel wall by both parenteral nutrition and the catheter, chronic inflammation and disruption of blood flow, compared to catheters which are directly inserted into a central vein [3]. Although it must be noted that this increased risk is most profound in patients treated for cancer or patients with chronic intestinal failure treated with TPN at home[5].

American national database studies, which included over 2000 pediatric patients, showed that patients treated for gastroschisis or intestinal atresia who received a central line are seemingly more at risk of CLABSI compared to pediatric patients in general, but they were limited in the amount of risk factors they could analyse [6, 7]. Moreover, they did not look into the risk of catheter related thrombosis which is why the incidence of this complication is still unknown.

Therefore, this retrospective cohort study aims to identify the incidence of and risk factors for CLABSI and central venous catheter associated thrombosis in patients treated for intestinal atresia and gastroschisis.

Methods

Patients and management

Our institute's data managers retrieved all children undergoing surgery for gastroschisis, intestinal atresia or a combination of both defined as complex gastroschisis between January 1998 and October 2021 from the Amsterdam university hospital database. The local medical ethical commission evaluated the study, it received the reference number W18_233#18.278. An opt-out letter was sent to patients and

parents, which they could return within one month if they did not wish to participate. Following this period, patient records were checked. Eventually, the data of the included patients was stored in Castor EDC [8]. The patient reports were read by a dedicated PhD-candidate (LES), in case of doubt a paediatric surgeon (JD) was consulted.

Current protocol

Our current protocol advises, in case of an estimated need of a central venous catheter for 30 days or less, the placement of a peripheral central venous catheter. These catheters are in general placed by the neonatologist in patients younger than one month and by the anaesthesiologist or interventional radiologist in patients older than one month. If central venous access is estimated to be needed for a period longer than 30 days a centrally placed, tunnelled catheter (Broviac©) is placed by the pediatric surgeon. No preventative measures other than basic hygiene, for instance antibiotic prophylaxis, are recommended to prevent CLABSIs. When it is expected that the catheter will be in place for longer than six weeks low molecular weight heparin is given to prevent thrombosis.

Data extraction

Patients were categorized according to a diagnosis of intestinal atresia or gastroschisis. A gastroschisis was deemed to be complex when both a gastroschisis and intestinal atresia were diagnosed. Mode of treatment for gastroschisis (SILO or primary closure) was extracted from surgical reports. Moreover the location of the atresia was noted as well as the type of atresia (using the Martin-Zarella classification) in case of jejunoileal atresias [9]. The following comorbidities were noted if present: duodenal web, annular pancreas, malrotation, midgut volvulus and meconium peritonitis.

Furthermore, information was extracted concerning: patients' sex, prematurity (defined as < 37 week gestational age), if the patient was diagnosed with trisomy 21, age at surgery, if the patient received an enterostomy as part of treatment, if the patient had a major postoperative complication (defined as Clavien-Dindo grade III or higher) in the first 30 days following surgery (excluding re-operations of placement of new central venous catheter only) [10], duration of hospital stay, number of abdominal surgical procedures received, mortality and length of follow-up.

The occurrence of a CLABSI was noted if an organism was cultured from the blood from a central venous catheter (one or two bottles) that was in place for at least two days without having a bacterial infection based on other aetiology. The occurrence of a central venous catheter associated thrombosis was noted only in case of clinical suspicion (e.g., unexplained thrombocytopenia or line occlusion) which was confirmed radiologically by ultrasound. Asymptomatic thrombosis was excluded. These complications (CLABSI and catheter associated thrombosis), as well as catheter removal due to the complication, were noted separately with a maximum of the first three consecutive central venous catheters placements in each patient.

For the first placed central venous catheter the following was extracted: complications directly occurring following catheter placement (incision on other side of the neck necessary because of problems

identifying jugular veins, postoperative catheter tip readjustment necessary due to improper location on the X-ray following placement or pneumothorax), time from first admission until insertion, if the catheter was inserted directly into a central vein (meaning in the internal or external jugular vein, subclavian vein or femoral vein) either initially or following failure of peripheral insertion) or if insertion was done via a peripheral vein (all other veins used), if the catheter was tunnelled, catheter dwell time (meaning duration between insertion and removal of the catheter), the organism cultured at CLABSI diagnosis (organisms were classified as common commensals using National Healthcare Safety Network (NHSN) list from the Centre for Disease Control and Prevention (CDC))[11], if other mechanical complications occurred (occlusion, dislocation or leakage), if death due to a central venous catheter complication occurred and if no central venous catheter associated complication occurred. It was also noted if the patient received a new central venous catheter up to the third central venous catheter. Occurrence of a CLABSI or a thrombosis were also noted for these central venous catheters.

Patients with missing information on date of catheter placement or removal or patients that were transferred to another hospital before catheter removal were excluded.

Statistical analysis

Descriptive characteristics were reported as median with range in case of non-normally distributed variables or mean ± standard deviation (SD) in normally distributed variables. Comparison between groups was performed using chi-squared test for categorical data, Student's T-test for parametric continuous data and the Mann-Whitney U test for non-parametric continuous data. CLABSI per 1000 days of duration of catheter stay was calculated using data from the first three inserted catheters. Lastly, a 1-Kaplan-Meier curve was composed with accompanying log-rank test to compare tunnelled versus non-tunnelled catheters in CLABSI occurrence.

Multivariable logistic regression analysis was performed on the outcome of CLABSI occurrence of the first inserted central venous catheter. The assumption of linearity of the logit of ordinal variables was assessed using the Box-Tidwell test. Backward Wald selection was used for selection of variables using the standard $p = 0.10$ for variable removal. Assessment of confounding (increase in B-coefficient of > 10%) and effect modification (significant interaction term). Significant risk factors were reported in odds ratio (OR) with 95% confidence intervals (95%-CI). Additionally, the adjusted R-squared is reported to show the proportion of the variance in the occurrence of CLABSI explained by the model. As part of a sensitivity analysis, a multivariate logistic regression analysis was repeated using only the CLABSIs that led to the removal of the central venous catheter as outcome variable.

Chi-squared testing was used to analyse if there was a significant association between tunnelled or centrally inserted catheters and thrombosis.

Results

Patient and surgical characteristics

In total 262 patients with intestinal atresia or gastroschisis were operated within the study period. In 22 patients there was no information on central venous catheter placement or removal and two patients were transferred to another hospital before catheter removal. Excluding these patients left a total of 238 patients. Baseline characteristics of these patients are displayed in Table 1. The type and location of the atresia in those treated for intestinal atresia and complex gastroschisis is provided in Table 2.

Out of all patients 74% (N = 175/238) were treated for intestinal atresia and 26% (N = 63/238) for gastroschisis. Out of all gastroschisis patients, 22% (N = 14/63) were treated for a complex gastroschisis which was 6% (N = 14/238) of the overall cohort. Gastroschisis was treated by primary closure in 64% (N = 40/63) of the patients. An enterostomy was created in 23% (N = 55/238) of all patients. Following surgery 22% (N = 53/238) of the children developed a Clavien-Dindo grade three or higher. Redo-surgery (due to adhesive obstructions, anastomotic leakage or stoma complications) accounted for 66% (N = 35/53) of these complications, whilst ICU admission accounted for 26% (N = 14/53) and death within 30 days following surgery for 8% (N = 4/53) of these complications. All deaths occurred in patients with associated trisomy 21 who experienced a postoperative infection (one caused by an anastomotic leakage, one CLABSI and two cases of sepsis of unknown origin) leading to multi-organ failure which resulted in their deaths.

Complications associated with central venous catheter placement

Table 3 provides an overview of the central venous catheter associated complications during and following insertion of the first central venous catheter. Out of all patients, a CLABSI developed in 34% (N = 82/238) and a catheter associated thrombosis in 7% (N = 16/238). This occurrence of CLABSI did not differ if we split the cohort in patients operated before or after the year 2010 (p = 0.98)

Following placement of the central venous catheter, postoperative readjustment of the catheter tip was the most common complication directly occurring following placement. It occurred occurring in 10% (N = 23/238) of the patients treated for intestinal atresia and in 21% (N = 13/63) of those treated for gastroschisis respectively. Of these readjustments, 35% (N = 8/23) occurred in tunnelled catheters whilst all other were non-tunnelled. Central venous catheter placement did not cause a pneumothorax in any of the patients. The central venous catheter was peripherally inserted in 28% (N = 65/238) of all patients (intestinal atresia, 30%, gastroschisis 19%) and directly into a central vein in 72% (N = 173/238) of all patients (intestinal atresia: 70%, gastroschisis: 81%). Furthermore, the central line was tunnelled in 73% (N = 173/238) of all patients (intestinal atresia: 76%, gastroschisis: 65%). The median catheter dwell time was 20 days (IQR: 13–30) in those treated for intestinal atresia and 25 (IQR: 14–18) days in those treated for gastroschisis.

A CLABSI developed in 35% (N = 82/238) and resulted in removal of the central venous catheter in 68% (N = 56/82) of the children. Appendix A provides an overview of the pathogens cultured from the blood showing 62% (N = 51/82) of the cultured bacteria were common commensals (CNS, S. Epidermis or S. Hominis). CLABSIs that were caused by common commensals did not lead to a significant higher rate of

removal of the central venous catheter than those caused by other pathogens (p = 0.14). Of all patients treated for intestinal atresia, 30% (N = 53/175) developed a CLABSI which occurred after a median of 16 days (IQR: 8–28). CLABSI occurred in 46% (N = 29/63) of the gastroschisis patients in a median of 19 days (IQR: 12–41). Patients that developed a CLABSI related to their first inserted central venous catheter stayed in the hospital for a median of 37 days (IQR: 22–67) whilst those that did not develop a CLABSI had a median length of stay of 24 days (IQR: 18–37 days) which was significantly shorter (p < 0.01). One patient's death was directly related to the CLABSI. This patient, treated for an intestinal atresia and diagnosed with trisomy 21, died due to ongoing respiratory and circulatory insufficiency following CLABSI development.

A central venous catheter associated thrombosis was seen in 7% (N = 16/238) of all patients. In those treated for intestinal atresia 7% (N = 12/175) thrombosis developed in a median of 11 days, whilst thrombosis occurred in 6% (N = 4/63) of the gastroschisis patients in a median of 19 days. The central venous catheter was removed in all cases of catheter related thrombosis. Therapeutic anticoagulant therapy was started in all cases without complications related to this treatment. such as bleeding. The occurrence of catheter associate thrombosis did not differ between the cohort operated before and after the year 2011 (p = 0.48)

No central venous catheter associated infection or thrombosis occurred in 62% (N = 108/175) and 40% (N = 25/63) of the patients treated for intestinal atresia and gastroschisis respectively.

A CLABSI developed in 46% (N = 27/59) and a thrombosis in 7% (N = 4/59) of the patients who received a second central venous catheter. A third catheter was placed in 25 patients. In these patients, a CLABSI developed in 24% (N = 6/25) and none developed a thrombosis. Taking into account the first three catheters inserted a total of 13 CLABSIs / 1000 catheter days were observed.

Risk factors for CLABSI and catheter related thrombosis

Multivariate logistic regression showed that patients who received an enterostomy as part of treatment (OR: 3.0; 95%-CI: 1.6–5.5) and those who received a non-tunnelled catheter (OR: 2.0; 95%-CI: 1.3–3.7) were significantly more at risk of CLABSI development. This model yields a Nagelkerke's R^2 of 10%. Excluded from the model were direct insertion into a central vein (p = 0.78), patient's sex (p = 0.76), preterm birth (p = 0.43), trisomy 21 diagnosis (p = 0.36) and experiencing a major postoperative complication (p = 0.12). A sensitivity analysis, including only CLABSIs that resulted in central venous catheter removal resulted in the identification of the same risk factors. Also, a separate analysis of all location of insertion did not show any location to be off significantly (p = 0.44) increased risk.

Birthweight was not included in the model due to the number of missing values, yet a separate T-test showed there was no significant difference (p = 0.68) in birthweight between those that experienced a CLABSI and those that didn't. Also, patients treated for a complex gastroschisis did not develop significantly more CLABSIs than patients treated for isolated gastroschisis (p = 0.08)

Catheter dwell time was found to be an effect modifier, differing significantly between tunnelled and non-tunnelled catheters. Therefore, this variable was excluded from the model. Stratifying both groups showed that the dwell time in non-tunnelled central venous catheter was significantly ($p < 0.01$) shorter than in tunnelled catheters. Tunnelled central venous catheters stayed inserted for a median of 23 days (IQR: 15–35) and non-tunnelled catheters a median of 14 days (IQR: 8–22). CLABSIs developed in a significantly shorter dwell time in non-tunnelled central venous catheters compared to tunnelled central venous catheters ($p = 0.02$). The Kaplan-Meier curve, shown in Fig. 1, visualizes this difference in time to CLABSI occurrence in tunnelled versus non-tunnelled catheters (log-rank test: $p < 0.01$).

A catheter related thrombosis occurred significantly more often in non-tunnelled central venous catheters ($p = 0.03$). Occurrence of thrombosis was not correlated with either peripheral insertion or direct insertion into a central vein of the catheter ($p = 0.34$).

Discussion

In our cohort of 238 patients with intestinal atresia or gastroschisis receiving a central venous catheter, the overall incidence of CLABSI was 35%. Out of the patients treated for intestinal atresia, 30% developed a CLABSI and 46% of the gastroschisis patients developed CLABSI. A catheter related thrombosis developed in 7% of all patients. In those treated for intestinal atresia 7% developed thrombosis whilst the same occurred in 6% of the patients treated for gastroschisis. Patients experiencing CLABSI stayed in the hospital significantly longer than those that did not. Moreover, children treated with an enterostomy and non-tunnelled catheters were significantly more at risk of CLABSI development Also, catheter dwell time was shorter and CLABSIs developed faster in non-tunnelled compared to tunnelled catheters. A catheter related thrombosis occurred significantly more often in non-tunnelled catheters, whilst there was no correlation with direct insertion into a central vein or peripheral insertion.

Previous studies in a general neonatal population showed that CLABSIs lengthen duration of hospital stay, increase costs and lead to severe complications including mortality [12]. Yet, there are just two studies that evaluated CLABSI and catheter related thrombosis as a primary outcome in neonates treated for intestinal atresia and gastroschisis. These studies retrieved their data from national databases using coding systems such as ICD-10. These studies report a CLABSI occurrence between 2–4% for those treated for gastroschisis, which is much lower than our cohort [6, 7]. Other studies report a higher occurrence, namely 18% in patients treated for intestinal atresia and 13% in children treated for gastroschisis [13, 14]. These studies were single centre retrospective cohort studies that reported on CLABSI as secondary outcome and which collected the data manually. National databases might suffer from underreporting of CLABSI and possibly coding errors since the care for patients suffering from these congenital birth defects is complex and complications are common. It is for instance remarkable that the database study reports a high CLABSI-rate per 1000-line days of 24 in patients treated for gastroschisis, whilst the numerator of this fraction (the incidence of CLABSI) is comparatively low (2%) and the denominator (catheter dwell time) is similar to this study (25 days). Other explanation for our higher incidence might be the definition used for CLABSI. The official CDC definition for CLABSI in young

patients demands two separate positive blood cultures in case of a common commensal organism such as CNS, next to signs of infection and no other site of infection than the central venous catheter [11]. At our hospital, a CLABSI is presumed following a single positive culture combined with clinical suspicion of CLABSI in case of no other cause of infection. In case of a common commensal positive blood culture, antibiotic treatment is mostly started without central venous catheter removal. When clinical deterioration occurs, the central venous catheter is eventually removed. If these common commensal positive cultures were caused by contamination instead of a real CLABSI, patients could be expected to improve significantly more without removal of the catheter. Yet, the rate of central venous catheter removal was similar when comparing the CLABSIs caused by common commensal and other positive cultures. Still, it might be that we over-diagnosed patients with CLABSI leading to catheter removal in patients that might have improved by watchful waiting which would be a form of action bias. Better adherence to the existent guidelines on pediatric parenteral nutrition might both decrease central venous catheter associated complications as overly cautious removal of the inserted central venous catheter[15]. Furthermore, prevention could maybe furthermore be realized by the usage of line-lock infusions. For instance, the usage of taurolidine has been shown to decrease the rate of CLABSIs in children who receive TPV at home and is therefore included in the guidelines for this specific cohort[15]. For the patients concerning our study, a well-designed study should be started to investigate the efficacy and safety of different line locks including taurolidine in preventing central line infections.

Previous studies described complex gastroschisis as risk factor and, interestingly, prematurity and low birthweight as protective for CLABSI in patients treated for gastroschisis[6, 7]. They suggested that this could be related to a longer NICU submission in premature and/or low birthweight infants which, due to CLABSI prevention protocols in place at the NICU, could lead to a decrease in CLABSIs. In our cohort, we could not confirm these risk factors. Therefore, it seems that, as the previous studies too suggested, these factors are not general risk factors but rather local ones differing from hospital to hospital. Their influences might be limited if all hospitals would adhere to the same guidelines. Studies in neonates and PICU patients in general described male sex, higher birthweight and centrally placed catheters as risk factors which we could also not confirm [4, 16].

The increased risk of CLABSI in patients who are treated by enterostomy formation, which in this cohort mostly consisted of patients with an intestinal atresia receiving an ileo- or jejunostomy, might be partly related to the risk of high-output enterostomies which occurs in 50–60% of these patients [17, 18]. This in turn could lead to malnutrition which will make these patients more susceptible for systemic infections originating from bacteria which, particularly in neonatal ill patients with intestinal obstructions, seem to translocate from the gut [19, 20] Since the amount of stoma output was not well described in our cohort, we could not evaluate the influence of high-output enterostomies on CLABSI.

When it comes to CLABSI prevention in our cohort, we show that tunnelled central venous catheters seem to be preferred over non-tunnelled central venous catheters most specifically when a long duration of parenteral nutrition is expected. However, previous studies show conflicting results. Some show that dwell time does not affect CLABSI-risk and that it occurs less often in non-tunnelled central venous catheters in

NICU patients in general [21]. We focussed specifically on a cohort of patients with congenital gastrointestinal diseases, which necessitates long-term parenteral nutrition. In the previous study in NICU patients, almost 50% of the non-tunnelled catheters were removed without complications within a week of dwell time, whilst this was the case in nearly 10% of the tunnelled catheters [21]. It thus seems that in this study patients who were less prone to long-term feeding difficulties were more likely to be treated by a non-tunnelled catheter. This could have resulted in selection bias which in turn could explain the difference with our cohort. Although some form of selection bias might have occurred in our cohort based on the patient's clinical status or the preference of the treating physician, it seems plausible that this bias is more profound in studies including multiple diseases.

The central venous catheter related thrombosis incidence in patients treated for intestinal atresia was found to be 8% in a previous study including 47 patients treated for jejunoileal atresia, which is similar to our results [13]. To our knowledge, there is no study describing the incidence of this complication in patients treated for gastroschisis. Our incidences are lower than the 6–30% reported in cohorts of children up to 16–18 years of age. This could be caused by the amount, commonly near 20%, of patients treated for cancer in these cohorts as well as older age. Treatment for cancer is in itself a risk factor for thrombosis [3, 22]. Furthermore, the inclusion of non-symptomatic thrombosis in these studies will have led to an increase in incidence whilst the clinical significance of these thrombosis is debatable. Still, it seems that this complication is not uncommon. It might be that lowering the threshold for giving prophylactic low molecular weight heparin, which at the moment is set at an expected catheter dwell time of six weeks in our clinic, might decrease the occurrence of thrombosis specifically in this cohort. However, the efficacy and safety of prophylactic low molecular weight heparin should be assessed in a well-designed trial in this population.

In older children, up to 18 years of age, it has been suggested that catheters inserted directly into a central vein decrease the risk of symptomatic thrombosis due to the comparatively larger lumen of the central veins [3]. In our cohort this hypothesis could not be proven.

Although the catheter was removed in all patients who experienced thrombosis, some suggest that spontaneous regression of the thrombosis within 28 days can occur in 50% of the children [23]. For this reason, an ongoing multicentre Dutch prospective observational cohort study (Trial registration: Dutch Trial Register. Registered 24 December 2013), which protocol has been published in 2018, aims to evaluate a new treatment strategy. In this protocol non-occlusive thrombosis in neonates admitted to the NICU is treated by "watchful waiting". In case of non-extension after 5 days, a thrombosis will be followed-up by ultrasound without anticoagulant treatment [23].

This study could not evaluate compliance to preventative measures (such as hand hygiene and skin preparation) which are in place to prevent CLABSI, due to the retrospective design [24]. This is a limitation of our study. Compliance to these measures has shown to able to decrease the incidence of CLABSI in neonates [25, 26]. Secondly, as explained previously, the definitions used for CLABSI might have resulted in different outcomes as would have been the case for catheter related thrombosis if we would have

included non-symptomatic thrombosis. In both cases we tried to use a definition which resulted in the clinically most relevant results. If we would have followed the official CDC definition for CLABSI more strictly our results would not have been a true reflection of the number of patients treated due to a presumed CLABSI. Although incidence might have differed, our sensitivity analysis showed that the same risk factors would have been identified if we had chosen to only include CLABSIs that led to catheter removal. The definition for catheter related thrombosis could have been widened by including non-symptomatic thrombosis. This would have increased our incidence, though presumably only slightly due to the rarity of non-symptomatic thrombosis in this cohort. Yet, the clinical relevance of non-symptomatic thrombosis is debatable which is why we chose not to include them. Lastly, some factors, such as catheter size, which specialist inserted the catheter, experience of the specialist, were not clearly described and could thus not be evaluated. Taking these limitations into account when interpreting our results, we still were able to approach the incidence and evaluate risk factors in a specified cohort which increases the interpretability of our results compared to studies including multiple age groups or diseases.

Conclusion

A CLABSI occurs in approximately a third of the patients treated for intestinal atresia or gastroschisis whilst a catheter related thrombosis occurs in one in fourteen patients. When in doubt which catheter to use for the administration of parenteral nutrition in these patients, a tunnelled catheter is preferred over a non-tunnelled since it is comparatively less at risk of catheter related infections and thrombosis. Moreover, the risk of CLABSI in this group of patients is increased following enterostomy formation. Besides adherence to uniform guidelines, it might be that a change in preventive measures for CLABSI, such as taurolidine as a line-lock infusion, and for thrombosis, such as starting low molecular weight heparin in when catheter dwell time is expected for shorter than six weeks, would decrease the occurrence of these complications in this cohort of patients. For this, well designed trials are necessary for these specific patients.

Declarations

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Level of evidence: II

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Tables

Table 1
Patient characteristics

Total number of patients = 238		**Count (% of total)**
Mean birthweight in grams (± Std)		2551 (652) *(Missing: 53)*
Male		124 (52%)
Premature		97 (41%) *(Missing: 13)*
Down syndrome		32 (13%)
Median age at surgery (IQR)		2 days (1–4)
Treatment for	Intestinal atresia	175 (73%)
	Gastroschisis	63 (27%)
Comorbidity*1	Duodenal web	28 (12%)
	Annular pancreas	24 (10%)
	Malrotation	22 (9%)
	Midgut volvulus	7 (3%)
	Meconium peritonitis	10 (4%)
Patients treated for complex gastroschisis		14 (6%)
Gastroschisis treated by primary closure*2		40 (64%)
Patients who received an enterostomy		55 (23%)
Clavien-Dindo ≥ III following surgery		53 (22%) *(Missing: 2)*
Median duration of hospital stay (IQR)		27 days (18–42)
Median number of abdominal procedures (IQR)		1 (1–2)
Mortality within 30 days		4 (2%)
Overall mortality		16 (7%)
Median months length of follow-up (IQR)		24 months (8–79)

**1: Five patients experienced a malrotation + duodenal web, one a malrotation + volvulus and one an annular pancreas + malrotation. *2: Of all complex gastroschisis patients, eight (57%) were treated by primary closure.*

Table 2
Classification of the intestinal atresias

		Intestinal Atresia (N = 175)	Complex gastroschisis (N = 14)
Location of the atresia	Pylorus	2 (1%)	0
	Duodenum	98 (56%)	0
	Jejunum	32 (18%)	2 (14%)
	Ileum	29 (17%)	9 (64%)
	Colon	7 (4%)	0
	Multiple locations	7 (4%)	3 (21%)
Type of jejunoileal atresia	Type 0	6 (9%)	0
	Type I	17 (25%)	2 (14%)
	Type II	16 (24%)	1 (7%)
	Type III-A	13 (19%)	1 (7%)
	Type III-B	4 (6%)	7 (50%)
	Type IV	11 (16%)	3 (22%)
	Unclear	1 (1%)	0

Table 3
Complications associated with the first inserted central venous catheter

Total number of patients included (N = 238)		**Intestinal atresia (N = 175)**	**Gastroschisis (N = 63)**
Complication directly associated to placement	*Incision other side neck necessary*	3 (2%)	3 (5%)
	Post-operative catheter tip readjustment necessary	10 (6%)	13 (21%)
	Pneumothorax	0	0
Enterostomy during central venous catheter		36 (21%)	6 (30%)
Median time from admission until insertion (IQR)		2 days (1–4)	0 days (0–1)
Place of insertion	*Internal Jugular*	43 (24%)	29 (46%)
	External Jugular	61 (35%)	14 (22%)
	Subclavian	15 (9%)	7 (11%)
	Femoral	3 (2%)	1 (2%)
	Superior limbs	13 (7%)	5 (8%)
	Saphenous magna	32 (18%)	3 (5%)
	Inferior limbs	8 (5%)	4 (6%)
Central venous catheter centrally inserted		122 (70%)	38 (81%)
Central venous catheter tunnelled		133 (76%)	41 (65%)
Central venous catheter dwell time (IQR)		20 days (13–30)	25 days (14–38)
CLABSI		53 (30%)	29 (46%)
Median time until CLABSI (IQR)		16 days (8–28)	19 days (12–41)
Thrombosis		12 (7%)	4 (6%)
Median time until thrombosis (IQR)		11 days (6–17)	17 days (14–35)
CLABSI and thrombosis at the same time		8 (5%)	4 (6%)
Removal due to other complications	*Occlusion*	2 (1%)	2 (3%)
	Dislocation	7 (4%)	8 (13%)
	Leakage	2 (1%)	0

Total number of patients included (N = 238)	Intestinal atresia (N = 175)	Gastroschisis (N = 63)
Death due to central venous catheter complication	1 (1%)	0
No central venous catheter complications	108 (62%)	25 (40%)
Received a new central venous catheter	33 (19%)	26 (41%)

Appendix

Appendix A is not available with this version.

Figures

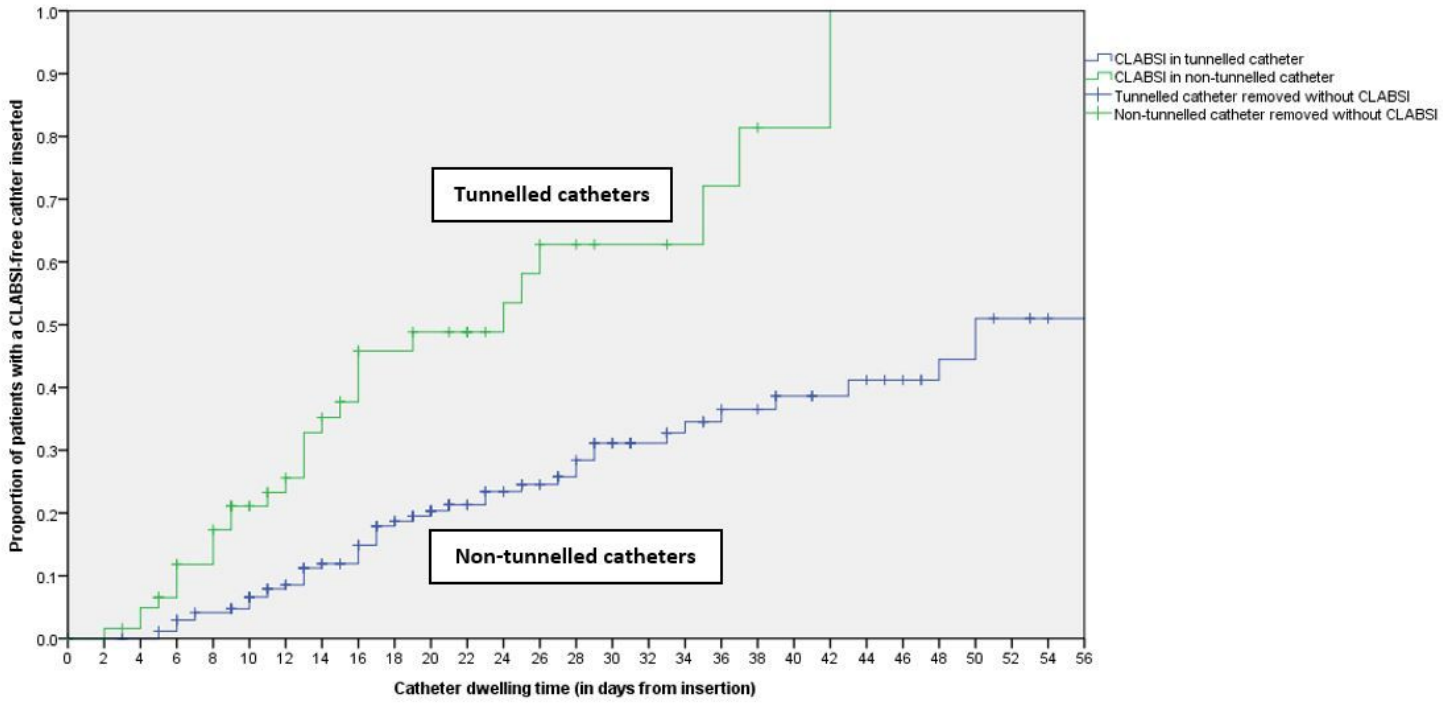

Figure 1

Time to CLABSI occurrence or removal comparing tunnelled and non-tunnelled catheters