

Complications of indwelling central venous catheters in pediatric liver transplant recipients

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Abstract: In pLT recipients, the advantages of ICVCs need to be weighed against the risk of complications. This single-center retrospective study aimed to review ICVC complications in our cohort of pLT recipients. We performed chart reviews of pLT patients having undergone transplant between 01/2000 and 03/2014 and who underwent ICVC placement either before or after LT. We identified 100 ICVC in 85 patients. Overall observation time was 90 470 catheter-days. There was no difference in catheter lifespan between those inserted pre- or post-transplant; 46% of ICVC presented a complication. Most frequent complications were MD and infection. The infection rate was 0.09 per 1000 catheter-days, and MD rate was 0.36 per 1000 catheter-days. Patients having received technical variant grafts were more at risk of complications. To the best of our knowledge, this is the first study examining ICVC complications in pLT recipients. We conclude that ICVC have a high rate of MD. Children receiving technical variants may be more at risk of complications. By removing ICVC in a select number of patients at six months post-insertion, we might avoid as much as 60% of complications.

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ICVCs are commonly used in adults and children with chronic conditions, such as intestinal failure, cystic fibrosis, and following an SOT (1–5). However, complications such as infection or thrombosis continue to plague patient quality of life by impacting the length of hospital stay and the number of hospital admissions. In addition, they expose immunosuppressed patients to infections and repeated surgery (6, 7).

In children, known risk factors for infections include frequency of ICVC handling (8) and patient age (9, 10). Age is also associated with

complications in general (9, 11), as is the use of TLCs (9). Younger age has been reported to be a risk factor for mechanical complications or thrombosis (11–13). Other risks and costs associated with ICVC comprise the need for surgery and general anesthesia, postoperative infection, air embolism, and dislocation of a catheter fragment (14). Re-implantation of an ICVC seems to be a risk factor for early infection in children with cancer (15).

Although SOT recipients are obvious candidates for ICVC, the benefits of such devices must be weighed against the risk of complications. Yet, there is very little literature to assist clinicians in their decision making. In our national referral center, we use ICVCs in the majority of pLT recipients for repeated blood draws and intravenous treatment. Therefore, our aim was to assess the frequency and type of complications in a representative cohort of pLT recipients with the goal to identify the potentially modifiable risk factors.

Abbreviations: ALF, acute liver failure; BA, biliary atresia; Comp, complications; CRP, C-reactive protein; Hb, hemoglobin; ICVC, indwelling central venous catheter; LT, liver transplant; MD, mechanical dysfunction; NoComp, no complication; pLT, pediatric liver transplant; Post-LT, post-liver transplantation; Pre-LT, pre-liver transplantation; SOT, solid organ transplant; TID, totally implantable devices; TLC, tunneled catheter.

Methods

After approval by the institutional ethics committee, we retrospectively reviewed the charts of patients transplanted between 01/2000 and 03/2014 who underwent ICVC placement. Catheters inserted and removed before LT were excluded. Only those removed after transplantation were considered for analysis. Both TID (Port-a-Cath®; B. Braun, Bard Access System, Melsungen, Germany) and TLCs (Broviac®; Bard Access System, Tempe, AZ, USA, Cook®, Cook Medical, Bloomington, IN, USA) were used. Devices were inserted using standard procedures by different pediatric surgeons during the study period. Catheters were managed according to local protocols by our center, by referring centers, or by home health companies.

We collected demographic and surgical data, as well as laboratory values within five days of ICVC insertion. Graft types were separated in whole liver and technical variant. A technical variant was any liver that was not whole, including split, reduced, and living-related donor. With regard to ICVC removal, we recorded the laboratory values within 48 h of the procedure. In addition, for those cases with ICVC infection, we gathered additional data including pathogen, antibiotic therapy, duration of bacteremia, catheter culture, and peripheral blood cultures. A left shift was defined as neutrophil band cells >500 per microliter. We used a time scale of 30 days for one month and 365 days for one yr.

Infections were defined following the Infectious Diseases Society of America 2009 guidelines (6). Thrombosis was diagnosed using Doppler ultrasound or contrast injection. The term “MD” was used for occlusions or displacement of the catheter. The catheter was defined as displaced if considerable changes in location of the catheter tip were deemed to be the cause of malfunction. “Occlusion” defined the inability to draw blood and inject without evidence of clear thrombosis or catheter displacement. We used the term “elective removal” for catheters removed for the following indications: nonuse, replacement of a TLC by a TID, and removal owing to growth of the patient. “Growth” was considered the indication for removal when the growth of the child caused a change in catheter location. “Other” was used for any other nonclassifiable causes. The complications (Comp) group included cases of infection, thrombosis, MD, and other. The group without complications (NoComp) included cases of elective removal and ICVC still in place at the end of the follow-up. Quick stands for patient prothrombin time over laboratory standard were expressed as a percentage.

Statistical analysis

For continuous variables, a Student test or a Wilcoxon test was used depending on variable distribution. K-sample test was used to compare medians. A chi-square test or a Fisher exact test was used to compare categorical variables. The Kaplan–Meyer test and log-rank test were used for survival analysis. A univariate logistic regression analysis was performed to identify the risk factors for catheter complications. All variables with a p value lower than 0.2 in the univariate model were included in the multivariate regression analysis. Statistical analyses were carried out with STATA software, version 13.0 (StataCorp, College Station, TX, USA).

Results

We identified 100 catheters in 85 patients. The observation time spanned 90 470 catheter-days

with a median follow-up of 18.9 months (IQR 4.8–47.2). Four patients died during follow-up, none from an ICVC-related complication. The median age at insertion was 14.3 months (IQR 8.25–40.7). The overall removal rate was 67% during follow-up, and the median ICVC lifespan was 16.1 months (IQR 3.6–36.4). Owing to the retrospective design of study, 33% of ICVC are still in place in the most recent pLT recipients.

Time of insertion

We identified 35 ICVC inserted before transplant (pre-LT) and 65 after transplant (post-LT) (Fig. 1). Diagnosis, surgical, and laboratory information are summarized in Table 1. Diagnoses were similar in the pre-LT and post-LT groups as was the proportion of children with BA and other cholestatic diseases 77.1% pre-LT and 69.2% post-LT (p value = 0.4). Pre-LT and post-LT populations did not differ significantly in terms of age or weight. However, coagulation factors and bilirubin were significantly different between pre-LT and post-LT groups. Nonetheless, the two groups did not differ in terms of frequency of overall complications or type of complication (Fig. 1), and there was no difference in device lifespan (Fig. 2).

Time and type of complications

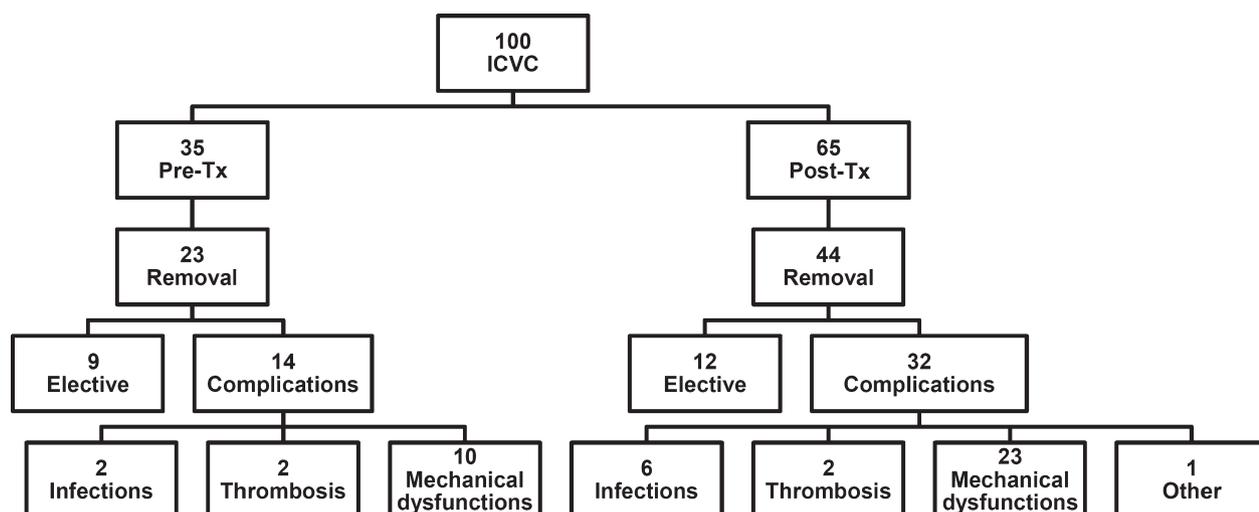
We identified 46 of 100 complications. The rate of complications was 0.5 per 1000 catheter-days. Table 2A compares and contrasts diagnosis, surgical, and laboratory data between groups with (Comp) and without (NoComp) complication. The Comp group included more partial grafts (p = 0.014). Moreover, Table 2B compares age and weight data between complication types. Due to the small sample size, we did not perform statistical analysis between complication types.

The median time to an ICVC complication was 8.5 months (IQR 3.4–31.9). Median time for the removal of a NoComp ICVC (elective removal) was 29 months (IQR 17–45.6), significantly longer than Comp ICVC (p = 0.007). As might be predicted, ICVC lifespan differed significantly between groups (p < 0.001).

Infections

We identified eight infections, of which two occurred in ICVC inserted pre-LT. The characteristics of infectious cases are outlined in Table 3. Median age at removal of infected catheters was 13.05 months (IQR 9.8–21.2). Duration of antibiotic therapy varied between patients from three days to 25 days. All eight infections occurred during the first year after LT,

(a)



(b)

	PreLT ICVC N=35		PostLT ICVC N=65		p value
	N	%	N	%	
Removal	23	65.7	44	67.7	0.8
Elective	9	39.1	12	27.3	0.37
Complication	14	60.9	32	72.7	0.7
Infection	2	14.3	6	18.8	0.6
Thrombosis	2	14.3	2	6.3	0.49
Mec dysfunction	10	71.4	23	71.8	1
Other	0	0	1	3.1	0.39

Fig. 1. Time of insertion and ICVC outcomes. (a) Descriptive overview of 100 ICVC inserted either pre- or post-LT (b) Comparison of outcomes according to time of insertion. Removal: both elective and removals for complication. Mec dysfunction: MD Pre-LT: inserted pretransplant; Post-LT: inserted post-transplant.

and seven of eight of infections occurred during the first year after ICVC insertion. The median lifespan of infected ICVC was 5.4 months (IQR 1.8–8.1). All infections occurred within 18 months of insertion. Our overall infection rate was 0.09 per 1000 catheter-days. Only one infection led to life-threatening septic shock (patient 5, Table 3). There was no significant difference in laboratory or surgical data between patients with and without infections. All infected ICVC were removal. ICVC type was not associated with incidence of infection: 7% of TID and 9% of TLC were infected (p value = 1).

MDs

We identified 33 MDs (71% of complications). The MD rate was 0.36 per 1000 catheter-days. Median age at insertion for these ICVC was 12.5 months (IQR 8.3–26.4). Median time before ICVC removal for MDs was 8.6 months (IQR 3.5–32.7). There was no significant difference in laboratory data between patients with and without MD. Children presenting with MD had received significantly more technical variants (p = 0.04). TLCs may be more at risk of MD. Indeed, 50% of TLC developed an MD, while MD was a problem in only 28.2% of TID (11/

Table 1. Patient characteristics at time of ICVC insertion

Diagnosis	Pre-LT		Post-LT		p value
	N = 35	%	N = 65	%	
BA	19	54.3	33	50.8	0.7
Other cholestatic	8	22.9	12	18.5	0.6
Wilson	0	0	2	3.1	0.5
Alpha 1 AT deficiency	0	0	2	3.1	0.5
ALF	0	0	8	12.3	0.048
Metabolic disease	2	5.7	3	4.6	1
Malignancy	4	11.4	0	0	0.013
Other	2	5.7	5	7.7	1
T1D	23	65.7	55	84.6	0.03
TLC	12	34.3	10	15.4	0.03

Insertion	Pre-TX		Post-TX		p value
	Median	IQR	Median	IQR	
Age (months)	9	7.4–46.4	16.8	11.1–40.1	0.09
Weight (kg)	7.5	5.8–17	9.9	7.9–14.3	0.11
Quick (%)	61.5	44–81	90.5	79–100	0.002
Factors VII–X (%)	45.5	31–63.5	74.5	62–100	0.001
Bilirubin ($\mu\text{mol/L}$)	236	108–407	21.5	13–44.5	<0.001
Hb (g/L)	89.5	79–105	100.5	86–112	0.06
Platelets (g/L)	202.5	126–269	218	135–296	0.5

Significant p values are in boldface.

22) (22/78), although this did not quite reach statistical significance ($p = 0.055$).

Thrombosis

We identified four thromboses (8.7%). The thrombosis rate was 0.044 per 1000 catheter-days. Median age at insertion of these ICVC was 9.0 months (IQR 7.4–25.6). Median time for ICVC removal because of thrombosis was

24 months (IQR 10.9–54.5). We did not perform detailed statistics because of the small sample size.

Risk factors for complications

Using a univariate model for complications in general, we identified technical variant grafts (OR 3.05 [CI 1.23–7.6]) as a risk factor. Conversely, age at insertion (OR 0.99 [CI 0.98–99]) ($p = 0.04$) and weight at insertion (OR 0.95 [CI 0.91–1]) seemed protective ($p = 0.08$) when they increase. The multivariate regression did not reveal any independent risk factors for overall complications (Table 4).

We looked for risk factors for complications in the pre-LT or post-LT populations. Using a univariate model, the use of technical variant grafts also emerged as a risk factor for patients having benefited from ICVC placement before LT (OR 2.9 [CI 1.01–8.9]), but not for patients in whom the ICVC was placed following LT.

Technical variants were also a risk factor (OR 2.8 [CI 1.03–7.9]) for MD, and the type of catheter TLC (OR 2.5 [CI 0.96–6.7; $p = 0.059$]) neared significance. The multivariate regression analysis confirmed that technical variant grafts were an independent risk factor for MD. We performed a *post hoc* analysis with transplantation type adjusted for age. In this model, partial grafts emerged as a risk factor for overall complications (OR 2.6 [CI 1.004–6.5], $p = 0.049$), but did not reach significance ($p = 0.06$) as a risk factor for MD (OR 2.6 [CI 0.9–7.5]).

No risk factors for infectious complications were identified. Only the diagnosis of ALF

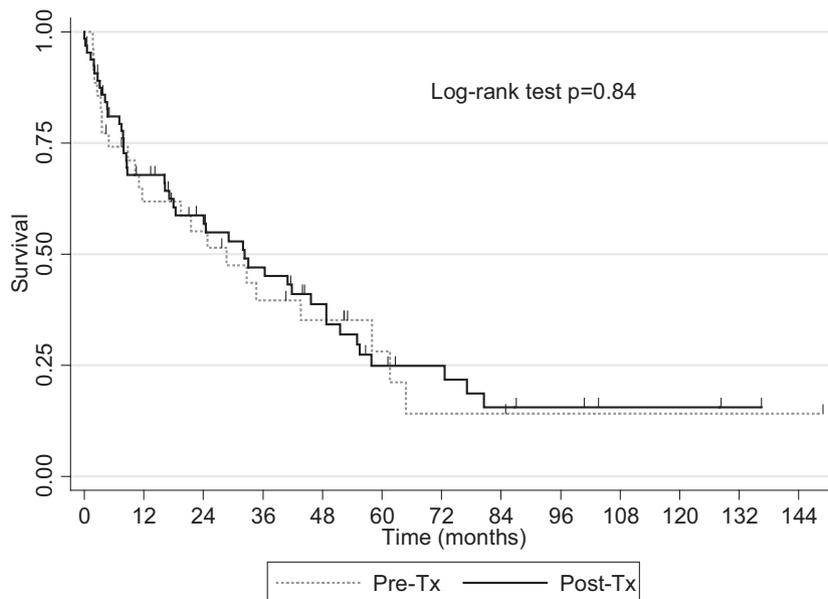


Fig. 2. Catheter lifespan: insertion pre-LT and post-LT. The median ICVC lifespan in the pre-LT group was 10.6 months (IQR 3.5–28.7) and 16.2 months (IQR 4.6–40.9) when the ICVC was placed post-LT. There was no significant difference in survival ICVC between the two groups ($p = 0.84$). Pre-LT: inserted pretransplant; Post-LT: inserted post-transplant.

Table 2. (A) Patient characteristics: complications (B) Characteristics of patients with complications; age and weight expressed as medians

(A)					
Diagnosis	NoComp		Comp		p value
	N = 54	%	N = 46	%	
BA	26	48.1	26	56.5	0.4
Other cholestatic	11	20.4	9	19.6	0.9
Wilson	1	1.8	1	2.1	1
Alpha 1 AT deficiency	1	1.8	1	2.1	1
ALF	4	7.4	4	8.7	1
Metabolic disease	5	9.3	0	0	0.06
Malignancy	4	7.4	0	0	0.12
Other	2	3.7	5	10.9	0.24
TID	45	83.3	33	71.7	0.16
TLC	9	16.7	13	28.3	0.16
Whole liver	23	42.6	9	19.6	0.014
Technical variant	31	57.4	37	80.4	0.014

Insertion	NoComp		Comp		p value
	Median	IQR	Median	IQR	
Age (months)	20.5	8.3–63.4	12.6	8.1–26	0.027
Weight (kg)	10	7.9–19.1	8.4	6.8–11	0.03

(B)				
	Mec dysfunction n = 33	Infection n = 8	Thrombosis n = 4	
Age at insertion (months)	12.5 (IQR 8.3–26.4)	13.0 (IQR 9.8–21.2)	9.0 (IQR 7.4–25.6)	
Weight at insertion (kg)	8.6 (IQR 6.5–11.7)	9.0 (IQR 6.6–11)	7.7 (IQR 6.9–9.3)	
Age at removal (months)	28.6 (IQR 13.1–68.3)	19.3 (IQR 15.7–33.2)	47.9 (IQR 18.3–80)	
ICVC age at removal (months)	8.6 (IQR 3.5–32.7)	5.4 (IQR 1.8–8.1)	24 (IQR 10.9–54.5)	
TID	22	6	4	
TLC	11	2	0	

Significant p values are in boldface.

Table 3. Patients with infected ICVC. All infections occurred post-LT, and all patients had positive blood cultures from the ICVC. “Catheter culture” indicates that the device was cultured following removal

Patients	Primary disease	Type of LT	Bacteria	Duration of bacteremia	Insertion	Central venous catheter	Peripheral blood culture	Catheter culture
P.1	ALF	Tech	<i>Staphylococcus Epidermidis</i>	18	Post-LT	TID	–	+
P.2	BA	Tech	<i>Escherichia Coli</i>	4	Post-LT	TID	–	–
P.3	BA	Whole	<i>S. epidermidis</i>	6	Post-LT	TID	+	–
P.4	BA	Tech	<i>E. coli and Acinetobacter spp.</i>	2	Post-LT	TLC	–	–
P.5	ALF	Tech	<i>Pseudomonas aeruginosa</i>	5	Post-LT	TID	+	+
P.6	BA	Tech	<i>S. epidermidis</i>	2	Post-LT	TID	–	+
P.7	BA	Tech	<i>Enterococcus Faecalis</i>	6	Pre-LT	TLC	–	–
P.8	SBC	Whole	<i>Stenotrophomonas maltophilia</i>	4	Pre-LT	TID	–	+

Tech, technical variant; SBC, secondary biliary cirrhosis; Whole, whole liver transplant.

showed a trend toward being a potential risk factor in the univariate model (OR 4.48 [CI 0.79–28.9]; p = 0.08). Given the low number of events, multivariate regression analysis was not performed.

To determine a possible cutoff for ICVC removal, we performed a subanalysis illustrated in Fig. 3. We looked at the lifespan of

catheters with infections, thrombosis, and MDs, respectively. Using a cutoff for systematic removal at six months post-insertion, we calculated that 50% of infections, 60% of mechanical complications, and 100% of thromboses might be avoided. All in all, 60% of complications could be avoided with such approach.

Table 4. Univariate and multivariate regression analyses for overall complications and mechanical complications

Univariate model	OR (CI)	p value	Multivariate model	OR (CI)	p value
Overall complications					
Diagnosis (no BA)	0.71 (0.32–1.6)	0.4	Age (months)	0.99 (0.97–1.02)	0.7
Technical variant	3.05 (1.23–7.6)	0.016	Weight (kg)	0.99 (0.9–1.1)	0.8
Deceased donor	0.45 (0.15–0.4)	0.16	Tunneled ICVC	2.25 (0.78–6.5)	0.13
Sex (male)	0.8 (0.36–1.76)	0.58	Technical variant	2.13 (0.74–6.13)	0.16
Age (months)	0.99 (0.98–0.99)	0.043			
Weight (kg)	0.95 (0.91–1)	0.08			
Tunneled ICVC	1.97 (0.75–5.15)	0.17			
Post-Tx inserted	1.5 (0.6–3.3)	0.37			
MD					
Diagnosis (no BA)	1.02 (0.44–2.37)	0.9	Tunneled ICVC	2.5 (0.92–6.7)	0.07
Technical variant	2.8 (1.03–7.9)	0.042	Technical variant	2.8 (1.01–7.9)	0.048
Time ins-LT	1 (0.99–1)	0.6			
Time ins-LT (>14 days)	1.11 (0.46–2.7)	0.8			
Age (months)	0.99 (0.98–1)	0.29			
Weight (kg)	0.98 (0.93–1.02)	0.36			
Tunneled ICVC	2.5 (0.96–6.7)	0.059			

Significant p values are in boldface.

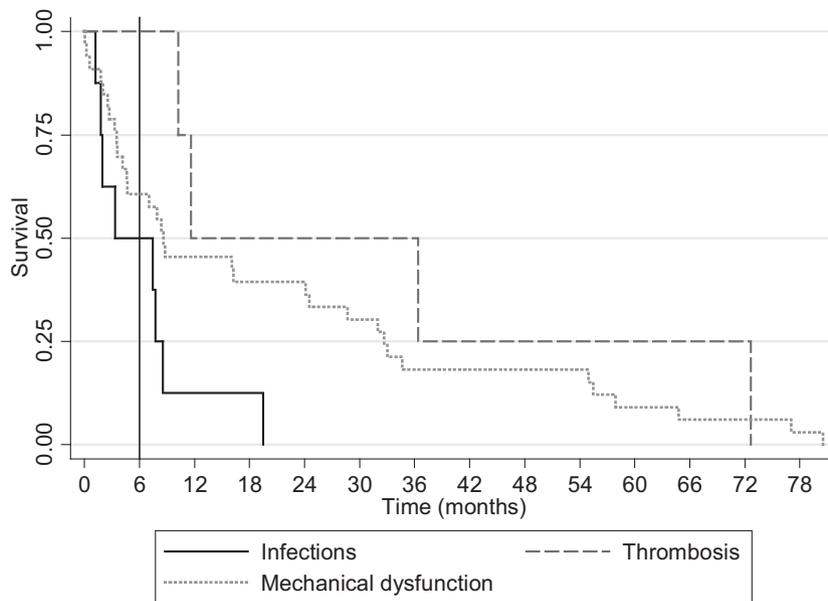


Fig. 3. ICVC lifespan according to the type of complication and proposed cutoff for elective removal to avoid complications (solid vertical line: six months after insertion).

Discussion

The use of ICVC in SOT candidates and recipients is controversial and varies between centers. Although they are frequently indicated, to the best of our knowledge, this the first single-center study examining the type and rate of ICVC complications in pLT recipients. Using strict definitions for complications, as many as 46% of ICVC developed a complication during the follow-up period, only one of which was life-threatening. The two most frequent complications were MD (71%) and infections (17%).

Although underlying diagnoses were similar, patients who received an ICVC pre-LT differed from the post-LT group in terms of laboratory

values. The children who benefitted from an ICVC insertion pre-LT were much sicker, as illustrated by a higher median serum bilirubin level (236 $\mu\text{mol/L}$ [IQR 108–407] vs. 21.5 $\mu\text{mol/L}$ [IQR 13–44.5], $p < 0.001$) and abnormal coagulation profile. Patients were more severely cholestatic. However, there was no difference in baseline diagnosis distinction between patients having undergone ICVC placement pre- or post-LT. TLC were used more frequently in the pre-LT group, while TID were more frequently used post-LT. This discrepancy can be explained by differing indications and by the lower weight and size of the pre-LT patients. Conversely, TID were favored post-LT likely

due to their longer lifetime and lower infectious risk (9, 10, 16, 17).

There was no significant difference in the causes of removal between pre-LT and post-LT catheters. There was no difference in lifespan or time to complications between the two groups. Thus, it would appear that when needed, ICVC insertion pre-LT does not come with an increased risk of complications.

There are few studies examining ICVC in pLT recipients with which to compare our series. Reports to date have focused on children with cancer or cystic fibrosis, and the populations studied have been diverse (9, 16). In the present study, we show that routine ICVC placement and use in pediatric LT candidates or recipients is ridden with complications, most of them, however, with the only clinical consequence of hastening removal.

Forty-six percent of ICVC developed complications, which is in contrast with other studies reporting somewhat lower rates (16, 18–20). Nonetheless, our rate of 0.5 complications/1000 catheter-days was lower than some reports (12, 19, 21). Part of this difference may be explained by different definitions of complications. Other explanations include personnel training. Indeed, unlike oncology units, staff on a surgical unit may be less familiar with ICVC use. What is more, many of our patients were managed at home by home health services or at outlying hospitals, all of which may use different protocols. However, we nonetheless observed an overall low rate of complications, which can probably be explained by the frequency of ICVC handling, less frequent than in an oncology unit. Further, in our cohort, when patients were seen at an outlying hospital or at their pediatrician's office, the ICVC were rarely used. Finally, pLT recipients typically have normal neutrophil function unlike children with cancer or following bone marrow transplantation. These reasons might explain the lower rate of infections and complications.

Younger children were at an increased risk of complications in the univariate analysis, confirming the findings of others (8–10, 22). Typically, this subset of patients are infants, much sicker at transplant than other candidates, and may present a more complicated post-LT course, thereby requiring more frequent or prolonged ICVC use. Although we can continue to improve pre-LT management, in particular nutrition, this variable seems difficult to modify. Finally, and in accordance with the idea that patient size matters, there was a trend toward fewer complications in the subset of patients transplanted for

metabolic indications, which typically undergo transplant at an older age.

Although MD (71% of complications, 0.36 MD/1000 catheter-days) was frequent in our series, the rate was within the range of previously published pediatric cohorts: Perdikaris et al. (23) reported 0.38 occlusions/1000 ICVC days, and other studies reported a mechanical complication rate of 0.45 per 1000 catheter-days (11) and 0.44 per 1000 catheter-days (24). It must be emphasized that our MD definition was broader than those used by other authors. Indeed, we pooled several complication types together owing to sample size.

Risk factors for MD included the use of technical variant grafts which will be discussed later. In addition, the use of TLC approached significance in the multivariate analysis, confirming other reports (10). All in all, the rate of MD was problematic in our population. Among other factors, this can be ascribed to the fact that the ICVC are either accessed by multiple caregivers or conversely are not accessed or cared for at regular intervals. Therefore, when the MD is noted, it is too late for catheter salvage using conventional methods (25).

Eight patients presented with infections (17.4% of complications causes) including one sepsis. This amounts to a rate of 0.09 infections per 1000 catheter-days, considerably lower than other reports. Reported rates of ICVC infections vary widely, depending on underlying diagnosis: 0.2–11/1000 catheter-days in one study (26) and 0.1–2.3/1000 catheter-days in pediatric cancer patients with a tunneled ICVC (27). Wagner et al. reported a rate of 1.97 for TLC and 0.18 for TID per 1000 catheter-days (10). In our series, infections occurred in the first year after transplantation (mean time [days] 142.6 [CI 43.7–241.5], median 166.5 [IQR 19–243]) when patients were seen on an outpatient basis. This is congruent with other reports that infections in outpatients are a known early complication (28). The pathogens identified in our patients are also in agreement with the literature (6, 8, 28–30). Only one patient developed sepsis (1.2% of patients; rate = 0.01/1000 catheter-days), which is lower than previous reports although it is difficult to conclude with only one event (19, 30). While numerous risk factors have been reported (8, 10, 16, 31), we were unable to identify any risk factors for ICVC infections probably due to the low number. In summary, in our cohort, infections are remarkably low considering that the patients are under immunosuppressive medications. Therefore, it is our opinion that in the right environment, the risk of infection should

not dissuade clinicians from using ICVC if clinically indicated.

The use of technical variant allografts emerged as a risk factor for overall ICVC complications in the univariate model, something not previously reported. However, this finding did not hold true in the multivariate analysis. Moreover, technical variant allograft was a risk factor for MD using multivariate regression analysis. Given that partial grafts may be associated with a more complicated postoperative course, one might postulate that the patient with a partial graft may be exposed to more ICVC handling, thereby increasing the risk for complications (32). Further, partial grafts are usually received by small children and infants, a population more prone to complications, as stated above and by others.

Based on our findings, we suggest ICVC removal at six months post-insertion in stable patients. Because most of the infectious complications occur in the first year post-insertion, we propose that early removal may be protective of infection to some degree. Moreover, thrombosis and MD can predispose to infection (26, 33), and time of utilization is a risk factor for thrombosis (13). Thus, almost 60% of complications could be avoided with ICVC removal at the six month. Of course, these potential advantages should be weighed against the patient's clinical condition, which may require more prolonged central venous access. For example, it may not be in the best interest of patients with a history of difficult blood draws, in small infants or in those with comorbidities warranting complex follow-up. Formal recommendation for this cutoff will require prospective validation.

Although to our knowledge this is the first detailed study examining the outcomes of ICVC in pediatric LT patients, it does present some limitations. First, it is a retrospective study and, as such, there are some missing data. Importantly, we are missing information about the standardized care of catheters managed in referring centers. Second, ICVC use differed between the pre-LT and post-LT groups. ICVC inserted before the transplantation were used more often for antibiotic therapy or parenteral nutrition, whereas post-transplant ICVC were used for blood draws. Third, we had a relatively small population in comparison with published studies of oncology patients, which may impact the statistical power. Fourth, the study period spans 15 yr. Finally, our definition of MD was broad and may have included undiagnosed thromboses contributing to the high rate of MD. Conversely, this could easily explain the low rate of thrombosis.

In conclusion, ICVC inserted before transplant were as safe as those inserted after. There was a high proportion of mechanical complications and a low rate of infections. Because patients receiving technical variant grafts are smaller, they may be at higher risk of complications. We propose to remove ICVC in selected patients at six months after insertion to avoid a large fraction of complications.

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Disclosures

The authors have no disclosures or conflicts of interest.

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Authors' contributions

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References

1. KRUL EJ, VAN LEEUWEN EF, VOS A, et al. Continuous venous access in children for long-term chemotherapy by means of an implantable system. *J Pediatr Surg* 1986; 21: 689–690.
2. BROVIAC JW, COLE JJ, SCRIBNER BH. A silicone rubber atrial catheter for prolonged parenteral alimentation. *Surg Gynecol Obstet* 1973; 136: 602–606.
3. HICKMAN RO, BUCKNER CD, CLIFT RA, et al. A modified right atrial catheter for access to the venous system in marrow transplant recipients. *Surg Gynecol Obstet* 1979; 148: 871–875.
4. BRINCKER H, SAETER G. Fifty-five patient years' experience with a totally implanted system for intravenous chemotherapy. *Cancer* 1986; 57: 1124–1129.
5. NIEDERHUBER JE, ENSMINGER W, GYVES JW, et al. Totally implanted venous and arterial access system to replace external catheters in cancer treatment. *Surgery* 1982; 92: 706–712.
6. MERMEL LA, ALLON M, BOUZA E, et al. Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 update by the Infectious Diseases Society of America. *Clin Infect Dis* 2009; 49: 1–45.
7. O'GRADY NP, ALEXANDER M, DELLINGER EP, et al. Guidelines for the prevention of intravascular catheter-related infections. Centers for Disease Control and Prevention. *MMWR Recomm Rep* 2002; 51: 1–29.

8. LEBEAUX D, FERNANDEZ-HIDALGO N, CHAUHAN A, et al. Management of infections related to totally implantable venous-access ports: Challenges and perspectives. *Lancet Infect Dis* 2014; 14: 146–159.
9. FALLON SC, KIM ME, FERNANDES CJ, et al. Identifying and reducing early complications of surgical central lines in infants and toddlers. *J Surg Res* 2014; 190: 246–250.
10. WAGNER M, BONHOEFFER J, ERB TO, et al. Prospective study on central venous line associated bloodstream infections. *Arch Dis Child* 2011; 96: 827–831.
11. FRATINO G, MOLINARI AC, PARODI S, et al. Central venous catheter-related complications in children with oncological/hematological diseases: An observational study of 418 devices. *Ann Oncol* 2005; 16: 648–654.
12. CESARO S, CORRO R, PELOSIN A, et al. A prospective survey on incidence and outcome of Broviac/Hickman catheter-related complications in pediatric patients affected by hematological and oncological diseases. *Ann Hematol* 2004; 83: 183–188.
13. ALBISETTI M, KELLENBERGER CJ, BERGSTRASSER E, et al. Port-a-cath-related thrombosis and postthrombotic syndrome in pediatric oncology patients. *J Pediatr* 2013; 163: 1340–1346.
14. LEE AC. Elective removal of cuffed central venous catheters in children. *Support Care Cancer* 2007; 15: 897–901.
15. NAM SH, KIM DY, KIM SC, et al. Complications and risk factors of infection in pediatric hemato-oncology patients with totally implantable access ports (TIAPs). *Pediatr Blood Cancer* 2010; 54: 546–551.
16. BABU R, SPICER RD. Implanted vascular access devices (ports) in children: Complications and their prevention. *Pediatr Surg Int* 2002; 18: 50–53.
17. BASS J, HALTON J, DROUET Y, et al. Central venous catheter database: An important issue in quality assurance. *J Pediatr Surg* 2011; 46: 942–945.
18. DILLON PA, FOGLIA RP. Complications associated with an implantable vascular access device. *J Pediatr Surg* 2006; 41: 1582–1587.
19. MUNCK A, MALBEZIN S, BLOCH J, et al. Follow-up of 452 totally implantable vascular devices in cystic fibrosis patients. *Eur Respir J* 2004; 23: 430–434.
20. FALLON SC, LARIMER EL, GWILLIAM NR, et al. Increased complication rates associated with Port-a-Cath placement in pediatric patients: Location matters. *J Pediatr Surg* 2013; 48: 1263–1268.
21. PINON M, BEZZIO S, TOVO PA, et al. A prospective 7-year survey on central venous catheter-related complications at a single pediatric hospital. *Eur J Pediatr* 2009; 168: 1505–1512.
22. CESCA E, DALL'IGNA P, BOSCOLO-BERTO R, et al. Impact of severe neutropenia and other risk factors on early removal of implanted central venous catheter (ICVC) in children with hematologic malignancies. *J Pediatr Hematol Oncol* 2014; 36: 541–544.
23. PERDIKARIS P, PETSIOS K, VASILATOU-KOSMIDIS H, et al. Complications of Hickman-Broviac catheters in children with malignancies. *Pediatr Hematol Oncol* 2008; 25: 375–384.
24. CASTAGNOLA E, FRATINO G, VALERA M, et al. Correlation between “malfunctioning events” and catheter-related infections in pediatric cancer patients bearing tunneled indwelling central venous catheter: Results of a prospective observational study. *Support Care Cancer* 2005; 13: 757–759.
25. VAN MIERT C, HILL R, JONES L. Interventions for restoring patency of occluded central venous catheter lumens. *Cochrane Database Syst Rev* 2012; 4: CD007119.
26. WOLF J, CURTIS N, WORTH LJ, et al. Central line-associated bloodstream infection in children: An update on treatment. *Pediatr Infect Dis J* 2013; 32: 905–910.
27. SCHOOT RA, VAN DALEN EC, VAN OMMEN CH, et al. Antibiotic and other lock treatments for tunneled central venous catheter-related infections in children with cancer. *Cochrane Database Syst Rev* 2013; 6: CD008975.
28. KELLY MS, CONWAY M, WIRTH KE, et al. Microbiology and risk factors for central line-associated bloodstream infections among pediatric oncology outpatients: A single institution experience of 41 cases. *J Pediatr Hematol Oncol* 2013; 35: e71–e76.
29. LOONEY WJ, NARITA M, MUHLEMANN K. *Stenotrophomonas maltophilia*: An emerging opportunist human pathogen. *Lancet Infect Dis* 2009; 9: 312–323.
30. WILDHABER B, KISTLER W, CAFLISCH U. Experiences with the Port-A-Cath system in children. *Schweiz Med Wochenschr* 2000; 130: 732–738.
31. RINKE ML, CHEN AR, BUNDY DG, et al. Implementation of a central line maintenance care bundle in hospitalized pediatric oncology patients. *Pediatrics* 2013; 130: e996–e1004.
32. MCDIARMID SV, ANAND R, MARTZ K, et al. A multivariate analysis of pre-, peri-, and post-transplant factors affecting outcome after pediatric liver transplantation. *Ann Surg* 2011; 254: 145–154.
33. YACOBOVICH J, BEN-AMI T, ABDALLA T, et al. Patient and central venous catheter related risk factors for blood stream infections in children receiving chemotherapy. *Pediatr Blood Cancer* 2015; 62: 471–476.