


# Retrospective analysis of the safety of peripherally inserted catheters versus implanted port catheters during first-line treatment for patients with diffuse large B-cell lymphoma

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## Abstract

**Objectives:** Both peripherally inserted central catheters (PICCs) and implanted port catheters (PORTs) are commonly used for the delivery of immunochemotherapy. We compared the safety of the two types of devices in a homogeneous and monocentric population of diffuse large B-cell lymphoma (DLBCL) patients who were treated with first-line immunochemotherapy by evaluating the numbers of catheter-related venous thromboses (VTs) and infections that occurred in the six months after implantation according to the type of device.

**Methods:** Using a propensity score, the adjusted relative risk (ARR) between the type of catheter and the occurrence of catheter-related complications (infection and/or VT) of interest was retrospectively determined.

**Results:** 479 patients were enrolled (266 PORTs/213 PICCs), and 26 VTs (5.4%) and 30 infections (6.3%) were identified in the period following PICC/PORT implantation. The adjusted relative risk (ARR) of catheter-related complications (infection and/or VT) according to the type of device was 2.6 (95% CI = 1.3–5.9,  $p = .0075$ ). This risk increase associated with the PICC device was significant for both infections (ARR = 3.2; 95% CI = 1.3–10.9) and thrombosis (ARR = 4; 95% CI = 1.5–11.6).

**Conclusion:** Our study supports the preferential use of PORTs for the first line of treatment for DLBCL patients.

## KEYWORDS

central venous catheter, diffuse large B-cell lymphoma, thrombosis

**Novelty Statement:** Both peripherally inserted central catheters (PICCs) and implanted port catheters (PORTs) are commonly used for the delivery of immunochemotherapy in DLBCL patients with no clear choice recommendations. We report a significant increased risk of 3–4 times for both infections and thrombosis with PICCs. Our study supports the preferential use of PORTs for the first line of treatment for DLBCL patients.

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## 1 | INTRODUCTION

Diffuse large B-cell lymphoma is the most frequent non-Hodgkin lymphoma (NHL) subtype in Western European countries and the United States. Currently, approximately 65% of patients can be cured by the gold standard combination of anthracycline-based chemotherapy and anti-CD20 monoclonal antibodies, namely, R-CHOP- or R-CHOP-like regimens.<sup>1</sup> Four to eight cycles are usually delivered every 14–21 days (6–8 x R-CHOP21 or RCHOP14), thereby justifying the usage of a central venous line to deliver safely drugs that must be centrally administered. Both peripherally inserted central catheters (PICCs) and implanted port catheters (PORTs) are commonly used in daily oncology practice for the delivery of chemotherapy and the collection of blood samples.<sup>2</sup> PORTs are traditionally used for chemotherapy administration, but their implantation and removal are invasive. Their use for short/intermediate-term chemotherapy is still the standard of care. In contrast, PICCs can be easily implanted and removed, particularly when patients become neutro/thrombocytopenic, and are now widely used for patients with cancer. The main complications of both types of central venous devices (CVDs) are thromboembolic events and infections.<sup>3</sup>

Clinical guidelines indicate no clear preference between PICCs and PORTs for the infusion of chemotherapy when the planned duration exceeds one month.<sup>3,4</sup> However, the results of a few randomised trials and a meta-analysis that were performed in non-haematological malignancies are consistent with a higher risk for catheter-related venous thrombosis (VT) and other adverse events with PICCs than with PORTs.<sup>2,5–8</sup>

While these complications are highlighted in the context of non-haematological cancers, they may be of particular concern in haematological malignancies that are characterised by significant immunodepression and frequent coagulation disorders. In a retrospective analysis, it was shown that patients with lymphoma were almost 4 times as likely to develop PICC-related VT as those with other types of cancer.<sup>9</sup> More specifically, among lymphomas, diffuse large B-cell lymphoma (DLBCL) is associated with a higher risk of thromboembolic events than follicular lymphoma (FL) or Hodgkin lymphoma (HL), and most of these events occur within three months after diagnosis.<sup>10</sup> Many other independent parameters have been associated with an increased risk of thromboembolic events in lymphoma patients, including history of thrombosis, obesity, mediastinal involvement, extranodal localisation, reduced mobility (ECOG performance status 2–4), neutropenia (1 G/L) or anaemia (< 10 g/dL), thereby leading to the definition of the thrombosis lymphoma score (ThroLy).<sup>11</sup>

In this context, the choice of intravenous device could be crucial for limiting the number of complications and ensuring treatment continuation. Notably, conventional central venous catheters (cCVCs) are associated with the highest risk of catheter-related complications; hence, these devices should no longer be used in haematological malignancies.<sup>12,13</sup> The aim of this study was to compare the safety of PICCs and PORTs in a homogeneous and monocentric population of DLBCL patients who were treated with first-line

immunochemotherapy by evaluating the numbers of thromboembolic events and infections that occurred in the six months following implantation according to the device that was used.

## 2 | PATIENTS AND METHODS

### 2.1 | Patient population

This retrospective study was conducted at the Cancer Institute Centre Henri Becquerel, Rouen, France. All patients who were diagnosed with DLBCL between January 2010 and April 2020 at this institution were screened. The inclusion criteria were patients older than 18 who were diagnosed with histologically proven primary DLBCL or transformed low-grade lymphomas that justified a first line of immunochemotherapy.

The exclusion criteria were ongoing systemic infection, platelet count <50 G/L, prothrombin time ratio (PR) <50% that was not attributed to anticoagulant therapy, haemophilia and superior vena cava syndrome. Patients who were undergoing curative anticoagulant therapy at the time of diagnosis were not excluded from the study. \*\*

### 2.2 | Central venous devices

The devices were centrally implanted by the same team using ultrasonography (US)-guided catheter placement. PICCs were implanted using the basilic or brachial vein, and PORTs were implanted in the internal jugular or subclavian vein. The PICC devices were PowerPICC SOLO2 (Becton Dickinson,) catheters with 4 Fr. single lumen. The PORT devices were X-PORT isp (Becton Dickinson) implanted ports with a 6 Fr. single lumen for patients with a body mass index (BMI) that exceeded 23 kg/m<sup>2</sup> and UltraSlimPort (Becton Dickinson) devices with a 6 Fr. single lumen for patients with BMI <23 kg/m<sup>2</sup>. All devices were tested and flushed immediately after implantation. A chest X-ray to confirm the position of the device after implantation was mandatory. After implantation, the PICCs were flushed every week using a 0.9% normal saline solution, and the occlusive dressing was changed as recommended.<sup>4</sup> In this retrospective study, the choice of the device was guided by patient preference, physician preference or availability/organisational considerations of the surgery department.

### 2.3 | End-points

The primary objective of this study was to compare the safety profiles of the two types of implanted devices, which were defined by the probability of a catheter-related serious adverse event (SAE) in the six months following implantation. According to the common terminology criteria for adverse events (CTCAE), version 5, catheter-related SAE was defined as either catheter-related

venous thrombosis (CR-VT) or infection (CR-I) of grade  $\geq 3$  or that induced a delay in chemotherapy administration of  $>7$  days or required the replacement of the implanted device or the use of curative anticoagulation.

Thromboembolic adverse events (AEs) were explored in cases of clinical suspicion, as in daily practice but without systematic screening. All thromboembolic AEs were confirmed by an ultrasound or computed tomography (CT) scan. Infection of the implanted devices was defined as either exit site infection or catheter-related bloodstream infection according to the French National Committee on Nosocomial Infections and Care-Related Infections (CTINILS)<sup>14</sup> (complete CTINILS criteria are provided as supplementary data). Purulence at the catheter insertion site or repeated occurrences of shivers after catheter flushing or manipulation were also considered infectious events, as in previous studies.<sup>15–17</sup> A sensitivity analysis was performed considering only infectious events according to the CTINILS criteria.

A composite parameter that was based on the combination of one or more of these complications (CR-VT and CR-I) was used as the primary endpoint. Separate analyses of CR-VT and CR-I were performed as secondary endpoints.

## 2.4 | Ethical and regulatory aspects

The study was approved by the Internal Review Board of the Centre Henri Becquerel (IRB number 2107B); all patients gave their consent for clinical retrospective analysis of their anonymous medical data.

## 2.5 | Statistical analysis

Based on preliminary results that were obtained by computer-based estimation by our database centre, we estimated the probability of thrombosis to be 1.95% using PORTs and 6.95% using PICCs and the probability of infections to be 5.81% using PORTs and 11% using PICCs. Based on these estimates, with a risk alpha of 5% and a risk beta of 10%, a sample size of 454 provided a 90% chance of correctly identifying the device with the higher risk of thrombosis/infections.

In this nonrandomised retrospective analysis, a propensity score-based analysis using inverse probability of treatment weighting was performed to reduce bias.<sup>18</sup> Briefly, the distributions of many measured putative confounders were summarised in a single score based on the probability of receiving a PICC versus a PORT (comparator population).<sup>19</sup> A logistic regression model was used to calculate the propensity score. The preselected variables in this model included age and sex, Ann Arbor stage, LDH level, *performance status* (ECOG scale), treatment with antiplatelet agents or anticoagulants, thrombosis past history, platelet count, PR, neutrophil and lymphocyte count, HIV status, type of chemotherapy, interval time between device implantation and chemotherapy initiation, socio-economic status, presence of a caregiver at home, cognitive or locomotor limitation, psychiatric condition, catheter laterality and date of catheter implantation.

To evaluate the association between device type and the occurrence of complications, we fitted a logistic regression model with a propensity score adjustment. Adjusted relative risks (ARRs) were computed using the marginal effects method with bootstrapping to calculate confidence intervals. The ARR of catheter complications for each considered risk factor, adjusted for the catheter type, was computed based on a modified propensity score that was calculated without the risk factor of interest. The results are presented in a forest plot. This analysis was performed with a descriptive purpose without correcting for multiple comparisons. Kaplan–Meier curves for the times between device implantation and events were computed and compared using likelihood-ratio tests. Statistical analyses were performed using R software R 4.1.0 and the main packages used were “boot” for bootstrap, “survey” for inverse probability weighting, “mice” for multiple imputation and “survival” for survival analysis. All tests were two-sided and  $p$ -values lower than .05 were regarded as statistically significant.

## 3 | RESULTS

### 3.1 | Population description

After selection according to the inclusion/exclusion criteria, 479 patients were retained for the analysis (Figure 1). Among them, 266 patients were treated using a PORT, and 213 were treated using a PICC. The main clinical features of the overall population and according to the type of intravenous implanted device are described in Table 1. Patients with a PICC and patients with an implantable PORT differed significantly in terms of age, performance status and chemotherapy regimen. PICC use was also more frequent among patients with lower PR, with antiplatelet or anticoagulant treatment, or with a history of thromboembolic events or locomotor disability. Left implantation was more frequent among patients with a PICC than with a PORT. PORTs were more frequently implanted before 2015, while PICC lines were more frequently implanted after 2015. In contrast, features such as sex, BMI, age-adjusted International Prognostic Index (aIPI), and Ann Arbor stage were similar between the two groups.

### 3.2 | Numbers of thrombotic and infectious events according to the type of device

Twenty-six TE (5.4%) events and 30 infections (6.3%) were identified in the six-month period following PICC/PORT implantation in this first line (1L) DLBCL population, which led to 50 catheter-related serious adverse events (10.4%). The flow chart of selection event is represented in Figure S1. Among the patients who experienced these adverse events, 6 experienced catheter-related septic thrombophlebitis, which is defined as the concurrent occurrence of both infection and thrombosis.

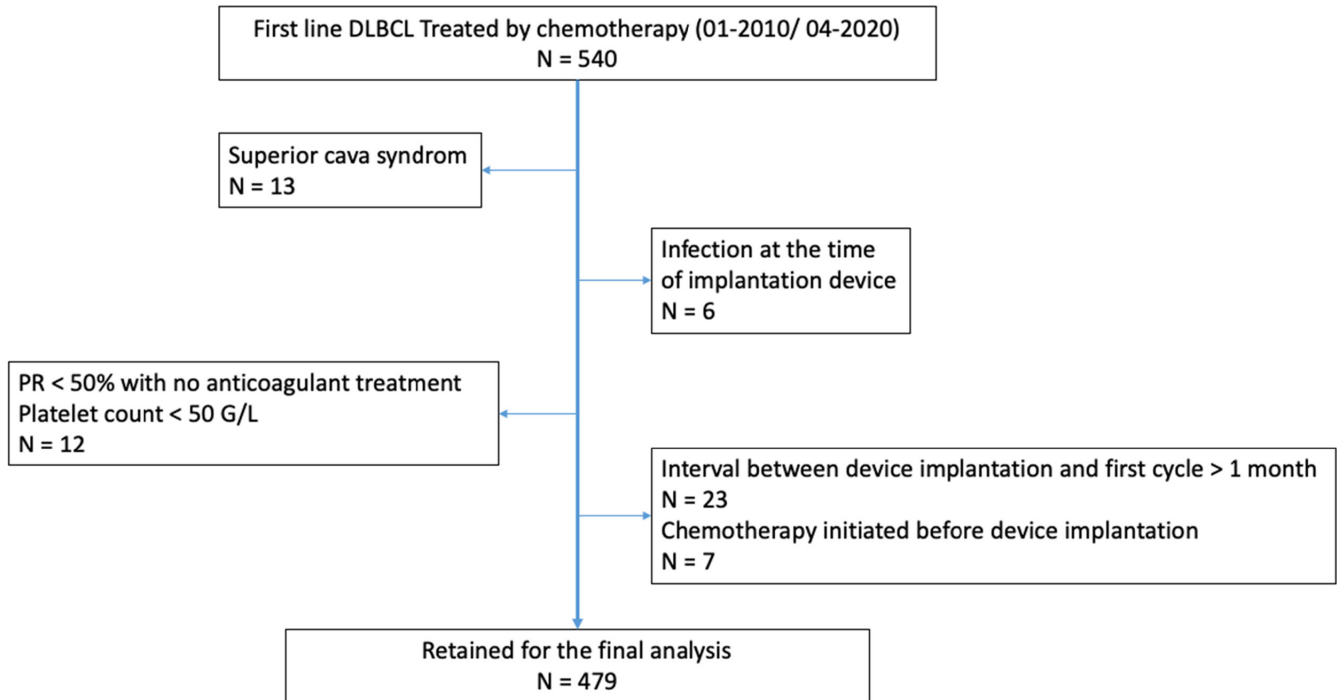


FIGURE 1 Flowchart of the study

Among the 26 venous thrombosis events that were confirmed by Doppler or CT scans in the overall cohort, the thrombosis locations were as follows: right basilic vein (x2), left basilic vein (x5), upper vena cava (x2), right internal jugular vein (x5), left internal jugular vein (x2), right subclavian vein (x6), left subclavian vein (x3) and not available (x1) (Table S1). Among patients with PICCs, the thrombus site was a basilic vein in 6/16 cases, a subclavian vein in 6/16 cases, an internal jugular vein in 2 cases and the upper vena cava in 1 case. Among patients with PORTs, most thrombosis sites were an internal jugular vein (5/10) or a subclavian vein (3/10). Among the 30 infectious events, 20 patients had catheter-related bloodstream infections, 9 patients had exit-site infections, and 1 patient experienced repeated occurrences of shivers after catheter flushing or manipulation without isolation of a pathogen (Table S1).

The majority of infectious events that were associated with PORTs were bloodstream infections (7/8), while 13 of the 22 infectious events in patients with PICCs were bloodstream infections. The identified pathogens were gram-positive cocci (GPC) in 10 cases, gram-negative bacilli (GNB) in 11 cases and other pathogens in 3 cases. In the PICC group, 9 of 16 infectious events with identified pathogens were caused by GNB versus 2 GNB infections over 8 infectious events with identified pathogens in the PORT group. The majority of the events, especially in the PICC group, occurred within the first three months following device implantation (Figure 2).

The ARR based on the propensity score according to the type of device is presented in Table 2. The results indicate that the PICC device is associated with a higher risk of catheter-related serious adverse events within 6 months after implantation, with an ARR of 2.6 [95% CI = 1.3–5.9],  $p = .008$ . This risk increase for the PICC device was significant for both infectious events (ARR = 3.2, 95% CI = [1.3–10.9],

$p = .015$ ) and venous thrombosis (ARR=4.0, 95% CI = [1.5–11.6],  $p = .009$ ) (Table 2). The estimated absolute risks of catheter-related serious adverse events in the propensity score analysis were 14% [8%–16%] in the PICC group and 5% [2%–8%] in the PORT group (absolute risk reduction: 9%). This means that the estimated number needed to treat (NNT) with a PORT rather than a PICC to avoid one complication is 11. The sensitivity analysis conducted when excluding infectious events outside of CTINILS criteria showed very similar results for catheter-related serious adverse events, with an ARR 2.5 [1.1–5.8],  $p = .02$ . This can be explained by the fact that half of these infectious events were septic thrombophlebitis and were therefore still reported as adverse events. When focusing only on infectious events, the comparison between PICC and PORT became non-significant after excluding non-CTINILS events (ARR 2.6 [0.9–8.2],  $p = .08$ ).

PICCs were withdrawn in 23 cases and PORTs in 7 cases. Among the 30 patients whose catheters were withdrawn, 22 had a catheter-related infectious event, and 8 had venous thrombosis without infection. Chemotherapy was postponed for 12 patients, among which 3 patients received PORTs and 9 patients received PICCs.

Figure 3 shows a forest plot for the ARR of catheter-related serious adverse events according to the potential risk factors that were considered in the propensity score analysis. Few factors were found to be associated with the risk of catheter complications outside of the highest LDH levels (ARR 3.8 [1.7–15.2]).

## 4 | DISCUSSION

To the best of our knowledge, we report the largest cohort of patients with DLBCL who were treated with first-line immunochemotherapy,

TABLE 1 Clinical and demographic features of the overall cohort and according to the type of device

Variable	PORT n = 266 (%)	PICC n = 213 (%)	p value
Age (years) (mean (sd))	64 (13)	67 (15)	.05
Gender			.49
Male	142 (53.4)	107 (50.2)	
Female	124 (46.6)	106 (49.8)	
Date of insertion of the central device			<.001
2010–2015	174 (65.4)	58 (27.3)	
2015–2020	92 (34.6)	155 (72.7)	
Catheter laterality		(NA = 1)	.002
Right	213 (80.1)	143 (67.1)	
Left	53 (19.9)	69 (32.4)	
Performance status	(NA = 2)	(NA = 8)	<.001
≤2	244 (91.7)	159 (74.6)	
>2	20 (7.5)	46 (21.6)	
Body mass index (mean(sd))	26.1 (4.9) (NA = 2)	26.8.8 (5.9)	.18
Caregiver at home	(NA = 14)	(NA = 2)	.04
No	60 (22.6)	68 (31.9)	
Yes	192 (72.2)	143 (67.1)	
Profession	(NA = 44)	(NA = 36)	.61
Working-class	66 (24.8)	62 (29.1)	
Craftsmen, business owners	21 (7.9)	11 (5.2)	
Managers and intellectual professions	36 (13.5)	24 (11.3)	
Employees	65 (24.4)	54 (25.4)	
Intermediate professions	34 (12.8)	26 (12.2)	
Days between catheter insertion and initiation of chemotherapy			<.001
0	59 (22.2)	77 (36.2)	
1–5	55 (20.7)	68 (31.9)	
5–13	68 (25.6)	50 (23.5)	
>13	84 (31.6)	18 (8.5)	
Mediastinal involvement		(NA = 1)	.11
No	169 (63.5)	124 (58.2)	
Lower than 7 cm	92 (34.6)	77 (36.1)	
Greater than 7 cm	5 (1.9)	11 (5.1)	
Ann Arbor stage	(NA = 1)		.71
Stade 1–2	62 (23.3)	38 (17.8)	
Stade 3–4	203 (76.3)	175 (82.2)	
aalPI			.08
0–1	61 (22.9)	35 (16.4)	
2–3	205 (77.1)	178 (83.6)	
LDH (UI/L)			.06

(Continues)

TABLE 1 (Continued)

Variable	PORT n = 266 (%)	PICC n = 213 (%)	p value
≤350	76 (28.6)	45 (21.1)	
>350	190 (71.4)	168 (78.9)	
Lymphocyte count (G/L) (mean (sd))	1.98 (1.94) (NA = 2)	1.82 (6.56)	.77
Platelet count (G/L) (mean (sd))	283 (110) (NA = 2)	299 (142)	.19
Neutrophil count (G/L) (mean (sd))	6.1 (3.4) (NA = 1)	7.0 (4.2)	.01
APTT	(NA = 3)		.13
≤1.2	245 (92.1)	190 (89.2)	
>1.2	18 (6.8)	23 (10.8)	
Prothrombin ratio	(NA = 1)		.03
≥70%	250 (94)	189 (88.8)	
<70%	15 (5.6)	24 (11.3)	
Chemotherapy			.01
RCHOP	132 (49.6)	86 (40.4)	
RMINICHOP	38 (14.3)	47 (22.1)	
RACVBP	49 (18.4)	27 (12.7)	
Other*	47 (17.7)	53 (24.9)	
History of thromboembolic events			.001
No	251 (94.4)	182 (85.4)	
Yes	15 (5.6)	31 (14.6)	
Anti-platelet treatment	(NA = 1)	(NA = 1)	.03
No	228 (85.7)	167 (78.4)	
Yes	37 (13.9)	45 (21.1)	
Anticoagulant drug	(NA = 1)		<.001
No	241 (90.6)	169 (79.3)	
Yes	24 (9)	44 (20.7)	
Psychiatric medical history			.56
No	234 (88.0)	191 (89.7)	
Yes	32 (12.0)	22 (10.3)	
Psychotropic drug	(NA = 1)		.49
No	223 (83.8)	184 (86.4)	
Yes	42 (15.8)	29 (13.6)	
Cognitive disorders			.25
No	240 (90.2)	185 (86.9)	
Yes	26 (9.8)	28 (13.1)	
Locomotor disability			.002
No	248 (93.2)	180 (84.5)	
Yes	18 (6.8)	33 (15.5)	

Abbreviations: aalPI, age-adjusted International Prognostic Index; APTT, activated partial thromboplastin time; NA, not available.

\*Other chemotherapy regimens included: R-MPV (R-methotrexate vincristine and procarbazine), R-C5R (R-COPADEM + R-CYM), R-CHP-polatuzumab, R-gemcitabine-oxaliplatin, R-CHOP-Tazemetostat, R-CHOP-Methotrexate.

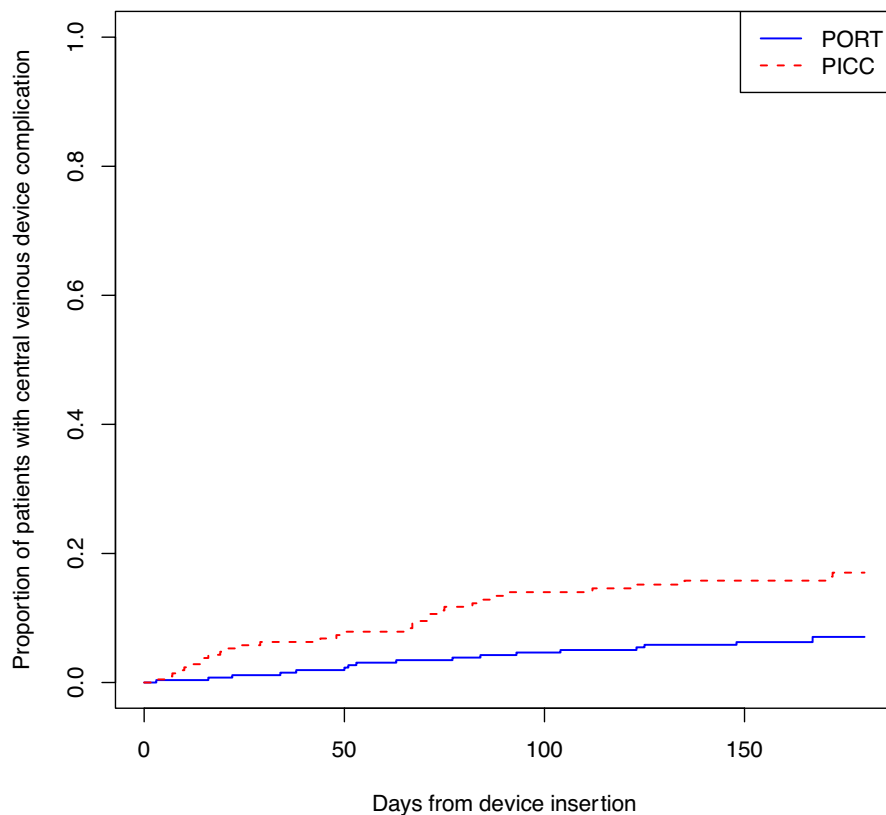


FIGURE 2 Kaplan-Meier curves for catheter-related serious adverse events

TABLE 2 Relative risk of venous thrombosis, infection and overall catheter-related serious adverse events adjusted by the propensity score according to the type of device

	Event <i>n</i> (%)	No event <i>n</i> (%)	ARR [CI95%]	<i>p</i> value
Event: catheter-related serious adverse event (CR-VT or CR-I)				
PORT	18 (6.8%)	248 (93.2%)	1	.008
PICC	32 (15.0%)	181 (85.0%)	2.6 [1.3– 5.9]	
Event: catheter-related infection (CR-I)				
PORT	8 (3.0%)	258 (97%)	1	.015
PICC	22 (10.3%)	191 (90%)	3.2 [1.3– 10.9]	
Event: catheter-related venous thrombosis (CR-VT)				
PORT	10 (3.8%)	256 (96.2%)	1	.009
PICC	16 (7.5%)	197 (92.5%)	4.0 [1.5–11.6]	

Abbreviations: ARR, adjusted relative risk; CI, confidence interval; CR-I, catheter-related infection; CR-VT, catheter-related venous thrombosis.

for which we describe thrombotic and infectious complications according to the type of central venous catheter that was used. We identify an estimated twofold increased risk of venous thrombosis and infectious complications in the 6 months following the implantation of PICC devices compared to PORTs. Importantly however, the number of postponed chemotherapy cycles remained low with the two types of devices; hence, there should not be a major effect on dose intensities, which is crucial for the treatment of DLBCL.

Several differences between PICCs and PORTs could explain this increased risk of complications associated with PICCs. The PORT device is directly inserted in a large diameter vein, while the PICC device is inserted in a basilic or brachial vein, with a lower diameter. A higher vein-to-catheter ratio has been described as associated with a reduction of blood flow resulting in a higher risk of thrombotic events.<sup>20</sup> In this study however, the PICC devices used were all small catheters (4 Fr.) in order to limit the risk of thrombotic events.<sup>21</sup> In terms of infections, migration of skin microorganisms along the catheter external surface is one of the main described mechanisms of catheter-related infections.<sup>22</sup> The external section of the PICC device is therefore likely to explain an increased risk of infection.

These results are in accordance with those reported in nonhaematological malignancies, as indicated by a comparison with systematic review data.<sup>23–25</sup> The rate of CR-VT, which was confirmed by Doppler or CT scans, was 5.4% in this DLBCL cohort. In comparison, in three randomised trials that involved solid tumours, the rate of CR-VT was 4.5%–7.2%.<sup>2,5,8</sup> Among these studies, the CAVA trial included patients with haematological malignancies, although in smaller numbers, which did not enable the authors to identify the preferred device in this group.<sup>8</sup> Additionally, it has been shown that despite a lower apparent cost associated with PICCs, the cost from a health care perspective is higher in cancer patients who receive a PICC than in those who receive a PORT, and discomfort is more frequently reported in the middle or at the end of treatment.<sup>5,26</sup>

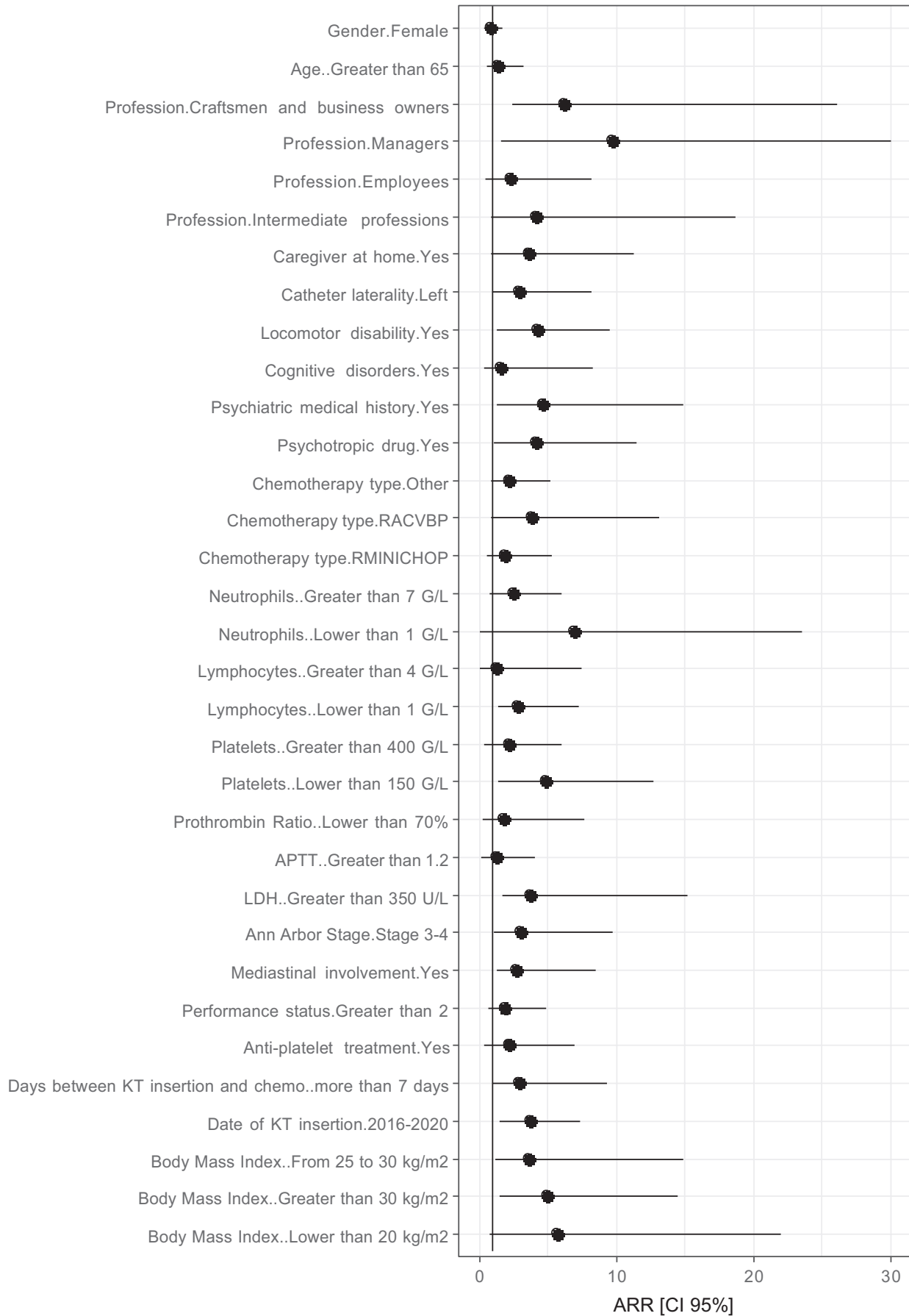


FIGURE 3 Forest plot of the adjusted relative risks for catheter-related serious adverse events



The comparison of the two device types is difficult to conduct, with studies that are either retrospective with limits inherent to the type of study, or randomised trials that in this context are often characterised by a high refusal rate (~50%), which suggest that patients who enrol in prospective trials are not necessarily representative.<sup>2,5</sup> The main limit of our study is its retrospective nature. The choice of the device was based on nonformalised criteria, which included mainly surgery accessibility or availability and the wait time of the anaesthesia-surgery department. Notably, we excluded specified high-risk situations, such as patients with superior vena cava syndrome.

Patients with PORTs versus PICCs differed significantly (Table 1) according to various clinical features, including performance status, interval between implantation and first chemotherapy cycle, anticoagulation usage and left implantation. These characteristics may influence the risk of complication. A Propensity-score based method was used to limit the impact of these confounders. Many potential confounders were included to reduce the potential selection bias to a minimum. However, this may result in overfitting the propensity score logistic regression and therefore in large confidence intervals. Therefore, care is needed in the interpretation of the magnitude of the effect that was shown. Another limit of this study is its single-centre design. The extent to which the results would apply to other types of devices than the ones used in our centre, other team habits or other patient populations, is uncertain. However, we show an increased risk of venous thrombosis with PICCs despite the use of low diameter PICC devices.

What are the practical consequences of these findings? The use of systematic anticoagulation to prevent central venous catheter complications in the field of haematological cancer is still a matter of debate. More specifically, no randomised trials have been conducted to evaluate thrombosis prophylaxis in lymphoma patients. In general, thrombosis prophylaxis in lymphoma patients is underused because of a potentially high risk of bleeding, which is related mainly to chemotherapy-induced thrombocytopenia.<sup>27</sup> Thromboembolic events are a frequent complication of DLBCL that occur particularly at diagnosis or during initial therapy and are associated with a worse prognosis.<sup>28,29</sup> A risk assessment model (RAM), namely, ThroLy, for the prediction of thromboembolic events in lymphoma has been developed and may be useful for guiding prophylaxis. However, this RAM was established in a heterogeneous population of lymphoid malignancies (NHL, HL, chronic lymphocytic leukaemia, and only 42% of aggressive lymphomas), where only 2/1820 patients developed CR-VT.<sup>11</sup> This suggests that this score is not directly applicable to select patients for CR-VT prophylaxis. Conversely, the Michigan risk score was developed in order to predict PICC-related thrombosis, in a heterogeneous population in which 6.2% were treated for active cancer.<sup>30</sup> In this score, active cancer was a risk factor of PICC-related thrombosis. However, considering the unknown proportion of patients with haematological malignancy, the extent to which this score can apply to lymphoma patients in order to guide prophylaxis is uncertain. Similarly, the prophylactic use of systemic antibiotics is not recommended before insertion. The available data are not sufficient for recommending for or against the routine use of antibiotic flush/lock therapy.<sup>4</sup>

Recently, the CAVA trial compared the complication rates and costs of three devices to establish the acceptability, clinical effectiveness, and cost-effectiveness of the devices for patients who are receiving systemic anticancer treatment. In this multicentric randomised trial, PORTs appeared to be more effective and safer than both Hickman catheters and PICCs. However, due to the small numbers of haematological malignancies in CAVA, the authors did not draw any conclusion in this subgroup.<sup>8</sup> Whereas current guidelines provide insufficient information for recommending one type of CVD over another,<sup>4</sup> our study provides data suggesting that PICCs are associated with more complications than PORTs for the first line of treatment for DLBCL patients. The choice of a device should take this into account, as well as patients' preference and anaesthetist/surgeon availabilities. Additionally, the choice of the device should take into account other risk factors of catheter complications (e.g. high LDH according to this study, or other risk factors of PICC-related VT according to the Michigan risk score, although data remain insufficient to draw specific recommendations according to risk factors. The use of a PICC could justify preventive measures such as the use of heparin thrombosis prevention, even if this procedure remains a matter of debate, and a prospective randomised trial in the setting of DLBCL would be of interest.

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#### CONFLICT OF INTEREST

The authors declare no potential conflicts of interest with respect to the authorship and/or publication of this article.

#### DATA AVAILABILITY STATEMENT

Data in this manuscript concern patient data and are not available in a public repository.

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#### REFERENCES

- Sehn LH, Salles G. Diffuse large B-Cell lymphoma. *N Engl J Med*. 2021;384(9):842-858.
- Taxbro K, Hammarskjöld F, Thelin B, et al. Clinical impact of peripherally inserted central catheters vs implanted port catheters in patients with cancer: an open-label, randomised, two-centre trial. *Br J Anaesth*. 2019;122(6):734-741.
- Chopra V, Flanders SA, Saint S, et al. Michigan appropriateness guide for intravenous catheters P. the michigan appropriateness guide for intravenous catheters (MAGIC): results from a multispecialty panel using the RAND/UCLA appropriateness method. *Ann Intern Med*. 2015;163(6 Suppl):S1-S40.
- Schiffer CA, Mangu PB, Wade JC, et al. Central venous catheter care for the patient with cancer: American society of clinical oncology clinical practice guideline. *J Clin Oncol*. 2013;31(10):1357-1370.
- Clatot F, Fontanilles M, Lefebvre L, et al. Randomised phase ii trial evaluating the safety of peripherally inserted catheters versus





- implanted port catheters during adjuvant chemotherapy in patients with early breast cancer. *Eur J Cancer*. 2020;126:116-124.
6. Patel GS, Jain K, Kumar R, et al. Comparison of peripherally inserted central venous catheters (PICC) versus subcutaneously implanted port-chamber catheters by complication and cost for patients receiving chemotherapy for non-haematological malignancies. *Support Care Cancer*. 2014;22(1):121-128.
  7. Pu YL, Li ZS, Zhi XX, et al. Complications and costs of peripherally inserted central venous catheters compared with implantable port catheters for cancer patients: a meta-analysis. *Cancer Nurs*. 2020;43(6):455-467.
  8. Moss JG, Wu O, Bodenham AR, et al. Group Ct. central venous access devices for the delivery of systemic anticancer therapy (CAVA): a randomised controlled trial. *Lancet*. 2021;398(10298):403-415.
  9. Zhang X, Huang JJ, Xia Y, et al. High risk of deep vein thrombosis associated with peripherally inserted central catheters in lymphoma. *Oncotarget*. 2016;7(23):35404-35411.
  10. Rupa-Matysek J, Gil L, Kazmierczak M, Baranska M, Komarnicki M. Prediction of venous thromboembolism in newly diagnosed patients treated for lymphoid malignancies: validation of the khorana risk score. *Med Oncol*. 2017;35(1):5.
  11. Antic D, Milic N, Nikolovski S, et al. Development and validation of multivariable predictive model for thromboembolic events in lymphoma patients. *Am J Hematol*. 2016;91(10):1014-1019.
  12. Fracchiolla NS, Todisco E, Bilancia A, et al. Clinical management of peripherally inserted central catheters compared to conventional central venous catheters in patients with hematological malignancies: a large multicenter study of the REL GROUP (rete ematologica lombarda - lombardy hematologic network, Italy). *Am J Hematol*. 2017;92(12):E656.
  13. Cortelezzi A, Moia M, Falanga A, et al. Group CS. Incidence Of thrombotic complications in patients with haematological malignancies with central venous catheters: a prospective multicentre study. *Br J Haematol*. 2005;129(6):811-817.
  14. Hadl S. *Comité Technique Des Infections Nosocomiales Et Des Infections Liées Aux Soins. Définition Des Infections Liées Aux Soins*. Ministère De La Santé, De La Jeunesse Et Des Sports DIRECTION GENERALE DE LA SANTE. 2007.
  15. Abdelkefi A, Torjman L, Ladeb S, et al. Randomized trial of prevention of catheter-related bloodstream infection by continuous infusion of low-dose unfractionated heparin in patients with hematologic and oncologic disease. *J Clin Oncol*. 2005;23(31):7864-7870.
  16. Castagnola E, Molinari AC, Giacchino M, et al. Incidence of catheter-related infections within 30 days from insertion of hickman-broviac catheters. *Pediatr Blood Cancer*. 2007;48(1):35-38.
  17. Abdelkefi A, Achour W, Ben Othman T, et al. Difference in time to positivity is useful for the diagnosis of catheter-related bloodstream infection in hematopoietic stem cell transplant recipients. *Bone Marrow Transplant*. 2005;35(4):397-401.
  18. Austin PC. An introduction to propensity score methods for reducing the effects of confounding in observational studies. *Multivariate Behav Res*. 2011;46(3):399-424.
  19. Webster-Clark M, Sturmer T, Wang T, et al. Using propensity scores to estimate effects of treatment initiation decisions: state of the science. *Stat Med*. 2021;40(7):1718-1735.
  20. Sharp R, Carr P, Childs J, et al. Catheter to vein ratio and risk of peripherally inserted central catheter (PICC)-associated thrombosis according to diagnostic group: a retrospective cohort study. *BMJ Open*. 2021;11(7):E045895.
  21. Balsorano P, Virgili G, Villa G, et al. Peripherally inserted central catheter-related thrombosis rate in modern vascular access era-when insertion technique matters: a systematic review and meta-analysis. *J Vasc Access*. 2020;21(1):45-54.
  22. Bouza E, Burillo A, Munoz P. Catheter-related infections: diagnosis and intravascular treatment. *Clin Microbiol Infect*. 2002;8(5):265-274.
  23. Chopra V, Anand S, Hickner A, et al. Risk of venous thromboembolism associated with peripherally inserted central catheters: a systematic review and meta-analysis. *Lancet*. 2013;382(9889):311-325.
  24. Pikwer A, Akeson J, Lindgren S. Complications associated with peripheral or central routes for central venous cannulation. *Anaesthesia*. 2012;67(1):65-71.
  25. Johansson E, Hammarskjöld F, Lundberg D, Arnlind MH. Advantages and disadvantages of peripherally inserted central venous catheters (PICC) compared to other central venous lines: a systematic review of the literature. *Acta Oncol*. 2013;52(5):886-892.
  26. Taxbro K, Hammarskjöld F, Juhlin D, Hagman H, Bernfort L, Berg S. Cost analysis comparison between peripherally inserted central catheters and implanted chest ports in patients with cancer-a health economic evaluation of the PICCPort trial. *Acta Anaesthesiol Scand*. 2020;64(3):385-393.
  27. Antic D, Jelcic J, Vukovic V, Nikolovski S, Mihajljevic B. Venous thromboembolic events in lymphoma patients: actual relationships between epidemiology, mechanisms, clinical profile and treatment. *Blood Rev*. 2018;32(2):144-158.
  28. Komrokji RS, Uppal NP, Khorana AA, et al. Venous thromboembolism in patients with diffuse large B-cell lymphoma. *Leuk Lymphoma*. 2006;47(6):1029-1033.
  29. Mahajan A, Wun T, Chew H, White RH. Lymphoma and venous thromboembolism: influence on mortality. *Thromb Res*. 2014;133(Suppl. 2):S23-28.
  30. Chopra V, Kaatz S, Conlon A, et al. The michigan risk score to predict peripherally inserted central catheter-associated thrombosis. *J Thromb Haemost*. 2017;15(10):1951-1962.

## SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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