American Journal of Infection Control 000 (2020) 1–8

Contents lists available at ScienceDirect

American Journal of Infection Control

journal homepage: www.ajicjournal.org

Major Article

Midline or long peripheral catheters in difficult venous access conditions? A comparative study in patients with acute cardiovascular diseases

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Key Words:
Catheter-related thrombosis
Catheter-related blood stream infection
Complication
Catheter survival
Incidence
Indwelling time

Background: Midline catheters (MCs) are commonly inserted in patients with difficult venous access (DVA) needing peripheral access. Recently, the alternative placement of ultrasound-guided long peripheral catheters (LPCs) has spread. However, no study has compared the reliability of the 2 devices. This study aims to compare the safety and reliability of MCs and LPCs in DVA patients.

Methods: A retrospective cohort study was conducted, enrolling 184 DVA patients. Polyurethane MCs and 2 lengths of polyethylene LPCs (8/10 cm and 18 cm) were compared. The independent effect of catheter type on uncomplicated catheter survival was determined through a Cox regression analysis.

Results: The relative incidences of overall catheter-related complications (CRCs) were 15.84 of 1,000, 10.64 of 1,000, and 6.27 of 1,000 catheter-days for 8/10 cm-LPCs, 18 cm-LPCs, and MCs, respectively. The relative incidences of catheter-related bloodstream infections were 0.72 of 1,000 for both length LPCs and 0.48 of 1,000 catheter-days for MCs. Compared to MCs, a significant increase in CRC risk for 8/10 cm LPCs (hazard ratio [HR] 5.328; 95% confidence interval [CI] 2.118-13.404; $P < 0.001$) was found, along with a nonsignificant trend toward an increased risk for 18 cm-LCPs (HR 2.489; 95% CI 0.961-6.448; $P = 0.060$).

Conclusion: MCs allow for longer uncomplicated indwelling times than LPCs. The decision regarding which catheter to use should consider the planned duration of intravenous therapy, the patient's clinical condition, and the cost of the device.

Up to 70% of hospitalized patients require vascular access.[1] In the vast majority of cases, a peripheral venous catheter (PVC) is placed, as this option represents the simplest and safest solution,[2] making it possible to administer, with a few specific exceptions, all the most commonly needed intravenous fluids and medications.[3,4] However, PVC placement may sometimes be challenging, in that some patients risk multiple failed attempts, thus, outlining a clinical condition known as difficult venous access (DVA).[5] Although in DVA patients the placement of central venous access seems to be an acceptable alternative, this option is associated with risks of immediate or delayed complications[6]; therefore, it should be reserved to very specific and restricted circumstances (e.g., administration of hyperosmolar, vesicants, or endothelium irritants products, advanced hemodynamic or oxyphoretic monitoring).

To ensure a peripheral access to DVA patients, a catheter can be inserted under ultrasound (US) guidance in deeper veins not recognizable through inspection or physical examination. However, traditional PVCs are not suitable for this use due to insufficient catheter length, which exposes the patients to a high risk of complications (e.g., extravasation or displacement).[7] In the absence of a precise indication for a central line, the US-guided placement of a midline catheter (MC) has been the traditional choice for over 30 years. More recently, the use of long peripheral catheters (LPCs) has been proposed as an intermediate option between conventional short PVCs and MCs,[8] and many guidewire-equipped catheters of various lengths have been progressively proposed by the industry.

Consequently, a clear distinction between MCs and LPCs is not yet obvious, either according to length or to tip position (which may depend on factors such as the anthropometric characteristics of the patient and the puncture site) or the type of biomaterial, while the only possible characterizing criterion could be related to the expected

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Conflict of interest: None to report.
Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

https://doi.org/10.1016/j.ajic.2019.12.025

duration of the catheters (Supplementary material). Therefore, the only clear difference between MCs and LPCs concerns the placement technique, since MCs require the same US-guided "modified Seldinger" technique used for peripherally inserted central catheters (PICCs),[9] while a faster method based on a "direct" Seldinger technique is indicated for LPCs. Another substantial difference is economic, since LPCs cost almost one-fourth that of MCs.[8,10] It is precisely these 2 last characteristics that have likely contributed to the rapid spread of the LPCs.

As a consequence, a tendency to consider the LPCs equivalent to MCs seems to have emerged. Indeed, over the years, LPCs have been called "short midlines," or even considered to be "midlines" tout-court.[11] A recent review included LPCs and MCs into a unique "midline" category, attributing them the same advantages in terms of complication rates and cost-benefit.[12] This confusion could lead to an indiscriminate choice of one or the other catheter. Unfortunately, the safety of the use of LPCs is supported by few studies,[13] and currently, no study has compared the reliability of LPCs and MCs in clinical practice. Thus, the aim of study is to compare the safety and reliability of midline catheters and LPCs of 2 different lengths in a population of DVA patients.

METHODS

Design, setting, and population

This is a retrospective cohort study conducted in the Cardiothoracic-Vascular Department of the University Hospital of Trieste, Italy. All consecutive adult DVA patients admitted from January 2014 to April 2019 were enrolled. DVA situations were identified in the presence of patients with a lack of readily visible or palpable veins when 3 or more cannulation attempts failed.[5] Patients with immediate life-threatening conditions or need for central venous access were excluded.

A minimum required sample size of 182 catheters was calculated based on the estimated difference between the complication rates of LPCs (19.7%)[14] and MCs (5.3%-5.9%).[15,16] This sample size enabled a type-I probability error of 5% and a desired statistical power of 80%.

Catheter characteristics and placement procedure

The catheters were categorized as MC or LPC based on the placement technique and the biomaterial. Polyurethane power injectables 4-5 Fr, 55 cm single-lumen PICCs, trimmed to a standard length of 20 cm were used as MCs, while polyethylene catheters (available in the following sizes: 3 Fr, 8 cm; 4 Fr, 10 cm; 4 Fr, 18 cm) were employed as LPCs. Both the LPC and the MC were inserted by a nurse specialized in vascular access.

After positioning the patient in a supine position with her/his upper arm in abduction, a complete US examination of the upper arm veins was conducted. Once identifying the most suitable vessel to cannulate, maximal aseptic barriers were adopted (surgical mask, cap, drape and gloves, sterile transducer cover, and US gel), and a wide skin surface around the puncture site was scrubbed with 2% chlorhexidine/70% alcohol solution. A tourniquet was positioned by a collaborator at the appropriate level of the arm. The identified vein was visualized in short axis and punctured with the needle under direct US guidance by using an "out-of-plane" approach. Once the needle tip was visualized within the vein and the blood flowed back through the needle, the guidewire was introduced and the needle removed. The technique differed at this point: for LPCs, the catheter was moved forward into the vein "over-the-guidewire" (direct Seldinger technique); for MCs, the microintroducer was inserted through the guidewire, which was subsequently removed, allowing the introduction of the catheter through the microintroducer (modified Seldinger technique), which was thus removed using a peel-away method.

For both procedures, the successful cannulation was confirmed by both the aspiration of blood and the direct US visualization of the catheter in the vessel. In the case of a failure, the needle was removed and the procedure was restarted; each needle puncture of the skin was considered a distinct attempt. At the end of the procedure, the catheter was secured with a sutureless system and the exit site covered with a transparent semipermeable dressing.

Catheter choice and postimplantation management

In the absence of specific recommendations, LPCs were assimilated to traditional PVCs, and thus, were considered for short-term use, chosen for patients who have an expected venous access need for up to 7-10 days; whereas, MCs were placed when the expected need exceeded this time frame.[4] The expected time was based on the planned duration of intravenous therapy at the time of placement. In the cases of a modification of the treatment plan, the catheters were kept in use as long as needed. The length and the caliber of the catheters was chosen based on the characteristics of the cannulated vein. Both LPC and MC were managed by bedside nurses based on the same hospital policy and synthesized as follows:

- The infusion of parenteral nutrition and high-osmolarity medications through these catheters was forbidden, while all antibiotics were infused only after an appropriate dilution.[17]
- After delivering any medication, infusion, or blood product, the catheter was flushed with 10-20 ml of normal saline using a "stop and go" technique.
- The catheter exit site was inspected daily for possible complications; the semipermeable dressing was replaced weekly or whenever necessary after providing an adequate scrubbing of the exit site with 2% chlorhexidine/70% alcohol solution.
- The routine replacement of the catheter was never planned, while the catheters were promptly removed when no longer needed or if a complication occurred.[4]

Miscellaneous study variables

Patient demographics and data on past medical history were collected, and the Charlson comorbidity index was calculated.[18]

Data on the catheter type, the diameter (millimeters between vein inner walls) of the cannulated vein and the derived catheter-to-vein diameter ratio, as well as the number of cannulation attempts were recorded.

Any antibiotic administered at least once through the catheter was registered. Moreover, patients taking antiaggregant or anticoagulant medications through an oral or subcutaneous route or receiving continuous intravenous infusion of sodium heparin were recorded as these conditions were considered as potential protective factors against venous thrombosis.

Study outcomes

The primary endpoint of the study was the uncomplicated indwelling time of the catheters, calculated as the interval (days) between the dates of placement and removal. The catheter removal at end of use without any complication, as well as the unplanned removal of an uncomplicated and still in-use catheter (e.g., accidental removal, patient death) was considered as good outcomes. Conversely, premature catheter removal due to a CRC was considered a poor outcome. For the study purposes, the following CRCs were identified:

- Catheter-related bloodstream infections (CR-BSI) were diagnosed based on: (1) a positive semiquantitative culture (>15 colony-forming units/catheter segment), whereby, the same microorganism

(species and antibiogram) is isolated from the catheter tip and peripheral blood, and (2) differential period of catheter versus peripheral blood culture positivity of >2 hours (differential time to positivity)[19]
- Catheter-related thrombosis (CRT) was diagnosed as: a contemporary presence of: (1) phlebitis, defined as the presence of 2 or more signs of pain, erythema, purulence, streak formation, or a palpable venous cord,[20] and (2) direct US visualization of blood clot around the catheter adhering to the vessel wall, or vein incompressible to the US compression test[21]
- Infiltration (i.e., leakage of the infused medication from the exit site), complete occlusion, and catheter fissuring.

Ethical considerations

At hospital admission, each enrolled patient signed an informed consent authorizing the use of her/his clinical data for research purposes. According to the hospital department authorities, a formal approval from an Institutional review board was not required as peripheral venous cannulation represented a routine intervention in everyday patient care. The investigation conforms to the principles outlined in the Declaration of Helsinki.

Statistical analysis

The median and interquartile range (IQR) were used to describe the continuous variables. The differences between groups were examined using the Mann–Whitney U test. The nominal variables were illustrated as a number and percentage, and the possible differences were tested using contingency tables and either the Pearson χ test or Fisher's exact test, depending on whether the variable had more than 5 observations in each cell or not, respectively.

CRCs were expressed as percentages and as the relative incidence per 1,000 catheter days.[22] When the patient was discharged to home or transferred to another hospital with an indwelling catheter, observations were right-censored at the time of the event (known survival). Unadjusted survival analysis was conducted by comparing Kaplan-Meier curves; the Mantel-Cox log rank test was used to calculate differences between the catheters' survival rates.

According to the study aim, the following catheter groups were compared: (1) MCs; (2) 18 cm LPCs; and (3) 8/10 cm LPCs. Multivariate Cox regression models with forward stepwise selection were used to estimate the time-to-event effect of the catheter groups on the risk of any CRC occurrence, adjusted for confounders known to increase the risk of CRC (e.g., catheter-to-vein ratio, comorbidity),[3,23-26] as well as for the infused medication showing significantly related to the occurrence of CRCs in bivariate analyses. All the categorical variables were considered as dummy variables (e.g., type of catheter: MC = 1, 18 cm LPC = 2, 8/10 cm LPC = 3; catheter-to-vein ratio: <45% = 0, ≥45% = 1; rifampicin: no = 0, yes = 1). The results were presented as a proportional hazard ratio (HR) with a corresponding 95% confidence interval (CI) and cumulative survival adjusted curves. For all tests, the statistical significance was set at an alpha level of $P = 0.05$. Statistical analyses were performed using the software SPSS Statistics for Windows, version 24.0 (IBM Corp., Armonk, NY).

RESULTS

During the study period, 186 DVA patients were enrolled; 2 patients (1 with MC and 1 with 8/10 cm LPC) were excluded because the catheters were removed within 24 hours after placement due to the interruption of the intravenous therapeutic plan. Consequently, 184 patients (age: median 70.0 years, IQR 63.0-77.0; males: n = 99; 53.8%; Charlson index: median 3.0, IQR 2.0-4.0) constituted the final study population. No significant difference ($P = 0.686$) was found between the male (median 70.0 years; IQR 62.0-77.0) and female ages (median 72.0 years; IQR 63.5-76.5).

MCs, 18 cm LPCs, and 8/10 cm LPCs were placed in 80 (43.5%), 48 (26.1%), and 56 (30.4%) cases, respectively. Patients receiving LPCs had a significantly higher Charlson index (both LPCs groups: Median 3.0, IQR 2.0-4.0; MC: Median 2.0, IQR 1.0-4.0; $P = 0.026$), while only a nonsignificant trend toward an older age was documented (8/10 cm LPCs: Median 73.0 years, IQR 63.0-77.5; 18 cm LPC: Median 72.5 years, IQR 67.5-77.0; MC: Median 68.5 years, IQR 59.0-75.0; $P = 0.069$). Most catheters were placed after a single attempt (n = 168; 91.3%), while in 15 cases (8.2%), 2, and in one case (0.5%), 3 attempts were needed. No difference was shown between the catheter groups according to the number of attempts (P=0.856). A higher vein-to-catheter ratio was documented for MCs (8/10 cm LPCs: Median 29.0, IQR 21.9-36.0; 18 cm LPCs: Median 29.6, IQR 23.6-32.5; MCs: Median 32.5, IQR 27.2-40.7; $P = 0.004$).

The administration of 25 different antibiotics was documented. Up to 5 different antibiotics (median 1.0; IQR 0.0-2.0) were infused through the same catheter. A statistically significant higher ($P < 0.001$) number of different antibiotics was infused through MCs (median 2.0; IQR 1.0-2.0) compared with 18 cm LPCs (median 1.0; IQR 0.0-2.0) and 8/10 cm LPCs (median 0.5; IQR 0.0-1.5). No difference was seen between the catheter groups in terms of specific antibiotics infused, except for ampicillin (8/10 cm LPC: n = 1, 1.8%; 18 cm LPC: n = 3, 6.3%; MC: n = 13, 16.3%; $P = 0.012$), oxacillin (8/10 cm LPC: n = 2, 3.6%; 18 cm LPC: n = 1, 2.1%; MC: n = 18, 22.5%; $P < 0.001$), and rifampicin (8/10 cm LPC: n = 6, 10.7%; 18 cm LPC: n = 4, 8.3%; MC: n = 19, 23.8%; $P = 0.032$). No difference was seen between groups according to either the administration of intravenous sodium heparin ($P = 0.392$) or patients receiving oral or subcutaneous antiaggregant or anticoagulant medications ($P = 0.148$).

The median indwelling time of the catheters was 14.0 days (IQR: 7.0-25.0), 3,546 catheter days overall. The maximum indwelling time was 54 days for 8/10 cm LPC, 48 days for 18 cm LPC, and 153 days for MCs. The indwelling time was significantly longer ($P < 0.001$) for MCs (Fig 1).

Thirty-one catheters (16.8%) were prematurely removed because of the occurrence of CRCs (Table 1). In all cases of symptomatic CRT, no thrombosis-related systemic complication was observed. The relative incidences of CRCs were 15.84, 10.64, and 6.27 cases for 1,000 catheter days for 8/10 cm LPCs, 18 cm LPCs, and MCs, respectively. The relative incidences of CR-BSI were 1.32/1,000 catheter days for 18 cm LPCs and 0.48 for MCs, while no CR-BSI cases were documented for 8/10 cm LPCs. Considering LPCs of both lengths, the incidence was 0.72/1,000 catheter days. MCs showed a significantly different uncomplicated survival time between the explored catheter groups (log rank 6.457; $P = 0.040$) (Fig 2a).

Having more than 2 different antibiotics (corresponding to a 75 percentile of the study population) infused through the catheters (no CRC: n = 22, 14%; any CRC: n = 9, 33.3%; $P = 0.013$) showed a statistically significant association with CRC incidences, as well as the infusion of 5 medications––ceftriaxone (no CRC, n = 5, 55.6%; any CRC: n = 4, 44.4%; $P = 0.045$), ciprofloxacin (no CRC: n = 12, 66.7%; any CRC: n = 6, 33.3%; $P = 0.049$), heparin (no CRC: n = 18, 100%; any CRC: n = 0, 0%; $P = 0.030$), levofloxacin (no CRC: n = 4, 44.4%; any CRC: n = 5, 55.6%; $P = 0.008$), and rifampicin (no CRC: n = 18, 62.1%; any CRC: n = 11, 37.9%; $P = 0.001$).

The final Cox proportional hazards model (log-likelihood 238.210; $P < 0.001$) showed a statistically significant increase in CRC risk for 8/10 cm LPCs and a nonsignificant trend toward an increased risk for 18 cm-LCPs compared with MCs (Table 2). The adjusted survival curves for the 3 catheter groups are reported in Figure 2b. The assumption of the Cox model was assessed by comparing the log-log transformation versus the log of survival time of the Kaplan-Meier curves for the catheter groups. Since the curves were approximately

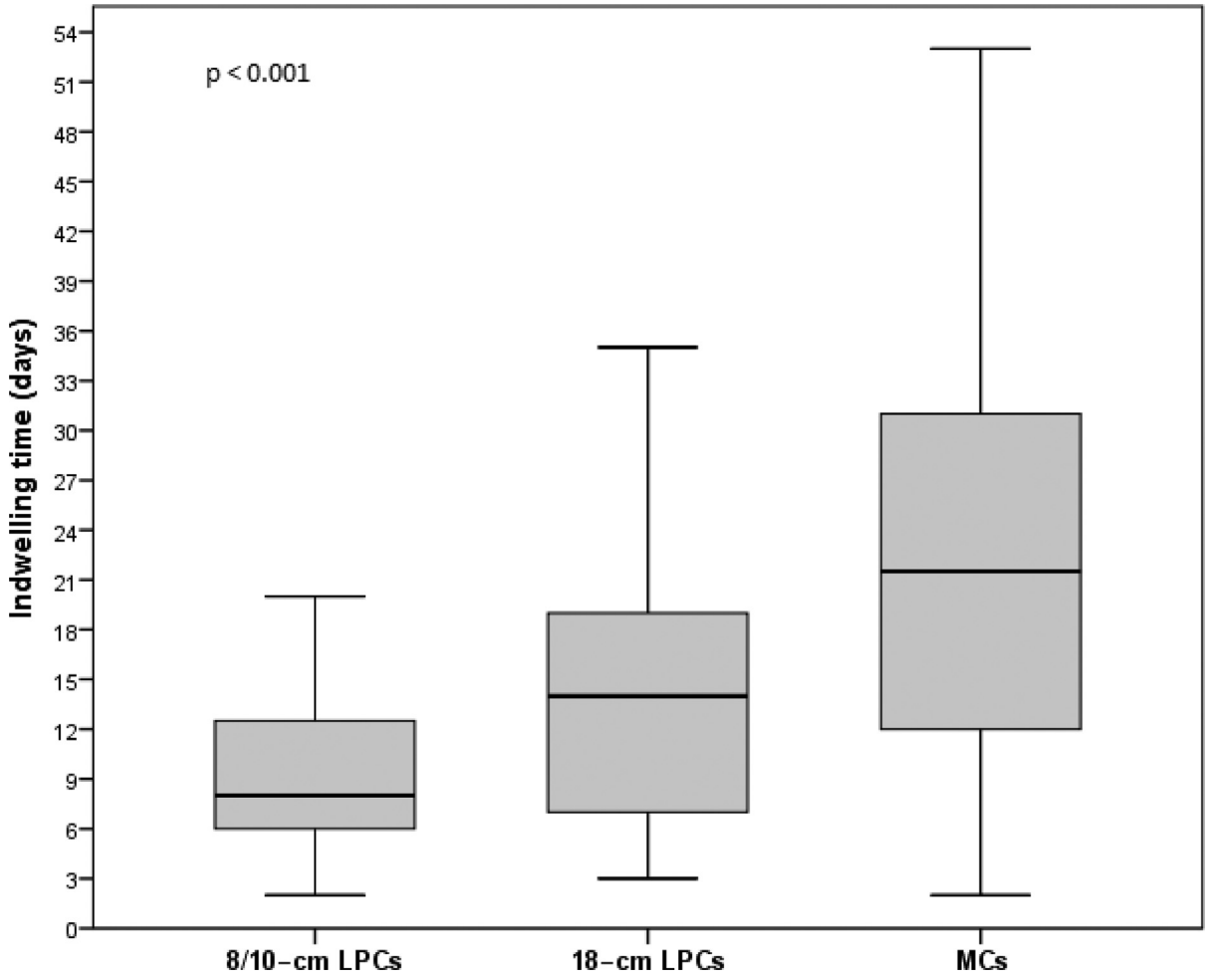

Fig 1. Differences between the median indwelling times of long peripheral catheters and midline catheters. Black horizontal line inside the boxes is the median. Box height is the interquartile range. Whiskers represent 1.5 × interquartile range.

LPCs, long peripheral catheters; *MCs*, midline catheters.

Table 1
Detailed outcomes of the catheters

Catheter outcome[#]	All catheters (n = 184)	8/10-cm LPCs (n = 56)	18-cm LPCs (n = 48)	MCs (n = 80)
No complication[*]	153 (83.2)	46 (82.1)	40 (83.3)	67 (83.8)
End of use[‡]	*91 (59.5)*	*33 (71.7)*	*29 (72.5)*	*29 (43.3)*
Inappropriate removal[§]	*10 (6.5)*	*2 (4.3)*	*2 (5.0)*	*6 (9.0)*
Accidental removal	*17 (11.1)*	*4 (8.7)*	*7 (17.5)*	*6 (9.0)*
Patient death	*4 (2.6)*	*1 (2.2)*	*1 (2.5)*	*2 (2.9)*
Patient discharged/transferred	*31 (20.3)*	*6 (13.0)*	*1 (2.5)*	*24 (35.8)*
Complications[†]	31 (16.8)	10 (17.9)	8 (16.7)	13 (16.2)
Complete catheter occlusion	*8 (25.8)*	*3 (30.0)*	*2 (25.0)*	*3 (23.1)*
Drug leakage from the exit-site	*11 (35.5)*	*6 (60.0)*	*2 (25.0)*	*3 (23.1)*
Catheter fissuration	*4 (12.9)*	*0 (0.0)*	*2 (25.0)*	*2 (15.4)*
Symptomatic CRT	*6 (19.4)*	*1 (10.0)*	*1 (12.5)*	*4 (30.8)*
CR-BSI	*2 (6.5)*	*0 (0.0)*	*1 (12.5)*[‖]	*1 (7.7)*[¶]

LPCs, long peripheral catheters; *MCs*, midline catheters; *CRT*, catheter-related thrombosis; *CR-BSI*, catheter-related bloodstream infection.

[*]: Catheter removed or end-of-observation in the absence of complications.

[†]: Unplanned catheter removal before completing the intravenous treatment.

[‡]: Catheter no longer clinically needed;

[§]: Catheter removed on the basis of rising temperature not attributable to a CR-BSI or CRT based on the applied diagnostic criteria (see Methods).

[‖]: Isolated bacterium: *Proteus Mirabilis*.

[¶]: Isolated bacterium: *Serratia Marcescens*.

[#]: Number (%).

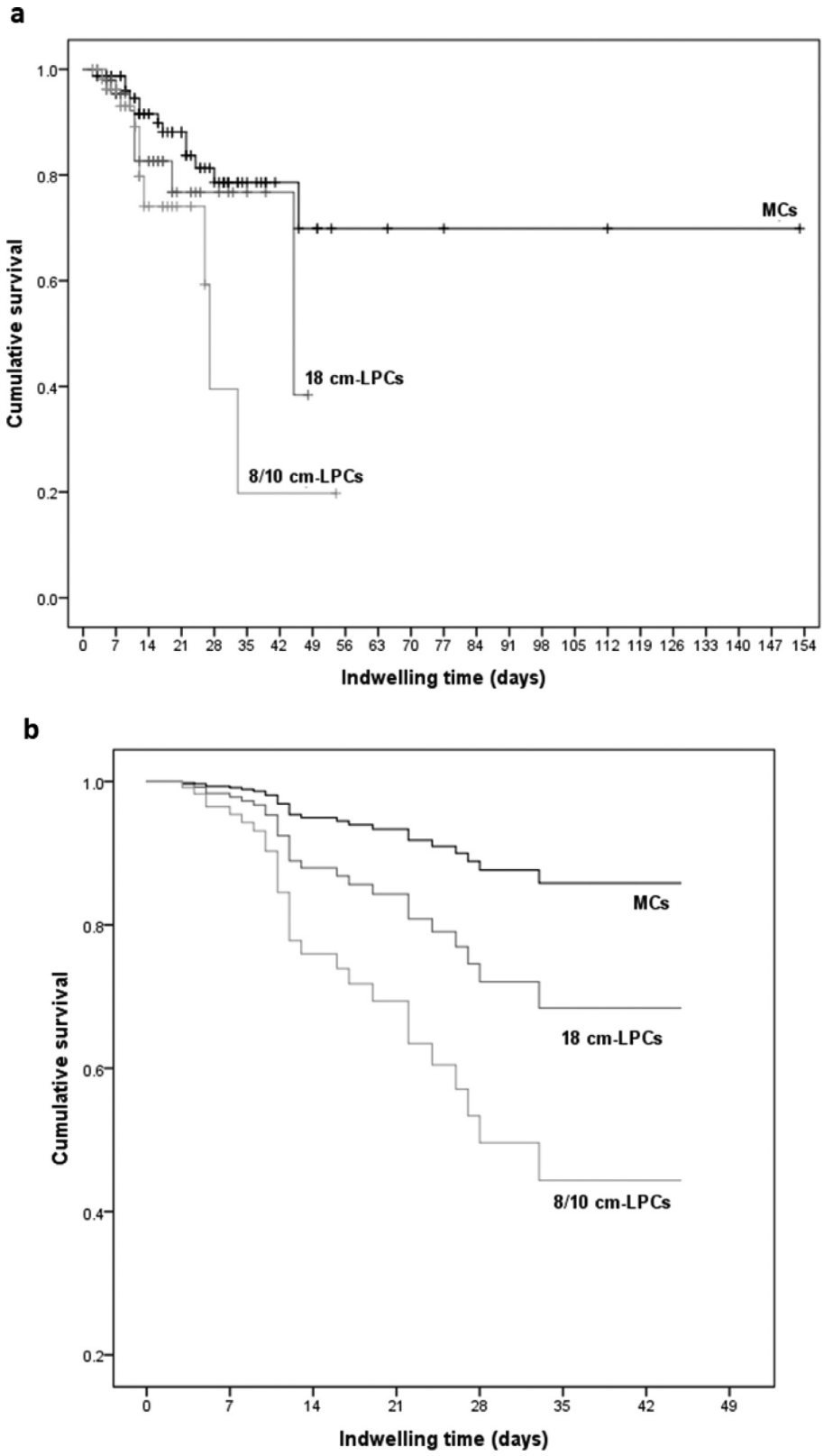

Fig 2. (a) Crude Kaplan-Meier survival curves for the compared catheter groups. (b) Adjusted Kaplan-Meier survival curves for the compared catheter groups as estimated with the multivariable Cox proportional hazards model.

LPCs, long peripheral catheters; *MCs*, midline catheters.

Table 2
Results of the multivariable Cox model

Predictor	HR (95% CI)	*P*-value
Catheter		
Midline	1.000	/
18-cm LPC	2.489 (0.961-6.448)	0.060
8/10-cm LPC	5.328 (2.118-13.404)	<0.001
Ciprofloxacin	3.423 (1.324-8.846)	0.011
Levofloxacin	3.505 (1.128-10.888)	0.030
Rifampicin	5.730 (2.423-13.551)	<0.001

HR, hazard ratio; *CI*, confidence interval; *LPC*, long peripheral catheter.
Variables excluded from the final model: Age, Charlson index, heparin, ceftriaxone, number of different antibiotics infused, vein-to-catheter ratio.

parallel and did not intersect with time (Fig 3), we assumed that the proportional hazard was constant over time.[27]

DISCUSSION

In a population of DVA patients, the use LPCs of different lengths demonstrated higher relative CRC incidences and a short uncomplicated indwelling time compared with MCs. To the best of our knowledge, this was the first study comparing midlines and LPCs.

According to the survival analysis, an LPC that has not demonstrated complications at a certain observation day had a much greater risk of having complications by the next day compared with an MC. In particular, the risk was more than 5-fold higher for an 8/10 cm LPC, while a more than doubled risk was seen in an 18 cm LPC, although without reaching statistical significance, perhaps because of the relatively small sample of this study. Since the proportional hazard ratio changed over time, by empirically observing the conditional (adjusted) survival curves,[28] we noticed that the LPC and MC outcomes appeared comparable only for less than one week after placement, becoming more marked with each subsequent day. Moreover, the unadjusted survival curves showed that only MCs ensured a long indwelling time (up to 22 weeks), with a risk of CRC substantially stable after the fourth week. These findings seemed to clearly indicate that LPCs were less reliable than MCs for extended use in DVA patients.

Unfortunately, in our population, modification of the treatment plan was quite frequent; thus, the indwelling time often exceeded the forecasted time interval, and in the absence of complications, the catheters were kept in use as long as needed. This is a well-known critical issue in choosing the most suitable device, given that clinically appropriate recommendations are frequently based on criteria like the duration of the treatment whose estimation is challenging.[29] This awareness has relevant implications for nurse decision-making in daily clinical practice.

Indeed, in addition to complication-related risks, every unplanned catheter removal may imply the need for a new catheter placement, determining avoidable patient discomfort, and increasing nurse workload. Moreover, every further cannulation attempt contributes to compromising the patient's "vascular heritage," whose health and preservation is strategic for any present and future therapeutic requirement.[30]

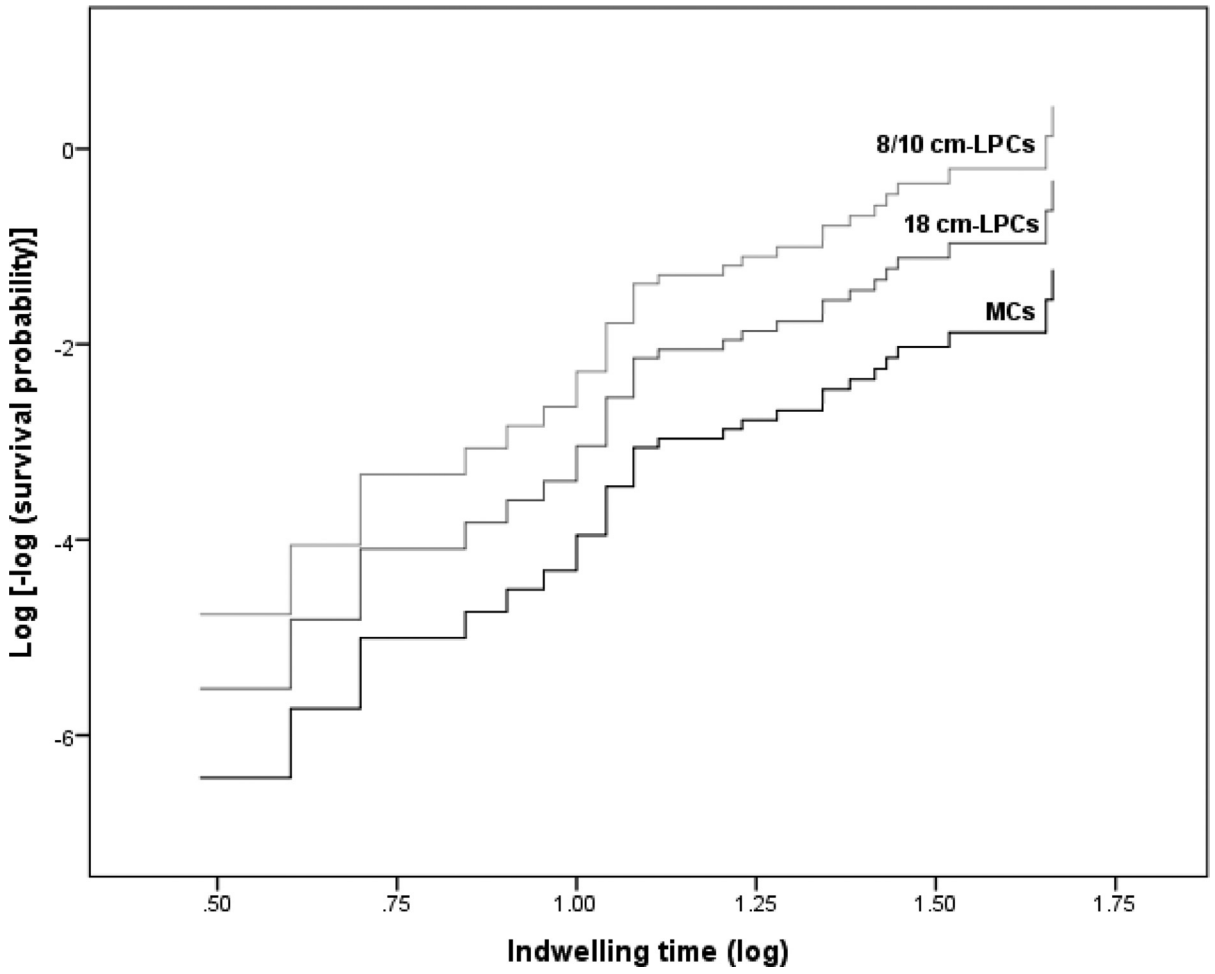

Fig 3. Graph to assess the proportional hazards assumption of the Cox model.
LPCs, long peripheral catheters; *MCs*, midline catheters.

In the present investigation, it is likely that uncomplicated catheter indwelling time may be even greater for some patients. In fact, we found that a number of catheters were perhaps too hastily removed on the basis of rising temperature alone. Although a CR-BSI should be suspected in patients with an indwelling intravascular device who present fever, chills, or other signs of sepsis,[31] a functioning catheter should not be removed on the basis of fever alone before having obtained confirmatory evidence that a CR-BSI is the cause.[3] While understanding the attention not to delay the treatment of a possible sepsis, the decision to remove the catheter should be made based on clinical judgment, after considering whether a source of infection is probable elsewhere or if the fever can be explained by a noninfectious cause.[19] In cases where—after discussing the risk-benefit balance—catheter salvage is deemed the best solution for an individual DVA patient, instillation into the catheter lumen of a solution combining a highly concentrated antibiotic and an anticoagulant (antibiotic lock therapy) might be considered to sterilize an infected catheter.[32]

The relative CR-BSI incidences seen in the study population for MCs (0.47/1,000 catheter days), it was comparable to what was reported by a recent clinical review (0.5/1,000 catheter days), as this rate was significantly lower than PICC (2.1-2.3/1,000) and central venous catheters (CVC) (2.4-2.7/1,000).[12] For LPCs, the overall relative CR-BSI incidence (0.72/1,000) was slightly lower than what was reported by a previous study (0.96/1,000).[14] However, it should be noted that no case of CR-BSI was documented for 8/10 cm LPCs, with an incidence lower than traditional PVCs (reported CR-BSI incidence: 0.2/1,000 catheter days).[12] These findings further support the assumption that either an MC or LPC, not a CVC, are the safest choice for a DVA patient when there is a need for peripheral venous access.

However, based on the above considerations, the choice between MCs and LPCs cannot be random. Thus, it is important to reflect on the possible reasons for such different outcomes for the catheters studied to optimize decision-making regarding the best catheter to be used in each individual patient. First, one aspect could be related to the various placement techniques, which might have been theoretically less traumatic for MCs than LPCs. Indeed, MC placement required a preliminary vein puncture using a small (21 gauge) needle, through which a very flexible nitinol-made guidewire was passed to allow the insertion of a complex microintroducer/dilator. Conversely, after puncturing the vein with a larger (19-20 gauge) needle and inserting a rather stiff steel-made guidewire, the LPC was introduced directly into the vein without the preliminary use of a dilator. Accordingly, having used both devices and a similar number of placement attempts, this potentially more traumatic placement might have contributed to an increase in CRC risk for LPCs.

A possible further explanation could be sought on the catheters themselves, as we compared polyethylene LPCs and polyurethane MCs. Polyethylene catheters are characterized by more stiffness and higher infective risk compared with polyurethane[4]; however, previous studies suggested that polyethylene LPCs are safe in acute DVA pediatric and adult inpatients,[14,33] and literature data on polyurethane-based catheters are controversial.[34-36] In our population, the catheter biomaterials may have contributed to affecting CRC occurrence.

As a third point, we considered the catheter-to-vein diameter ratio as a potential independent risk factor in adjusting the multivariate analyses because of its strong theoretical rationale (briefly: the indwelling device can favor thrombogenesis by inducing blow flow to become slower and turbulent)[37] and results in previous research[23-25]: The higher the ratio, the higher the risk for CRC. In the present study, the vein-to-catheter ratio did not affect the risk of CRC. However, it should be noted that, although in our population the 45% recommended threshold was only seldom overcome, a higher vein-to-catheter ratio was documented for MCs despite their lower risk for complications. This finding should not be surprising, given that the vein-to-catheter ratio was measured at the insertion point. Considering that anatomically the caliber of venous vessels tends to increase progressively as they approach the large thoracic vessels, the vein-to-catheter ratio may have been overall more favorable for longer catheters if considered at the level of the catheter tip, which represents the most critical point for the risk of complications related to the characteristics of administered drugs—the greater blood flow ensured by the higher venous caliber present several centimeters distally to the insertion point should have ensured a more rapid medication dilution and transport. In addition to the MCs (20 cm long), this consideration could be made for 18 cm LPC (both MCs and LPCs tips may be potentially located near the axillary vein thanks to their length), partly explaining the different outcomes between longer and shorter LPCs documented in the present investigation.

A final factor could be related to the administration of some medications, which resulted independently associated to a worse catheter outcome. Interestingly, patients in the MC group had fewer complications despite receiving a higher number of antibiotics, most often rifampicin. This may suggest that the overall characteristics of the medications to be infused should be taken into consideration for the catheter choice, although the current guidelines do not offer a specific and differentiated recommendation within peripheral catheters.

Based on previous research and on the findings of the present investigation, to overcome the above criticalities, a customized approach should be adopted for each individual DVA patient to extend the potential of the catheter life while preventing catheter-related complications. In light of the possible unpredictability of the actual time of use of the catheter, we believe it is not appropriate to select an MC for all DVA patients requiring a PVC, as this choice would result in unjustifiably higher costs. A possible strategy should consider, in addition to the estimated intravenous therapy duration, other patient conditions potentially predictive of an unexpected prolongation of the catheter stay (e.g., unstable clinical conditions, high comorbidity) to support the choice of an MC or an LPC. When the choice falls on LPCs, it may be suggested to choose the longest catheter compatible with the characteristics of the cannulated vessel. However, the MC should be considered a first choice in patients with major bilateral anatomical limits assessed through an upper arm vein US scan, to avoid using the only available vessel with a catheter that could, if necessary, not ensure a sufficient indwelling time and which may be difficult to replace.

Limitations

This study has some limitations, mainly related to the retrospective design, which may limit the generalizability of the results. The LPC and MC populations were not comparable in terms of comorbid conditions. This difference may have affected the rate and timing of the complication. Furthermore, data about medications were limited to having or not administered them through the catheters. Variables such as the number of infusion days and the daily frequency of administration may have affected the explored outcome, and were not considered.

Finally, in several patients, the observation ended while the catheters were still in use and no complication occurred. Having this study based on a time-to-event outcome, the actual complicated/uncomplicated indwelling times could certainly have been longer in both catheter groups, which possibly affecting the study results.

CONCLUSION

MCs can ensure a significantly longer and uncomplicated time of use compared with LPCs. According to our results, MCs and LPCs should not be considered as a unique and indistinct category of peripheral catheters. The most appropriate solution for each individual patient should be carefully considered before choosing and placement the device, taking into consideration both the planned intravenous therapy duration, the cost of the device, the characteristics of the patient's "venous

heritage," as well as the patient's overall clinical condition as a potential predictor of a longer than expected need for the venous access.

Further, larger prospective studies are needed to confirm our results and to explore the safety and reliability of LPCs in daily clinical practice, also taking into account never before considered variables, such as the vein-to-catheter ratio at the catheter's tip level and more precise data on the administered medications.

Acknowledgments

The authors thank the whole staff of the Cardiothoracic-Vascular Department for their valuable collaboration.

SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.ajic.2019.12.025.

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