Insertion site and risk of peripheral intravenous catheter colonisation: A post hoc analysis of the CLEAN 3 study including more than 800 catheters

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Short Report

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Abstract

Aim: Although uncommon, infections associated with peripheral intravenous catheters (PIVCs) may be responsible for severe life-threatening complications and increase healthcare costs. Few data are available on the relationship between PIVC insertion site and risk of infectious complications.

Methods: We performed a post hoc analysis of the CLEAN 3 database, a randomised 2x2 factorial study comparing two skin disinfection procedures (2% chlorhexidine-alcohol or 5% povidone iodine-alcohol) and two types of medical devices (innovative or standard) in adults patients before admission to a medical ward. PIVC insertion sites were grouped into five groups: hand, wrist, forearm, cubital fossa and upper arm. We evaluated the risk of risk of PIVC colonisation (*i.e.*, tip culture eluate in broth showing at least one microorganism in a concentration of at least 1000 Colony Forming Units per mL) and positive PIVC tip culture (*i.e.*, PIVC-tip culture eluate in broth showing at least one microorganism regardless of its amount) using multivariate Cox models.

Results: Overall, we included 823 PIVCs with known site of insertion that were sent to the laboratory for quantitative culture. After adjustment for confounding factors, PIVC insertion in the wrist or the cubital fossa was associated with an increased risk of positive and colonised tip culture. In other words, insertion of a PIVC into a site of the upper limb other than the wrist or the cubital fossa reduced the risk of colonised PIVC (HR 0.57 [0.35-0.92], p=0.020) and of positive PIVC tip culture (HR 0.75 [95%CI, 0.55-1.02], p=0.065).

Introduction

Peripheral intravenous catheters (PIVCs) are the most widely used medical devices in hospitals [1]. Every year, 2 billion PIVCs are sold worldwide [2]. Of these, 50% are subject to mechanical (accidental removal, dislodgment, leakage from insertion site, occlusion), vascular (phlebitis, diffusion) or infectious (local or bloodstream infection [BSI]) complications leading to PIVC failure [3]. PIVC failure is responsible for treatment interruptions which can be detrimental to patients. In addition, BSIs prolong hospitalisation and increase treatment costs and mortality [4]. In a retrospective study conducted from January 2018 to March 2020, among the 9833 patients visiting our emergency department and hospitalised in a medical ward after insertion of a PIVC, 25 cases (0.2%) of PIVC-related BSI were identified. Of these, major complications occurred in nine patients (36%) including six deaths, one severe sepsis requiring intensive care unit admission, one thoracic spondylodiscitis, one mitral valve endocarditis and one deep pre-sacral abscess. Median additional hospital stay costs were estimated at €5,587 per case [5].

National guidelines have been developed to reduce the occurrence of these complications and to improve patient outcome. They include disinfecting hands with a hydro-alcoholic solution when handling the catheter or the line, preparing the skin with 2% chlorhexidine-alcohol, inserting the PIVC once the work area is dry using the no-touch technique, and applying a transparent film dressing over the PIVC insertion site.

The choice of insertion site to limit complications is still a matter of debate. Numerous studies have been conducted to identify risk factors for non-infectious complications. Overall, the upper extremities should be preferred to the lower limbs to reduce these complications, while avoiding the wrist and cubital fossa [6]. Little is known about the choice of PIVC insertion site to reduce the infectious risk. Therefore, we analysed data collected during the CLEAN 3 trial to determine the risk of PIVC colonisation according to insertion site [7].

Materials And Methods

CLEAN 3 was a randomised, 2x2 factorial clinical trial carried out at Poitiers University Hospital in France. The trial has two main objectives: (1) to demonstrate the superiority of skin preparation with 2% chlorhexidine-alcohol over 5% povidone iodine-alcohol in preventing PIVC colonisation, and (2) to demonstrate the superiority of a set of innovative devices

including integrated PIVC, zero-reflux needless-connectors, disinfecting caps and single-use prefilled flush syringes over standard PIVC in extending the time elapsed between PIVC placement and PIVC failure. The investigators obtained written informed consent before study inclusion. The French Southwest and Overseas Ethics Committee and the French Drug Safety Agency approved the trial.

The trial enrolled adult patients (age ≥ 18 years) visiting the Emergency Department and requiring a single PIVC for a predictable duration of at least 48 hours before being admitted to medical wards. Main exclusion criteria were known allergies to chlorhexidine or povidone iodine; suspicion of BSI at PIVC insertion; participation to another clinical trial aimed at reducing PIVC complications; skin injury at PIVC insertion site; PIVC placement in extremely urgently situation; suspicion of difficult PIVC insertion suspected; and previous enrolment in the trial.

Patients were assigned to one of four groups according to the modalities of skin disinfection (2% chlorhexidine-alcohol or 5% povidone iodine-alcohol) and type of devices used (innovative or standard). PIVC were inserted and handled according to the French guidelines. PIVC insertion sites were selected according to the inserter and grouped into five areas (Figure 1): hand, wrist, forearm, cubital fossa and upper arm. At PIVC removal, PIVC tips were sent to the main laboratory for quantitative culture.

Catheter colonisation was defined as a PIVC-tip culture eluate in broth showing at least one microorganism in a concentration of at least 1000 colony forming units per mL (CFU/mL). A *positive culture* was defined as a PIVC-tip culture eluate in broth showing at least one microorganism regardless of its amount. Characteristics of patients and PIVC, and risk factors for PIVC complications were collected prospectively by research staff.

Statistical analysis

Characteristics of patients and PIVC were described as median (Interquartile range [IQR]) or number (proportion) as appropriate. First, we performed univariate analyses to identify associated covariates for PIVC colonisation and positive PIVC culture. Then, we performed multivariate Cox models adjusted for risk factors of PIVC colonisation or positive PIVC culture. Skin preparation (2% chlorhexidine-alcohol or 5% povidone iodine-alcohol) and type of devices (standard or innovative) were *a priori* forced into the model, as there were stratification covariates in CLEAN 3. Finally, we grouped the wrist and cubital fossa on one side, and the other three insertion sites on the other, as PIVC insertion at a joint site is more likely to result in PIVC dislodgment or dressing disruption, both factors increasing infectious risk. Analyses were performed using R 4.0.2 (R-project, Vienna, Austria) and *survival 3.5-7* package. A p-value equal to or lower than 0.05 was considered as significant.

Results

Between Jan 7, 2019, and Sept 6, 2019, 1316 patients were eligible in CLEAN 3 study and 1000 were enrolled. Of these, 177 PIVC were excluded for insertion failure (n=6), consent withdrawal (n=5), lack of PIVC tip culture (n=143) and insertion site unknown (n=23). Table 1 summarised the characteristics of the 823 patients and PIVC included in the current study. Tables S1 and S2 provide univariate analyses to identify covariates associated with PIVC colonisation or positive PIVC culture, respectively. Using adjusted multivariate Cox models, PIVC insertion in the cubital fossa or wrist increased the risk of PIVC colonisation (HR [95% CI], 1.68 [0.93 - 3.03] and 2.21 [1.12 - 4.36]) and of positive PIVC culture (1.49 [1.02 - 2.18] and 1.59 [0.98 - 2.59]), respectively (Table 2). After pooling insertion sites into two groups, PIVC insertion into an upper limb site other than a joint (wrist and cubital fossa) reduced the risk of PIVC colonisation (0.57 [0.35-0.92], p = 0.020) and of positive PIVC culture (0.75 [0.55-1.02], p = 0.065).

Discussion

We carry out a *post hoc* analysis of CLEAN 3 database to assess the link between PIVC insertion site and its infectious risk. The value of the CLEAN 3 database is that it is recent and include almost 1000 PIVCs with few missing data. Moreover, we used research staff to ensure high quality data collection and we sent over 85% of PIVC tips to the laboratory for culture. We used catheter colonisation instead of PIVC-related BSI as it is by far a much more common event and is regularly used as a surrogate of PIVC-related BSI because colonisation usually precedes BSI [8]. Using PIVC-related BSI would have required inclusion of tens of thousands of PIVC, which is difficult to achieve with the collection of large amounts of data and the sending of PIVC tips for culture.

In our study, PIVC insertion at the wrist or cubital fossa increased the risk of infectious complications. These findings are in agreement with the literature. In a retrospective study of 24 cases of PV-related BSI in adult patients, PIVC involved were more frequently inserted in the cubital fossa and less frequently inserted in the back of hand [5]. These findings were confirmed by a prospective cohort study involving 400,000 PIVC. In this study, hand insertion reduced the risk of PIVC-related BSI (HR 0.42, 95% CI 0.18-0.98, p = 0.046) compared with proximal insertion sites [9].

We believe that insertion sites close to the joints could lead to PIVC dislodgment, thus damaging the endothelium of the vein and enabling bacteria from the insertion site to penetrate the body. These two components increase the risk of phlebitis and infectious complications. Moreover, the joints compromise the hold of the polyurethane dressing. Dressing disruption is a well-known major risk factor of infectious complications associated with vascular catheters [10].

Our study has several limitations. Firstly, this is a *post-hoc* analysis of a single-centre study, which may compromise the external validity of the results. However, the large number of patients included and the wide range of medical conditions presented makes it possible to explore a representative sample of the general population. Secondly, only patients visiting our emergency department were included. PIVC inserted in emergency departments are at greater risk of infectious complications. However, only experienced nurses took part in the study, guidelines to prevent PIVC-related BSI were rigorously applied and PIVC inserted urgently were excluded. Thirdly, the study was not randomised according to insertion site. However, we did multivariate analyses taking into account all covariates of interest to identify independent factors associated with PIVC-related infectious complications.

The choice of the insertion site for a PIVC depends on a variety of factors, including the quality of the patient's venous network, the diameter of the catheter to be inserted, patient comfort and the risk of infectious and non-infectious complications. Our study suggests that the wrist and cubital fossa should be avoided whenever possible to reduce the risk of infectious complications. Prevention measures should consider the insertion site to reduce the risk of severe infections associated with PIVC.

Abbreviations

BSI : Bloodstream Infection

CFU : Colony Forming Units

HR : Hazard Ratio

IQR : Interquartile Range

PIVC : Peripheral Intravenous Catheter

Declarations

Ethics approval and consent to participate

For CLEAN 3 study, the investigators obtained written informed consent before study inclusion. The French Southwest and Overseas Ethics Committee and the French Drug Safety Agency approved the trial.

This study, a post hoc analysis, did not require an ethics committee approval.

Consent for publication

This manuscript doesn't contain any individual person's data in any form.

Availability of data and materials

The CLEAN 3 database is available on the Poitiers University Hospital statistical platform. CLEAN 3 database has not been published.

All data generated or analysed during this study are included in this published article and its supplementary information files.

Competing interests

OM, JG, BD, MB conceived the study.have received funding from Becton Dickinson™ for conference presentations.

NB received a Mobility grant from the Swiss National Science Foundation (Grant number: P400PM_183865)

NM has no competing interest linked to the study. NM received honorarium from Fisher and Paykel society for lectures.

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Becton Dickinson™ had no role in the conceptualization, design, data collection, analysis, decision to publish, or preparation of the manuscript.

Authors' contributions

OM, JG, NM, BD, MB and NB conceived the study.

BD wrote the first draft of the manuscript.

OM, JG, NM, BD, MB, NB undertook critical appraisal and revision of the manuscript.

NM and NB provided statistical expertise.

All authors read and approved the final manuscript prior submission.

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Tables

Table 1. Patients and catheters characteristics

	Hand		Wrist		Forearm		Cubital fossa		Upper arm	
	123	(15)	103	(12)	321	(38)	255	(30)	21	(2)
Gender, male	51	(41)	52	(50)	178	(55)	120	(47)	18	(86)
Age, years	75	[65-86]	82	[64-88]	79	[64-87]	72	[63-85]	75	[70-87]
Body mass index, kg/m^2	27	[23-31]	26	[22-30]	24	[22-27]	25	[23-29]	25	[23-28]
Antiseptic group										
2% chlorhexidine-alcohol	70	(57)	44	(43)	158	(49)	139	(55)	9	(43)
5% povidone iodine-alcohol	53	(43)	59	(57)	163	(51)	116	(45)	12	(57)
Devices group										
Standard	67	(54)	55	(53)	152	(47)	110	(43)	12	(57)
Innovative	56	(46)	48	(47)	169	(53)	144	(56)	9	(43)
Chronic disease*										
Diabetes	39	(32)	17	(17)	62	(19)	43	(17)	6	(29)
Dyslipidemia	26	(21)	11	(11)	71	(22)	53	(21)	4	(19)
COPD	16	(13)	9	(9)	31	(10)	23	(9)	5	(24)
Chronic heart failure	20	(16)	24	(23)	57	(18)	36	(14)	6	(29)
Chronic renal failure	9	(7)	4	(4)	22	(7)	13	(5)	2	(10)
Long-term corticosteroids	2	(2)	5	(5)	14	(4)	5	(2)	0	(0)
Immune deficiency	4	(3)	0	(0)	7	(2)	3	(1)	1	(0)
Haematological malignancy	2	(2)	5	(5)	10	(3)	4	(2)	0	(0)
Autoimmune disease	4	(3)	1	(1)	12	(4)	11	(4)	0	(0)
Unknown	20	(16)	19	(18)	43	(13)	34	(13)	6	(29)
None	30	(24)	37	(36)	103	(32)	105	(41)	3	(14)
Antibiotics in the last 15 days	7	(6)	11	(11)	29	(9)	22	(9)	0	(0)
Time with catheter in place, hours	43	[24-66]	39	[23-70]	42	[20-67]	32	[17-58]	47	[21-66]
Colonisation of catheter tip	9	(7)	16	(16)	20	(6)	27	(11)	1	(5)

Positive culture of catheter tip	28	(23)	27	(26)	54	(17)	58	(23)	6	(29)

Data are n (%) or median [IQR]. COPD = Chronic Obstructive Pulmonary Disease. *Some patients may have more than one chronic disease

Table 2. Adjusted hazard ratio by different insertion sites for catheter colonisation and positive catheter culture using multivariate Cox models.

Catheter colonisation				
53/823				
		Hazard Ratio	95% CI	p value
Insertion site				
Forearm	20 (6)	-	-	-
Hand	9 (7)	1.29	[0.58 - 2.85]	0.5
Upper arm	1 (5)	0.67	[0.09 - 5.03]	0.7
Cubital fossa	27 (11)	1.68	[0.93 - 3.03]	0.084
Wrist	16 (16)	2.21	[1.12 - 4.36]	**0.022**
Positive catheter culture				
173/823				
		Hazard Ratio	95% CI	p value
Insertion site				
Forearm	54 (17)	-	-	-
Hand	28 (23)	1.43	[0.89 - 2.29]	0.14
Upper arm	6 (29)	1.81	[0.77 - 4.25]	0.2
Cubital fossa	58 (23)	1.49	[1.02 - 2.18]	**0.038**
Wrist	27 (26)	1.59	[0.98 - 2.59]	0.061

Data are n/N or n (%). CI = Confidence Interval

Figures

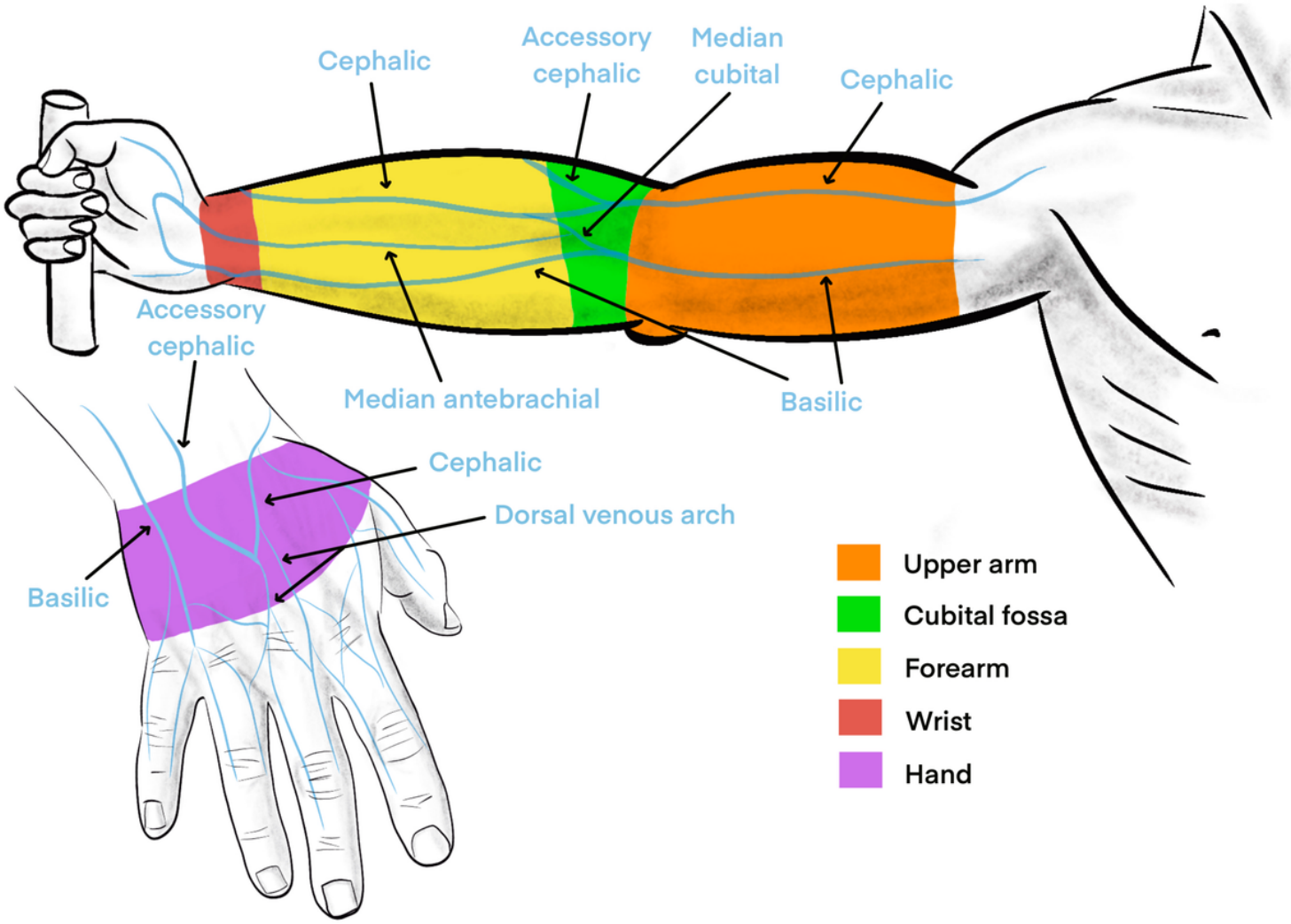

Figure 1

Legend not included with this version

Supplementary Files

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- S2Univariateandpositiveculture07032024copie.docx