

NCC/IBL aanvraagbon A105010960

Materiaal	Obx	PPN 416443087,243157886 (OCN)	
Titel	The journal of vascular access		
Deel			
Auteur			
Corporatie	Vascular Access Society		
Jaar/Editie	2000		
Uitgave	Milano Wichtig		
Serie/Sectie			
ISBN/ISSN	1724-6032	ISBN-13	
Plaatscode	416443087 ; Elektronisch document ; ; 2000 V1 1 -		
Jaar	2018-00-00	Datum indienen	09-08-2018 07:51
Volume	19	Datum plaatsing	09-08-2018 07:51
Aflevering	3	Afhandelen voor	
Leenvorm	KOPIE	Datum rappel	06-09-2018
Leveringswijze	E	Aantal rappels	
Coöperatiecode(s)	R	Geplaatst bij	0036/0003
Aanvraagidentificatie	In bezit bij bibliotheek		
Auteur artikel	van Loon FH		
Artikel	Pain upon inserting a peripheral intravenous catheter		
Bladzijden	258-265	PPN artikel	
Bron			
Opmerking	N276		
Componist			
Artiest			
Bewerker/Samensteller			
Bezetting			
Vorm uitgave			
Moeilijkheidsgraad			
Aanvrager	0803	Bibliotheektype	Algemene bibliotheek (L)
Aanvrageridentificatie		Particulier	N
Eindgebruiker			
Klant			
Opmerkingen			
Afleveradres post	Catharina Ziekenhuis Medische Bibliotheek Postbus 1350 5602ZA Eindhoven		
E-mail	infobib@catharinaziekenhuis.nl		
Telefoon	040-2398438		
Opmerking m.b.t. kosten			
		Stuur rekening?	N
Factuuradres	Clearing House		

[1] origineel gestuurd
[2] kopie gestuurd
[3] overige

[4] nog niet aanwezig
[5] niet aanwezig
[6] niet beschikbaar

[7] uitgeleend
[8] wordt niet uitgeleend
[9] bibliografisch onjuist
[0] bij de binder

Aantal eenheden 8

Aanvraagnummer A105010960

Pain upon inserting a peripheral intravenous catheter: Size does not matter

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The Journal of Vascular Access
2018, Vol. 19(3) 258–265
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sagepub.co.uk/journalsPermissions.nav
DOI: 10.1177/1129729817747531
journals.sagepub.com/home/jva
SAGE

Abstract

Background: Approximately 1.2 billion peripheral intravenous catheters are inserted across the world annually. It is known that intravenous cannulation may be a painful procedure, which affects cognitive abilities by increasing anxiety and discomfort.

Aim: We hypothesized that inserting a smaller sized peripheral intravenous catheter has a lower level of pain sensation compared to a larger sized catheter.

Methods: This observational, cross-sectional study was conducted between May and October 2016, in which surgical patients, aged 18 years or older, were eligible to participate. Experienced anesthesiologists and nurse anesthetists routinely obtained peripheral intravenous access according to the standards of care. The primary outcome was pain (verbal numeric rating scale, 0–10) upon intravenous cannulation.

Results: A total of 1063 patients were included and they were divided into four groups: group 1, 22 gauge (N = 29); group 2, 20 gauge (N = 447); group 3, 18 gauge (N = 531); and group 4, sized over 18 gauge (N = 56). Inserting an 18-gauged peripheral intravenous catheter resulted in the lowest pain score (3.2 ± 2.0). As a result of the multivariate linear analysis, five factors were significantly associated with pain upon inserting a peripheral intravenous catheter (sex, American Society of Anesthesiology classification, a patients risk profile on the A-DIVA scale, site of cannulation on the extremity, and whether or not the attempt was successful); however, the size of the inserted peripheral intravenous catheter had no significant relation to the primary outcome.

Conclusion: Inserting a smaller sized peripheral intravenous catheter did not result in a lower pain sensation. Moreover, to prevent pain upon inserting a peripheral intravenous catheter, an unsuccessful attempt must be avoided.

Keywords

Catheterization, peripheral, pain, vascular access devices

Date received: 6 January 2017; accepted: 6 November 2017

Introduction

It has been reported that approximately 1.2 billion peripheral intravenous catheters (PIVCs) are inserted in hospitalized patients across the world annually.¹ Moreover, nearly four out of five patients admitted to the hospital receive a PIVC, which makes PIVC insertion one of the most commonly practiced invasive procedures by both medical and nursing staff.^{2–4} Furthermore, intravenous cannulation is usually the first procedure performed by anesthesiologists and nurse anesthetists on patients presenting for procedures that require anesthesia or procedural sedation.

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A PIVC is a small hollow catheter that is advanced over a needle into a peripheral vein through the skin. PIVC placement is indicated for short-term use in many clinical situations, such as administration of intravenous medications, fluids, antibiotics, or blood products. Common sites of cannulation are the cephalic or basilic veins of the upper extremity, of which the antecubital fossa and the dorsum of the hand are commonly preferred sites for routine intravenous cannulation.^{5,6} The superficial veins of the lower limbs may also be cannulated; however, these tend to be avoided because they are associated with a higher risk of infection, phlebitis, and embolism.^{5,7,8}

Factors influencing the site selection for PIVC placement are the general condition of the vein, types of drugs to be administered, duration of intended therapy, and size of the catheter versus size of the vein.^{5,7} In clinical anesthesia practice, the size of the inserted PIVC depends on the clinical situation, while a larger sized PIVC has an increased speed of administration of intravenous fluids.^{2,9} The size of the chosen catheter is normally determined by the expected surgical complexity, complications, and blood loss, ranging between 22 and 14 gauge in clinical practice.^{2,10}

It is common for PIVC insertion to be a painful and invasive procedure, which therefore increases the anxiety and discomfort experienced by patients.^{11–14} This affects their cognitive abilities and causes discomfort both mentally and physically.¹⁵ To add to this, the anticipated pain prior to and upon cannulation significantly elevates a patient's level of anxiety.⁶ Moreover, as concluded by Macario et al.,¹⁶ discomfort from PIVC insertion was found to be the fifth most important clinical problem in anesthesia practice.

However, it seems trivial that inserting a PIVC with a smaller diameter is thought to be less painful compared to a larger sized PIVC; no consensus was reached regarding this statement.^{2,9} Thus, we hypothesize that inserting a smaller sized PIVC has a lower level of pain sensation compared to a larger sized PIVC when no additional analgesic technique has been applied. In addition to this hypothesis, we propose to identify factors that have an impact on pain during peripheral intravenous cannulation.

Materials and methods

Design

This observational, cross-sectional study was conducted between May and October 2016 and was performed in the operating theater complex of Catharina Hospital (Eindhoven, The Netherlands). The institutional review board (Catharina Hospital, Eindhoven, The Netherlands) approved the study protocol (ref: 2013-59), and written informed consent was obtained from all patients.

Participants

Inclusion criteria are as follows: patients 18 years or older were eligible to participate in this study if scheduled for

any surgical procedure, regardless of their American Society of Anesthesiology (ASA) classification, demographics, and medical history. Exclusion criteria are as follows: patients were excluded if they did not understand or answer the questionnaire (due to physical or communicational disorders), were unresponsive, or when a PIVC had already been inserted. Patients received usual care throughout the study and were a-selective included by the dependent practitioners during the study period. As a part of hospital policy, patients received premedication, consisting of 1 g acetaminophen administered orally, approximately 60 min before cannulation, and no sedative premedication was administered.

Outcome measures

The primary outcome measure was pain felt during peripheral intravenous cannulation with the size of the inserted PIVC. Pain was scored on the verbal numeric rating scale (VNRS) for pain, which is a one-dimensional measurement scale for pain intensity in adults and is a segmented numeric version of the visual analog scale (VAS). The pain VNRS is a single 11-point numeric scale with “0” representing no pain and “10” representing the worst pain imaginable. Although a valid and reliable scale to measure pain intensity, the pain VNRS evaluates only one component of the pain experience and pain intensity.¹⁷ Nevertheless, VNRS is an appropriate scale to measure pain upon intravenous cannulation and is simple to administer.^{18,19} As secondary outcomes, this study tried to identify which, if any, of the independent variables of patient's demographics (sex, age, body mass index (BMI), and ASA classification) or data related to the procedure of inserting a PIVC (puncture in the dominant site, site of cannulation on the extremity, diameter of the target vein, practitioner, whether or not the puncture was successful, and a patient's risk for a difficult intravenous access as measured on the A-DIVA scale) had a relation to pain upon inserting a PIVC.¹⁰ Data were collected by the depending anesthesiologist or nurse anesthetist during performing the procedure of intravenous cannulation, by asking the patient or from the preoperative anesthesia chart, and registered on score forms; completed score forms were included in the dataset and analyzed. To minimize bias and to maximize the validity of the results, both practitioners and patients were not aware of the primary outcome, and for that reason were blinded to the outcome measure pain during intravenous cannulation.²⁰ The pain scores were collected and recorded directly after performing each attempt by the dependent practitioner.

Procedure

Experienced anesthesiologists and nurse anesthetists routinely obtained peripheral intravenous access. PIVCs sized 14–22 gauge were inserted, and the size of the inserted catheter depended on the clinical situation and was chosen

by the practitioner (Venflon Pro Safety; BD Infusion Therapy AB, Helsingborg, Sweden). Intravenous cannulation was performed according to practice guidelines, as described in a previous publication by Gorski⁸ and van Loon et al.¹⁰ Veins on the dorsal and ventral surfaces of the upper extremity were considered for peripheral cannulation, including the metacarpal, cephalic, basilic, and median veins. Peripheral intravenous cannulation was defined as successful if the practitioner was able to inject a saline flush without signs of extravasation or infiltration in the surrounding tissues.^{5,8}

Statistical analyses

A difference in experienced pain felt during intravenous cannulation of at least a relative 30% of difference on the VNRS between the study groups was denoted to be clinically relevant.²¹ The sample size needed was calculated as at least 41 patients for each group, assuming a mean difference of 30% regarding the baseline pain score from a previous study at $\alpha = 0.05$ and $\beta = 0.80$.¹⁰ The post hoc power was calculated as 0.80. Power analysis was performed using G*Power (G*Power version 3.1.9.2; Christian Albrechts Universität, Kiel, Germany).²² The Kolmogorov–Smirnov test assessed the normality assumption for continuous variables. Continuous variables with a normal distribution were expressed as the mean and standard deviation, while those without a normal distribution were expressed the median and interquartile range. Discrete variables were expressed as frequencies with percentages. Comparison of variables between the study groups of inserted PIVCs was performed using one-way analysis of variance (ANOVA) testing (with Bonferroni post hoc analyses) or Chi-square testing, as appropriate. Stepwise multivariate linear regression technique was used to provide correlations between variables, in which items with a significant relationship to the primary outcome from a univariate linear regression technique were entered to determine the significance of the relationships between variables with the primary outcome. The stepwise method was utilized as the primary method of regression analysis in order to remove independent variables that did not make a significant contribution to the primary outcome variable. Items were removed from this model using a backward elimination process, with the removal criteria set at an α value of 0.01 as the level of significance, to obtain a model with a minimal set of variables and a maximal correlation coefficient (R^2). Throughout the study, a p value less than 0.05 was denoted to be statistically significant. SPSS (version 21.0; SPSS Inc., Chicago, IL, USA) was used for statistical analysis.

Results

A total of 1063 patients were included in this study, whose demographic characteristics are represented in Table 1. Throughout the study, 1408 peripheral intravenous punctures

were carried out with a first-attempt success ratio of 83%. For the analysis, patients were retrospectively subdivided into study groups based on the size of the inserted PIVC after an successful attempt, of which four groups were created: group 1, 22-gauged PIVC ($N = 29$); group 2, 20-gauged PIVC ($N = 447$); group 3, 18-gauged PIVC ($N = 531$); and group 4, PIVC sized over 18 gauge, including 17- and 14-gauged PIVCs ($N = 56$).

Inserting an 18-gauged PIVC resulted in a statistically significant lowest pain score of 3.2 ± 2.0 , compared to other size PIVCs ($F = 7.04$, $df = 3$, $p < 0.001$), as shown in Table 2. Notwithstanding the statistically significant difference in pain sensation upon cannulation with an 18-gauged PIVC, a clinically significant difference was only detected in patients in whom an 18-gauged PIVC was inserted, compared to a 22-gauged PIVC or a PIVC sized over 18 gauge. The mean pain score of the total study cohort was 3.3 ± 2.2 .

As a result of the univariate linear regression analyses, a total of nine variables had a significant relation to the outcome of interest (pain upon cannulation): sex; ASA classification; BMI; PIVC in the dominant site; site of cannulation on the extremity; diameter of the vein; practitioner; A-DIVA risk profile; and whether or not the attempt was successful (Table 3). Nonetheless, no significant relationship could be detected between pain upon cannulation and the size of the inserted PIVC as a result of this univariate analysis ($B = -0.01$ (95% confidence interval (CI) = -0.22 to $+0.20$), $p = 0.91$, standard error (SE) = 0.11).

These significant variables from the univariate analyses were included in a multivariate linear regression analysis, including the variable size of the inserted PIVC. As a result of this analysis, five factors were significantly associated with the pain experienced upon inserting a PIVC (sex, ASA classification, site of cannulation on the extremity, A-DIVA risk profile, and whether or not the attempt was successful), as shown in Table 4. Actually, inserting a PIVC successfully at the first attempt on the dorsum of the hand in male patients with an ASA classification 1 and a low-risk profile on the A-DIVA scale resulted in the lowest pain score ($R^2 = 0.32$, $F = 82.11$, $df = 6$, $p < 0.001$). In contrast, the size of the inserted PIVC had no significant relation to the primary outcome within this multivariate analysis.

Discussion

The aim of this observational study was to demonstrate whether or not inserting a smaller sized PIVC has a lower level of pain sensation compared to a larger sized PIVC, when no additional analgesic technique has been applied. Additionally, we proposed to identify factors that had an impact on pain during peripheral intravenous cannulation. The hypothesis was rejected as a result of this study, concluding that inserting an 18-gauged PIVC resulted in the lowest pain score (3.2 ± 2.0). Both the

Table 1. Demographic characteristics.

	22 gauge (N = 29)	20 gauge (N = 447)	18 gauge (N = 531)	>18 gauge (N = 56)
Sex				
Male	8 (28%)	150 (34%)	282 (53%)	30 (54%)
Female	21 (72%)	297 (66%)	249 (47%)	26 (46%)
Age (years)	51.0 ± 22.4	50.9 ± 17.1	56.7 ± 17.4	60.1 ± 16.3
BMI	26.3 ± 5.8	28.6 ± 8.1	27.3 ± 6.2	25.5 ± 4.2
ASA classification				
ASA 1	13 (45%)	134 (30%)	125 (24%)	11 (20%)
ASA 2	6 (21%)	207 (46%)	239 (45%)	31 (55%)
ASA 3	9 (31%)	103 (23%)	160 (30%)	9 (16%)
ASA 4	1 (3%)	3 (1%)	7 (1%)	5 (9%)
PIVC in dominant site				
Yes	14 (48%)	319 (71%)	310 (58%)	32 (57%)
No	15 (52%)	128 (29%)	221 (42%)	24 (43%)
Site of cannulation				
Dorsum of the hand	20 (69%)	302 (68%)	226 (43%)	8 (14%)
Lower arm	6 (21%)	95 (21%)	158 (29%)	16 (28%)
Elbow crease	3 (10%)	50 (11%)	138 (26%)	30 (54%)
Upper arm			9 (2%)	2 (4%)
Diameter of the vein	2.0 ± 0.2	2.6 ± 0.2	3.4 ± 0.3	4.5 ± 0.5
Practitioner				
Nurse anesthetist	23 (79%)	409 (91%)	465 (88%)	41 (73%)
Anesthesiologist	6 (21%)	38 (9%)	66 (12%)	15 (27%)
Successful attempt				
Yes	14 (48%)	342 (77%)	476 (90%)	49 (88%)
No	15 (52%)	105 (23%)	55 (10%)	7 (12%)
A-DIVA risk profile				
Low-risk	12 (41%)	336 (75%)	474 (89%)	50 (89%)
Medium-risk	8 (28%)	59 (13%)	40 (8%)	4 (7%)
High-risk	9 (31%)	52 (12%)	17 (3%)	2 (4%)

BMI: body mass index; ASA: American Society of Anesthesiology; PIVC: peripheral intravenous catheter; A-DIVA: difficult intravenous access in adult patients. Demographics of patient characteristics and procedure-related data represented per study group: group 1 (control group), PIVC size 22 gauge; group 2, PIVC size 20 gauge; group 3, PIVC size 18 gauge; and group 4, PIVC sized over 18 gauge including 17- and 14-gauged PIVCs. Sex was represented as an absolute number (proportions). Age (years) was represented as the mean ± standard deviation. BMI (kg/m²; kilograms body-weight per squared length in meters) was represented as the mean ± standard deviation. ASA classification was represented as an absolute number (proportions). PIVC in the dominant site was represented as an absolute number (proportions). Site of cannulation was represented as an absolute number (proportions). Diameter of the target vein (mm) was represented as the mean ± standard deviation. Practitioner was represented as an absolute number (proportions). Successful attempt was represented as an absolute number (proportions). A-DIVA risk profile (determined by the A-DIVA score) was represented as an absolute number (proportions).

Table 2. Pain scores upon intravenous cannulation.

	22 gauge (N = 29)	20 gauge (N = 447)	18 gauge (N = 531)	>18 gauge (N = 56)
Pain score	4.3 ± 2.8 ^a	3.4 ± 2.5 ^b	3.2 ± 2.0 ^c	4.4 ± 2.3

Pain scores were measured on the verbal numeric rating scale (VNRS). Data were represented as the mean ± standard deviation after assessing the normality assumption by Kolmogorov–Smirnov testing for all the study groups: group 1 (control group), 22-gauged peripheral intravenous catheter (PIVC) (D=0.166, df=29, p=0.187); group 2, 20-gauged PIVC (D=0.157, df=447, p=0.200); group 3, 18-gauged PIVC (D=0.159, df=531, p=0.200); and group 4, PIVC sized over 18 gauge, including 17- and 14-gauged PIVCs (D=0.172, df=56, p=0.200). Statistical analyses were performed using the one-way ANOVA test (with Bonferroni post hoc analyses), whereas ^ap=0.04 when compared to patients in which an 18-gauged PIVC was inserted; ^bp=0.01 when compared to patients in which a PIVC was inserted sized over 18 gauge; and ^cp<0.001 when compared to patients in which a PIVC was inserted sized over 18 gauge (F=7.04, df=3, p<0.001).

smallest (22-gauged) and the biggest sized (over 18-gauged) PIVCs resulted in the highest pain scores during intravenous cannulation, with pain scores of 4.3 ±

2.8 and 4.4 ± 2.3, respectively. As a result of regression analyses, five factors were significantly associated with pain upon intravenous cannulation and had an

Table 3. Univariate linear regression analyses.

	B coefficient	95% CI	p value	Standard error
Size of the PIVC	-0.01	-0.22 to +0.20	0.91	0.11
Sex	0.30	0.03-0.57	0.03	0.14
ASA classification	0.59	0.42-0.76	<0.001	0.09
BMI	0.03	0.01-0.05	0.01	0.01
PIVC in dominant site	0.42	0.14-0.70	0.01	0.14
Site of cannulation	0.41	0.25-0.57	<0.001	0.08
Diameter of the vein	0.31	0.20-0.42	<0.001	0.06
A-DIVA risk profile	1.63	1.42-1.84	<0.001	0.11
Practitioner	0.20	0.11-0.28	<0.001	0.04
Successful attempt	3.09	2.79-3.34	<0.001	0.16

PIVC: peripheral intravenous catheter; ASA: American Society of Anesthesiology; BMI: body mass index; A-DIVA: difficult intravenous access in adult patients. The results of univariate linear regression analyses, including factors with a significant relation to pain on the procedure of inserting a PIVC sized 22 gauge (referent category), 20 gauge, 18 gauge, or >18 gauge (17 and 14 gauge). Sex: male (referent category) and female. ASA classification: 1 (referent category), 2, 3, or 4. BMI (kg/m²): kilograms bodyweight per squared length in meters. PIVC in dominant site: yes (referent category) or no. Site of cannulation: dorsum of the hand (referent category), lower arm, elbow crease, or upper arm. Diameter of the target vein (millimeters). A-DIVA risk profile (determined by the A-DIVA score): low risk (referent category), medium risk, or high risk. Practitioner: nurse anesthetist (referent category) or anesthesiologist. Successful attempt: yes (referent category) or no.

Table 4. Multivariate linear regression analysis.

	B coefficient	95% CI	p value	Standard error
Size of the PIVC	0.35	-0.74 to +1.01	0.13	0.01
Sex	0.34	0.11-0.57	0.01	0.12
ASA classification	0.28	0.13-0.43	<0.001	0.10
Site of cannulation	0.17	0.03-0.32	0.02	0.07
A-DIVA risk profile	0.56	0.31-0.82	<0.001	0.13
Successful attempt	2.52	2.13-2.90	<0.001	0.13

PIVC: peripheral intravenous catheter; ASA: American Society of Anesthesiology; A-DIVA: difficult intravenous access in adult patients; CI: confidence interval. The results of the multivariate linear regression analyses, including factors with a significant relation to pain upon the procedure of inserting a PIVC sized 22 gauge (referent category), 20 gauge, 18 gauge, or >18 gauge (17 and 14 gauge). Sex: male (referent category) and female. ASA classification: 1 (referent category), 2, 3, or 4. Site of cannulation: dorsum of the hand (referent category), lower arm, elbow crease, or upper arm. A-DIVA risk profile (determined by the A-DIVA score): low risk (referent category), medium risk, or high risk. Successful attempt: yes (referent category) or no. The B coefficient for the constant variable was 4.12 (95% CI: 3.51-4.72, $p < 0.001$). R^2 for the multivariate analysis was 0.32 with pain upon the procedure of inserting a PIVC as the depending variable ($F = 82.11$, $df = 6$, $p < 0.001$).

independent relation to this outcome of interest: sex; ASA classification; A-DIVA risk profile; site of cannulation on the extremity; and whether or not the attempt was successful. The size of the inserted PIVC had no significant relation to the primary outcome.

The lowest pain score was registered in patients in whom the PIVC was inserted successfully at the first attempt on the dorsum of the hand in male patients with an ASA classification 1 and a low-risk profile on the A-DIVA scale. Noteworthy is the decent influence of an unsuccessful attempt on the level of pain sensation, which had an apparently higher impact on pain sensation compared to the other variables. However, the five variables in the multivariate analyses had a statistically significant relation to the outcome of interest independently, while only inserting a PIVC successfully at the first attempt had a clinically significant effect on pain sensation upon

intravenous cannulation. The effect size of the other variables on the level of pain sensation upon inserting a PIVC was limited.

As concluded by Rivera et al.,² it is generally agreed that a larger sized PIVC allows faster transfusion with less hemolysis or risk for thrombosis, but carries a higher risk for pain and phlebitis. Smaller gauges, in contrast, are thought to have exactly the opposite advantage for array and risk profile. The presented pain scores of PIVCs sized over 18 gauge, as a result of our study, are in accordance with the study of Rivera et al.² However, we were not able to prove the statement about lower pain scores in smaller sized catheters, as was concluded in the volunteer-based study by Brown.⁹ In addition, we believe that pain, as experienced during intravenous cannulation, depends more on the cannulation site and patient characteristics than on the inserted size of the PIVC.

The clarifications for differences in the experienced pain between the sites of intravenous cannulation are unclear. Nevertheless, cannulation on the dorsum of the hand was thought to be more painful compared to the antecubital fossa due to the tougher skin and greater density of nociceptors on this site.^{6,23,24} However, this study showed the opposite results while suggesting insertion of a PIVC on the dorsum of the hand in an effort to minimize pain during the procedure. Nevertheless, the risk for accidental removal and occlusion seems to be higher on the dorsum of the hand, as concluded by the trial of Wallis et al.²⁵ To add to this, Bregenzer et al.²⁶ even showed a higher incidence of PIVC obstruction in patients with a PIVC inserted on the dorsum of the hand compared to other cannulation sites on the upper extremity. Thus, it seems that catheter insertion in high-mobility areas contribute to the development of traumatic phlebitis or complications, which should be taken into account before choosing a cannulation site.^{27,28} Site selection should likewise be determined based on the indication for PIVC placement, the time needed for intravenous treatment, the diameter of the vein, patients' preferences, and the risk of complications due to the cannulation site.

An unsuccessful first attempt at inserting a PIVC is more often seen in patients in whom a smaller sized PIVC was inserted. This was in line with the predicted A-DIVA score; patients in whom a smaller sized PIVC was inserted were more often classified in a high-risk profile.¹⁰ The A-DIVA score is based on the five variable additive A-DIVA scale, which is a reliable predictive rule that implies the probability to identify patients with a difficult intravenous access prospectively. Logically, the diameter of the target vein was smaller in the group of patients with the highest A-DIVA score compared to those with a low-risk profile. As shown in this study, a successful first attempt resulted in both statistically and clinically significant lower pain scores compared to unsuccessful attempts. Moreover, pain as experienced by patients increased with further attempts to insert a PIVC. Possibly, this is a result of the relationship between fear or anxiety and pain as experienced by the patient, of which it is known that pain levels are higher in patients experiencing fear or anxiety upon an invasive procedure.²⁹⁻³¹ Successful PIVC placement at the first attempt was mostly seen in patients in whom an 18-gauge sized catheter was used, in comparison to the higher failure ratio in those patients with a 22-gauged PIVC inserted. This can be explained by the fact that a smaller sized PIVC was used in patients with a predicted difficult intravenous access, and thus, in those patients, a failed first attempt at inserting a PIVC could likewise be expected, because of smaller peripheral veins, for instance. Based on these findings, attention must be paid to patients with a high-risk profile according to the A-DIVA scale, and thus to those with a predicted difficult intravenous access, to avoid an unsuccessful attempt.

As stated in the results, male patients had a lower level of pain sensation compared to female patients, although there is no clear and consistent pattern of sex differences in human pain sensitivity.³² Despite this, a possible clarification can be that male patients had bigger sized veins and a lower risk profile on the A-DIVA scale against females. It is known that patients with a high ASA physical status are at an increased risk for intraoperative mortality, and the complexity of both the surgical procedure and anesthesia increases simultaneously with an increasing ASA classification.^{33,34} For this reason, larger sized PIVCs were more frequently inserted in this group of patients to achieve faster administration of fluids, which can explain the lower pain scores in patients with a lower ASA physical status.

As stated before, needle-related procedures induce anxiety, fear, and distress in patients due to pain from the intravenous puncture.^{12,13} To reduce this pain, several techniques had been studied in which anesthetic agents seem to play an important role. The ideal agent for pain upon intravenous cannulation should be effective, quick, pain-free, and cheap and would cause no side effects.³⁵ Injected local and topical anesthetics are most commonly used for analgesic effects.³⁶ Topical anesthetic cream, although effective for smaller cannulas, and adjuvant delivery methods, such as heat, iontophoresis, and ultrasound, have been explored, but are not commonly used.^{12,36} Newer anesthetic delivery methods, such as use of a pressurized aerosolized spray, may be quick and effective but remain costly.³⁶ Ethyl chloride and other vapocoolants are likely to have an analgesic effect in reducing pain during intravenous cannulation and are not likely to make cannulation more difficult or cause serious adverse events.³⁵ No analgesic techniques were applied in this study, because, first, we proved the baseline level of pain as experienced during intravenous cannulation and identify patient- and procedure-related factors for pain upon inserting a PIVC, and second, because we applied an easy and practical approach without additional techniques. However, combining the results of this study with the most effective and efficient analgesic technique will possibly result in an approach with lower pain scores.

Pain is a subjective experience; every individual uses the word pain based on their own experience with tissue damage.³⁷ According to this statement, it seems trivial that pain scores differ between patients, but is present in every intravenous puncture due to a local damage of the tissue. Pain induces a stress response, while the human stress response is innately tied to the immune function through a cascade of hormonal releases driven by the autonomic nervous system.³⁸ Increased stress can lead to elevated levels of hormones, which may inhibit immune response and wound healing. Pain and anxiety have also been linked to lowered pain thresholds through increased activation of the entorhinal cortex of the hippocampal formation. Consequently, pain and anxiety can contribute to a number

of negative medical outcomes, including longer recovery times.^{15,39,40} As so stated, reducing the level of experienced pain can simply increase a patient's degree of comfort.⁴¹

Limitations

In spite of the large number of patients included in this study, they were not equally distributed among the different study groups. The smaller number of patients included in the 22-gauged and over 18-gauged PIVC groups was not consistent with the number of patients in the 20-gauged and 18-gauged PIVC groups, which can influence the statistical power of the analysis. Hence, attention must be paid to the risk for type I errors. With such a large sample size, it is more likely that the hypothesis test will detect a small difference anyway. For this reason, this study focused on clinically significant results. However, the total cohort of patients included in this study, with respect to their distribution according to the inserted PIVC sizes, was representative of the clinical situation. The dependent practitioner determined the inserted size of the PIVC based on the expected surgical complexity and blood loss and the diameter of the target vein. To increase the level of evidence of research upon the studied subject, controlled trials and blinded studies should be created, while keeping ethical considerations in mind. Nonetheless, our results seem to be of clinical relevance and applicable due to the large population of included patients. The proper choice of the cannulation site can be a simple and effective method of pain reduction upon intravenous cannulation, but further research should focus on validation of the results of this study in combination with the most effective and efficient analgesic technique. We believe that combining analgesic techniques with the anatomical and physiological aspects of a patient can create a more painless cannulation upon PIVC placement. Furthermore, multiple attempts to insert a PIVC increased the pain significantly. Predicting the risk for a difficult intravenous access in the individual patient with the A-DIVA scale can guide the use of additional techniques (such as ultrasound) and, on that account, increase the success ratio of inserting a PIVC. We suggest further research to focus on increasing the success ratio for PIVC placement, in combination with the results on experienced pain during PIVC placement.

Conclusion

In summary, inserting a smaller sized PIVC did not result in a lower pain sensation. Nevertheless, the lowest pain score was registered in patients in whom the PIVC was inserted successfully at the first attempt on the dorsum of the hand in male patients with an ASA classification 1 and a low-risk profile on the A-DIVA scale. To prevent pain on inserting a PIVC, an unsuccessful attempt must be avoided, especially in those patients with a predicted high-risk profile on the

A-DIVA scale. However, choosing less painful sites will help to gain the confidence and cooperation of the patient. The appropriate size of the PIVC as well as the cannulation site should be carefully selected based on the indication for PIVC placement, the diameter of the vein, and the risk of complications after placement.

Acknowledgements

The authors thank the anesthesia personnel for help with the data collection and taking care of patients. F.L. is the main investigator and involved in study conception and design, drafting of the article, and analysis and interpretation of data. L.P. and W.A. helped in collecting data and critical revision of the article. A.D. participated in critical revision of the article. A.B. is involved in study conception and design, collecting data, and critical revision of the article.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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