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## Research Article

# Feasibility and Functions of Central Venous Catheters *versus* Peripherally Inserted Central Venous Catheters - @

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## ABSTRACT

Safety, risk of complications and the functional feasibility among different kinds of central venous access are still a matter of debate. Not many clinical trials have reported a comparison of complications and patency of CVCs *versus* Peripherally Inserted Catheters (PICC) as central venous access for indoor patients with advanced gastrointestinal disorder. The aim of the present study was to compare CVCs and PICCs regarding function, complications and convenience in a controlled clinical study on patients aimed for oncology surgery aimed for cure. Distributions of patients were comparable. Malignant diagnoses were significantly higher among CVC-patients. CVCs and PICCs were used for treatment during equal number of days, without any significant complication rates and with comparable number of days on antibiotics and other potent drugs. The overall cumulative hazard (risk) for treatment interruptions, due to either full-filled clinical indications or due to any complication among the subgroups of patients did not differ. Central Venous Catheter and Peripheral Inserted Central Venous Catheter, for central venous access, did not differ among consecutive unselected patients with serious gastro-intestinal disorders.

**Keywords:** Central venous catheterization; Peripherally inserted central catheter; Central venous access; Central venous catheter thrombosis; Deep venous thrombosis; Adverse event; Gastrointestinal surgery

## INTRODUCTION

Safe and cost benefits in the use of a central venous access have remained a matter of debate in the clinical care of patients subjected to fluid and pharmacology treatments. Available options are multiluminal catheters as compared to different kinds of peripherally inserted central venous catheters [1]. Central Venous Catheters (CVC) enable reliable intravenous administration of medication, fluids, intensive care monitoring of central haemodynamics, chemotherapy treatment, parenteral nutrition and blood sampling based on different kinds of central access modalities such as centrally inserted CVC, tunneled CVC, Port-a-Cath and Peripherally Inserted Central Venous Catheters (PICC). There are different kinds of catheters within each application from different manufacturers, materials and multiluminal items for insertion with or without imaging guidance. Accordingly, it has been difficult to assess optimal applications and items for different medical indications and patients in classic randomized studies. Important aspects among items are patient feasibility, different kinds of side effects, complications. The experience in the medical team to provide technical solutions as well as run the system with unfrequent problems as well as high functionality are factors that may all be translated into medical costs. There are still need for clinical trials comparing CVC and the PICC applications in unselected patients regarding complications, side effects and patency between these principally different techniques [2]. It may be suggestive that direct approach and entrance in central large vessels close to lung and mediastinal compartments could differ to peripheral insertions, particularly related to patient convenience and appearance of serious infections and subsequent sepsis. The aim of the present investigation was therefore to compare overall outcomes between CVC and PICC in unselected patients. Due to a large number of emergency-treated patients we have to report our results as rather a consecutive controlled treatment report.

## MATERIAL AND METHODS

### Study population

Patients older than 18 years and hospitalized for treatment with need of central venous lines were included during 2014-2015 at Sahlgrenska University Hospital in the West Region of Sweden, in a Center for Upper Gastrointestinal cancer surgery. Study end-points were patency, function, and complication requiring catheter removal, thrombophlebitis, pneumo- or haemothorax. Anaesthesiologists performed all CVC insertions. PICCs were inserted by a registered nurse or anesthesiologists depending on personal competence and

preferences. The study protocol followed all patients, where baseline-data, catheter days, patient experience and complications were registered during hospital stay and signed for validity.

The original plan was a conventional randomized clinical trial, but due to substantial enrolment of patients outside office hours with limited knowledge in PICC insertions in large number of patients, we choose to present information in two ways; outcome in randomized patients (R) and outcomes for the total number of included patients (T). Written informed consent was obtained in all patients. Randomization was based on birthdate as described elsewhere [3]. A total of 149 patients were included, where 103 (76 + 27) strictly followed randomization (R). Thus, protocol violations were usually related to allocations for PICC: [CVC ( $n = 112$ ), PICC ( $n = 37$ )].

### Catheter type and insertion technique

Both CVC and PICC are well known items for central venous access [4]. CVC insertions were all performed in operation rooms under sterile conditions by anesthesiologists. PICCs were either inserted by a register nurse or by anesthesiologists familiar with the procedures, few guided by imaging. A chest radiograph confirmed central line locations. PICC were 5F or 6F, 1-2 PowerPICC SOLO<sup>®</sup>2; (Bard Access Systems, Inc, Salt Lake City, UT). Triple-lumen catheters were 7F, with two 18-gauge lumens and one 16-gauge lumen, made by Arrow International (Teleflex Medical, Research Triangle Park, NC). Quadruple-lumen catheters were 8.5F, with two 18-gauge lumens, one 16-gauge lumen, and one 14-gauge lumen made by Arrow International. The overall cost for each PICC line-set (including all sterile material, cloths and sutures) was 77.6€ and 31.8€.

### Data collection

Data on gender, age, weight, BMI, associated diagnosis (Table 1), and antibiotic, antithrombotic, corticosteroid treatment are shown (Table 2). Insertion registrations were side, venous localization, numbers of lumen, complications at follow up, reason for removal and catheter inconvenience. Registered complications were local infection on site, occlusion, unsuccessful insertion, pneumonia, septicaemia, thrombophlebitis, pneumo- and hemothorax (Table 3). Biochemical tests immediately before insertions included: Na (sodium)/s, K (potassium)/s, Hemoglobin, leukocytes, thrombocytes, C-reactive protein, Partial thromboplastine time, Prothrombine complex, liver enzymes and creatinine/s (Table 4).

### Statistics

Results are presented as standard statistics (mean, median,

**Table 1:** Patient characteristics and diagnoses in randomized patients (R) or in the total number of patients valuated per protocol (T).

		CVC	PICC	<i>p</i> <
Randomized patients (R)		76 (74%)	27 (26%)	
Total number of patients (T)		112 (75%)	37 (25%)	
Gender (F/M)	R	39/37	10/17	n.s.
	T	55/57	15/22	n.s.
Age (years)	R	66.4 ± 10.9 (SD)	65.1 ± 12.7 (SD)	n.s.
	T	66.1 ± 10.7 (SD)	61.8 ± 14.5 (SD)	<i>p</i> < 0.06
Weight (kg)	R	73.1 ± 1.5	75.4 ± 2.8	n.s.
	T	75.1 ± 1.4	73.4 ± 2.3	n.s.
BMI: Body Mass Index	R	25.3 ± 0.5	25.3 ± 0.9	n.s.
	T	25.8 ± 0.4	24.8 ± 0.8	n.s.
Malignant diagnosis	R	61/78 = (78%)	19/27 = (70%)	n.s.
	T	92/112 = (82%)	23/37 = (62%)	<i>p</i> < 0.002
Associated diagnosis (numbers) :				
Randomized patients (R)	- Diabetes mellitus	10	7	
	- Cardiopulmonary	17	9	
Total number of patients (T)	- Diabetes mellitus	19	10	
	- Cardiopulmonary	34	17	
Mean, SEM, SD BMI: Body Mass Index				

**Table 2:** Days on drugs and the distributions of catheters with complete function among such groups in randomized patients (R) and in the total number of patients evaluated per protocol (T).

	CVC	PICC	<i>p</i> <
Antibiotic treatment postop day one			
R	38/76 = 50%	12/27 = 44%	n.s.
T	99/112 = 88%	29/37 = 78%	<i>p</i> < 0.004
Antithrombotic treatment day one			
R	74/76 = 97%	23/27 = 85%	n.s.
T	103/112 = 92%	30/37 = 81%	<i>p</i> < 0.06
Corticosteroid treatment day one			
R	3	2	n.s.
T	4	2	n.s.
Days on antibiotics			
R	14 ± 1	12 ± 2	n.s.
T	15 ± 1	17 ± 3	n.s.
Days on anti-thrombotic treatment			
R	16 ± 1	12 ± 1	n.s.
T	17 ± 1	14 ± 3	n.s.
Mean, SEM			

**Table 3:** Catheter characteristics, insertions, complications, reasons for catheter removal and patients' subjective experience during treatment in randomized patients (R) and in the total number of patients evaluated per protocol (T).

		CVC-R	PICC-R	CVC-T	PICC-T	<i>p</i> <
Insertion site right/ dx		59/15	19/8	90/18	26/11	<i>p</i> < 0.09
Venous localization						
	Basilica	0	17	0	18	
	Brachialis	0	5	0	5	
	Cephalica	0	3	0	5	
	Jugularis	22	0	31	0	
	Subclavia	52	0	77	0	
	Not registered	2	2-Jan	4	9	
Numbers of lumen						
	One	1	2	4	10	
	Two	23	24	32	25	<i>p</i> < 0.001
	Three	39	0	56	0	
	Four	13	1	18	1	
	Not registered	0	0	2	1	
Complication at follow up						
none		56	20	80	27	
local infection		3	1	6	1	
occlusion		6	1	2	3	n.s.
unsuccessful insertion	1	1	1	1		
pneumonia		1	1	1	1	
septicemia		1	0	1	0	
thrombophlebitis	1	1	1	1		
hemo-/ pneumothorax	0	0	0	0		
other		7	2	20	3	
Reason for Catheter removal						
end of treatment	56	18	81	25	n.s.	
death		2	1	2	1	
change of catheter	3	4	4	4		
complication		7	1	9	4	
other or not registered	8	3	16	3		
Catheter inconvenience according to patients						
	None		45	13	65	<sup>14</sup> <i>p</i> < 0.09
	Mild to moderate	8	2	13	2	
	Severe		0	1	1	2
	Not registered	23	11	33	19	

Numbers the statistical testing compared catheters with different numbers of lumens among subgroups (venous localization, catheter lumen, complications, catheter removals, inconvenience) in CVC-R vs PICC-R or CVC-T vs PICC-T as indicated by the vertical lines related to the observations in bold.

SEM, SD) as indicated in tables. Statistical testing was performed by ANOVA;  $p < 0.05$  was considered statistically significant in two-tailed test; otherwise stated non-significant (n.s.) =  $p > 0.05$ . Statistical analyses were both performed on randomized patients (R) and on all patients (T) comparing CVC *versus* PICC. The log rank test according to Kaplan Meier was used to evaluate catheter patency over time between CVC and PICC among patient groups.

## Ethics

The studies have been performed according to the Declaration of Helsinki. This Study was approved by Gothenburg University Board for Ethics. Dnr 492-11

## RESULTS

Randomization was appropriate in 103 patients (R) allocated to CVC ( $n = 76$ ) and to PICC ( $n = 27$ ). A total number of 149 patients (T) received CVC ( $n = 112$ ) or PICC ( $n = 37$ ). Randomized patients did not differ in any characteristics at time of inclusion (Table 1). More patients (75%) received CVC compared to PICC when they were grouped according to the total number of patients (T). Drug treatments were comparable among randomized patients, while more CVC-patients were given antibiotics (88%) compared to the PICC-patients (78%) regarding all patients (T) ( $p < 0.004$ ) seen in table 2.

Applications of the various catheter items are provided in table 3, with statistically significant differences on numbers of catheter lumens among patient subgroups ( $p < 0.001$ ). Otherwise, no significant differences were observed for insertion side (right/left), venous localization, complications at follow up, insertion success rate and reasons for catheter removal or concerning catheter inconvenience for the patients (VAS scale from 0-10 divided in 3 equal groups = none, mild to moderate, and severe inconvenience) (Table 3).

Biochemical test results before catheter insertions are provided in table 4 among patient groups. Randomized PICC-patients had significantly higher blood Leukocytes/s in combination with elevated CRP (in both R and T groups).

CVC- and PICC-patients showed small differences in either the number of days with catheters or in days in hospital (Table 5).

The overall cumulative hazard (risk) for treatment interruptions, due to either full-filled clinical indications or due to any complication among the subgroups of patients did not differ ( $p < 0.80$ ) (Figure 1)

## DISCUSSION

Reports appear during the 1990<sup>th</sup> usually focusing on Peripherally Inserted Central Catheters (PICC) [5,6]. Subsequently, numerous publications have evaluated the feasibility of different PICC catheters, indicating that PICCs were easy to insert, without the need of doctor assistance, less troublesome for the patients since the catheter did not involve areas close to the neck and therefore easier to manage [7-10]. However, mechanical irritation of inserted vessels, related to the kind of infused solutions, increased incidence of thrombosis, thrombophlebitis and catheter-related infections were, however, frequently observed [11]. More recent publications discuss the topics for example side effects of each type catheter, among others the risk of serious deep venous thrombosis, the need for thrombosis prophylaxis drugs, the optimal dressing, chemotherapy and antibiotic infusion in each type of catheter in both adults and in children [12-16].

More clinical treatments may be carried out on home basis to

**Table 4:** Biochemical data immediate before insertion of catheters in randomized patients (R) and in the total number of patients evaluated per protocol (T).

CVC		PICC		P <	
Na (mmol/L)	R	140 ± 0.4		140 ± 1	n.s.
	T	140 ± 1		140 ± 1	n.s.
K (mmol/L)	R	4.2 ± 0.4		4.1 ± 0.1	n.s.
	T	4.2 ± 0.04		4.1 ± 0.01	n.s.
Hemoglobin (g/L)	R	128 ± 2		132 ± 4	n.s.
	T	128 ± 1		126 ± 4	n.s.
Leukocytes (10 <sup>6</sup> /L)	R	7.5 ± 0.3		10.8 ± 1.2	$p < 0.004$
	T	7.8 ± 0.5		10.3 ± 0.9	$p < 0.01$
Trombocytes (/L)	R	268000 ± 11000	287000 ± 24000	n.s.	
	T	269000 ± 9000	287000 ± 20000	n.s.	
C-reactive protein (mg/L)	R	15 ± 3		49 ± 16	$p < 0.001$
	T	16 ± 3	52 ± 13	$p < 0.004$	
Partial thromboplastine time (seconds)	R	35 ± 0.5		36 ± 0.9	n.s.
	T	35 ± 0.4	36 ± 0.8	n.s.	
Prothrombin complex (relative to reference plasma)					
	R	1.0 ± 0.01	1.0 ± 0.03	n.s.	
	T	1.0 ± 0.02	1.1 ± 0.03	n.s.	
ASAT (ukat/L)	R	0.6 ± 0.09		0.8 ± 0.2	n.s.
ALAT (ukat/L)	T	0.7 ± 0.08		0.8 ± 0.2	n.s.
Alkaline phosphatase (ukat/L)					
	R	2.4 ± 0.4		2.3 ± 0.6	n.s.
	T	2.6 ± 0.4	2.3 ± 0.5	n.s.	
Bilirubin (umol/L)	R	14 ± 3		10 ± 1	n.s.
	T	17 ± 3		14 ± 3	n.s.
Creatinine (umol/L)	R	79 ± 3		70 ± 3	n.s.
	T	78 ± 2		102 ± 21	$p < 0.06$

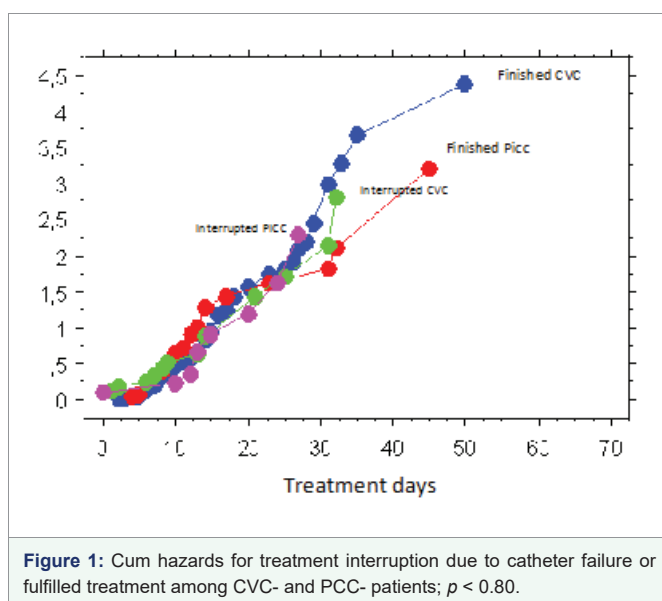
Mean, SEM, Na: Sodium; K: Potassium; ASAT: Aspartate Aminotransferase; ALAT: Alanine Aminotransferase

support cost benefit calculations. Therefore, safe and long lasting catheter functions are warranted with few side effects.

Patients evaluated in multidisciplinary board conferences for either chemotherapy or in combination with surgical treatments are usually provided CVCs, Port-a-Caths and sometimes PICCs. Such patients demand venous access in preparation of demanding medical interventions [17]. In 2011 a review of the literature on PICCs was published, which recommended additional investigations for evaluations of benefits and side effect compared to traditional CVCs [18]. Accordingly, our aim of the present study was to compare overall function, benefits and eventual shortcomings of PICCs *versus* CVCs on unselected patients referred to our institution for advanced medical investigations and treatments. All included patients had the need of central venous access for a longer period of time. Our purpose was to perform a classic randomised trial, but high violation of the

**Table 5:** Number of days with catheters in function and the number of in-hospital days in randomized patients (R) and in the total number patients evaluated per protocol (T).

CVC		PICC	$p <$		
Catheter days					
Randomized patients (R)		15 ± 1		12 ± 1	n.s.
Total number of patients (T)		15 ± 1		16 ± 2	n.s.
Days in hospital					
Randomized patients (R)		16 ± 1		14 ± 1	n.s.
Total number of patients (T)		17 ± 1		17 ± 2	n.s.
Mean, SEM					



protocol, because of limited confidence during on call service, skewed the possibility to full-fill pre-study statistical power estimations. After 2 years of patient inclusions (2014-2015) we therefore decided to report our result per protocol; i.e. as a consecutive prospective study. We also provide results separately for strictly randomized patients. The merit of this report seems to be that results did not differ among groups according to randomization or per protocol (T).

A variety of results are available in published reports related to various patient-groups and medical conditions. Although, still there are a limited amounts of randomized clinical trials. Until 2008, only one randomised prospective study comparing PICC and CVC had been published [19]. It included 51 vs 51 patients and only for nutritional support. The results showed higher rates of thrombophlebitis with PICC line insertion and also more difficult to insert compared to the standard subclavian approach. In 2011 one cohort study included 239 patients only including patients from the intensive care unit. They saw an incidence of deep venous thrombosis in 27.2% of the PICC patients and 9.6% of the CVC patients ( $p = 0.0007$ ) [20]. A single-centre RCT in 2016 [21] enrolled 124 patients. This was only comparing different dressing and securement methods to prevent PICC failure.

A fairly large retrospective cohort study was published in 2015 including 200 CVC and 200 PICC line patients [22]. The incidence of catheter-related deep venous thrombosis was uncommon with no

significant difference in complication-rates was observed. But also the PICC should be aggressively discontinued when no longer needed.

Regarding cost benefit calculations, it is depending on who, doctor or nurse, insert the catheter. Is it inserted bedside, in the radiology department or in the OR?. This study does not aim for economical calculations. There is a need for studies that have addressed this issue specifically, to draw any conclusion in this matter.

PICC-line insertion and use appears as a safe venous device for chemotherapy delivery, although 15% failures have to be accounted for, when planning PICC insertions for chemotherapy [23]. Thrombotic and infectious complications should be uncommon following either PICC or CVC insertions, without significant difference in observed complication rates have been reported [22]. The incidence of thrombotic events in patients on oncology treatment due to haematological disorders was significantly lower when long-term skin tunnelled venous catheters were used compared to PICC line in retrospective analyses [24]. Accordingly, a randomized trial comparing PICCs *versus* long-term skin tunnelled venous catheters is warranted. Increasing lumen numbers of the PICC is a potential risk-factor, evaluated in orthopaedic patients on long-term antibiotic treatment for bone infections [25]. The risks of tip-malpositioning, thrombophlebitis and catheter dysfunction may favour clinical use of centrally placed catheters instead of peripherally inserted central catheters, without any observed difference in catheter-related infection rates [26]. Power-injectable PICCs have many advantages in the ICU: multipurpose central lines for any type of infusion, for hemodynamic monitoring, and for high-pressure injection of contrast media during radiological procedures. Their maintenance is associated with an extremely low rate of infective and non-infective complications [10].

Our study has of course weaknesses. One is the amount of patients enrolled in each arm. The lack of limited confidence during on call service with PICC insertion. This is one of the big problems in performing a randomized clinical trial. The timing of the study. One comparing method should be as familiar for the persons involved as the other. There are a variety of lumens in each comparing catheter and also different kinds of Brands. Our strength is that doctors and nurse involved in inserting the catheter are very few and also very familiar with the different kind of catheters (PICC and CVC) also with the Brands and lumens. We also have nurses aimed for follow up of the patients when discharged from the hospital or moved to another hospital in the region.

On the other hand the result showed no significant differences comparing the two catheter-methods involved.

In conclusion, the present study aimed to be a complete randomized evaluation to compare Central Venous Catheter *versus* Peripheral inserted central venous catheter with central venous placement for all kind of treatments according to medical indications showed essentially no important medical difference between CVC and PICC evaluated in 149 prospective and consecutive patients. A strength in our study is that strictly randomized patients, although with limited numbers, showed the same results, suggesting that the risk for by chance distributions of important events were unlikely behind equal results between CVC and PICC in unselected patients with serious gastrointestinal disease. Thus, the choice for CVC or PICC catheters may be selected on other merits than pure medical indications such as costs, practical and local experience and personal preferences.





## AUTHOR CONTRIBUTIONS

CE, the guarantor of this article had full access to the data and take responsibility for the integrity of the methods used for data collection and the appropriateness and honesty of the analyses and drafted the main text and figure generation with critical revision offered by KL, MH, BMI and SL. KL personally reviewed and conducted the statistical analysis and figure generation and supported critical revision of the draft. MH and SL performed almost all of the PICC insertions. The CVC were inserted by a doctor specialized in anaesthesiology and intensive care. Learning curve in how to perform an insertion of a PICC and CVC was not included, all including doctors were very familiar with each procedure. LR supported the start of the study as head of the Department of Surgery at Hospital of Skaraborg and Head of the Department of Anaesthesiology and Intensive Care Unit at Sahlgrenska University Hospital and also contributed with manuscript draft revision and critical revision. All authors reviewed the final manuscript and agreed to its submission.

## OTHER CONTRIBUTIONS

We appreciate the assistance of Ulla Körner and Lena Gunnebo RNs, who assisted us with design of the database and the collection of the primary data in our database and Professor Sven-Erik Ricksten and Johan Snygg MD PhD for support on performing the study.

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## STUDY REGISTRATION

ISRCTN70648637-<http://www.controlled-trials.com/ISRCTN70648637/>.

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