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## **OPEN** Assessing infection related to short-term central venous catheters in the perioperative setting

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Central venous catheter (CVC) cannulation can be accompanied by serious complications. The appearance of catheter-related infections is associated with high morbimortality. The aim of this study is to evaluate the incidences of colonization and central line-associated bloodstream infections (CLABSI) in short-term CVCs in the elective surgery setting, as well as to analyze the related risk factors. Prospective observational study including patients undergoing elective surgery with a CVC inserted perioperatively. Patients with current infection, taking preoperative antibiotics, those planning to have CVC for longer than 14 days, those under 18 years old, and those refusing to participate were excluded. Patients without cultures at the moment of CVC retrieval were not included. 200 patients were included, with a mean catheter duration of 6.8±3.1 days, and a total duration of 1,358 days. Incidence of colonized catheters was 6% (8.84/1000 catheter-days), and 3.5% had CLABSI (5.15/1000 catheter-days). Catheter duration was longer in patients whose CVCs had been removed due to suspected infection (p < 0.0001). The risk factors for catheter colonization were a history of oncological disease (p = 0.022), ischemic heart disease (p = 0.019), as well as jugular venous catheterization (p = 0.019). No relationship was detected between colonization and operator experience (p = 0.050), ultrasound-guided cannulation (p = 0.565), or number of attempts (p = 0.379). The risk factors for CLABSI were: age over 60 years (p = 0.041) and oncological disease (p = 0.021). CLABSI was neither related to operator experience (p = 0.178), ultrasound-guided cannulation (p = 0.373), or number of attempts (p = 0.379). Although CVCs were in place for a short time and in a controlled setting, we observed high incidences of colonization and CLABSI. The risk of catheter colonization depends on other factors rather than catheter duration.

Keywords Central venous catheterization, Perioperative instrumentation, Catheter related infections, Bacteremia, Perioperative period/Therapy, Complications

Cannulation of central venous catheters (CVC) is often necessary in the elective surgery setting. However, a downward trend in its insertion by anesthesiologists has been identified, with an increase in their placement by other medical specialties<sup>1</sup>. This trend may be due to increased awareness that its insertion can be accompanied by mechanical complications or catheter-related infections<sup>2</sup>. Even though the incidence of these infections is lower than that caused by other clinical care devices<sup>3</sup>, they are associated with longer duration of mechanical ventilation, longer intensive care unit (ICU) and hospital stays, as well as increased healthcare costs<sup>4</sup>.

The use of real-time ultrasound during catheter introduction has been shown to reduce the risk of mechanical complications related to the procedure, such as pneumothorax or carotid puncture. Ultrasound-guided cannulation improves first-attempt success rates, and reduces cannulation-time<sup>5</sup>. However, ultrasound may increase the risk of bacteremia due to contamination during catheter insertion by suboptimal skin asepsis or failure to maintain aseptic conditions during the technique<sup>6</sup>. Thus, interventions aimed at ensuring compliance with measures to prevent catheter-related infections must be implemented, considering the specificities of the

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ultrasound-guided technique<sup>7</sup>. Research evaluating the effect of employing aseptic techniques has been shown to reduce the incidence of catheter-associated bacteremia<sup>8</sup>.

The arrival of microorganisms to the CVC can occur through 3 routes: extraluminal, intraluminal and hematogenous<sup>9</sup>. Infection related to short-term devices (less than 14 days) occurs mainly through the extraluminal route due to the passage of microorganisms of the skin during insertion, or by the subsequent colonization of the skin entry point of the catheter<sup>10</sup>. Even after a single day of CVC insertion, inflammatory changes have been observed in the corresponding veins<sup>11</sup>. The main objective of this study is to evaluate the incidence of colonization and CLABSI associated with short-term CVC in patients undergoing elective surgery. As secondary objectives, we evaluated the risk factors related to catheter colonization and central line-associated bloodstream infections (CLABSI).

## Materials and methods

This prospective observational study was approved by the Ethics Committee of the Hospital Universitario de Gran Canaria Doctor Negrín, Las Palmas de Gran Canaria, Spain (code #150030), and written informed consent was obtained from all subjects participating in the trial. The trial was registered prior to patient enrollment at clinicaltrials.gov (NCT05495646).

All patients undergoing elective surgery who were planned to have a CVC inserted perioperatively were included. Exclusion criteria were: patients showing signs or symptoms of current infection such as fever, altered consciousness, hypotension, leukocytosis, platelet disturbances, liver or renal disfunction, etc., or those taking preoperative antibiotics, patients who already have CVC inserted before surgery, patients under 18 years old, and patients who refused to participate. As this study is focused on short-term catheters, those placed for less than 14 days, patients who would need to have CVC inserted for longer than 14 days were also excluded. Data of patients who did not had cultures obtained when catheters were removed (tip catheter, central and peripheral hemocultures) were excluded from the analysis. This research was carried out according to the Declaration of Helsinki, following good clinical practice. The manuscript follows the STROBE guidelines<sup>12</sup>.

## Study protocol

Prior to anesthetic induction, patients who met the inclusion criteria were selected and informed consent was signed. After anesthetic induction, the criteria for CVC access and technique were made by the anesthesiologist responsible for the clinical management of the patient. The medical team in charge of patient perioperative management were unaware of the nature of the study, so their clinical decisions would not be influenced by this study. After the insertion of a 3-lumen CVC (Arrowg + ard Blue<sup>\*</sup> Three-Lumen CVC, Arrow International LLC, Morrisville, USA), a chest x-ray was performed per protocol on all patients to verify the correct placement of the tip of the catheter and rule out the appearance of immediate complications. Daily monitoring of catheters was carried out by investigators not related to clinical management of patients. Transparent sterile dressing was used to cover the entry point of the catheters, following our center's routine clinical practice. In case of suspicion of infection by the medical staff in charge of patients, due to local and/or systemic signs, two blood cultures from venipuncture, a blood culture from the catheter and a culture from the tip were extracted. The removal of the device was done using an aseptic technique, and a distal 5 cm, sectioned with a sterile scalpel, was sent to the microbiology laboratory for culture.

The following variables were collected: age, gender, body mass index, cervical circumference, and smoking habits; comorbidities were recorded: diabetes mellitus, respiratory and cardiac diseases, cancer, immunosuppression (including corticosteroid therapy and neutropenia), previous solid organ transplant, and chronic kidney disease. Data related to surgery were collected: type and duration, intraoperative bleeding, and use of blood transfusions and vasopressors. Data related to CVC insertion were also collected: operator experience, approach, technique used, total time spent, number of punctures until success, use of ultrasound, and need to change approach. The CVC approaches found were: right/left internal jugular vein by anatomical references or guided by ultrasound [Ultrasound GE Healthcare Venue (General Electric Company, New Jersey, USA)], right/left subclavian vein by anatomical references, and right/left infraclavicular axillary vein guided by ultrasound. Subsequently, patients were monitored during their hospital stay, and the following information was recorded: immediate and postoperative complications related to the catheter, postoperative complications during the hospital stay, postoperative treatments, duration of the catheter and reason for removal, local or systemic signs of infection, positive cultures, and final diagnosis related to the catheter.

#### Aseptic measures

Aseptic measures are intended to reduce the probability of infection of a catheter inserted in a central vein. The aseptic measures used both in the insertion and maintenance of the catheter were those usual in clinical practice, following the recommendations of the guidelines for the prevention of infections related to intravascular catheters<sup>13</sup>: surgical handwashing before catheter insertion; cleaning the skin with 2% chlorhexidine alcohol before inserting the CVC; allowing the antiseptic solution to dry before the puncture; barrier precautions, such as wearing a surgical cap, mask, sterile gloves, and sterile gown; semi-permeable transparent sterile dressing to cover CVC entry, but also allowing continuous inspection of the entry point; removing unnecessary catheters; avoiding wetting the catheter while the patient is bathing; replacing administration sets no more frequently than at 96 h intervals, but at least every 7 days in patients not receiving blood products, or lipid emulsions; changing systems used for the infusion of blood products or lipid emulsions within 24 h of starting the infusion; and changing connectors no more frequently than every 72 h, or according to the manufacturer's instructions.

Ultrasound-guided cannulation is the use of real-time ultrasound to visualize the target vein and surrounding structures and also the advancing needle tip<sup>14</sup>. The recommendations followed in the ultrasound-guided cannulations were the following<sup>7</sup>: exploring the area with ultrasound to recognize anatomical anomalies and

variants of normality prior to skin antisepsis, without sterile sheath or gel; performing asepsis prior to hand disinfection and putting on sterile gloves; surgical hand disinfection and putting on sterile gloves; skin cleaning with a 2% chlorhexidine alcohol preparation; allowing the antiseptic solution to dry before the puncture; barrier precautions, such as wearing a cap, mask, sterile gloves, and sterile gown; covering the ultrasound probe and connecting cables with a sterile sheath; using sterile single-dose gel inside and outside the sheath; placing the probe transverse to the vessels to identify the vein, performing the puncture out of plane at the midpoint of the probe and vertical to the entry point into the skin; and ensuring that the needle tip is never in contact with the probe sheath.

Definitions<sup>15</sup>:

- Catheter colonization: isolation of a microorganism from a 5-cm segment of the catheter tip after its removal, without clinical signs of infection.

- Exit site infection: Local signs of infection at the catheter entry point (redness, induration, warmth, and leakage of purulent material), without bacteremia.

- Bacteremia or fungemia probably related to catheter: in the absence of catheter culture, sepsis without another apparent reason, with positive blood culture, in which the symptoms disappear 48 h after CVC removal.

- Central line-associated bloodstream infections (CLABSI): isolation of the same microorganism in a blood culture from a peripheral vein and in a quantitative or semiquantitative culture of the CVC tip in a patient with clinical symptoms of sepsis, without another apparent reason.

#### Sample size calculation

The primary objective of this study was to estimate the rates of catheter colonization and CLABSI in short-term CVCs in the elective surgical setting. Although not much literature has been published regarding colonization rates in short-term CVCs, CLABSI rates around 4% have been reported in critically ill patients<sup>16</sup>. To a conservative approach in the sample size calculation, a rate of 5% was assumed in the elective surgical setting. Considering this, with a 95% confidence interval and a 3% error margin, 200 patients are needed to accurately estimate the prevalence of CLABSI in the study population.

### Statistical analysis

Data were analyzed using SPSS 20.0 (Statistical Package for Social Sciences, IBM). Categorical variables are expressed as frequency and percentage. To compare frequencies between non-infected patients and patients with positive catheter tip culture or CLABSI, Chi-square test was used. Quantitative variables are expressed as mean  $\pm$  SD. We used Shapiro–Wilk's test to analyze the normality of data. Quantitative variables were compared between groups using t-test for independent samples in cases of variables with normal distribution, and Mann–Whitney U-test when the distribution of variables could not be adjusted to normality. For each risk factor assessed, Odds Ratio (95% CI) was calculated for the qualitative variables, and mean differences (95% CI) for the quantitative variables. A p-value < 0.05 was considered statistically significant.

## Results

Between August 2023 and February 2024, 249 patients were included for whom the need for intraoperative CVC insertion was deemed necessary. Of these, catheter tip culture could not be retrieved in 49 patients after removal of the CVC (Fig. 1).

Baseline characteristics and Central venous catheter insertion technique.

The descriptive analysis of the sample is shown in Table 1. Tables 2 and 3 show the characteristics of the CVC insertion and the postoperative management of the patients. Mean catheter duration was  $6.8 \pm 3.1$  days, with a total catheter duration of 1,358 days.

Catheter infection and postoperative management of patients.

Catheters were removed due to lack of use in 84% of the cases (with a mean duration of  $6.4 \pm 2.8$  days), due to suspected infection in 14.5% (mean duration of  $8.9 \pm 3.6$  days), and due to malfunction in the 1.5% of cases (average duration of  $6.3 \pm 2.5$  days) (Table 3). Catheter duration was longer in those patients whose CVCs had been removed due to suspected infection (p < 0.0001).

The prevalence of colonized catheters was 6% (12 patients, 8.84/1000 catheter-days), 3.5% suffered from CLABSI (7 patients, 5.15/1000 catheter-days), and the entry point infection prevalence was 0.5% (1 patient, 0.74/1000 catheter-days). Bacteremia of unknown origin affected 2.5% of patients (5 cases, 3.68/1000 catheter-days) (Table 3).

Risk factors for central venous catheter infection.

Table 4 shows the relationship between a positive culture at the tip of the catheter, or CLABSI, and patients' baseline risk factors, and issues related to the technique of CVC insertion. We did not detect a connection between catheter tip infection and patients' postoperative treatment: antibiotics (p=0.687), corticosteroids (p=0.895), parenteral nutrition (p=0.078), renal replacement therapy (p=0.067), or invasive mechanical ventilation (p=0.212). Vasoactive support was required in 33.3% of patients who had a positive culture, compared to 7.8% of patients who did not have a positive catheter tip culture (p<0.0001). We also did not detect a relationship between CLABSI and the administration of corticosteroids (p=0.795). However, patients with CLABSI received more antibiotic therapy (100% vs. 54.9%, p=0.018), parenteral nutrition (57.1% vs. 10.4%, p<0.0001), renal replacement therapy (14.3% vs. 0.5%, p<0.0001), invasive mechanical ventilation (42.8% vs. 6.2%, p<0.0001) and vasoactive support (42.8% vs. 9.3%, p=0.004). The duration of CVC was significantly higher in patients with positive catheter tip culture (9.05±3.07 days vs. 6.53±2.97 days, p=0.002) o CLABSI (11.00±2.58 days vs. 6.64±2.99 days, p<0.0001).

Postoperative complications found during hospital stay were: postoperative pneumonia (4 patients, 2%), atrial fibrillation (3 patients, 1.5%), anastomotic leakage (2 patients, 1%), and postoperative bleeding (1 patient,

		N=200	
Gender male, n (%)		123 (61.5)	
Age, years		$61.6 \pm 13.0$	
	<40 years old	17 (8.5)	
Age, n (%)	40-60 years old	56 (28.0)	
	>60 years old	127 (63.5)	
BMI, kg·m <sup>-2</sup>		$28.7\pm4.8$	
	<24.9 kg·m <sup>-2</sup>	60 (30.0)	
	25-29.9 kg·m <sup>-2</sup>	80 (40.0)	
BMI, n (%)	30-34.9 kg·m <sup>-2</sup>	36 (18.0)	
	35-39.9 kg·m <sup>-2</sup>	17 (8.5)	
	>40 kg·m <sup>-2</sup>	7 (3.5)	
Cervical diameter > 40 cm, n (%)		34 (17.0)	
Smokers, n (%)			
	Cancer	115 (57.5)	
	Diabetes Mellitus	44 (22.0)	
	COPD/Asthma	32 (16.0)	
$C_{am}$ arbidition $\pi(0/)$	Ischemic heart disease	25 (12.5)	
Comorbidities, n (%)	Immunosuppression	18 (9.0)	
	Chronic kidney disease	16 (8.0)	
	Heart failure	9 (4.5)	
	Transplantation	4 (2.0)	
	General and Digestive Surgery	80 (40)	
	Urology	27 (13.5)	
	Neurosurgery	25 (12.5)	
Survival Specialty p (%)	Thoracic Surgery	25 (12.5)	
Surgical Specialty, n (%)	Spinal Surgery	23 (11.5)	
	Vascular Surgery	16 (8.0)	
	Orthopedics and Trauma Surgery	3 (1.5)	
	Maxillofacial Surgery	1 (0.5)	
Duration of surgery, min		$161\pm 66$	
Intraoperative bleeding, ml		$198 \pm 144$	
Intraoperative blood transfusion, n (%)		7 (3.0)	
	Ephedrine	24 (12.0)	
Intraoperative vasoactive support, n (%)	Phenylephrine	19 (9.5)	
	Norepinephrine	7 (3.5)	

 Table 1. Patients' characteristics. Data are expressed as absolute and relative frequencies or mean  $\pm$  SD.

0.5%). No relationship was found between postoperative complications and CLABSI or positive catheter tip culture (Table 4).

Microorganisms detected in central line infections.

The distribution of pathogens detected in CVC tips and causing CLABSI is shown in Fig. 2. No relationship was found between the pathogen detected and the non-modifiable variables: gender (p=0.402), age (p=0.167), BMI (p=0.182), neck circumference>40 cm (p=0.852), history of cancer (p=0.083), diabetes mellitus (p=0.505), COPD/asthma (p=0.887), ischemic heart disease (p=0.054), immunosuppression (p=0.557), chronic kidney disease (p=0.609), cardiac failure (p=0.510) or transplantation (p=0.934). There was also no relationship found with the modifiable variables: operator's experience (p=0.333), the approach (p=0.506), ultrasound-guided cannulation (p=0.189), cannulation time (p=0.790), the need to change side (p=0.887), the number of attempts (p=0.980), or the difficulty in entering the guidewire (p=0.774) (Table 5).

## Discussion

In this prospective study analyzing short-term CVCs through cultures of those inserted prior elective surgery, 6% were colonized, with a CLABSI prevalence of 3.5%. Therefore, it could be expected that the rate of CLABSI would have been higher in case the duration of catheters had been longer. Knowing how many complications are associated from short-term CVCs in an elective surgical setting lets us infer what might happen when catheters remain a longer period, or are placed under suboptimal conditions.

The prevalences and incidences of infectious complications after CVCs are variable according to the studied populations<sup>17</sup>. A CLABSI prevalence of 0.02% has been reported in the general population<sup>18</sup>, while it can reach 3.7% in patients admitted to the emergency department<sup>19</sup>. In susceptible patients due to disease or treatment,

			N=200
Operator, n (%		Medical specialist	93 (46.5)
		Resident doctor	107 (53.5)
Vein Approach, n (%)		Right internal jugular	153 (76.5)
		Left internal jugular	27 (13.5)
		Right subclavian	8 (4.0)
		Left subclavian	8 (4.0)
		Axilar	4 (2.0)
Tralations of (0	1)	Ultrasound-guided	56 (28.0)
Technique, n (%)		Anatomical landmarks	144 (72.0)
Canalization longer than 10 min, n (%)		31 (15.5)	
Need to change side, n (%)		14 (7.0)	
		On the first attempt	85 (42.5)
	Without ultrasound	Second attempt	31 (15.5)
0 (0()		More than two attempts	11 (5.5)
Success, n (%)		On the first attempt	43 (21.5)
	With ultrasound	Second attempt	16 (8.0)
		$\begin{tabular}{ c c c c } \hline U & U & U & V & V & V & V & V & V & V &$	14 (7.0)
	1	None	174 (87.0)
Immediate complications, n (%)		Difficulty passing the guide/catheter	21 (10.5)
		Arterial punction	5 (2.5)
		None	184 (92.0)
Complications detected in the postoperative period, n (%)		Inadequate position	12 (6.0)
		Cervical hematoma	1 (0.5)
		Pneumothorax	3 (1.5)

**Table 2**. Characteristics of the central venous catheter insertion technique. Data are expressed as absolute and relative frequencies.

prevalence is 26.4%, with a 13.2 cases/1000 catheter-day rate of infection<sup>20</sup>. In critical care patients, prevalence is 4.28%<sup>16</sup>, with a 1.14/1000 catheter-day rate of infection<sup>21</sup>. This infection rate is higher in patients admitted to the ICU than in the rest of inpatients<sup>22</sup>. The recorded incidence of CLABSI in hospitalized patients is 0.40 infections/1000 catheter-days<sup>23</sup>. Although the rate is superior in surgical patients, the implementation of aseptic techniques has reduced the incidence of catheter-related infections (CRI) (from 2.7 to 1.1 cases/1000 catheter-days), CLABSI (from 0.8 to 0.5/1000 catheter-days), and even the colonization of the catheter (from 4.5 to 2.6/1000 catheter-days)<sup>24</sup>. Putting these measures into practice has demonstrated to reduce the CRI (OR 0.46 (95% CI 0.23–0.92), p = 0.029), and the colonization of catheters (OR 0.58, 95% CI 0.34–0.98, p=0.042)<sup>24</sup>. This same research group carried out a re-evaluation years later with a larger sample size, observing that the effect of measures was maintained over time in terms of incidence of CRI and CLABSI, but the colonization rate rose again to 4.1/1000 catheter-days<sup>18</sup>.

In the perioperative scenario, measures to reduce the appearance of CLABSI are effective, reducing prevalence from 5.05 to 2.28%, and infection rate from 5.17 to 2.27/1000 catheter-days<sup>25</sup>. However, CLABSI and catheter colonization rates were higher in our research. This higher incidence could be attributed to doing cultures of catheter tips in all patients, while previous studies only performed cultures in patients suspected of infection. Colonization is a predisposing factor for CRI and CLABSI<sup>18</sup>. The mere suspicion of CLABSI can lead to the unnecessary catheter removal in up to 55% of cases<sup>22</sup>. However, the suspicion of infection leading to its removal may not be sufficiently sensitive to rule out the possibility of colonization. Prophylactic antibiotics administered in the perioperative period may mask the symptoms. So, patients with catheter colonization are asymptomatic, but culture of catheters would demonstrate that they are colonized. Since the catheter duration in our study was less than one week, there was not enough time for a colonized catheter to cause CLABSI. The occurrence of CLABSI increases hospital mortality<sup>26</sup>, but the risk of CLABSI has a greater impact on mortality than the occurrence of CLABSI itself<sup>21</sup>. Therefore, it is imperative to take measures to reduce this risk.

There are non-modifiable risk factors that depend on patients' characteristics, while others depend on clinical practice and can be changed. In our study, cancer and ischemic heart disease were associated with colonization, while age over 60 years<sup>27</sup>, cancer, and heart failure were associated with CLABSI. Immunocompromised patients, and those with chronic kidney disease did not have a higher risk, contrary to previous literature<sup>20,25,27,28</sup>. In routine clinical practice, these patients could have received more meticulous care and medications to prevent nosocomial infections. Male gender has also been defined as a risk factor<sup>18</sup>, but we could not appreciate this relationship. Among the technique-related factors, we did not detect a relationship between complications and the operator's experience, or the technique employed. However, we confirmed that jugular approach has a higher prevalence of colonization than subclavian or axillary approaches<sup>18,20,23</sup>. This increased colonization rate in the jugular access may be due to asymptomatic thrombosis highly prevalent in the surgical population due to

Postoperative management and pat	ient evolution		N=200	
	Lack of use	168 (84.0)		
Catheter removal, n (%)	Suspected infection	29 (14.5)		
	Malfunction	3 (1.5)		
Postoperative treatment, n (%)	Antibiotics	113 (56.5)		
	Corticoids	36 (18.0)		
	Parenteral nutritie	Parenteral nutrition		
	Vasoactive support	rt	21 (10.5)	
	Invasive mechanic ventilation	15 (7.5)		
	Renal replacemen	it therapy	2 (1.0)	
	T 1	Induration	23 (11.5)	
	Local symptoms	Erythema	5 (2.5)	
	Fever	26 (13)		
	Tachycardia	13 (6.5)		
	Tachypnea	6 (3.0)		
	Leukocytosis	14 (7)		
Patients' symptoms and signs, n (%)	Leukopenia	1 (0.5)		
	Obtundation	1 (0.5)		
	$\begin{array}{c c} \mbox{Local symptoms} & \hline rever & 5 (2.3) \\ \hline \mbox{Fever} & 26 (1) \\ \hline \mbox{Tachycardia} & 13 (6) \\ \hline \mbox{Tachycardia} & 13 (6) \\ \hline \mbox{Tachycardia} & 13 (6) \\ \hline \mbox{Tachycardia} & 14 (7) \\ \hline \mbox{Leukocytosis} & 14 (7) \\ \hline \mbox{Dotundation} & 1 (0.5) \\ \hline \mbox{Obtundation} & 1 (0.5) \\ \hline \mbox{Oliguria} & 6 (3.0) \\ \hline O$	6 (3.0)		
		6 (3.0)		
	Hypotension	13 (6.5)		
	Bleeding disorders		3 (1.5)	
		2 (1.0)		
	Colonization	12 (6.0)		
Catheter related infection, n (%)	CLABSI	7 (3.5)		
	Entry point infect	1 (0.5)		
Bacteremia of unknown origin, n (%)			5 (2.5)	
Death, n (%)			1 (0.5)	

 Table 3.
 Postoperative management and symptoms/signs of patients. Data are expressed as absolute and relative frequencies.

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vascular trauma and perioperative inflammation<sup>29</sup>. We could not compare other technique-related factors, such as the number of lumens<sup>18,21,24</sup>, or the use of hygiene measures<sup>23</sup>. Despite their short duration, we confirmed the relationship between catheter duration and complications<sup>16,18,21,25,27</sup>. Given that the mean duration of CVCs in our sample was 6 days, we question the recommendation that keeping catheters for up to 7 days can be "safe" to avoid CLABSI<sup>21</sup>. Each additional day a patient has a CVC increases the risk of asymptomatic colonization turning into fatal CLABSI. Finally, there are risk factors that are influenced by clinical practice, that depend on clinical evolution. We confirmed that patients with catheter colonization needed more vasopressor support, while those developing CLABSI required not only more vasopressors but also more antibiotics, renal replacement therapy, and invasive mechanical ventilation. The relationship between CVC infectious complications and parenteral nutrition has been widely described<sup>19,25,27</sup> as well as with the use of antibiotics<sup>27</sup>. The other factors detected are associated with a more severe illness<sup>21</sup>. In a critical care context, this would have resulted in a higher APACHE-II score was not prospectively calculated.

The main cause of CLABSI in our sample were coagulase-negative Staphylococcus, followed by gram-negative bacilli, as in previous studies<sup>18,24,25,30</sup>. Candida did not cause CRSI even though they were also on catheter tips, probably because most of included patients was not receiving immunosuppressants, and cannulation was performed in a controlled setting<sup>20,21</sup>. Many other of microorganisms isolated in the tips did not provoke CLABSI, but having left the catheter in for longer could have given rise to a greater diversity of microorganisms provoking CLABSI<sup>30</sup>.

The search for prognostic tools for early diagnosis of complications favors the initiation of early treatment and a decrease in postoperative morbidity and mortality<sup>31</sup>. In the septic patient, serum Butyrylcholinesterase (BChE) has been shown to mirror the changes of other inflammation biomarkers, such as C-Reactive Protein, Procalcitonin, interleukins (IL-4, IL-6 and IL-10), or tumor necrosis factor Alpha (TNF-a). Thus, the sustained reduction in serum BChE might be used to assess patient outcome 90 days following the onset of sepsis<sup>32</sup>. Furthermore, decreased BChE on the first and third postoperative days after colorectal surgery has been associated with a higher risk of surgical site infection, but not sepsis<sup>33</sup>.

Our study had several limitations due to its design. This was a single-center study from a tertiary university hospital treating only adults, and our results may not be applicable to other centers, patient groups or catheter

	Catheter tip culture						
	Positive (n=19)	Negative (N=179)	OR (95% CI) or md (95% CI)	p	CLABSI (N=7)	OR (95% CI) or md (95% CI)	p
Male gender, n (%)	17 (89.5)	106 (59.2)	0.43 (0.15–1.24)	0.053	6 (85.7)	1.06 (1.01–1.11)	0.180
Age, years	$63.2 \pm 14.7$	$61.1 \pm 12.9$	1.67 (-4.54-7.87)	0.562	$71.6\pm7.4$	10.28 (0.48-20.08)	0.008
Age>60 years old, n (%)	16 (84.2)	111 (62.0)	1.09 (0.43-2.74)	0.202	7 (100)	0.95 (0.91–0.99)	0.041
BMI, kg⋅m <sup>-2</sup>	28.6±3.8	$28.8 \pm 4.9$	-0.12 (-2.41-2.16)	0.820	$26.4\pm0.7$	-2.34 (-5.97-1.29)	0.212
BMI > 35 kg·m <sup>-2</sup> , n (%)	1 (5.2)	23 (12.8)	2.45 (0.34-17.56)	0.342	1 (14.3)	0.96 (0.93-1.99)	0.335
Neck circumference > 40 cm, n (%)	2 (10.5)	32 (17.9)	1.09 (0.34-3.54)	0.335	2 (28.6)	1.23 (1.53–9.88)	0.407
Smokers, n (%)	4 (21.0)	56 (31.3)	1.53 (0.53-4.42)	0.422	2 (28.6)	0.54 (0.13-2.36)	0.980
Cancer, n (%)	17 (89.5)	98 (54.7)	1.48 (1.18-2.29)	0.022	7 (100)	1.09 (1.04–1.84)	0.021
Diabetes mellitus, n (%)	6 (31.6)	38 (21.2)	0.79 (0.30-2.07)	0.442	2 (28.6)	0.70 (0.14-3.51)	0.669
COPD/Asthma, n (%)	4 (21.0)	28 (16.6)	1.02 (0.31-3.28)	0.687	2 (28.6)	1.14 (0.14–9.17)	0.356
Ischemic heart disease, n (%)	6 (31.6)	19 (10.6)	0.31 (0.13-0.74)	0.019	1 (14.3)	0.96 (0.93–0.99)	0.884
Immunosuppression, n (%)	0 (0)	18 (10.0)	0.89 (0.85-0.94)	0.128	0 (0)	0.96 (0.93–0.99)	0.397
Chronic kidney disease, n (%)	0 (0)	16 (8.9)	0.89 (0.85-0.94)	0.153	0 (0)	0.96 (0.93-0.99)	0.427
Cardiac failure, n (%)	2 (10.5)	7 (3.9)	0.85 (0.13-5.67)	0.240	2 (28.6)	0.28 (0.04-2.11)	0.002
Transplantation, n (%)	0 (0)	4 (2.2)	0.90 (0.86-0.95)	0.489	0 (0)	0.96 (0.94–0.99)	0.700
Intraoperative bleeding, ml	$200 \pm 100$	$198 \pm 151$	2.21 (-66.63-71.05)	0.961	$186\pm56$	-12.73 (-122.55-97.09)	0.827
Duration of surgery, min	$156 \pm 62$	$161 \pm 67$	15.98 (-36.73-26.32)	0.773	$175\pm66$	15.22 (-35.04-65.49)	0.567
Intraoperative vasoactive support, n (%)	4 (21.0)	45 (25.9)	0.80 (0.28-2.29)	0.840	1 (14.3)	0.50 (0.06-4.05)	0.925
Intraoperative transfusion, n (%)	0 (0)	6 (3.3)	0.90 (0.86-0.94)	0.420	0 (0)	0.96 (0.94-0.99)	0.636
Resident doctor operator, n (%)	7 (36.8)	100 (55.9)	0.51 (0.21-1.23)	0.050	2 (28.6)	0.65 (0.15-2.84)	0.178
Left or right internal jugular veins, n (%)	19 (100)	159 (88.8)	1.12 (1.06–1.18)	0.019	7 (100)	1.04 (1.01–1.07)	0.369
Ultrasound-guided, n (%)	7 (36.8)	49 (27.4)	0.67 (0.28-1.61)	0.565	3 (42.8)	0.97 (0.19-4.87)	0.373
Cannulation longer than 10 min, n (%)	3 (15.8)	28 (16.6)	1.02 (0.32-3.30)	0.750	1 (14.3)	0.91 (0.11-7.29)	0.905
Need to change side, n (%)	3 (15.8)	11 (6.1)	0.40 (0.13-1.21)	0.167	0 (0)	0.96 (0.93–0.99)	0.460
Success after >2 attempts, n (%)	2 (10.5)	31 (17.3)	0.82 (0.20-3.35)	0.379	2 (28.6)	1.17 (0.15–9.29)	0.379
Difficulty passing the guide, n (%)	2 (10.5)	19 (10.6)	1.00 (0.25–4.04)	0.093	0 (0)	0.96 (0.93–0.99)	0.582
Other postoperative complications, n (%)	0 (0)	10 (5.0)	1.11 (1.06–1.16)	0.293	0 (0)	1.04 (1.01–1.07)	0.537

**Table 4.** Relationship between having a positive catheter tip culture or catheter-related bacteremia and patientrisk factors, or those related to the technique. Data are expressed in absolute and relative frequencies ormean  $\pm$  SD. CLABSI: central line-associated bloodstream infection. OR (95% CI): Odds Ratio (95% ConfidenceInterval); md (95% CI): mean differences (95% Confidence Interval).

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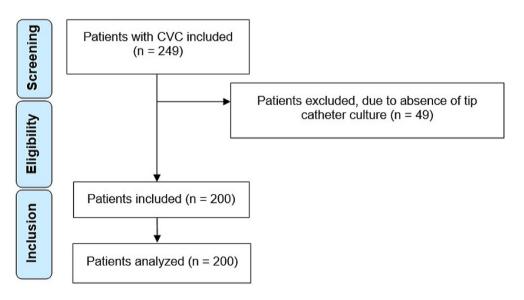
types. As a pragmatic prospective clinical study, patients were not selected, and attending anesthesiologists inserted CVCs. Due to its pragmatic design and having performed this study in the perioperative setting, mainly jugular approach. Although jugular approach might be the most suitable for this setting, it is not free of complications. Therefore, neither the appropriateness of its indication nor the perioperative medication was controlled. Furthermore, patients were submitted to different surgeries and hence the diversity of data we found. However, only by conducting the study in this way could the current rate of short-term CVCs colonization be known in routine clinical practice, as well as the CLABSI rate. As with all observational studies, we cannot account for cofounders that have not been addressed, and our results cannot be interpreted as causal. Larger studies examining the effect of short-term CVCs in a more homogeneous population (i.e. a specific type of surgery or patient) would give a more precise information regarding its real effect and the consequences of related complications.

## Conclusions

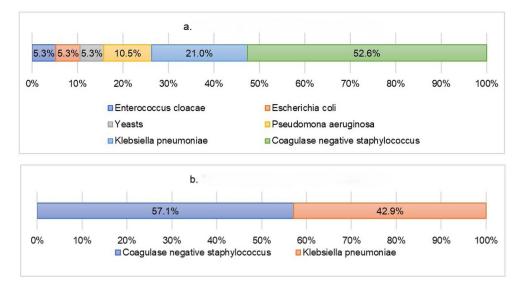
This prospective observational study carried out in elective surgery in which short-term CVCs were canalized under aseptic conditions, shows a high incidence despite catheters being in place for less than a week. The duration of catheters should be shortened as much as possible to avoid complications, but colonization risk depends more on other factors.

	Gram-negative bacilli (n=11)	Gram-positive cocci (n=7)	Yeasts (n=1)	p
Male gender, n (%)	9 (81.8)	7 (100)	0 (0)	0.402
Age, years	70.7±10.0	66.6±12.6	29	0.009
Age>60 years old, n (%)	10 (90.9)	5 (71.4)	0 (0)	0.167
BMI, kg⋅m <sup>-2</sup>	27.3±2.1	30.9±3.3	22.9	0.010
BMI > 35 kg·m <sup>-2</sup> , n (%)	0 (0)	1 (14.3)	0 (0)	0.182
Neck circumference > 40 cm, n (%)	1 (9.1)	1 (14.3)	0 (0)	0.852
Smokers, n (%)	3 (27.3)	1 (14.3)	0 (0)	0.699
Cancer, n (%)	9 (81.8)	6 (85.7)	0 (0)	0.083
Diabetes mellitus, n (%)	3 (27.3)	3 (42.8)	0 (0)	0.505
COPD/Asthma, n (%)	1 (9.1)	1 (14.3)	0 (0)	0.887
Ischemic heart disease, n (%)	1 (9.1)	3 (42.8)	1 (100)	0.054
Immunosuppression, n (%)	0 (0)	0 (0)	0 (0)	0.557
Chronic kidney disease, n (%)	0 (0)	0 (0)	0 (0)	0.609
Cardiac failure, n (%)	1 (9.1)	1 (14.3)	0 (0)	0.510
Transplantation, n (%)	0 (0)	0 (0)	0 (0)	0.934
Intraoperative bleeding, ml	187.5±9.8	228.6±99.4	350	0.232
Duration of surgery, min	185.0±65.0	141.4±41.4	240	0.169
Intraoperative vasoactive support, n (%)	2 (18.2)	1 (14.3)	1 (100)	0.072
Intraoperative transfusion, n (%)	0 (0)	0 (0)	0 (0)	0.874
Resident doctor operator, n (%)	5 (45.4)	2 (28.6)	0 (0)	0.333
Internal jugular veins, n (%)	11 (100)	7 (100)	1 (100)	0.506
Ultrasound-guided, n (%)	5 (45.4)	0 (0)	0 (0)	0.189
Cannulation longer than 10 min, n (%)	2 (18.2)	0 (0)	0 (0)	0.790
Need to change side, n (%)	1 (9.1)	0 (0)	0 (0)	0.887
Success after >2 attempts, n (%)	9 (81.8)	7 (100)	1 (100)	0.980
Difficulty passing the guide, n (%)	1 (9.1)	0 (0)	0 (0)	0.774
Other postoperative complications, n (%)	0 (0)	0 (0)	0 (0)	0.757

**Table 5**. Relationship between the pathogens detected and patient risk factors, or those related to thetechnique. Data are expressed in absolute and relative frequencies or mean ± SD.



## Fig. 1. Patient Flow chart diagram.



**Fig. 2.** Microorganisms identified in cultures. Figure 2a: Microorganisms isolated from central venous catheter tips (n = 19). Figure 2b: Bacterial agents found in patients with CLABSI (n = 7). Data are expressed as relative frequencies. CVC: central venous catheter; CLABSI: central line-associated bloodstream infection.

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## Data availability

The data presented in this study are available on request from the corresponding author.

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## **Author contributions**

A. B.-B., Y. D.-D., H. T.-M., O. P.-R. and A. R.-P. contributed to the conception and design of the study; A. B.-B., Y. D.-D., H. T.-M., S, C.-D., L. V.-S. and N. O.-B. contributed with the acquisition of the data; A. B.-B., Y. D.-D. and N. O.-B. performed the analysis and interpretation of the data; A. B.-B., Y. D.-D., and A. R.-P. drafted the manuscript; All authors contributed to revision of the manuscript. All authors read and approved the final manuscript.

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## Declarations

## **Competing interests**

The authors declare no competing interests.

## Ethics approval and consent to participate

This study was approved by the Ethics Committee of the Hospital Universitario de Gran Canaria Doctor Negrín, Las Palmas de Gran Canaria, Spain (IRB approval #150030). Written informed consent was obtained from all subjects participating prior to their enrollment in the trial.

## Additional information

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