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ORIGINAL ARTICLE

Skin insertion site culture for the prediction of primary bloodstream infection

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Abstract

Purpose Previous studies have analyzed the capability of skin insertion site culture to predict catheter-related bloodstream infection (CRBSI). However, there has been not analyzed its capability to predict primary bloodstream infection (PBSI), that include CRBSI and bloodstream infection of unknown origin (BSIUO). The novel objective of our study was to determine the capability of insertion skin site culture to predict CRBSI and primary bloodstream infection (PBSI), that include CRBSI and bloodstream infection of unknown origin (BSIUO).

Material and methods Observational and prospective study in one Intensive Care Unit. Patients with some central venous catheter (CVC) at least during 7 days and suspected catheter-related infection (CRI) (new episode of fever or sepsis) were included. Cultures of insertion skin site, paired blood samples, catheter-tip, and other clinical samples were taken. Capability of insertion skin site culture to predict CRBSI and PBSI was determined.

Results We included 108 CVC from 96 CRI suspicion episodes. The causes that motivated CRI suspicion were 20 (18.5%) PBSI, 44 (40.7%) other infections, and 44 (40.7%) unknown. Among the 20 PBSI, 11 (55%) were CRBSI and 9 (45%) were BSIUO. Negative predictive value of insertion skin site culture to predict CRBSI was 95% (87–98%) and to predict PBSI was 85% (76–91%).

Conclusions The new finding of our study was that skin insertion site culture had a good negative predicted valued for the prediction of CRBSI and PBSI.

Keywords Bloodstream infection · Prediction · Skin insertion site culture

Introduction

Recent guidelines for the management of intravascular catheter-related infection (CRI) recommended that the routinely immediate removal of the central venous catheter

Highlights
- Skin insertion site culture for prediction of CRBSI and PBSI
- Skin insertion site culture had a good negative predicted valued for the prediction of CRBSI and PBSI

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(CVC) is not necessary in patients who are hemodynamically stable, without immunosuppressive therapy, intravascular foreign bodies or organ transplantation, and no suppuration at the insertion site or bacteremia/fungemia [1–3].

There are several arguments against the routinely immediate CVC removal when CRI is suspected, such as that critically ill patients frequently develop fever due other causes [4], vascular catheterization by new puncture entails risk of serious mechanical complications [5], and the absence of differences in outcome between the early CVC removal and watchful waiting group when CRI is suspected [6, 7].

Therefore, the use of conservative methods for the diagnosis of CRI that allow keeping the catheter in situ can have the advantage of avoiding unnecessary removal of the catheter and the potential risk of mechanical complications [8]. The semiquantitative cultures of CVC insertion skin site is one of those conservative methods. Previous studies have analyzed the capability of skin insertion site culture to predict catheter-related bloodstream infection (CRBSI) or CVC tip colonization [9–16]. CRBSI has been defined in those studies as a positive blood culture by recognized pathogen, CVC tip colonization with the same microorganism, and no other apparent infection source. However, there has been not analyzed its capability to predict primary bloodstream infection (PBSI) that include CRBSI and bloodstream infection of unknown origin (BSIUO) [17]. Thus, the novel objective of our study was to determine the capability of insertion skin site culture to predict CRBSI and PBSI.

Methods

Design and subjects

We performed a prospective and observational study between June 2020 and January 2021 with the approval of the Institutional Ethic Review Board of the Hospital Universitario de Canarias (Tenerife, Spain). The requirement of written informed consent was waived due to the only change of our daily clinical practice by the study was the skin insertion site culture (which is a noninvasive procedure that is internationally accepted for CRBSI diagnosis in the daily clinical practice) and due to that the prohibition of patient visits by the public health outbreak policy of Spanish Government due to the context of COVID-19 pandemia.

We included patients admitted to Intensive Care Unit underwent to some CVC at least during 7 days and CRI was suspected. CRI was suspected when a patient developed a new episode of fever or sepsis. Fever was considered as temperature ≥ 38 °C. Sepsis was defined according to Sepsis-3 Consensus criteria of 2016 [18].

Variables recorded

The following variables were recorded for each patient: age, sex, diagnosis on admission, diabetes mellitus, renal replacement therapy previously to admission, chronic obstructive pulmonary disease (COPD), asthma, chronic liver disease, smoking, parenteral nutrition previously to admission, corticosteroids previously to admission, immunosuppressive therapy previously to admission, hematological tumor, solid tumor, human immunodeficiency virus, corticosteroids at sepsis, immunosuppressive therapy at sepsis, parenteral nutrition at sepsis, propofol at sepsis, renal replacement therapy at sepsis, temperature, lactic acid, glucose, creatinine, protein, albumin, C-reactive protein, procalcitonin, leukocytes, neutrophils, platelets, international normalized ratio (INR), activated partial thromboplastin time (aPTT), pressure of arterial oxygen/fraction inspired of oxygen (PaO_2/FIO_2), Sepsis-related Organ Failure Assessment (SOFA) score [19], time of CVC, site of CVC, aspect of skin insertion site, culture of skin insertion site, death at 30 days, and time alive during first 30 days.

Sample collections

The following samples were collected from each patient: insertion skin site culture, paired blood samples, catheter-tip, and other clinical samples. Superficial swab from insertion site of approximately 3-cm area of skin was taken after dressing and rubbing the area around the insertion site with a cotton swab wet with sterile saline. Paired blood samples were taken from peripheral vein, with 10-ml blood sample in each one and separated by 15 min. Catheter-tip sample was taken after scrubbing the skin surrounding the insertion site with 2% chlorhexidine and cutting off the tip (distal 5-cm segment) using sterile scissors. Patients without blood culture, catheter tip culture, and skin insertion site cultures were excluded of the analysis.

Definitions

We used criteria of European Centre for Disease Prevention and Control (ECDC) to define infections [17]. Catheter-tip colonization was considered as significant growth of a microorganism on the CVC tip (≥ 15 colony-forming units) by semi-quantitative method described by Maki et al. [20]. Insertion skin site colonization was considered as significant growth of a microorganism on semi-quantitative culture (≥ 15 colony-forming units per plate). BSIUO was defined as bloodstream infection of unknown origin (verified during survey and no source found). PBSI include CRBSI and BSIUO; thus, some PBSI had positive CVC tip colonization and others not.

Statistical analysis

Continuous variables are reported as means and standard deviations, and categorical variables as frequencies and percentages. We used Mann–Whitney T test to compare continuous variables between groups. Comparison of categorical variables between groups was performed using chi-square test. We obtained the sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio, and negative likelihood ratio of the insertion skin site culture to determine the capability of insertion skin site culture to predict CRBSI and PBSI. All values were calculated with a 95% confidence interval. $P < 0.05$ were considered statistically significant. Statistical analysis was performed with SPSS 17.0 (SPSS Inc., Chicago, IL, USA).

Results

We included 108 CVC from 96 episodes of CRI suspicion. The causes of clinical symptoms that motivated CRI suspicion were the following: 20 (18.5%) PBSI, 44 (40.7%) secondary to other infections, and 44 (40.7%) unknown origin. Among the 20 PBSI, 11 (55%) were CRBSI and 9 (45%) were BSIUO. The site of CVC was 25 (23.1%) subclavian, 53 (49.1%) jugular, and 30 (27.8%) femoral.

We found that the group of CVC developing CRBSI (n = 11) compared to CVC group without it (n = 97) had more rate of positive culture of skin insertion site (p = 0.001) and of female (p = 0.03); however, no significant differences were found in rate of death (p = 0.99), time of CVC, site of CVC, aspect of skin insertion site, and in the other variables that were recorded (Table 1).

We found that the group of CVC developing PBSI (n = 20) compared to CVC group without it (n = 88) had more rate of positive culture of skin insertion site (p = 0.03); however, no significant differences were found in rate of death (p = 0.78), time of CVC, site of CVC, aspect of skin insertion site, and in the other variables that were recorded (Table 2).

We found 15 cases of positive culture of skin insertion. We found that the culture of skin insertion site was positive in 6 of 11 cases of CRBSI and negative in 88 of 97 cases without CRBSI (Table 3). We found that the culture of skin insertion site was positive in 6 of 20 cases of PBSI and negative in 79 of 88 cases without PBSI (Table 4). Table 5 describes sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio, and negative likelihood ratio of insertion skin site culture to predict CRBSI and PBSI.

Discussion

Previous studies have been found that culture of skin insertion site had a good negative predicted valued for the prediction of the CRBSI or CVC tip colonization [9–16]. Novel aspects of our research were that we studied the capability of skin insertion site culture for predict CRBSI and PBSI. The new finding of our study was that skin insertion site culture had a good negative predicted valued for the prediction of CRBSI and PBSI. Thus, that the probability of not having PBSI if the result of skin insertion site culture is negative is high.

Previous studies analyzed CRBSI defined as a positive blood culture by recognized pathogen (or two positive blood cultures by skin contaminant microorganism) obtained from a peripheral vein and CVC tip colonization with the same microorganism. However, we analyzed PBSI for the first time. The studies that have analyzed the capability prognosis of skin insertion site culture have many differences between them. Some studies included all patients removing CVC [11, 15, 16], and other studies include only patients who CVC were removed due to catheter related infection suspicion [9, 10, 12–14]. Some studies determined the ability of skin insertion site culture to predict CVC colonization tip [9, 11], and other studies to predict CRBSI [10, 12–16]. Some studies did not include femoral CVC [14–16], and only one study reported an important rate of femoral CVC removed (26%) [13]. Some studies included CVC with any time of catheterization [13], other studies only included CVC with more than 48 h of catheterization [12, 14], and other studies only included CVC with more than 7 days of catheterization [10, 15, 16].

In the most of previous studies was analyzed the culture of skin insertion site and hubs together, and culture only of skin insertion site was analyzed only in a study [16]. However, in the study by the team of Bouza et al. were included all patients removing CVC and only 24% were removed due to CRI suspicion [16]. Besides, in the study by Bouza et al., femoral CVC was not reported [16], and this may be a point of interest due to femoral site is associated with higher CRBSI risk [21].

Recent guidelines for the management of CRI recommended that immediate CVC removal is not necessary routinely in patients who are hemodynamically stable, without immunosuppressive therapy, intravascular foreign bodies or organ transplantation, and no suppuration at the insertion site or bacteremia/fungemia [1–3]. If any of these conditions is present, the strategy of watchful waiting and maintain CVC to microbiological results could be adopted. In addition, we believe that in the decision of watchful waiting or immediate CVC removal in patients with suspected CRI should take into account the vascular

Table 1 Characteristics of CVC developing and not catheter-related bloodstream infection (CRBSI)

Data	Non CRBSI (n = 97)	CRBSI (n = 11)	P-value
Culture positive of skin insertion site, n (%)	9 (9.3)	6 (54.5)	0.001
Aspect of skin insertion site, n (%)			0.34
Normal	57 (58.8)	8 (72.7)	
Inflammation	34 (35.1)	2 (18.2)	
Non-purulent exudate	4 (4.1)	0	
Purulent exudate	2 (2.1)	1 (9.1)	
Time of CVC (days)–median (p 25–75)	9 (7–12)	9 (8–12)	0.41
Site of CVC, n (%)			0.66
Subclavian	22 (22.7)	3 (27.3)	
Jugular	49 (50.5)	4 (36.4)	
Femoral	26 (26.8)	4 (36.4)	
Age, years (p 25–75)	65 (56–72)	63 (52–70)	0.37
Sex female, n (%)	30 (30.9)	0	0.03
Admission diagnostic, n (%)			0.17
Medical	72 (74.2)	9 (81.8)	
Surgical	18 (18.6)	0	
Traumatology	7 (7.2)	2 (18.2)	
Diabetes mellitus, n (%)	30 (30.9)	4 (36.4)	0.74
Renal replacement therapy previously to admission, n (%)	3 (3.1)	1 (9.1)	0.35
COPD, n (%)	14 (14.4)	0	0.35
Asthma, n (%)	5 (5.2)	1 (9.1)	0.48
Chronic liver disease, n (%)	4 (4.1)	0	0.99
Smoking, n (%)	15 (15.5)	1 (9.1)	0.99
Parenteral nutrition previously to admission, n (%)	2 (2.1)	0	0.99
Corticosteroids previously to admission, n (%)	5 (5.2)	0	0.99
Immunosuppressive therapy previously to admission, n (%)	5 (5.2)	1 (9.1)	0.48
Hematological tumor, n (%)	0	1 (9.1)	0.10
Solid tumor, n (%)	1 (1.0)	0	0.99
Human Immunodeficiency Virus, n (%)	1 (1.0)	0	0.99
Corticosteroids at sepsis, n (%)	16 (16.5)	1 (9.1)	0.99
Immunosuppressive therapy at sepsis, n (%)	3 (3.1)	0	0.99
Parenteral nutrition at sepsis, n (%)	16 (16.5)	2 (18.2)	0.99
Propofol at sepsis, n (%)	37 (38.1)	4 (36.4)	0.99
Renal replacement therapy at sepsis, n (%)	13 (13.4)	1 (9.1)	0.99
Temperature, median, °C (p 25–75)	37.4 (36.4–37.8)	37.0 (35.5–37.5)	0.15
Lactic acid, median mmol/L (p 25–75)	0.9 (0.8–1.5)	1.5 (0.8–1.5)	0.31
Glucose (g/dL)–median (p 25–75)	125 (102–148)	114 (103–142)	0.67
Creatinine (mg/dl)–median (p 25–75)	0.8 (0.5–1.4)	0.7 (0.6–0.9)	0.93
Protein (g/L), median (p 25–75)	5.7 (5.3–6.1)	5.8 (5.0–6.0)	0.61
Albumin (g/L), median (p 25–75)	2.8 (2.7–3.3)	2.8 (2.6–2.8)	0.87
C-reactive protein (mg/gl), median (p 25–75)	95 (38–151)	94 (24–169)	0.90
Procalcitonin (ng/ml) – median (p 25–75)	0.3 (0.1–0.7)	0.1 (0.1–0.3)	0.21
Leukocytes, median $\times 10^3/mm^3$ (p 25–75)	11.4 (8.4–15.0)	11.0 (8.0–12.2)	0.45
Neutrophils, median $\times 10^3/mm^3$ (p 25–75)	9.0 (6.3–12.0)	7.9 (5.7–9.9)	0.46
Platelets, median $\times 10^3/mm^3$ (p 25–75)	246 (183–334)	254 (146–335)	0.68
INR, median (p 25–75)	1.1 (1.0–1.2)	1.1 (1.0–1.2)	0.58
aPTT, median seconds (p 25–75)	30 (27–33)	29 (22–33)	0.81
PaO_2/FIO_2 ratio, median (p 25–75)	293 (217–316)	284 (202–346)	0.74
SOFA score, median (p 25–75)	4 (3–6)	4 (2–6)	0.66
Deaths at 30 days, no. (%)	26 (26.8)	3 (27.3)	0.99
Time alive during first 30 days (days), median (p 25–75)	30 (23–30)	30 (6–30)	0.79

CVC central venous catheter, *COPD* chronic obstructive pulmonary disease, *INR* international normalized ratio, *aPTT* activated partial thromboplastin time, *PaO_2/FIO_2* pressure of arterial oxygen/fraction inspired oxygen, *SOFA* Sepsis-related Organ Failure Assessment

Table 2 Characteristics of CVC developing and not primary bloodstream infections (PBSI)

Data	Non PBSI (n = 88)	PBSI (n = 20)	P-value
Culture positive of skin site, n (%)	9 (10.2)	6 (30.0)	0.03
Aspect of skin insertion site, n (%)			0.31
Normal	50 (56.8)	15 (75.0)	
Inflammation	32 (36.4)	4 (20.0)	
Non-purulent exudate	4 (4.5)	0	
Purulent exudate	2 (2.3)	1 (5.0)	
Time of CVC (days), median (p 25–75)	9 (7–12)	10 (8–12)	0.60
Site of CVC, n (%)			0.84
Subclavian	21 (23.9)	4 (20.0)	
Jugular	42 (47.7)	11 (55.5)	
Femoral	25 (28.4)	5 (25.0)	
Age, years (p 25–75)	65 (56–72)	64 (54–72)	0.65
Sex female, n (%)	28 (31.8)	2 (10.0)	0.06
Admission diagnostic, n (%)			0.09
Medical	63 (71.6)	18 (90.0)	
Surgical	18 (20.5)	0	
Traumatology	7 (8.0)	2 (10.0)	
Diabetes mellitus, n (%)	30 (34.1)	4 (20.0)	0.29
Renal replacement therapy previously to admission, n (%)	3 (3.4)	1 (5.0)	0.57
COPD, n (%)	12 (13.6)	2 (10.0)	0.99
Asthma, n (%)	5 (5.7)	1 (5.0)	0.99
Chronic liver disease, n (%)	4 (4.5)	0	0.99
Smoking, n (%)	14 (15.9)	2 (10.0)	0.73
Parenteral nutrition previously to admission, n (%)	2 (2.3)	0	0.99
Corticosteroids previously to admission, n (%)	5 (5.7)	0	0.58
Immunosuppressive therapy previously to admission, n (%)	5 (5.7)	1 (5.0)	0.99
Hematological tumor, n (%)	0	1 (5.0)	0.19
Solid tumor, n (%)	1 (1.1)	0	0.99
Human Immunodeficiency Virus, n (%)	1 (1.1)	0	0.99
Corticosteroids at sepsis, n (%)	13 (14.8)	4 (20.0)	0.52
Immunosuppressive therapy at sepsis, n (%)	3 (3.4)	0	0.99
Parenteral nutrition at sepsis, n (%)	13 (14.8)	5 (25.0)	0.32
Propofol at sepsis, n (%)	35 (39.8)	6 (30.0)	0.46
Renal replacement therapy at sepsis, n (%)	13 (14.8)	1 (5.0)	0.46
Temperature, median, °C (p 25–75)	37.4 (36.6–37.8)	37.2 (35.0–38.0)	0.52
Lactic acid, median mmol/L (p 25–75)	0.9 (0.8–1.4)	1.2 (0.8–1.5)	0.35
Glucose (g/dL), median (p 25–75)	125 (102–149)	126 (106–145)	0.83
Creatinine (mg/dl), median (p 25–75)	0.8 (0.5–1.5)	0.7 (0.6–0.9)	0.37
Protein (g/L), median (p 25–75)	5.7 (5.3–6.1)	5.9 (5.0–6.0)	0.82
Albumin (g/L), median (p 25–75)	2.8 (2.7–3.3)	2.8 (2.6–2.8)	0.41
C-reactive protein (mg/gl), median (p 25–75)	98 (38–143)	86 (31–168)	0.83
Procalcitonin (ng/ml), median (p 25–75)	0.3 (0.1–0.8)	0.1 (0.1–0.4)	0.37
Leukocytes, median $\times 10^3/mm^3$ (p 25–75)	11.5 (8.3–14.7)	11.0 (8.3–13.4)	0.80
Neutrophils, median $\times 10^3/mm^3$ (p 25–75)	8.5 (6.3–12.0)	8.9 (5.8–12.0)	0.99
Platelets, median $\times 10^3/mm^3$ (p 25–75)	246 (180–334)	261 (200–325)	0.87
INR, median (p 25–75)	1.1 (1.0–1.2)	1.1 (1.0–1.2)	0.83
aPTT, median seconds (p 25–75)	30 (27–33)	29 (26–33)	0.97
PaO_2/FIO_2 ratio, median (p 25–75)	293 (229–335)	253 (200–300)	0.33
SOFA score, median (p 25–75)	4 (3–6)	5 (2–7)	0.91
Deaths at 30 days, no. (%)	23 (26.1)	6 (30.0)	0.78
Time alive during first 30 days (days), median (p 25–75)	30 (22–30)	30 (21–30)	0.72

CVC central venous catheter, *COPD* chronic obstructive pulmonary disease, *INR* international normalized ratio, *aPTT* activated partial thromboplastin time, *PaO_2/FIO_2* pressure of arterial oxygen/fraction inspired oxygen, *SOFA* Sepsis-related Organ Failure Assessment

Table 3 Test results of insertion skin site culture and existence of catheter-related bloodstream infection (CRBSI)

	CRBSI (n = 11)	Non CRBSI (n = 97)	Total (n = 108)
Positive insertion skin site culture	6 (54.5%)	9 (9.3%)	15 (13.9%)
Negative insertion skin site culture	5 (45.5%)	88 (90.7%)	93 (86.1%)

Table 4 Test results of insertion skin site culture and existence of primary bloodstream infections (PBSI)

	PBSI (n = 20)	Non PBSI (n = 88)	Total (n = 108)
Positive insertion skin site culture	6 (30.0%)	9 (10.2%)	15 (13.9%)
Negative insertion skin site culture	14 (70.0%)	79 (89.8%)	93 (86.1%)

accessibility (since that in some cases, new vascular catheterization may be very difficult due to poor vascular access) and the risk of mechanical complications (since that in same cases, as severe coagulopathy or respiratory disease could appears life-threatening complications). Thus, the development of methods for the diagnosis of CRBSI without CVC removal can contribute to unnecessary CVC removal and to reduce mechanical complications due to CVC. We think that the approach of skin insertion site culture could help in the decision of watchful waiting avoiding routinely immediate CVC removal in patients with suspected CRI.

Some limitations must be recognized in our study. First, we have not taken other non-invasive cultures to compare its capability to predict PBSI with skin insertion site culture. Second, we have not registered all CVC to know the incidence of PBSI and the rate of skin insertion site culture positive in all CVC. Third, we have not reported what proportion of CVC was excluded due to have not all culture (blood, catheter tip, and skin insertion site culture).

Conclusion

The new finding of our study was that skin insertion site culture had a good negative predicted valued for the prediction of CRBSI and PBSI.

Abbreviations aPTT: Activated partial thromboplastin time; CRBSI: Catheter-related bloodstream infection; CRI: Catheter-related infection; CVC: Central venous catheter; COPD: Chronic obstructive pulmonary disease; FIO_2: Fraction inspired of oxygen; INR: International normalized ratio; PaO_2: Pressure arterial of oxygen; PBSI: Primary bloodstream infection; SOFA: Sepsis-related Organ Failure Assessment score

Author contribution LL conceived, designed, and coordinated the study; participated in acquisition and interpretation of data; and drafted the manuscript. ML and AM conceived and designed the study and participated in acquisition and interpretation of data. APL, AGM, MC, and MLM participated in acquisition of data. AJ participated in the interpretation of data. All authors revised the manuscript critically for important intellectual content, made the final approval of the version to be published, and were agreed to be accountable for all aspects of the work.

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Availability of data and material The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval This study was carried out with the approval of the Institutional Ethic Review Board of the Hospital Universitario de Canarias (Tenerife, Spain). The requirement of written informed consent was waived due to the only change of our daily clinical practice by the study was the skin insertion site culture (which is a noninvasive procedure that is internationally accepted for CRBSI diagnosis in the daily clinical practice) and due to that the prohibition of patient visits

Table 5 Capacity of insertion skin site culture to predict catheter-related bloodstream infection (CRBSI) and primary bloodstream infections (PBSI)

	CRBSI	PBSI
Sensitivity and 95% CI	55% (25–82%)	30% (13–54%)
Specificity and 95% CI	91% (83–95%)	90% (81–95%)
Positive predicted value and 95% CI	40% (17–67%)	40% (17–67%)
Negative predicted value and 95% CI	95% (87–98%)	85% (76–91%)
Positive likelihood ratio and 95% CI	5.88 (2.58–13.40)	2.93 (1.18–7.30)
Negative likelihood ratio and 95% CI	0.50 (0.26–0.96)	0.78 (0.58–1.05)

CI confidence intervals

by the public health outbreak policy of Spanish Government due to the context of COVID-19 pandemia.

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Conflict of interest The authors declare no competing interests.

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