

**Risk factors for bloodstream infection and influence on mortality rate***Fatores de risco para infecção de corrente sanguínea e influência na taxa de mortalidade**Factores de riesgo para la infección del flujo sanguíneo e influencia en la tasa de mortalidad*Rosimeire Faria da Silva<sup>1</sup>, Clesnan Mendes-Rodrigues<sup>1</sup>, Eliana Borges Silva Pereira<sup>1</sup>, Denise Von Dolinger de Brito Röder<sup>1</sup>, Fabíola Alves Gomes<sup>1</sup>

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**ABSTRACT**

**Objective:** To evaluate the main risk factors for catheter-related bloodstream infection (ICSRC) and its effects on the outcome of death in patients admitted to an adult intensive care unit (ICU). **Methods:** Retrospective study performed at an ICU. Data on potential risk factors for ICSRC (sociodemographic profile, unit and insertion pathway, responsible for the dressing) were collected and the death outcome was evaluated. **Results:** 268 central venous catheters (CVC) were inserted in 209 patients, 13.4% with at least one ICSRC and 36.36% of the patients died; 11.9% of the CVC were punctured in the jugular vein and 13.8% in the subclavian vein infected. Length of stay longer than 14 days and place of insertion of the CVC outside the ICU increased the chances of infection in the subclavian and jugular routes (OR: 2.25 and 0.27). The chances of infection in the jugular route increased with tracheostomy (OR: 3.83). The risk of death increased with ICSRC, hospitalization for trauma and APACHE > 22. **Conclusion:** Evaluation and intervention in the conditions of insertion and care of the CVC outside the ICU seems to be the crucial point for the decrease of the infections and mortality of patients subsequently admitted to the ICU.

**Descriptors:** Catheter-Related Infections, Catheters, Intensive Care Units, Risk Factors.

**RESUMO**

**Objetivo:** avaliar os principais fatores de risco para infecção de corrente sanguínea relacionada ao cateter (ICSRC) e seus efeitos no desfecho de óbito, em pacientes internados em uma unidade de terapia intensiva (UTI) adulto. **Métodos:** Estudo retrospectivo, realizado em uma UTI. Foram coletados dados sobre os fatores de risco potenciais para ICSRC (perfil sociodemográfico, unidade e via de inserção, responsável pelo curativo) e avaliado o desfecho óbito. **Resultados:** 268 cateteres venosos centrais (CVC) foram inseridos em 209 pacientes, sendo 13,4% com pelo menos uma ICSRC e 36,36% dos pacientes evoluíram para óbito; 11,9% dos CVC puncionados na veia jugular e 13,8% na veia subclávia infectaram. O tempo de permanência maior que 14 dias e local de inserção do CVC fora da UTI aumentaram as chances de infecção nas vias subclávia e jugular (OR: 2,25 e 0,27). As chances de infecção na via jugular aumentaram com traqueostomia (OR: 3,83). O risco de óbito aumentou com ICSRC, internação por trauma e APACHE >22. **Conclusão:** A avaliação e intervenção nas condições de inserção e cuidados do CVC fora da UTI parece ser o ponto crucial para diminuição das infecções e mortalidade dos pacientes posteriormente admitidos na UTI.

**Descritores:** Infecções relacionadas a cateter, Cateteres, Unidades de terapia intensiva, Fatores de risco.

**RESUMÉN**

**Objetivo:** evaluar los principales factores de riesgo para la infección del flujo sanguíneo relacionado con el catéter (ICSRC) y sus efectos en el desenlace de defunción, en pacientes internados en una unidad de terapia intensiva (UCI) adulto. **Métodos:** Estudio retrospectivo, realizado en una UTI. Se recolectar datos sobre los factores de riesgo potencial para ICSRC (perfil sociodemográfico, unidad y vía de inserción, responsable del curativo) y evaluado el desenlace de la muerte. **Resultados:** 268 catéteres venosos centrales (CVC) fueron insertados en 209 pacientes, siendo el 13,4% con al menos una ICSRC y el 36,36% de los pacientes evolucionó a muerte; El 11,9% de los CVC puncionados en la vena yugular y el 13,8% en la vena subclavia infectaron. El tiempo de permanencia mayor que 14 días y lugar de inserción del CVC fuera de la UTI aumentaron las posibilidades de infección en las vías subclavia y yugular (OR: 2,25 y 0,27). Las posibilidades de infección en la vía yugular aumentaron con traqueotomía (OR: 3,83). El riesgo de muerte aumentó con ICSRC, internación por trauma y APACHE > 22. **Conclusión:** La evaluación e intervención en las condiciones de inserción y cuidados del CVC fuera de la UTI parece ser el punto crucial para disminuir las infecciones y mortalidad de los pacientes posteriormente admitidos en la UTI.

**Descriptoros:** Infecciones Relacionadas con Catéteres, Catéteres, Unidades de Cuidados Intensivos, Factores de Riesgo.

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## INTRODUCTION

Central venous catheters (CVC) are subject to monitoring, administration of fluids, medications, blood products and parenteral nutrition<sup>1, 2</sup>. Despite the advantages of using CVC there are associated risks, since catheter-related bloodstream infection (CABSI) and colonization are the most common adverse outcomes among catheter-related infections, raising mortality and cost of hospitalization<sup>3, 4</sup>.

The ICSRC stands out as the main risk and complication resulting from the use of this device, being confirmed clinically and by laboratory tests. If the association between catheter and blood infection is not confirmed by laboratory tests, but CVC is the most likely cause of infection, it is defined as bloodstream infection associated with the catheter<sup>3</sup>.

ICSI are important causes of morbidity and mortality among critically ill patients<sup>3</sup>. In the United States, CABSI rates in intensive care units (ICUs) are approximately 80,000 cases each year, while 250,000 cases of bloodstream infection (ICS) have been estimated to occur annually, regardless of the patient's hospitalization unit.

There are four recognized pathways for catheter contamination: migration of skin microorganisms into the catheter insertion site into and through the catheter surface with colonization of the catheter tip; direct contamination of catheter or catheter hub by contact with contaminated hands, fluids or devices; contamination of the catheters by hematogenic route from another source of infection; and contamination of the infusion<sup>3</sup>.

CABSI results from inadequate hygiene and catheter installation and management procedures. These include breaking the aseptic technique into catheter insertion, inadequate hand hygiene during handling, inadequate skin hygiene at the site of catheter insertion, suboptimal location of

catheters, and unnecessary placement of catheters<sup>3</sup>. Other risk factors include the age of the patient, the presence of comorbidities, as well as the duration of catheterization and hospitalization<sup>1</sup>.

In this context, the objective of this study was to evaluate the main risk factors for CABSI and their effects on the outcome of death in patients admitted to an adult ICU.

## METHODS

### Study scenario

This is a retrospective, documentary study, carried out from July 2013 to January 2014, in a general ICU, of a Brazilian university hospital of tertiary care. The adult ICU, site of the study, consists of 30 beds occupied by clinical and surgical patients of various specialties, aged up to 14 years.

### Inclusion criteria

The study included patients aged from 14 years who had at least one CVC nontunneled inserted into the subclavian vein, internal femoral or jugular lasting at least 48 hours, being punctured in the ICU or outside (in another unit of the same or other hospital). They were only included in the CVC study for fluid therapy or drug administration. Patients with incomplete or illegible data on medical records or on epidemiological surveillance records, with peripherally inserted central catheters, pulmonary artery catheters, and hemodialysis catheters were excluded.

### Data collection

Data were collected on the following potential risk factors for CRFRS: age, sex, reason for ICU admission (dichotomized in clinical or traumatologic cause), insertion pathway and CVC placement site (inserted inside or outside the ICU), score Acute Physiology and Chronic Health Evaluation (APACHE II), length of time of each

catheter, length of ICU stay, presence of infection, professional responsible for CVC dressing and microorganism present in culture.

In the months of July to September of 2013 the dressings of the CVC were performed by any professional of the nursing team (Nursing Assistants, Nursing Technicians and Nurses). In the month of October of 2013 there was a change in the dressing performer, and this month was excluded from the analysis. From the month of October 2013 until January 2014 the dressing of CVC was carried out exclusively by the Nurse. The dressing performer was inserted as the professional variable responsible for the dressing (nursing team or nurse).

Data collection was not blind, using uncontrolled cohorts of available charts during the study period. In addition, internal forms of the Hospital Infection Control Service (HICS) of these patients were accessed for data collection on infections. The HICS of the hospital already performed ICSRC surveillance for all ICU patients using CVC, using the definitions of the Centers for Disease Control and Prevention (CDC)<sup>3</sup>. A device day (catheter-day) was defined by a patient with a single CVC for a total or partial period of 24 hours. Patient-related infection with a further 48 hours of CVC insertion was considered as ICSRC, with cultures of positive catheter-tipped microorganisms and no other recognized source of infection. All infections were diagnosed by the HICS of the hospital.

#### **Ethical issues**

The study was approved by the Research Ethics Committee of the Federal University of Uberlândia under number 1042790/2015, in accordance with the Resolution 466/2012 of the National Health Council.

#### **Statistical analysis**

All quantitative variables were binary dichotomized for analysis, based on the low frequency of some strata or values. The association between the presence or absence of CVC infection was evaluated only for binary classification. To test the association between the occurrence of infection and use of the CVC, the Independence Chi-Square Test (for variables with all expected frequencies greater than 5) or Fischer's Exact Test (for variables with at least one lower expected frequency that 5). This analysis was performed separately for the catheters that were punctured in the subclavian and jugular veins, and, additionally, independent of the puncture site. The catheters punctured in the femoral vein were not included in the analysis because of low sampling and no infection in the sample (n=8).

To assess the impact of the catheter puncture order in the same patient were conducted two analyzes. In the first analysis, only the first puncture was considered in each patient. In the second, they were analyzed only the 2nd and 4th catheters punctured the patient; In this case, the presence of a previous catheter with infection was included. The catheters had to be grouped by the low number of 3rd and 4th puncture catheters. In these analyzes, each CVC was considered as a sample, and its covariates were calculated independently.

The risk factor analysis was also performed for the outcome of death (0: survival, 1: death), in which case the results referring to the catheters in the femoral route were also included in the analysis and each patient was individually sampled. The catheterization time was the sum of the time of each of the patient's CVC.

The odds ratios (OR) were calculated for all covariates and the three approaches: infection in the catheters in the jugular veins, subclavian vein catheters in and death outcome. For this, simple logistic regression was used, using the outcome as the dependent variable and the covariates of the

profile as the independent variables. In addition, a multiple regression analysis was performed, with all covariates included in the individual analyzes. In this case, the method of selection of backward variables with inclusion and exclusion criteria of variables was adopted, with a probability of 0.10. Variables with a significance probability between 0.05 and 0.10 were maintained to improve the robustness of the multiple regression model.

**RESULTS**

During the study period, 268 CVC were inserted in 209 patients, of which 76 patients (36.36%) progressed with death outcome. Regarding the profile of patients, males predominated among the 209 patients (66.51%, 139 men), the mean age of patients was 51.38 years (standard deviation 19.83; range, 14-97) with an APACHE II median score of 19.28 (standard deviation 7.84, range, 2-52). The reason for hospitalization for clinical reasons was prevalent (61.24%, 128 patients). The mean length of stay in ICU patients was 18.8 days (standard deviation, 14.81, range, 4-92) (Table 1).

As to the catheter insertion site, 139 patients (66.51%) had at least one CVC inserted into the subclavian vein, 92 patients (44.02%) in the jugular vein and only eight patients (3.83%) in the femoral vein (Table 1). The mean CVC time was 14.81 days (standard deviation ± 11.09, range 4 - 67), when assessed independently of the insertion site (Table 1). Patients had a mean of 1.28 catheters per hospital stay (standard deviation ± 0.55, interval, 1-4).

Table 1. Profile of patients evaluated for central venous catheter infection in an Intensive Care Unit, Uberlândia, Minas Gerais, Brazil, 2013-2014.

Variable	No		Yes	
	n	%	N	%
Catheter infection	181	86.60	28	13.40
Mortality	133	63.64	76	36.36
Had at least one jugular access	117	55.98	92	44.02
Had at least one subclavian access	70	33.49	139	66.51
Had at least one femoral access	201	96.17	8	3.83
Presence of tracheostomy	159	76.08	50	23.92
Dressing performed by a nurse	123	58.85	86	41.15
Trauma hospitalization	128	61.24	81	38.76
Age > 60 years	130	62.20	79	37.80
Time of catheter stay	130	62.20	79	37.80
APACHE II > 22	142	67.94	67	32.06
Length of stay in ICU > 14 days	111	53.11	98	46.89
Sex	Female	70 (33.49)		
	Male	139 (66.51)		
Location of catheter puncture	Out of ICU	139 (66.51)		
	In ICU	70 (33.49)		
	Mean ± DP		Range	
Age (years)	51.38 ± 19.83		14 - 97	
APACHE II	19.28 ± 7.84		2 - 52	
Number of catheters due to hospitalization	1.28 ± 0.55		1 - 4	
Number of catheters with infection	0.15 ± 0.41		0 - 2	
Length of catheter stay (days)	14.81 ± 11.09		4 - 67	
Length of ICU stay (days)	18.8 ± 14.81		4 - 92	

Most patients (66.51%, 139 patients out of 209) had at least one CVC inserted outside the ICU. Of the 268 catheters, 34 (12.7%) presented infection (Table 2). When evaluating the prevalence of infection by puncture, of the 101 catheters punctured in the jugular vein, 12 had infection (11.9%); of the 159 punctures in the subclavian vein, 22 had infection (13.8%); and none of the eight catheters punctured in the femoral vein had infection.

Table 2. Profile of patients evaluated for central venous access infection in an Intensive Care Unit (ICU), Uberlândia, Minas Gerais, Brazil, 2013-2014.

Predictor	Stratum	Access infection				p <sup>a</sup>	OR (IC <sub>95%</sub> ) p
		No (n=234)		Yes (n=34)			
		n	%	n	%		
Sex	Male	86	84.31	16	15.68	ns	0.65(0.31-1.35)ns
	Female	148	90.24	18	10.97		
Internação por trauma	No	145	86.83	22	13.17	ns	0.89(0.41-1.88)ns
	Yes	89	88.12	12	11.88		
Age > 60 anos	No	151	88.30	20	11.69	ns	1.27(0.61-2.65)ns
	Yes	83	85.57	14	14.43		
APACHE II >22	No	154	87.50	22	12.50	ns	1.05(0.49-2.23)ns
	Yes	80	86.96	12	13.04		
Puncture site	Out of ICU	167	84.34	31	15.66	*	0.24(0.07-0.82) <sup>a</sup>
	In ICU	67	95.71	3	4.28		
Order catheter puncture	1st	184	87.62	26	12.38	ns	1.13(0.48-2.65)ns
	2nd or more	50	86.21	8	13.79		
Responsible for dressing	Team	141	87.57	20	12.42	ns	1.06(0.51-2.20)ns
	Nurse	93	86.92	14	13.08		
Tracheostomy	No	181	88.29	24	11.70	ns	1.42(0.64-3.16)ns
	Yes	53	84.12	10	15.87		
Catheter stay time > 14 days	No	178	89.45	21	10.55	ns	1.97(0.92-4.18)ns
	Yes	56	81.16	13	18.84		
ICU time > 14 days	No	157	89.71	18	10.29	ns	1.81(0.87-3.75)ns
	Yes	77	82.80	16	17.20		
Length of stay > 14 days	No	112	91.06	11	8.94	ns	1.92(0.89-4.12)ns
	Yes	122	84.14	23	15.86		

Legend: bi: OR (95% CI) p: Odds Ratio and 95% confidence interval, ns: p>0.05, \*p<0.05. <sup>a</sup> the probability based on the chi-square test with continuity correction. <sup>b</sup> probability for the

estimation of parameter  $b_1$  (regression coefficient) of the univariate logistic regression model.

The profile of microorganisms in the 34 cultures related to infections was very diverse with: *Ac. baumannii* (n = 3); *C. albicans* (n = 3), *C. parapsilosis* (n = 2), *E. faecalis* (n = 1), *E. faecium* (n = 1), *Elizabethking meningoseptica* (n = 1), *P. aeruginosa* (n = 3), *S. aureus* (5), *S. epidermidis* (n = 6), *S. haemolyticus* (n = 1), *S. hominis* (n = 1), *S. marcesens* (n = 1) and *Steno maltophilia* (n = 1). The resistance profile was not evaluated in this study. A total of 3,114 day catheters and 34 ICSRC were identified, all confirmed with laboratory tests. The infection rates evaluated were 10.92 infections per 1000 day catheters (34 infections/3111 catheters per day x 1000); 162.67 infections per 1000 patient-days (34 infections/209 patients x 1000) and 133,97 patients with infection per 1000 patients (28 patients with infection/209 patients x 1000).

Regardless of the site of insertion of the CVC, there was no relation of the profile of the patients evaluated with the occurrence or not of the CABS, except in relation to the place of placement of the CVC. There was a higher incidence of infection in punctured catheters outside the ICU (Table 2).

In the univariate analysis, when the risk factors for the occurrence of SCID were individually assessed for each puncture site, there was no relation of the profile of patients with punctured catheters in the jugular vein, except for those using tracheostomy, with a higher presence of infected catheters in patients with tracheostomy (26.36%, 5/19) compared to those without tracheostomy (15.73%, 14/89) ( $p = 0.046$ ), which evidenced an increased risk of infection (OR = 3.82,  $CI_{95\%} = 1.06-13.78$ ) (Table 2).

When the catheters were evaluated separately for the subclavian route, only the catheter's residence time (greater than 14 days) was dependent on the presence or absence of

infection ( $p = 0.045$ ; results not shown). The presence of CVC for more than 14 days increased infection (24.39%, 10 infections in 41 cases), while those with less than 14 days had less infection (10.17%, 12 infections in 118 cases), which resulted in increased risk for infection with CVC over 14 days of stay (OR = 2.85;  $CI_{95\%} = 1.12$  to 7.22). The non-significant results were not shown for these analyzes (Table 2).

In the multivariate analysis, when the predictors of risk of CABS were evaluated, regardless of the site of insertion of the CVC, it is observed that only risk predictors are the location of placement, with insertion in the ICU decreasing the chances of infection (OR = 0.217,  $CI_{95\%} = 0.06-0.74$ ), and CVC permanence for more than 14 days increasing the chances of infection (OR=3.32;  $CI_{95\%}=1.27-8.67$ ).

Independently evaluating each insertion site of the CVC, it is observed that for the subclavian route only the time of permanence of the CVC over 14 days is a significant predictor of the risk of ICSRC, which increases the chances of infection (OR = 3.32;  $CI_{95\%} = 1.27-8.67$ ), and in the jugular route only the use of tracheostomy increases the chances of infection (OR=3.83;  $CI_{95\%}=1.06-13.78$ ) (Table 3).

In the multivariate analysis, for the evaluation of the order of placement of the CVC, when it was performed restricting the first catheter inserted in each patient, with ICU puncture, the risk of infection decreased (OR = 0.23,  $CI_{95\%} = 0,07-0,82$ ) and ICU patients' time spent in ICU longer than 14 days increased the chances of ICSRC (OR = 3.37;  $CI_{95\%} = 1.39-8.16$ ). When the analysis was restricted from the 2nd to the 4th inserted catheter, the existence of a previous catheter with infection was the only significant predictor of the risk of CABS that increased considerably (OR = 22.00,  $CI_{95\%} = 3.59-134.89$ ) (Table 3).

Table 3. Multiple logistic regression for the occurrence of central venous access infection in an Intensive Care Unit (ICU), under different models, Uberlândia, Minas Gerais, Brasil, 2013-2014.

Model	Predictor	b <sup>i</sup> (EP)	p	OR (IC <sub>95%</sub> )
Independent of puncture site	Constant	-1.91(0.24)	<0.001	
	Puncture site	-1.53(0.63)	0.015	0.22(0.06-0.74)
	Catheter stay> 14 days	0.81(0.39)	0.040	2.25(1.04-4.87)
Subclavian infection	Constant	-1.99(0.31)	<0.001	
	Puncture site	-1.17(0.67)	0.079	0.31(0.08-1.15)
	Catheter stay> 14 days	1.20(0.49)	0.014	3.32(1.27-8.67)
Jugular infection	Constant	-2.37(0.39)	<0.001	
	Tracheostomy	1.34(0.65)	0.040	3.83(1.06-13.79)
1st Catheter	Constant	-1.98(0.29)	<0.001	
	Puncture site	-1.45(0.64)	0.024	0.23(0.07-0.82)
	ICU stay> 14 days	1.21(0.45)	0.007	3.37(1.39-8.16)
2nd to 4th catheter	Constant	-3.09(0.72)	<0.001	
	Previous Catheter Infection	3.09(0.92)	0.001	22.00(3.59-134.89)
Death	Constant	-1.10(0.28)	<0.001	
	Catheter infection	1.45(0.47)	0.002	4.26(1.69-10.74)
	Hospitalization for trauma	-0.87(0.35)	0.013	0.42(0.21-0.83)
	APACHE >22	1.59(0.34)	<0.001	4.88(2.51-11.65)
	Tracheostomy	-0.67(0.40)	0.090	0.51(0.23-1.11)
	Puncture site	0.65(0.34)	0.059	1.90(0.98-3.73)

Legend: *i*-th regression coefficient estimate, EP: standard error, OR (95% CI): Odds Ratio and 95% confidence interval. The probability for the bi-parameter estimation (regression coefficient).

When risk factors for death were assessed individually, the significant predictors for death were: patients with CABSÍ that increased the odds of death (OR = 3.19, CI<sub>95%</sub> = 1.14-7.25), puncture site with an ICU puncture that increased the chances of death (OR = 1.81, CI<sub>95%</sub> = 1.01-3.28), reason for hospitalization due to trauma hospitalization that reduced the chances of death (OR = 0.42 , CI<sub>95%</sub> = 0.23-0.78), age over 60 years that also increased the odds of death (OR = 2.24, CI<sub>95%</sub> = 1.26-4.01) and APACHE II> 22 that increased the odds of death (OR = 4.82, CI<sub>95%</sub> = 2.59-8.98). The other predictors were not predictive factors of the chances of death (Table 4).

Table 4. Profile of the patients evaluated for the occurrence of the death outcome (n = 133) and survival (n = 76) as a function of the central venous access infection profile in an Intensive Care Unit (ICU), Uberlândia, Minas Gerais, Brasil, 2013-2014.

Predictor	Stratum	Survival		Death		p <sup>a</sup>	OR (IC <sub>95%</sub> )
		n	%	n	%		
Age > 60 years	No	92	70.77	38	29.23	**	2,24(1,26-4,01)**
	Yes	41	51.90	38	48.18		
Sex	Male	41	58.57	29	41.43	Ns	0,72(0,40-1,30)ns
	Female	92	66.19	47	33.81		
Hospitalization for trauma	No	72	56.25	56	43.75	**	0,42(0,23-0,78)**
	Yes	61	75.31	20	24.69		
APACHE>22	No	107	75.35	35	24.65	**	4,82(2,59-8,98)**
	Yes	26	38.81	41	61.19		
Puncture site	Outside of the ICU	95	68.35	44	31.65	Ns	1,81(1,01-3,28)*
	In the ICU	38	54.29	32	45.71		
Jugular catheter	No	73	62.39	44	37.61	Ns	0,88(0,50-.56)ns
	Yes	60	65.22	32	34.78		
Subclavian catheter	No	46	65.71	24	34.29	Ns	1,14(0,63-2,09)ns
	Yes	87	62.59	52	37.41		
Femoral catheter	No	129	64.18	72	35.82	ns <sup>b</sup>	1,79(0,44-7,38)ns
	Yes	4	50.00	4	50.00		
Catheter infection	No	122	67.40	59	32.60	Ns	3,19(1,41-7,25)**
	Yes	11	39.29	17	60.71		
Tracheostomy	No	99	62.26	60	37.74	Ns	0,78(0,40-1,52)ns
	Yes	34	68.00	16	32.00		
Responsible for the dressing	Team	76	61.79	47	38.21	Ns	0,82(0,46-1,46)ns
	Nurse	57	66.28	29	33.72		
Number of catheters >1	No	106	66.25	54	33.75	Ns	1,60(0,83-3,07)ns
	Yes	27	55.10	22	44.90		
Catheter stay >14 days	No	88	67.69	42	32.31	Ns	1,58(0,89-2,82)ns
	Yes	45	56.96	34	43.04		
ICU time >14 days	No	28	56.00	22	44.00		
	Yes	67	60.36	44	39.64	Ns	0,74(0,42-1,30)ns
	No	66	67.35	32	32.65		

Legend: OR (95% CI): Odds Ratio and 95% confidence interval, ns: p> 0.05; \* p <0.05; \*\* p <0.01. <sup>a</sup> probability based on the chi-square test with continuity correction or the Fisher exact test (¥). <sup>b</sup> probability for parameter b1 (regression coefficient) of the univariate logistic regression model.

In multivariate analysis, significant predictors of the risk that increased the odds of death were: patients with CABSÍ (OR = 4.26; IC<sub>95%</sub> = 1.69 to 10.74%) and APACHE II> 22 (OR = 4.88 ; CI<sub>95%</sub> = 2.51-11.65). Differently from the univariate analysis, it was observed that the location of the catheter puncture and the presence of tracheostomy were not predictors of death when other covariates were included in the model (Table 4).

**DISCUSSION**

We found 13.4% of CABSÍ among the CVC, and 36.36% of the patients died. Regarding the puncture route of the catheter, 11.9% of the CVC punctured in the jugular vein and 13.8% in the subclavian vein infected. Length of stay longer than 14 days and place of insertion of the CVC outside the ICU increased the chances of infection

in the subclavian and jugular routes (OR: 2.25 and 0.27). The chances of infection in the jugular vein increased with the presence of tracheostomy (OR: 3.83). The risk of death increased with the presence of CABSÍ, hospitalization for trauma and APACHE > 22. These data show that the profile of patients in our study is consistent with other Brazilian studies in which male predominates, older than 50 years, APACHE II greater than 17 and most patients hospitalized for clinical reasons<sup>5-7</sup>. However, the mortality rate among patients with CABSÍ in our study was higher than rates reported in other ICU studies<sup>5, 7-10</sup>. Mortality rates have already been reported as higher for South America, and there is a strong relationship between infection rates and mortality in ICUs<sup>5</sup>.

An important finding was the increased chances of infection of the second catheter when the previous catheter was infected. This finding raises the discussion of the reasons for catheter replacement. Apparently the replacement of the catheter by itself does not reduce the risk of infection of the new catheter, suggesting that it should be performed prior to signs of infection, as an alternative proposed by some authors<sup>11</sup>. Our sample of this group was small, but the risk increased 22-fold, showing not to be a marginal effect.

Prospective studies should assess the effect of early change and determination of the best management for CVC replacement or which factors are associated with this increased risk. Early replacement of the catheter was not a factor that decreased the chances of infection in some studies<sup>3</sup>, which evidences the interference of other factors. Reinforcing this interference, another study also demonstrates that the second episode of catheterization does not affect infection rates, motivated by the adequacy in adherence to prevention protocols<sup>12</sup>. Many guidelines and authors do not indicate routine catheter replacement, except in the condition of non-

functioning of the catheter or suspicion of catheter colonization<sup>8</sup>.

We observed a high infection rate when compared to the literature, with an expected value for incidence below 4.4% and infection density of 2.7 infections per 1000 catheters-day<sup>13</sup>. This may be a result of poor adherence to standard precautionary mechanisms in the institution studied, such as hand hygiene<sup>14</sup>, participation in training<sup>15</sup>, which is consequently associated with outbreaks of multiresistant bacteria in these units<sup>16</sup>. In spite of this, actions such as continuing education and implantation of protocols have been shown to be effective in reducing rates of bladder catheter-related infections, as observed in the same institution and unit studied<sup>17</sup>. Contrary to what has been observed here, in this last study, the executioner's change had a positive impact on infection rates, but was connected to a multifactorial set of actions. To think that dressing has little impact on infection rates is unexpected, but one explanation would be that manipulation of the catheter is more relevant than curative alone, since it is a direct route of contamination. This reinforces the need for specific actions for each type of health care-related infection (HRI).

The access route may be more associated with colonization of catheter lumen than with insertion point or pathway. Strategies to change these rates can be complex and depend on multiple aspects. Implementing multifaceted quality improvement interventions with daily checklists, goal setting, and clinician request are not, for example, able to reduce in-hospital mortality<sup>18</sup>. Multimodal strategies may also not be effective in behavior change<sup>14</sup>. There is a need for a specific planning for each objective with a clear survey of the causes and risk factors involved in the process. Strategies such as bundles have been effective in many situations, both in reducing mortality and in infection rates<sup>19</sup>. This study evidences the need for bundles proposed for ICUs

to take into account the patient's previous history before ICU admission.

In the present study there were more CVC implants in the subclavian pathway compared to the jugular vein. Puncture in the femoral vein was little used in the sample, which did not allow discussion of the specific risk factors of the latter pathway. The femoral route is the last option according to CDC guidelines<sup>3</sup>. We do not set the criteria for choosing each route, which in a way makes it difficult to interpret the predilection by one way or another. Some studies have demonstrated that the CVC insertion site may be an important risk factor for the development of CABS<sup>20</sup>, although we did not observe this in our study, but we observed that each access route had different risk factors when evaluated individually. The catheters inserted into the jugular vein were more prone to colonization than those inserted into the subclavian vein, which would justify tracheostomy as a risk factor for the jugular pathway. This may be related to factors favoring colonization of the skin near the jugular vein or tracheostomy, for example, oropharyngeal secretions, temperature increase, difficulties in the immobilization of the catheter and in the dressing<sup>21</sup>.

The impact of the catheter insertion site on the risk of infection remains controversial. In our study, there was no significant difference in the CABS rates between insertion in the subclavian and jugular veins. Some studies have shown that subclavian site catheterization was associated with a lower risk of HFRS and deep venous thrombosis, and a higher risk of pneumothorax compared to jugular or femoral sites<sup>20, 22, 23</sup>. According to another study, when the risk of CSBI is considered, the subclavian route is no longer the undisputed site of choice in ICU patients, and the internal jugular vein may be initially chosen. The subclavian vein maintains its first-choice

classification when the risk of colonization is considered<sup>24</sup>.

Insertion of the catheter out of the ICU also increased the chances of infection. Apparently, IRAS prevention strategies should contemplate the entire hospitalization flow of the patient, and can not be restricted to emergency or ICU units. Bundles or other prevention techniques applied to the ICU may be ineffective if factors preceded by ICU patient hospitalization are not corrected and included in the prevention protocol. Length of stay and risk of infection are dependent on the type of catheter, its use, and may be variable depending on the profile of each unit and its care planning<sup>13, 25</sup>.

The duration of the catheter increased the chance of CABS, and the duration of CVC use was the main determinant factor most commonly found for the development of ICSRC<sup>13, 25</sup>. Some studies have already shown that after a period of more than 10 days of permanence of the device there is an increase in the probability of acquiring CABS<sup>21</sup>. Therefore, the shorter the CVC stay time, the lower the probability of developing complications related to the catheter, reducing hospital stay time and related costs<sup>26</sup>. In our study, the length of time the patient remained in the ICU does not seem to be related to the chance of CABS, although the length of time the patient stays in the ICU could be an indicator of severity and indirect risk and serve as an alert for patients with a long stay from CVC.

No significant difference was identified between the incidence of CABS when the dressing was performed by any member of the nursing team or exclusively by the nurse. One of the hypotheses raised is that the evaluated nursing team of the ICU is composed of professionals with ample experience and constantly receive training in the unit. Added to this fact, most of the professionals in this unit in the positions of Auxiliary or Nursing Technician have a higher education degree in Nursing, despite being hired to another position.



The training above the job post has become a constant in the labor market of Nursing<sup>27</sup>. Some authors suggest that experienced, qualified and well-trained staff to maintain and remove CVCs improve CABSIs rates and reduce associated costs<sup>3, 26</sup>, therefore, the team's profile may have been the factor that influenced the absence of differences of the CABSIs between the performer of the dressing.

It is observed that the significant predictors of death risk that increased the chances of death were catheter infection and APACHE II > 22. Agarwal et al.<sup>28</sup> also found that a high APACHE II index was associated with mortality (N = 201) (OR 51.1, 95% CI: 1.0-1.1), as expected. The presence of infection has also been observed as a major risk factor for mortality in the literature<sup>5, 29-31</sup>. The mortality rate obtained in our study is much higher than other studies, 39.5%<sup>29</sup> and 19.2%<sup>32</sup>. When the data were adjusted, insertion of the catheter in the ICU was not significant for the risk of death. Probably, this scenario only reflects the early admission of severe ICU patients with the central access puncture in the unit.

CABSIs remains a challenging problem in the management of critically ill ICU patients. Therefore, limiting the indication and the time of use of CVC are primordial factors. Our study demonstrated that the risk factors for CABSIs were unit of CVC placement and stay for more than 14 days. Simple preventive measures and periodic review of the need to use CVC will be beneficial in decreasing infection rates in hospitals with significant catheter use burden in ICU patients.

#### Limitations

Our study has some limitations. First, its observational design, since different insertion sites were not randomly assigned, which did not allow sufficient sampling of femoral catheters, and this fact could cause bias in the profile analysis. Second, it was a monocentric study and only

reflects the reality of a hospital structure, so the results can not be extrapolated to other scenarios even with important indications for the management of critical patients. We were also not able to recover the reasons for the catheter site change, which does not allow us to conclude that the puncture of the second access was in some cases guided by some early sign of infection.

#### CONCLUSION

We observed different risk factors for each CVC access route. However, the insertion unit of the catheter (outside the ICU) and the residence time greater than 14 days in both cases increased the chances of infection. The risk of infection from the second catheterization was 22 times higher when the previous catheter was infected. And both the presence of CVC infection, hospitalization for trauma and Apache > 22 were related to the higher risk of death. The evaluation of CVC insertion conditions outside the ICU and prevention and education actions seem to be crucial points for the reduction of infections and mortality in the UTIS, since the history of pre-admission care in the ICU has proved to be an important factor risk for patients.

#### REFERENCES

1. Frampton GK, Harris P, Cooper K, Cooper T, Cleland J, Jones J, et al. Educational interventions for preventing vascular catheter bloodstream infections in critical care: evidence map, systematic review and economic evaluation. *Health Technol Assess.* 2014;18(15):1-5.
2. Tao F, Jiang R, Chen Y, Chen R. Risk Factors for Early Onset of Catheter-Related Bloodstream Infection in an Intensive Care Unit in China: A Retrospective Study. *Med Sci Monit.* 2015 Feb;21:550-6.

3. O'Grady NP, Alexander M, Burns LA, Dellinger EP, Garland J, Heard SO, et al. and the Healthcare Infection Control Practices Advisory Committee (HICPAC). Guidelines for the prevention of intravascular catheter-related infections. *Clinical Infectious Diseases*. 2011 May;52(9):162-93.
4. Zimlichman E, Henderson D, Tamir O, Franz C, Song P, Yamin CK, et al. Health care-associated infections: a meta-analysis of costs and financial impact on the US health care system. *JAMA Intern Med*. 2013 Dec;173(22):2039-46.
5. Vincent JL, Rello J, Marshall J. International study of the prevalence and outcomes of infection in intensive care units. *JAMA*. 2009 Dec;302(21):2323-29.
6. Freitas ERFS. Perfil e gravidade dos pacientes das unidades de terapia intensiva: aplicação prospectiva do escore APACHE II. *Rev Latino-Am Enfermagem*. 2010 Jun;18(3):317-23.
7. Silva E, Dalfior Junior L, Fernandes HS, Moreno R, Vincent JL. Prevalência e desfechos clínicos de infecções em UTIs brasileiras: subanálise do estudo EPIC II. *Rev Bras Ter Intensiva*. 2012 Jun;24(2):143-50.
8. Fletcher S. Catheter-related bloodstream infection. *Continuing Education in Anaesthesia Critical Care & Pain*. 2005 Oct;5(2):49-51.
9. Klevens RM, Edwards JR, Richards CL Jr, Horan TC, Gaynes RP, Pollock DA, et al. Estimating health care-associated infections and deaths in U.S. hospitals, 2002. *Public Health Rep*. Mar/Apr 2007;122(2):160-6.
10. Hajjej Z, Nasri M, Sellami W, Gharsallah H, Labben I, Ferjani M. Incidence, risk factors and microbiology of central vascular catheter related bloodstream infection in an intensive care unit. *J Infect Chemother*. 2014 Mar;20(3):163-8.
11. Mermel LA, Allon M, Bouza E, Craven DE, Flynn P, O'Grady NP, et al. Clinical Practice Guidelines for the Diagnosis and Management of Intravascular Catheter-Related Infection: 2009 Update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2009 Jul;49(1):1-45.
12. Castelli GP, Pognani C, Stuani A, Cita M, Paladini R. Central venous catheter replacement in the ICU: new site versus guidewire exchange. *Minerva Anestesiol*. May 2007;73(5):267-73.
13. Shah H, Bosch W, Thompson KM, Hellinger WC. Intravascular Catheter-Related Bloodstream Infection. *Neurohospitalist*. 2013 Jul;3(3):144-51.
14. Pereira EBS, Jorge MT, Oliveira EJ, Ribeiro Júnior AL, Santos LRL, Mendes-Rodrigues C. Evaluation of the Multimodal Strategy for Improvement of Hand Hygiene as Proposed by the World Health Organization. *J Nurs Care Qual*. 2017 Apr/Jun;32(2):E11-E19.
15. Sousa Neto RL, Mendes-Rodrigues C. Continuing Education Program: a comparative study between voluntary and mandatory regimes applied to a patient safety course. *J Patient Saf Infect Control*. 2017 Jan/Apr;5:45-6.
16. Rossi Gonçalves I, Ferreira ML, Araujo BF, Campos PA, Royer S, Batistão DW, et al. Outbreaks of colistin-resistant and colistin-susceptible KPC-producing *Klebsiella pneumoniae* in a Brazilian intensive care unit. *J Hosp Infect*. 2016 Dec;94(4):322-9.
17. Mendes-Rodrigues M, Pereira EBS, Sousa Neto RL, Resende J, Fontes AMS. Could legal requirements in nursing practice trigger actions that would change the rates of urinary tract infections? A case study in Brazil. *Am J Infect Control*. 2017 May;45(5):536-8.
18. Cavalcanti AB, Bozza FA, Machado FR, Salluh JI, Campagnucci VP, Vendramim P, et al. Effect of a Quality Improvement Intervention With Daily Round Checklists, Goal Setting, and Clinician Prompting on Mortality of Critically Ill Patients: A Randomized Clinical Trial. *JAMA*. 2016 Apr;315(14):1480-90.
19. Pereira JP, Fernandes Jr CJ, Sousa AG, Akamine N, Santos GPD, Cypriano AS, et al. Improving performance and outcome (mortality) after implementation of a change-bundle approach

for management of septic patients. *Einstein*. 2008;6(4):395-401.

20. Wyatt CM, Vassalotti JA. We still go for the jugular: implications of the 3SITES central venous catheter study for nephrology. *Kidney Intl*. 2016 Mar;89(3):522-4.

21. Bicudo D, Batista R, Furtado GH, Sola A, Medeiros EAS. Risk factors for catheter-related blood stream infection: a prospective multicenter study in Brazilian intensive care units. *Braz J Infect Dis*. 2011 July/Aug;15(4):328-31.

22. Parienti JJ, Cheyron D, Timsit JF, Traoré O, Kalfon P, Mimoz O, et al. Meta-analysis of subclavian insertion and nontunneled central venous catheter-associated infection risk reduction in critically ill adults. *Crit Care Med*. 2012 May;40(5):1627-34.

23. Parienti JJ, Mongardon N, Mégarbane B, Mira JP, Kalfon P, Gros A, et al. Intravascular Complications of Central Venous Catheterization by Insertion Site. *N Engl J Med*. 2015 Sep;373(13):1220-29.

24. Arvaniti K, Lathyris D, Blot S, Apostolidou-Kiouti F, Koulenti D, Haidich AB. Cumulative Evidence of Randomized Controlled and Observational Studies on Catheter-Related Infection Risk of Central Venous Catheter Insertion Site in ICU Patients: A Pairwise and Network Meta-Analysis. *Crit Care Med*. 2017 April;45(4):e437-e448.

25. Gahlot R, Nigam C, Kumar V, Yadav G, Anupurba S. Catheter-related bloodstream infections. *Int J Crit Illn Inj Sci*. 2014 Apr/Jun;4(2):162-7.

26. Higuera F, Rangel-Frausto MS, Rosenthal VD, Soto JM, Castañón J, Franco G, et al. Attributable Cost and Length of Stay for Patients With Central Venous Catheter-Associated Bloodstream Infection in Mexico City Intensive Care Units A Prospective, Matched Analysis. *Infect Control Hosp Epidemiol*. 2007 Jan;28(1):31-5.

27. Wermelinger MCMW, Lima JCF, Vieira M. A formação do auxiliar e do técnico em enfermagem: a 'era SUS'. *Divulgação em Saúde para Debate*. 2016;56:36-51.

28. Agarwal R, Gupta D, Ray P, Aggarwal AN, Jindal SK. Epidemiology, risk factors and outcome of nosocomial infections in a respiratory intensive care unit in North India. *J Infect*. 2006 Aug;53(2):98-105.

29. Oliveira AC, Kovner CT, Silva RS. Nosocomial Infection in an Intensive Care Unit in a Brazilian University Hospital. *Rev. Latino-Am. Enfermagem*. 2010 Mar/Apr;18(2):233-9.

30. Prowle JR, Echeverri JE, Ligabo EV, Sherry N, Taori GC, Crozier TM, et al. Acquired bloodstream infection in the intensive care unit: incidence and attributable mortality. *Crit Care*. 2011;15(2):1-11.

31. Dasgupta S, Das S, Chawan NS, Hazra A. Nosocomial infections in the intensive care unit: Incidence, risk factors, outcome and associated pathogens in a public tertiary teaching hospital of Eastern India. *Indian J Crit Care Med*. 2015 Jan;19(1):14-20.

32. Toufen Junior C, Franca SA, Okamoto VN, Salge JM, Carvalho CRR. Infection as an independent risk factor for mortality in the surgical intensive care unit. *Clinics*. 2013 Ago;68(8):1103-8.

**COLLABORATIONS**

Silva RF, Mendes-Rodrigues C, Pereira EBS, Röder DVDB and Gomes FA contributed at all stages of the research project that originated the present article. In addition, they collaborated in all stages of creation and revision of published material

**CONFLICTS OF INTEREST AND DECLARATION**

The authors declare no conflicts of interest.

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