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

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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 catéteres 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 infeccções e mortalidade dos pacientes posteriormente admitidos na UTI.

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

RESUMÊN

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 (UTI) adulto. Métodos: Estudio retrospectivo, realizado en una UTI. Se recolectan 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 jugular (OR: 2,25 y 0,27). Las posibilidades de infección en la vía jugular 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.

Descrientes: Infecciones Relacionadas a 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. Despite the advantages of using CVC there are associated risks, since catheter-related bloodstream infection (CRBSI) and colonization are the most common adverse outcomes among catheter-related infections, raising mortality and cost of hospitalization.

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.

ICSIs are important causes of morbidity and mortality among critically ill patients. In the United States, CRBSI 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.

CRBSI 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. Other risk factors include the age of the patient, the presence of comorbidities, as well as the duration of catheterization and hospitalization.

In this context, the objective of this study was to evaluate the main risk factors for CRBSI 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). 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 Fisher’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.

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.
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 CABSI, 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, CI95% = 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 CCV over 14 days of stay (OR = 2.85; CI95% = 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 CABSI 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, CI95% = 0.06-0.74), and CVC permanence for more than 14 days increasing the chances of infection (OR=3.32; CI95%=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; CI95% = 1.27-8.67), and in the jugular route only the use of tracheostomy increases the chances of infection (OR=3.83; CI95%=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, CI95% = 0 , 07-0.82) and ICU patients' time spent in ICU longer than 14 days increased the chances of ICSRC (OR = 3.37; CI95% = 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 CABSI that increased considerably (OR = 22.00, CI95% = 3.59-134.89) (Table 3).
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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.

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

DISCUSSSION

We found 13.4% of CABSI 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 catheter 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 CABSI, 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. However, the mortality rate among patients with CABSI in our study was higher than rates reported in other ICU studies. Mortality rates have already been reported as higher for South America, and there is a strong relationship between infection rates and mortality in ICUs.

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. 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, 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. 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.

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. This may be a result of poor adherence to standard precautionary mechanisms in the institution studied, such as hand hygiene, participation in training, which is consequently associated with outbreaks of multiresistant bacteria in these units. 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. 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. Multimodal strategies may also not be effective in behavior change. 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. 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. 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 CABSI, 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.

The impact of the catheter insertion site on the risk of infection remains controversial. In our study, there was no significant difference in the CABSI 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. 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.

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.

The duration of the catheter increased the chance of CABSI, and the duration of CVC use was the main determinant factor most commonly found for the development of ICSRC. 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 CABSI. 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. In our study, the length of time the patient remained in the ICU does not seem to be related to the chance of CABSI, 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 CABSI 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\textsuperscript{27}. Some authors suggest that experienced, qualified and well-trained staff to maintain and remove CVCs improve CABSI rates and reduce associated costs\textsuperscript{3, 26}, therefore, the team's profile may have been the factor that influenced the absence of differences of the CABSI 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.\textsuperscript{28} 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\textsuperscript{5, 29-31}. The mortality rate obtained in our study is much higher than other studies, 39.5% \textsuperscript{29} and 19.2%\textsuperscript{32}. 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.

CABSI 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 CABSI 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


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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