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RISK FACTORS OF CENTRAL VENOUS CATHETER RELATED INFECTIONS IN INTENSIVE CARE PATIENTS

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This study investigates the incidence of and risk factors for Central Venous Catheter (CVC) infection in intensive care patients of Military Medical Academy in Sofia. CVCs were prospectively studied in patients who had lines inserted in general or neurosurgical intensive care and were expected to have the line in situ for at least 7 days.

Catheters were cultured for CVC related infections and blood culture done when indicated. In 29% there is a CVC related infection and in 24.26% - a CVC related sepsis. After adjustment of duration of catheterization, independent predictors of CVC related infections were type of catheter, insertion site, sex, and Acute Physiology Chronic Health Evaluation (APACHE).

Multivariate discriminant analysis was used in order to find out significantly important factors for CVC infection an sepsis. The variables entered into the model were those found to be statistically significant (p ¡ 0.005) on multivariate analysis. The criterion for entering a variable into the model was the values of Mahalanobis statistics and the corresponding values of F-statistics [11]. The software package use for statistical analysis was STATISTIKA 5.0.

1. Introduction

During the last several years, the management of acutely ill patients or patients requiring long-term intravenous therapy has changed because of the widespread

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use of CVCs. The major medical complication associated with the use of intravascular devices is infection. With the possible exception of pulmonary artery catheters, CVCs have the highest reported rates of infection of all intravascular catheters [4], [8]. Data from North America indicate that CVCs used for a short-term account for 90% of all vascular catheter related bloodstream infections [1]. A multicentre Australian study found the relative risk of CVC-sepsis was 64 times higher than the observed rate of sepsis with peripheral vein catheters [4]. This presents a significant problem for the care of critically ill patients who are already highly susceptible to infection due to their underlying disease, but require CVCs for administration of medications, fluids and blood products, as well as for haemodynamic monitoring.

A number of factors may contribute to the risk of CVC-infection. These include insertion site, duration of catheterization , type of catheter, diagnostic group, sex, characteristics of the patients themselves, Acute Physiology Chronic Health Evaluation score (APACHE), etc. [4], [8], [1].

We undertook a prospective study of all new CVCs inserted into patients in the intensive care unit in order to identify risk factors for CVC - infection and sepsis.

2. Patients and measurements

The study was conducted during an one-year period in the intensive care units (12-bed) of Military Medical Academy in Sofia. Patients eligible for the study were those who had had the central line inserted in intensive care unit and were expected to have the line in situ for at least 7 days. 70 CVCs inserted in 68 patients (female and male) were evaluated prospectively to determine the frequency and risk factors associated with catheter-related infection and sepsis. 3 types of catheters are used: "Balton", "Cavafix" and "Vigon". Data obtained for each catheter included the patients' medical diagnoses and APACHE score on the first catheter day, the use of other invasive devices, clinical and laboratory data pertaining to infection, the anatomical location of the CVC (v. subclavia, v. jugularis and v. femoralis), the condition of insertion site, the number of days the catheter had been in place.

3. Statistical methods

A catheter related infection was suspected in 29% of the total number of lines (70) and in 24.26% there was a CVC-sepsis. Multivariate discriminant analysis was developed to identify most relevant factors predisposing to infection and sepsis. The software package STATISTICA 5.0 was used [7]. The variables entered into

the model were those found to be statistically significant (< 0.05). The forward stepwise method was used. CVC-related infection was the dependent variable. Independent variables in our model were:

- The insertion site: v. subclavia, v. jugularis and v. femoralis;
- The diagnostic group;
- The type of CVC: "Balton", "Cavafix" and "Vigon";
- The duration of catheterization;
- Sex;
- APACHE: min = 2, max = 29.

At the first step we found out that the most significant factor for CVC infection and sepsis is "The type of CVC" signed as "CATHETER" (Table 1.)

	Wilks' Lambda	Partial Lambda	F(2,66)	p-level	Toler.	R-Sqr.
CATHETER	1.00	.85	5.81	.005	1.00	0.00

Table 1

The level of significance is p=0.00473. The classification of the cases is given in Table 2.

Group	% Corr.	n	i	s
n	100	32	0	0
i	0	20	0	0
s	0	16	0	1
Total	47.82	68	0	1

Table 2

As one may notice, 100% of the cases are distinguished on the base of the variable CATHETER. But this delimitation is not satisfactory because the cases "Infection (i)" and "Sepsis (s)" are attached to the class of "No infection (n)". Table 3 and Table 4 present correspondingly the Mahalanobis distances and level of F-statistics.

INFECTION	n	i	s
n	0.00	.34	1.02
i	.34	0.00	.18
s	1.02	.18	0.00

Table 3

INFECTION	n	i	s
n	–	.048	.001
i	.048	–	.212
s	.001	.212	–

Table 4

The next variable entered into the model is "The insertion site" signed as "VENA". The level of significance is p=0.013. The result is: both factors "CATHETER" and "VENA" exert essential influence on the model - correspondingly level of significance p=0.003 and p=0.013 (see Table 5).

	Wilks' Lambda	Partial Lambda	F(2,66)	p-level	Toler.	R-Sqr.
CATHETER	.89	.83	6.47	.002	.98	.019
VENA	.85	.87	4.60	.013	.98	.019

Table 5

So, till this moment of analysis it could be seen that in the greater part of the cases "No infection (n)" and "Sepsis (s)" are distinguished (about 81% and 82% correspondingly) on the base of these two factors. The cases of "Infection (i)" are equally (10 and 10) attached to the classes "No infection (n)" and "Sepsis (s)" (see Table 6).

Group	% Corr.	n	i	s
n	81.2	26	0	6
i	0	10	0	10
s	82.3	3	0	14
Total	47.82	68	0	1

Table 6

These results could be interpreted as follows: the factor "The insertion site" determines whether the infection will grow to sepsis. The Mahalanobis distances and the level of significance of F-statistics for this model are shown on Table 7 and Table 8.

INFECTION	n	i	s
n	0.00	.48	2.05
i	.48	0.00	.60
s	2.05	.60	0.00

Table 7

INFECTION	n	i	s
n	–	.070	.000
i	.070	–	.085
s	.000	.085	–

Table 8

At the next step the independent variable APACHE was entered into the model (p=0.008). Adding this variable makes possible the categorization of the cases of "Infection (i)" from the cases of "Sepsis (s)" (10 to (n), 6 to (i) and 4 to (s)) (see Table 9.).

	Wilks' Lambda	Partial Lambda	F(2,66)	p-level	Toler.	R-Sqr.
CATHETER	.74	.87	4.84	.011	.95	.046
VENA	.77	.83	6.40	.003	.90	.099
APACHE	.74	.86	5.20	.008	.88	.117

Table 9

Group	% Corr.	n	i	s
n	78.1	25	4	3
i	30.0	10	6	4
s	70.6	2	3	12
Total	62.3	37	13	19

Table 10

The Mahalanobis distances and the level of significance of F-statistics for this model are shown on Table 11 and Table 12.

INFECTION	n	i	s
n	0.00	.55	2.79
i	.55	0.00	1.88
s	2.78	1.88	0.00

Table 11

INFECTION	n	i	s
n	–	.107	.000
i	.107	–	.002
s	.000	.002	–

Table 12

At the last step the variable "SEX" was entered (p=0.07). This model is shown on Table 13.

	Wilks' Lambda	Partial Lambda	F(2,66)	p-level	Toler.	R-Sqr.
CATHETER	.68	.86	5.10	.008	.94	.055
VENA	.74	.79	7.95	.001	.85	.153
APACHE	.69	.84	5.84	.005	.86	.137
SEX	.64	.92	2.73	.072	.92	.074

Table 13

Using the values of the Wilks' Lambda we can consider the contribution of each of the parameters in the model. The most considerable parameter is SEX with Wilks' Lambda equal to 0.64. The next two parameters are CATHETER and APACHE. The most nonsignificant parameter is VENA.

The classification of the cases now is 10 to (n), 6 to (i) and 3 to (s).

Group	% Corr.	n	i	s
n	78.1	25	4	3
i	30.0	10	6	4
s	70.6	2	3	12
Total	62.3	37	13	19

Table 14

So, this variable does not give better classifications of the cases. The Obtained results for Mahalanobis distances and level of significance of F-statistics for this model are similar to these shown in Table 11 and Table 12.

4. Discussion

Catheters were cultured for CVC related infections and blood culture done when indicated. In 29% there is a CVC related infection and in 24.26% - a CVC related sepsis. Up to 20 different risk factors for catheter related infections in intensive care patients have been reported. These relate to catheter selection and composition, choice of insertion site, care of insertion site, infusate and apparatus, patient characteristics and duration of catheterization. The relative importance of one risk factor over another is difficult to assess given that in most studies only univariate analysis has been performed and estimating the risk of each factor while controlling the others has not been attempted.

In our investigation 6 risk factors were included: type of catheter, insertion site, duration of catheterization, diagnostic group, sex and APACHE. We

performed a multivariate analysis to assess the major determinants of catheter related infections in our patients and found that after controlling the duration of catheterization, the independent predictors for catheter related infection and sepsis were type of catheter ($p < 0.005$), insertion site ($p < 0.015$), APACHE ($p < 0.008$) and sex ($p < 0.072$).

The fact that insertion site is more likely to influence infection has been reported elsewhere [6], [3], [9]. The relationship CVC infection – APACHE scores is reported in [10], [5], but in our study the level of significance is lower.

Duration of catheterization and diagnostic group was not found in multivariate analysis to add to the risk of infection. Resent Australian and USA studies suggested that there may be a marked increase in the risk of CVC related infections in some patients with dwell times longer than 5 days. This studies tested only for the effect of catheter type for insertion and did nor control statistically other risk factors. However, there is some evidence to suggest that the routine replacement of CVCs does not necessary reduce the risk of infection [4].

The variable "type of catheter" in medical sense corresponds to different techniques of CVC insertion. The result that this is the most significant factor for CVC infection and sepsis is unexpected for our medical doctors. There are a small number of studies which include this risk factor.

In our future work we plan to include about 60 new patients and add new risk factors as microbiological parameters, number of lumens of CVC, etc. We plan to correct our results using theory of Mixture of Continuous and Categorical Variables in Discriminat Analysis presented by Krzanowski [2].

REFERENCES

[1] P. J. Collignon. Intravascular catheter-associated sepsis: a common problem. *Medical J. of Australia* **161** (1994), 374–378.

[2] W. J. Krzanowski. Mixtures of Continuous and Categorical Variables in Discriminant Analysis. *Biometrics* **36** (1980), 493–499.

[3] S. W. McDonald, A. J. B. McNally et al. Comparison of technical Success and Outcome of Tunneled Catheters inserted via Jugular and Subclavian Approaches. *J.V.I.R* **11** (2000), 225–231.

[4] McKinly, A., Finfer S., Ward R., Penfold J. Incidence and predictors of central venous catheter related infection in intensive care patients. *Anesth. Intensive Care* **27** (1999), 164–169.

[5] L. A. Mermel. Prevention of Intravascular Catheter Related Infections. *ANN. Inter. Med.* **132**, *5* (2000), 391–402.

[6] L. A. Mermel, Farr, B. M., Sheretz, R. J. et al. Guidelines for the Management of Intravascular Catheter – Related Infections. Infect. Control. *Hosp. Epidemiol.* **22** (2001), 222–242.

[7] StatSoft, Inc. (1995). STATISTICA for Windows [Computer program manual]. Tulsa, OK: StatSoft, Inc., 2325 East 13th Street, Tulsa, OK 74104, (918) 583-4149, fax: (918) 583-4376.

[8] E. Tacconelli, Tumbarello M., Pittiruti F., Leone F., Lucia M.B., Caudia R., Ortona L., Eur. J. Clin. Microbiol. Infect. Dis. **16** (1997), 203–209.

[9] J. F. Timsit, Brunell, F., Cheval, C. et al. Use of Tunneled Femoral Catheters of Prevent Catheter - Related Infection. A randomized Controled Trial. *Ann. Intern. Med.* **130** (1999), 729–735.

[10] J. F. Timsit, J.C. Boyer, J. M. et al.Center Vein Catheter – Related Trombosis in Intensive Care Patients. Incidence Risk Factors, and Relationship with Catheter Related Sepsis. *Chest* **144** (1998), 207–213.

[11] D. L. Vandev, P. Mateev. Statistics with PRAVETZ 82. Nauka i Izkustvo, Sofia, 1998.

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