Blood cultures on internal medicine: utilization profile and clinical implications

Hemoculturas em medicina interna: perfil de utilização e implicações clínicas

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ABSTRACT

Introduction: recent literature suggests that excessive use of blood cultures could prolong length of stay and hospital costs. Moreover, low positive rates have been reported and positivity predictive scores have recently been proposed. **Methods:** we conducted an observational prospective study in an Internal Medicine department of a university reference hospital analysing data from all patients to whom BC was requested. **Results:** blood cultures were performed in 39.9% of 414 admissions. Patients with blood cultures had higher length of stay and underwent more laboratory and imaging diagnostic tests. Global positivity rate was of 7.5%. Patients fulfilling sepsis criteria had a higher positivity rate (21.7%) and there were no positive blood cultures in patients without sepsis, namely in cases of isolated c-reactive protein elevation, leucocytosis or fever. In addition, blood cultures results were not a determinant of antibiotic adjust or de-escalation. **Conclusions:** our data suggest that the use of BC should be done essentially in patients with sepsis criteria, reducing its unnecessary use, although more studies are required to validate such practice.

Keywords: Blood Culture. Sepsis. Internal Medicine. Microbiology.

RESUMO

Introdução: o uso excessivo de hemoculturas tem sido associado a aumento do tempo de internamento e de custos hospitalares. Adicionalmente, a literatura médica reporta taxas de positividade abaixo do esperado, levando à criação de índices de predição de positividade. **Métodos:** estudo prospectivo observacional conduzido numa enfermaria de Medicina Interna de um hospital terciário, com recolha de dados de todos os doentes a quem foram realizadas hemoculturas. **Resultados:** em 414 admissões, foram colhidas hemoculturas em 39.9%. Os doentes a quem foram colhidas hemoculturas tiveram maior tempo de internamento e mais exames laboratoriais e imagiológicos pedidos. 7,5% das hemoculturas foram positivas. Nos doentes com critérios de sepsis a taxa de positividade das hemoculturas foi 21,7% e não houve nenhuma hemocultura positiva em doente sem critérios de sépsis, nomeadamente em doentes com elevação isolada de proteína c-reactiva, leucocitose ou febre. O resultado da hemocultura não foi um determinante de de-escalação antibiótica. **Conclusões:** este estudo sugere que as hemoculturas devem ser colhidas essencialmente em doentes com sepsis, podendo esta prática diminuir o seu sobreuso.

Palavras-chave: Hemocultura. Sepse. Medicina Interna. Microbiologia.

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Conflict of interest
The author(s) declare(s) that there is no conflict of interest regarding the publication of this paper.

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Introduction

Blood cultures (BC) remain the gold standard for the diagnosis of bloodstream infections. Positivity rates in unselected settings vary between 9 and 20% [1] and in patients fulfilling sepsis criteria can be as high as 66%.[2] Widespread use of BC has been thoroughly debated.[1,3]. Recent papers suggest that overuse of BC may be responsible for prolonging hospital length of stay (LoS) and higher hospital costs, without relevant impact on mortality.[4] Direct utility of BC when measured by therapeutic changes based on its results is limited. According to a study by Corbo et al in 355 admissions for community acquired pneumonia, only in 5% of patients the antibiotic was changed based on BC results.[5]

Simple measures can be taken in order to optimize and rationalize the use of BC, namely adoption of more strict criteria and emphasis on the importance of microbiological analysis of other biological products like urine, sputum or pleural liquid.[6] Such practices can reduce BC use as much as 18% with important cost-reductions.[6,7] Efforts have been made for the development of BC positivity prediction tools, either based on integrated scores or focused on independent variables, but none has achieved convincing results. Severity of infection still seems to be the strongest predictor of BC positivity[8,9] and more in depth information on BC overuse and related clinical outcomes is crucial.

The aim of our study was to characterize in the setting of an Internal Medicine Department the use and burden of BC, its indications and utility and its relationship with clinical outcome variables.

Material and Methods

An observational study was conducted with information gathered from the clinical files of all discharged patients during 3 months in an Internal Medicine (IM) department of a university reference hospital. The main variables included: age; gender; presumptive diagnosis of infection; LoS; death; number and result of BC; reason to order BC; clinical setting (Emergency department [ED] vs ward) and number of imagiologic and laboratory exams ordered.

Data were collected using a structured form designed specifically for this study. Blood cultures were ordered according to medical criteria of the attending physicians and there were no prestudy orientations. Blood cultures were collected using the standard microbial detection systems available in the hospital (BacT/ALERT®, Biomérieux Inc. Durham, N.C., EUA and BD BACTEC™, Becton, Dickinson and Company, Shannon, Ireland) and no data was obtained concerning the puncture-site or details of the procedure.

The unit for analysis was the series of BC done at the same time in a given patient (BC episode) and not the individual BC. The following agents were considered skin contaminants: Coagulase-negative staphylococcus; *Propionibacterium* spp; *Peptostreptococcus* spp; *Corynebacterium* spp; *Micrococcus* spp. Blood culture episodes were classified as: i) positive (at least two BC were positive for specimens other than contaminants); ii) dubious (only one of the BC had an isolated specimen or if the isolate was one of the contaminants) and iii) negative (no specimens identified).

The analysis was divided in subgroups: patients with/without infection, according to the diagnosis used by clinicians on medical files; patients with/without BC and patients with/without sepsis (Surviving Sepsis Campaign criteria applied by the investigators.[10]

For statistical analysis SPSS version 21 (IBM Inc.) was used. Discrete variables were described with frequency tables and continuous variables with means and standard deviations. Chi-square test was used for bivariate analysis of dichotomous variables and t-student test for continuous variables. Multivariate scenarios were analysed with binary logistic regression. Results were considered significant for p values below 0.05.

Results

A total of 414 admissions were analysed, with a predominance of female gender (54.8%), mean age of 73.0 years, mean LoS of 7,4 days (11.7 in patients with BC) and an overall mortality rate of 9,4%. Blood cultures were performed in 165 admissions (39.9%) and characterization of patients is detailed in table 1. Mortality rate was consistently more elevated in the patients in whom BC were performed (17.0%). Subgroup analysis of patients with and without infection criteria revealed higher mortality in the first group (13,5% vs 4,7%). Higher mortality in patients to whom BC were collected

persists even in the group of patients without infection criteria, although less pronounced.

Out of 464 individual BC, 201 BC episodes were considered. The mean number of BC per episode was 2.8 (range from 1 to 5) as described in table 2. The group with BC had higher mean laboratory and imagiologic exams ordered per patient (figure 1).

The global positivity rate of individual BC was 7.5%, but this value was significantly higher for BC ordered in the ED (15.4%). All positive BC were done in patients with sepsis criteria (table 3).

Blood culture usefulness was assessed using as surrogate the change of antibiotic strategy as consequence of BC result. From all the 201 BC episodes, antibiotic therapy was used in 172 at any point of the episode. In 63 of those the antibiotic was changed during hospital stay (31.3%), but only 21 (12.2%) were based on the BC result, even in cases classified as dubious. Moreover, only in 10 cases there was antibiotic de-escalation based on positive or dubious BC result, representing less than 5% of all the BC episodes.

Table 1: Comparison between patients with or without blood cultures.

	All patients	Patients without BC	Patients With BC	p-value (bivariate analysis)	p-value (multivariate analysis)	Odds Ratio
Admissions	414 (100%)	249 (60.1%)	165 (39.9%)			
Gender (female)	54.8%	57.8%	50.3%	0.93	0.384	N/S
Mean age (years)	73.0	71.9	74.6	0.003	0.578	N/S
LoS (mean days)	7.4	4.6	11.7	< 0.0001	< 0.0001	1.126
Mortality	33	11 (4.4%)	28 (17%)	< 0.0001	< 0.0001	1.762
Mortality in patients with presumptive infection	39 (13.5%)	4 (4.9%)	26 (18.3%)	< 0.0001		
Mortality in patients without infection	9 (4.7%)	7 (4.2%)	2 (8.7%)	< 0.0001		

(Bivariate analysis with chi-square or t-student. Multivariate analysis [logistic regression] included gender, mean age, LoS, mortality and presumptive infection for the dependent variable “performing blood culture” [n: total number of admissions; LoS: length of stay])

Table 2: Number of blood cultures drawn by episode of blood culture.

	Number of episodes	% of episodes
1 BC drawn	8	4.0
2 BC drawn	138	68.7
3 BC drawn	45	22.3
4 BC drawn	7	3.5
5 BC drawn	3	1.5
Total of BC drawn	201	100.0

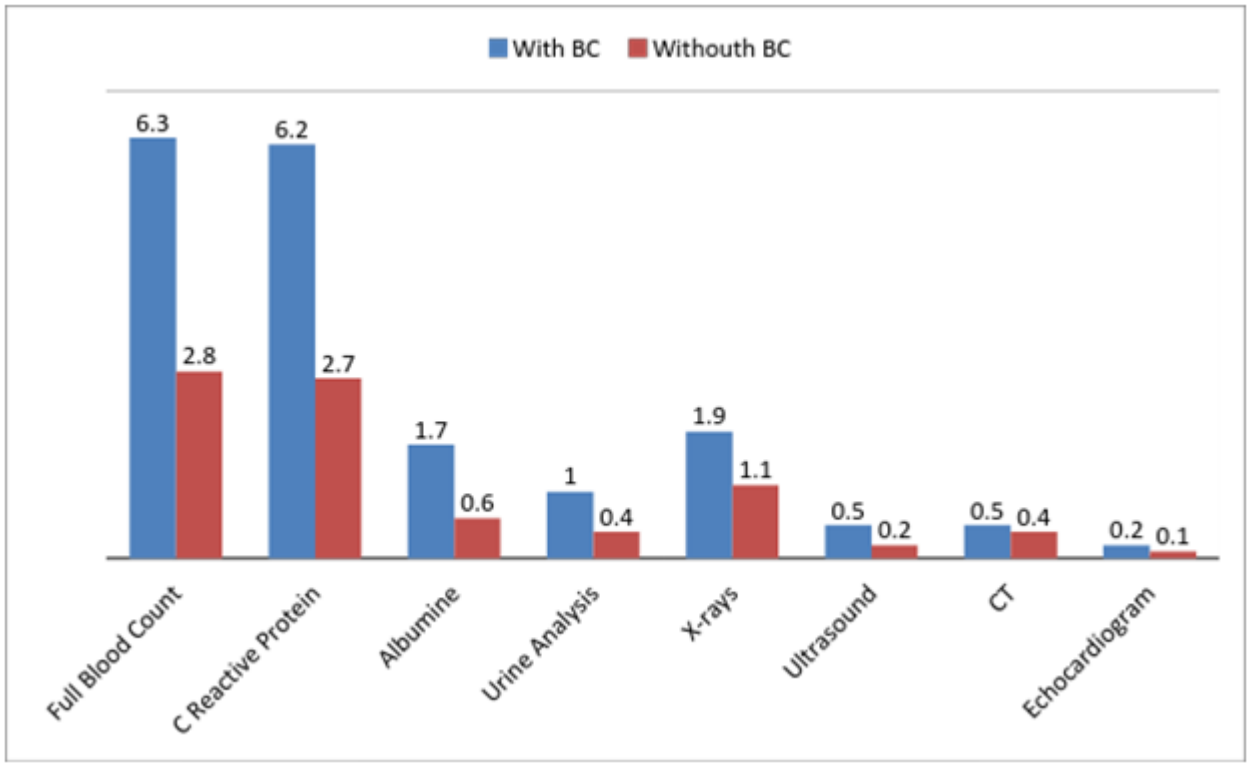

Figure 1: Laboratorial and imagiological exams per patient (means), according to BC ordering. (BC: Blood Culture; CT: Computorized tomography)

Table 3: BC positivity according to setting and reason to order BC.

	BC Positive	BC Dubious	BC Negative	Total
Setting				
ED	4 (15.4%)	2 (7.7%)	20 (76.9%)	26
Ward	11 (6.2%)	14 (7.9%)	152 (85.9%)	177
Reason to order BC				
Sepsis	15 (8.6%)	13 (7.4%)	147 (84.0%)	175
Leucocytosis *	0 (0%)	0 (0%)	2 (100.0%)	2
CPR elevation *	0 (0%)	1 (6.3%)	15 (93.8%)	16
Fever *	0 (0%)	0 (0%)	7 (100.0%)	7
Control	0 (0%)	0 (0%)	3 (100.0%)	3
Total n (%)	15 (7.5%)	15 (7.5%)	171 (85.1%)	201

(BC: Blood culture; ED: Emergency department; CPR: C-reactive protein; * - patients without sepsis criteria)

Discussion and Conclusion

These results on the use of BC in an Internal Medicine ward reveal an excessive utilization and moreover patients to whom BC are ordered have higher LoS, more exams ordered and higher mortality. Such results can not be directly attributed BC ordering itself, but rather it is likely that clinicians request of BC is related to the perception of unclear diagnosis and to the severity of the underlying clinical condition. This is particularly relevant in internal medicine wards, where multiple comorbidities, severe infectious or non-infectious diseases and complications during hospital stay are frequent.[4,11,12]

Our positivity rate is slightly lower than in other series, which can be attributed to the several BC performed in patients with low-severity infection, namely patients who do not meet sepsis criteria.[13] It has been proposed that severity of infection may be the best predictor of positivity of BC, but the way to assess this remains controversial.[14] Scores have attempted to predict positivity, since it has been suggested that more precise criteria is required.[15] Shapiro et al,[13] for instance, gathered information concerning patients' history, co-morbidities, physical examination and laboratory results that were incorporated in a scale that determined with high sensitivity which patients would benefit from BC. However, our work suggests that the presence of sepsis criteria might be the most relevant single marker to reduce the number of BC, although this requires further validation. Thus, improvement in sepsis recognition may be more useful and simple than the application of complex positivity prediction scores.

The fact that in our series BC results were not a determinant of antibiotic changes or de-escalation indicates reduced usefulness of BC in this setting. Blood cultures are known to have higher positivity rates in patients with more severe infections and further studies may clarify in which situations BC do have a real impact on clinical outcomes.[16] Site of infection may also play a role in deciding the true value of performing a BC.[17] More than deciding in which patients to order a BC, our study helps to select patients in whom BC could be avoided. As previously described,[18,19] many BC are ordered to patients with simple elevation of C-reactive protein, leucocytosis or fever, and in this setting positivity rates can be extremely low, as documented in our study, where there was no single positive BC in this context.

The clinical setting has been proposed as a relevant factor in excessive BC ordering,[1,6] and in fact it has been suggested that ED and night-shift physicians ordered more tests in the assumption that this was the expected practice by the attending physician. However, our study indicates that the BC collected on ED had a higher positivity rate, suggesting a good degree of appropriateness in this setting. In any case, the emphasis should be put on the importance of clinical recognition of sepsis, irrespective of clinical setting.

In conclusion, this study suggests that in patients admitted in an Internal Medicine wards it is reasonable to perform BC essentially on patients who fulfil current sepsis criteria. Further studies may clarify in which situations BC offer true benefit to the patient, in order to define more precisely its use.

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