Predicting resistant etiology in hospitalized patients with blood cultures positive for Gram-negative bacilli

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ABSTRACT

Objective: To develop a risk-scoring tool to predict multidrug-resistant (MDR) etiology in patients with bloodstream infections (BSI) caused by Gram-negative bacilli (GNB).

Methods: A prospective multicenter study analyzed patients with BSI hospitalized in 31 Internal Medicine wards in Italy from March 2012 to December 2012. Patients with BSI caused by MDR-GNB (non-susceptible to at least one agent in three antimicrobial categories) were compared to those with BSI due to susceptible GNB. A logistic regression to identify predictive factors of MDR-GNB was performed and the odds ratio (OR) were calculated. A score to predict the risk of MDR was developed.

Results: Of 533 BSI episodes, 253 (47.5%) were caused by GNB. Among GNB-BSI, 122 (48.2%) were caused by MDR-GNB while 131 (51.8%) by non-MDR GNB. At multivariate analysis transfer from long-term care facility (OR 9.013, 95% CI 1.089–74.579, p = 0.041), hospitalization in the last 3 months (OR 2.882, 95% CI 1.202–6.759, p = 0.026) were factors independently associated with MDR etiology. A score ranging from 0 to 10 was useful to recognize patients at lowest risk (0 points: Negative Likelihood Ratio 0.10) and those at highest risk (> 6 points, Positive Likelihood Ratio 11.8) of GNB bacteremia due to a MDR strain.

Conclusions: Specific predictors of MDR etiology are useful to calculate probabilities of MDR etiology among hospitalized patients with blood cultures positive for GNB.

1. Introduction

Over the past decade, Gram-negative bacilli (GNB) have emerged as the leading cause of bloodstream infections, outnumbering Gram-positive pathogens as causes of nosocomial bloodstream infections [1]. The burden of multidrug-resistant (MDR) GNB, including extended-spectrum β-lactamases (ESBLs)-producing Enterobacteriaceae, carbapenem-resistant Enterobacteriaceae (CRE), MDR Pseudomonas...
aeruginosa or Acinetobacter baumannii has substantially increased worldwide and is becoming a major threat for public health [2–4].

The treatment of bloodstream infections caused by these strains is challenging because of their high morbidity and mortality rates [5–7]. A delayed adequate antimicrobial therapy is associated with increased mortality in severe infections that have the potential to progress to septic shock [8]. Thus, the rapid identification of organisms is critical to enable early appropriate antimicrobial therapy. Unfortunately, the median time-to-positivity of blood cultures in patients with GNB bacteremia is 10.6 h and ranges from 5.9 to 49.8 h [9]. Furthermore, additional time is necessary to obtain species identification and susceptibility test results [9,10]. In the last years, new diagnostic assays have been developed to produce results faster than traditional susceptibility testing methods [11]. However, these techniques are used to identify bacteria at species level and not their resistance profile, and are not routinely used in the clinical practice. For these reasons, after initial identification of GNB from blood cultures, the clinical evaluation remains the milestone to identify those patients who have the highest risk of MDR bloodstream infections and to ensure the early initiation of empirical broad-spectrum antimicrobial therapy.

The aim of this study is to develop a simple risk-scoring tool that can be used to assess the probabilities of MDR etiology among hospitalized patients with blood cultures positive for GNB.

2. Materials and methods

2.1. Study design and setting

A prospective multicenter observational study of consecutive patients with bloodstream infections hospitalized in 31 internal medicine units from 14 different Italian regions was conducted from March 1, 2012, to December 31, 2012 (SNOOPII Study) [12]. A minimum of 15 patients was requested to each participating center. Fig. 1 shows the geographical distribution of participating centers. All included patients were daily monitored from the bloodstream infection onset until the end of hospitalization. Approval of the study protocol was obtained from the institutional review boards at each hospital, which waived the requirement for obtaining informed consent. The study has been conducted under the auspice of the Federation of Association of Executives of Hospital Internists (FADOI).

2.1.1. Inclusion and exclusion criteria

All consecutive patients ≥18 years of age admitted to the hospital with bloodstream infection or developing a bloodstream infection during hospitalization were included in the study. A bloodstream infection was defined according to the standard definitions of the Centers for Disease Control and Prevention (CDC) [13]. Investigators in charge for the enrollment were physicians trained for the identification of patients with signs of bloodstream infection. Only patients with positive blood cultures were included in the study.

2.1.2. Data collection

A standard clinical record form was used to collect all patients’ information in each center. All data were collected at the time of the positivity of blood cultures. Detailed instructions explaining the aim of the study, instructions for data collection, and definitions for various items were available for all investigators before starting data collection. Demographic data such as age and date of hospital admission were recorded. Moreover, for each patient the investigators recorded past medical history, reasons for hospital admission, comorbidities assessed by the Charlson comorbidity index. Information about comorbid medical conditions, such as diabetes, cardiovascular disease, chronic obstructive pulmonary disease (COPD), liver disease, cancer was obtained through medical record review. Chronic kidney disease was defined according to Kidney Disease Outcomes Quality Initiative (K/DOQI) guidelines [14]. Information about the presence of obstruction, recent urinary-tract surgery or trauma and change of urinary catheter prior to BSI was not recorded. Neutropenia was defined as an absolute neutrophil count of < 500 cells/mm³ within 30 days before the bloodstream infection [15].

The presence of a medical device (peripherally inserted central catheter, dialysis catheter, central venous catheter or implanted line) and urinary catheters or nephrostomy tubes was recorded. Relevant therapies including cytotoxic chemotherapy, systemic corticosteroids, immunosuppressive agents or radiation therapy in the 3 months prior to bloodstream infection were documented. Immunosuppressive therapy was defined as use of steroids (prednisolone > 0.5 mg/kg/d or equivalent for > 1 month), chemotherapy or anti-tumor necrosis factor, cyclophosphamide, azathioprine, methotrexate, mycophenolate mofetil, or calcineurin inhibitors therapy within the past 3 months. Information about previous splenectomy and administration of

![Fig. 1. Geographical distribution of the 31 Internal Medicine units from 14 different Italian regions participating to the study.](image-url)
intravenous immunoglobulin during the hospitalization has been recorded.

According to the National Healthcare Safety Network, the probable source of bloodstream infection was assessed according to the available clinical and microbiological information and classified by the investigators using the following categories: genitourinary tract, respiratory tract, gastro-intestinal, skin and soft tissue, surgical site infection, line-related, endocarditis, or unknown [16]. Length of stay was calculated as the number of days from the date of admission to the date of discharge.

2.1.3. Measures

For each patient the investigators daily recorded clinical and biochemical parameters, use of vasopressor agents (including dopamine, epinephrine, norepinephrine), renal function (assessed by the estimation of glomerular filtration rate [GFR] through the Cockcroft-Gault equation), hepatic function. Mental status to define if patients was alert, disoriented, stuporous or comatose was daily evaluated. Information on arterial blood gases was gathered, and the PaO$_2$/FiO$_2$ ratio was calculated. Severity of acute illness was assessed at the time of the positive blood cultures by using the National Early Warning Score (NEWS) and Modified Early Warning Score (MEWS) [17]. Bloodstream infections episodes were classified as: (i) nosocomial, if a positive blood culture was obtained from patients who had been hospitalized for 48 h or longer; (ii) health care–associated, if a positive blood culture was obtained from a patient at the time of hospital admission or within 48 h of admission if the patient fulfilled any of the following criteria:

- received intravenous therapy at home or had self-administered intravenous medical therapy in the 30 days before the bloodstream infection;
- received wound care or specialized nursing care through a health care agency, family, or friends;
- attended a hospital or hemodialysis clinic or received intravenous chemotherapy in the 30 days before the bloodstream infection;
- was hospitalized in an acute care hospital for 2 or more days in the 90 days before the bloodstream infection;
- resided in a nursing home or long-term care facility;

(iii) community-acquired, if a positive blood culture obtained at the time of hospital admission or within the 48 h after hospital admission for patients who did not fit the criteria for a health care–associated infection [18].

2.2. Microbiological analysis

Microbiological examinations were performed on sputum, urine and blood according to standards of practice. All isolates from patients were identified in a central Microbiology laboratory from each study site by using automated methods such as BacT/Alert (BioMerieux; Marcy-L’Étiole, France) and Vitek2 microbroth dilution (BioMerieux), according to EUCAST interpretative standards. MDR bacteria were defined as microorganisms non-susceptible to at least one agent in three or more antimicrobial categories [19,20].

<table>
<thead>
<tr>
<th></th>
<th>GNB MDR+ N = 122</th>
<th>GNB MDR- N = 131</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Escherichia coli</td>
<td>77 (63.1%)</td>
<td>87 (66.4%)</td>
<td>0.583</td>
</tr>
<tr>
<td>Klebsiella spp</td>
<td>19 (15.6%)</td>
<td>19 (14.5%)</td>
<td>0.812</td>
</tr>
<tr>
<td>Pseudomonas spp</td>
<td>4 (3.3%)</td>
<td>5 (3.8%)</td>
<td>0.817</td>
</tr>
<tr>
<td>Acinetobacter spp</td>
<td>7 (5.7%)</td>
<td>0</td>
<td><strong>0.005</strong></td>
</tr>
<tr>
<td>Enterobacter spp</td>
<td>3 (2.5%)</td>
<td>12 (9.2%)</td>
<td><strong>0.024</strong></td>
</tr>
<tr>
<td>Proteus mirabilis</td>
<td>6 (4.9%)</td>
<td>1 (0.8%)</td>
<td><strong>0.044</strong></td>
</tr>
<tr>
<td>Bacteroides fragilis</td>
<td>1 (0.8%)</td>
<td>3 (2.3%)</td>
<td>0.349</td>
</tr>
<tr>
<td>Providencia stuartii</td>
<td>2 (1.6%)</td>
<td>0</td>
<td>0.141</td>
</tr>
<tr>
<td>Others</td>
<td>3 (2.5%)</td>
<td>4 (3.1%)</td>
<td>0.773</td>
</tr>
</tbody>
</table>

ESBL = extended spectrum β-lactamases; KPC = Klebsiella pneumoniae carbapenemase; GNB = Gram-negative bacilli; MDR = multi-drug resistant; pip-taz = piperacillin-tazobactam.

* Others: 1 Fusobacterium necrophorum; 1 Brucella; 1 Brucella + E. coli; 1 Salmonella spp.; 1 Citrobacter braakii; 1 Serratia marcescens; 1 Sphingomonas paucinobilis.
2.3. Study groups and outcome of the study

Out of all episodes of GNB bloodstream infection, two study groups were identified: MDR - group, including patients with bloodstream infection caused by susceptible GNB strains, and MDR+ group, including patients with bloodstream infection caused by a MDR-GNB. A comparison between patients belonging to the 2 study groups was performed. The outcome of the study was the identification of risk factors independently associated with MDR etiology in patients with GNB bacteremia.

2.4. Statistical analysis

Statistical analysis was performed using commercially available statistical software packages (SPSS, version 20.0; SPSS, Inc., Chicago, IL and R, version 3.0.2; R development core team, Vienna, Austria). Continuous variables were compared by Student's t-test if normally distributed and the Mann–Whitney U test if non-normally distributed. Categorical variables were evaluated using χ² or the two-tailed Fisher's exact test. Values for continuous and categorical variables are expressed as the mean ± standard deviation (SD) or median (interquartile ranges) (IQR) and percentage of the group from which they are derived, respectively. Multivariate analysis to identify independent risk factors for MDR etiology was performed using a logistic regression model. All variables were considered initially for the multivariate analysis. The final multivariate model was then selected via a stepwise selection optimizing the Akaike Information Criterion. Odds ratio (OR) and 95% confidence intervals (CIs) were calculated to evaluate the strength of any association.

A new score predicting the risk of MDR etiology was developed. The score values were derived by rounding the beta coefficients (logarithm of the OR). We evaluated discrimination using receiver operating characteristic curves (ROC) and positive and negative likelihood ratios (LR). The calibration of the model was evaluated by the goodness-of-fit Hosmer-Lemeshow χ² statistic. We calculated sensitivity and specificity for the cut-off point of the score in order to predict MDR etiology. Statistical significance was established at ≤0.05. All reported P values are 2-tailed.

3. Results

Overall, 533 bloodstream infections have been initially included in the study. Of these, 253 (47.5%) were caused by GNB and were included in the final analysis. Among GNB bloodstream infections, 122 (48.2%) episodes were caused by MDR-GNB while 131 (51.8%) by non-MDR GNB. The study flow diagram is shown in Fig. 2. As shown in Table 1, the most frequent isolated species were Escherichia coli, followed by Klebsiella pneumoniae and Pseudomonas aeruginosa. Of 122 MDR strains, we detected 92 (75.4%) ESBL-producing Enterobacteriaceae, 18 (14.8%) CRE (10 Klebsiella pneumoniae, 5 E. coli, 2 P. mirabilis, and 1 Providencia spp), 4 Pseudomonas strains (3.3%), 1 Sphingomonas paucimobilis (0.8%), and 7 (5.7%) Acinetobacter spp. (6 A. baumannii and 1 A. lwoffii). Fig. 3 describes the percentage of MDR organisms for each microbial species.

Table 2 describes demographics, clinical features and outcomes of patients included in the MDR+ and MDR-groups. The 2 groups did not differ for underlying comorbid conditions and for clinical signs during bloodstream infection episode. The most common source of infection in both groups was the genitourinary tract. Patients with MDR-GNB bloodstream infection were older, had been more frequently hospitalized and subjected to antibiotic treatments in the last three months and had more frequently an indwelling urinary catheter. As shown in Table 3, at multivariate analysis transfer from a long-term care facility (LTCF) (OR 9.013, 95% CI 1.089–74.579, p = 0.041), hospitalization in the last 3 months (OR 2.882, 95% CI 1.580–5.259, p = 0.001), presence of urinary catheter (OR 2.315, 95% CI 1.202–4.459, p = 0.012), antibiotic therapy in the last 3 months (OR 1.882, 95% CI 1.041–3.405, p = 0.036) and age ≥ 75 years (OR 1.866, 95% CI 1.076–3.237,
Table 2
Clinical features and outcomes of patients with bacteremia due to MDR Gram-negative bacilli compared to those with bacteremia caused by non MDR Gram-negative bacilli.

<table>
<thead>
<tr>
<th>NGB MDR+</th>
<th>NGB MDR−</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GNB = Gram-negative bacilli; MDR = multidrug-resistant; LTCF = long-term care facility; CI = confidence interval.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Demographic characteristics

| Age, years, median (IQR) | 80 (69–85) | 74 (69–82) | 0.492 |
| Gender, male | 78 (63.9%) | 64 (48.9%) | 0.016 |
| Hospital admission in the last 3 months | 70 (58.2%) | 38 (28.6%) | < 0.001 |

Antibiotic therapy in the last 3 months

<table>
<thead>
<tr>
<th>Way of acquisition</th>
<th>Community-acquired</th>
<th>Healthcare associated</th>
<th>Nosocomial</th>
<th>Transfer from LTCF</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>61 (46.6%)</td>
<td>31 (23.4%)</td>
<td>28 (20.7%)</td>
<td>12 (9.0%)</td>
</tr>
</tbody>
</table>

Comorbid conditions

<table>
<thead>
<tr>
<th>Source of infection</th>
<th>Intravenous catheter</th>
<th>CVC</th>
<th>Skin or soft tissue</th>
<th>Respiratory tract</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutropenia</td>
<td>4 (3.3%)</td>
<td>3 (2.2%)</td>
<td>0.632</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>15 (12.3%)</td>
<td>31 (25.4%)</td>
<td>0.028</td>
<td></td>
</tr>
<tr>
<td>Liver disease</td>
<td>20 (16.2%)</td>
<td>22 (17.5%)</td>
<td>0.168</td>
<td></td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>27 (21.1%)</td>
<td>31 (23.3%)</td>
<td>0.002</td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal disorder</td>
<td>16 (13.1%)</td>
<td>31 (25.4%)</td>
<td>0.168</td>
<td></td>
</tr>
<tr>
<td>CVC</td>
<td>5 (4.1%)</td>
<td>3 (2.2%)</td>
<td>0.411</td>
<td></td>
</tr>
</tbody>
</table>

Table 3
Multivariate analysis of risk factors for bacteremia due to MDR-GNB.

<table>
<thead>
<tr>
<th>Variables</th>
<th>OR</th>
<th>95.0% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transfer from LTCF</td>
<td>9.013</td>
<td>1.089</td>
<td>74.579</td>
</tr>
<tr>
<td>Hospitalization in the last 90 days</td>
<td>2.882</td>
<td>1.580</td>
<td>5.259</td>
</tr>
<tr>
<td>Indwelling urinary catheter</td>
<td>2.315</td>
<td>1.202</td>
<td>4.549</td>
</tr>
<tr>
<td>Antibiotic therapy in the last 90 days</td>
<td>1.882</td>
<td>1.041</td>
<td>3.405</td>
</tr>
<tr>
<td>Age ≥ 75 yrs</td>
<td>1.866</td>
<td>1.076</td>
<td>3.237</td>
</tr>
</tbody>
</table>

Table 4
Risk score for MDR etiology among patients with blood cultures positive for GNB.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pitt bacteremia score</td>
<td>0-1</td>
</tr>
<tr>
<td>2-4</td>
<td></td>
</tr>
<tr>
<td>5-7</td>
<td></td>
</tr>
<tr>
<td>MEdS, median (IQR)</td>
<td>7 (5-8)</td>
</tr>
<tr>
<td>Charlson Comorbidity Index, median (IQR)</td>
<td>3 (2-5)</td>
</tr>
</tbody>
</table>

Table 5
Percentage of GNB-MDR strains according to score.

<table>
<thead>
<tr>
<th>Score</th>
<th>Number of patients MDR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>1</td>
<td>18</td>
</tr>
<tr>
<td>2</td>
<td>43</td>
</tr>
<tr>
<td>3</td>
<td>76</td>
</tr>
<tr>
<td>4</td>
<td>33</td>
</tr>
<tr>
<td>5</td>
<td>34</td>
</tr>
<tr>
<td>6</td>
<td>27</td>
</tr>
<tr>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>≥ 8</td>
<td>10</td>
</tr>
</tbody>
</table>

p = 0.026) were factors independently associated with bloodstream infection due to MDR-GNB.

Table 4 summarizes the derived score and the points assigned to each variable. The score ranges from 0 to 10. Table 5 shows the exact percentage of MDR strain for each value of the score. Fig. 4 shows the ROC curve of this score system. The AUC of our model was 0.735 (95% CI 0.674–0.796, p < 0.001). The Hosmer-Lemeshow test was successful (p = 0.2), indicating good calibration. The score was considered negative if = 0 (none item satisfied), while it was positive if > 6. When the score was negative, the positive LR was 0.10. The threshold to define a positive score was 6. When the score was > 6 the positive LR was of 11.8.

4. Discussion

This multicenter prospective study reveals some specific predictors of MDR etiology in patients with GNB bacteremia hospitalized in medical wards, such as transfer from a LTCF, hospitalization and antibiotic therapy in the previous 90 days, presence of urinary catheter and age ≥ 75 years. These factors were weighted to develop a simple tool showing a good performance that can be used from clinicians to calculate probabilities of MDR etiology at time of blood cultures positive for GNB. From a clinical standpoint, when physicians receive from microbiology laboratory the notification of positive blood cultures for GNB, the absence of any identified risk factor (score 0) might be useful to exclude a MDR etiology before the sensitivity test analysis results are
available. Conversely, a positive score (> 6) alert physicians about a possible MDR etiology and the need of a more aggressive empiric antibiotic therapy.

Since the delay to initial administration of effective antimicrobial therapy is the strongest predictor of survival with significant decreases in survival for every hour delay, the early start of an adequate antibiotic therapy is strongly recommended in patients with bloodstream infection [21,22]. To this end, clinical microbiology laboratories experienced revolutionary changes in the methods used for organism identification. A significant innovation is the matrix-assisted laser desorption ionization-time of flight (MALDI-TOF) mass spectrometry, which represents a rapid and robust method for accurate microbial identification [23]. However, after the initial identification of infecting pathogen a certain time (at least 24 h in the clinical practice) could be necessary to determine susceptibility profiles of isolated organism to antimicrobial agents [10]. At this time, after receiving the alert from microbiology laboratory about the blood cultures positivity for GNB, clinicians should evaluate in each patient the presence of risk factors for resistant etiology.

Based on the weight of single risk factors we propose an easy tool to stratify the risk of MDR etiology in a hospitalized patient with positive blood cultures for GNB. A negative score (no positive item) indicates that the MDR etiology could be excluded with a good level of confidence (negative LR = 0.10). Conversely, a positive score (> 6) should strongly rise the suspicion of the presence of a bloodstream infection due to a MDR-GNB (positive LR 11.8). A negative score was associated with negative LR of 0.10, indicating a large decrease of post-test probability of disease, while a positive score was associated with positive LR > 10 suggesting a large increase of post-test probability of disease [24]. However, clinicians face a ‘grey zone’ (score from 1 to 6 points), in which the decision to ensure or not a broad-spectrum therapy should be supported by clinical judgment, together with, if possible, the most advanced microbiological techniques such as molecular biology [25].

It is to consider that different molecular diagnostic methods such as real-time PCR (qPCR), PCR-based reverse blot hybridization assay mass spectrometry (REBA), microarray and loop-mediated isothermal amplification-based systems are currently available for bacterial identification and discrimination of antimicrobial susceptibility [26]. Some of them allow the rapid detection of GNB and their ESBL, AmpC, and carbapenemase resistance genes [27]. The costs and the limited availability of these techniques and dedicated personnel able to use them justify the need of a clinical judgment to either confirm or streamline antibiotic therapy for patients suffering from bloodstream infections.

Among identified risk factors, transfer from a LTCF resulted as the strongest factor associated with the risk of MDR etiology. The reasons for harboring MDR-GNB among this patient population include poor functional status, presence of pressure ulcers, wound management, advanced dementia, and previous antimicrobial exposure [28,29]. Unfortunately, no data about the type of antimicrobial treatments were available among patients from LTCF in our study. However, our study confirm that antimicrobial stewardship programs is a pressing need in LTCF and has recently become a ‘hot topic’ [30]. The fact that antimicrobial stewardship programs in LTCF have tended to be less well organized and less resourced could in part explain the strong association between LTCF and MDR etiology, emerging from our study [31].

The presence of an indwelling urinary catheter was another independent predictor of MDR etiology. Importantly, a total of 191 (75.5%) patients with a GNB bloodstream infection had an indwelling catheter. Urinary catheterization has been identified as risk factor for acquiring ESBL-producing Enterobacteriaceae, probably reflecting the frequency of healthcare manipulations [32]. Furthermore, urinary sphincter status is one of the main factors significantly associated with the isolation of ESBL or carbapenemase-producing Enterobacteriaceae [33].

The strength of our study is its prospective and multicenter nature. Moreover, in order to standardize data collection, case report forms were prepared by the coordinating center and were sent to all
participating sub-investigators and detailed instructions were available for all investigators before starting data collection. Anyway our study has some limitations. First, Italy is a country with high prevalence of MDR organisms, and our findings cannot be generalized to other countries with low prevalence of antibiotic resistance. Second, we found a strict correlation between MDR etiology and transfer from a LTCF, which may depend on the specific organization of Italian health care system, which ensure LTCF admission to elderly patients with poor functional status and multiple comorbidities; thus, the risk for MDR may be increased compared to that observed in similar facilities from other countries. Third, although the total number of patients from LTCF was low, transfer from LTCF resulted the strongest factor associated with MDR etiology. Larger scale confirmatory studies would need to validate our results. Finally, although its multicenter design, the final sample of bloodstream infections due to MDR strains was relatively small.

In conclusion, we identified specific predictors of MDR etiology among patients with blood cultures positive for GNB. In the clinical practice, a certain time, often 24 h or more, could spend between the positivity of the blood cultures and the results of the susceptibility tests. In this interval of time, clinicians should identify patients at high risk for MDR-GNB in order to start adequate therapy as early as possible. Knowledge of predictors of MDR etiology could provide an easy, fast and bedside instrument for the clinician to decide or not initiation of a broad-spectrum antibiotic therapy covering potentially MDR pathogens.

Learning points

✓ After the initial identification of an infecting pathogen from the bloodstream, a certain time (at least 24 h in the clinical practice) could be necessary to determine susceptibility profiles of isolated organism to antimicrobial agents. In this period clinicians should be able to identify patients who have the highest risk of MDR infections and start a broad spectrum antibiotics to ensure a safe bacterial coverage.

✓ In our study, transfer from a long-term care facility, hospitalization in the last 3 months, urinary catheter, antibiotic therapy in the last months and age ≥75 years were factors independently associated with bloodstream infections due to MDR Gram-negative bacilli.

✓ A negative score (no positive item) indicated that the MDR etiology could be excluded with a good level of confidence. Conversely, a positive score (>6) should strongly raise the suspicion of the presence of a bloodstream infection due to a MDR Gram-negative strain. Clinicians face a “grey zone” (score from 1 to 6 points), in which the decision to ensure or not a broad-spectrum therapy should be supported by clinical judgment, together with, if possible, the most advanced microbiological techniques such as molecular biology.

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