ORIGINAL ARTICLE

Predicting Multidrug-Resistant Gram-Negative Bacterial Colonization and Associated Infection on Hospital Admission

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OBJECTIVE. Isolation of multidrug-resistant gram-negative bacteria (MDR-GNB) from patients in the community has been increasingly observed. A prediction model for MDR-GNB colonization and infection risk stratification on hospital admission is needed to improve patient care.

METHODS. A 2-stage, prospective study was performed with 995 and 998 emergency department patients enrolled, respectively. MDR-GNB colonization was defined as isolates resistant to 3 or more classes of antibiotics, identified in either the surveillance or early (≤48 hours) clinical cultures.

RESULTS. A score-assigned MDR-GNB colonization prediction model was developed and validated using clinical and microbiological data from 995 patients enrolled in the first stage of the study; 122 of these patients (12.3%) were MDR-GNB colonized. We identified 5 independent predictors: age > 70 years (odds ratio [OR], 1.84 [95% confidence interval (CI), 1.06–3.17]; 1 point), assigned point value in the model), residence in a long-term-care facility (OR, 3.64 [95% CI, 1.57–8.43); 3 points), history of cerebrovascular accidents (OR, 2.23 [95% CI, 1.24–4.01]; 2 points), hospitalization within 1 month (OR, 2.63 [95% CI, 1.39–4.96]; 2 points), and recent antibiotic exposure (OR, 2.18 [95% CI, 1.16–4.11]; 2 points). The model displayed good discrimination in the derivation and validation sets (area under ROC curve, 0.75 and 0.80, respectively) with the best cutoffs of < 4 and ≥4 points for low- and high-risk MDR-GNB colonization, respectively. When applied to 998 patients in the second stage of the study, the model successfully stratified the risk of MDR-GNB infection during hospitalization between low- and high-risk groups (probability, 0.02 vs 0.12, respectively; log-rank test, $P < .001$).

CONCLUSION. A model was developed to optimize both the decision to initiate antimicrobial therapy and the infection control interventions to mitigate threats from MDR-GNB.

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The prevalence of multidrug resistance (MDR) among gram-negative bacteria (GNB) is increasing, both in healthcare-associated and community-acquired infections, and MDR-GNB has become a major public health threat globally.[1–4] Compared with infections due to antimicrobial-susceptible GNB, infections due to MDR-GNB increase the risk of inappropriate initial antimicrobial therapy and consequently contribute to the increased length of hospital stay, medical costs, and mortality in patients with sepsis.[5–8] These infections are especially challenging for first-line physicians, who usually make crucial decisions in treating septic patients without available microbiological test results.[8,9] In addition, delayed identification or lack of recognition of a patient with MDR-GNB colonization increases the risk of nosocomial contamination and spread of MDR-GNB between healthcare workers and patients, thus introducing significant infection control issues and an increased disease burden in the healthcare system.[10,11] Thus, the early identification of patients at risk of MDR-GNB colonization or infection at the time of admission is a critical issue, from both a clinical and an infection control perspective. Early detection optimizes treatment outcomes by the appropriate choice of initial antimicrobial therapy and helps prevent the nosocomial spread of MDR-GNB through implementation of specific infection

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PREVIOUS PRESENTATION: This study was presented in part at the 51st Interscience Conference on Antimicrobial Agents and Chemotherapy, Chicago, Illinois, on September 19, 2011, and at the 7th Asian Conference on Emergency Medicine in Tokyo, Japan, on October 24, 2013.

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control interventions. However, universal microbiological surveillance for every patient that is admitted to identify MDR-GNB colonized patients is both time and resource consuming.[12,13] A risk-stratified surveillance strategy to identify patients harboring MDR-GNB prior to the implementation of stringent infection control interventions is a more reasonable and field-applicable approach. Several predictive models have been developed by researchers with the aim of stratifying patients at risk of antimicrobial-resistant GNB colonization or infection. However, these models have limitations, including the use of a retrospective study design,[14–17] a narrow focus on a specific antimicrobial-resistant organism, such as MDR *Acinetobacter baumannii* or extended-spectrum β–lactamase-producing *Enterobacteriaceae*,[14–21] the use of an inpatient study population,[16–18,21] or the need for prior culture results as a predictive variable.[16–21] Studies using clinical culture results may only misclassify patients colonized with antimicrobial-resistant GNB as noncolonized, which inevitably introduces an information and classification biases in these studies.[14–18,21] Therefore, to develop an MDR-GNB prediction model that addresses these limitations, a prospective, active-surveillance, culture-based study that targets community patients is required to assist first-line physicians in their risk-stratification and clinical decisions.

We hypothesized that certain clinical characteristics could independently predict different risk levels of colonization by MDR-GNB. A prediction model integrating information regarding these factors could effectively stratify patients with differential risks of MDR-GNB colonization. We also hypothesized that the risk of infection with MDR-GNB was correlated with the risk of MDR-GNB colonization. We aimed to develop a score-based prediction system that more accurately identified community-based patients at risk of being colonized by MDR-GNB at the time of hospital admission and at risk of subsequent infection during hospitalization.

PATIENTS AND METHODS

Study Design and Setting

The National Taiwan University Hospital is a 2,200-bed teaching hospital providing both primary and tertiary care in northern Taiwan. The hospital has a busy emergency department (ED) with more than 100,000 visits annually, with 20% of hospitalized patients admitted through the ED. We conducted this ED-based prospective study to develop an MDR-GNB colonization prediction model (COP model) in the first stage of this study, which was then tested in the second stage of the study via the field applicability of this model in identifying ED patients at risk of developing MDR-GNB infection. In the first stage, conducted from April 1, 2009, to September 30, 2009, 995 ED patients were enrolled and underwent active microbiological surveillance before admission. Clinical and microbiological data collected at this stage were used in the derivation and validation of the COP model. The second stage, conducted from September 1, 2015, to November 30, 2015, in which 998 ED patients were enrolled, was designed to assess the usefulness of the COP model in predicting the occurrence of MDR-GNB infection during the subsequent hospitalization course. The study was approved by the institutional review board of the hospital, and the requirement for written consent was waived.

Selection of Participants

In the first stage of this study, all adult patients (≥16 years of age) who stayed at the ED Observation and Extended Care Area awaiting admission to the medical wards were actively screened by research nurses every Tuesday and Thursday during the study period. After an explanation of the study was given and oral consent was obtained, patients were interviewed using a standardized recording form by a single study investigator. Universal active surveillance cultures from anterior nares swab, posterior pharyngeal wall (throat) swab, urine, and areas of skin breakdown if presented were consistently collected by a single research nurse. To achieve high compliance with active surveillance within the ED setting, we did not obtain perianal swab cultures.

Clinical cultures to identify potential infection were also collected based on the judgment of the ED primary care physician. We reviewed all early clinical cultures (within 48 hours of admission)[14,15] for every study patient to prevent the active surveillance cultures from missing any potential MDR-GNB colonized cases.[22] A patient was identified as MDR-GNB colonized if the patient had a positive culture result for MDR-GNB from either the active surveillance culture or early clinical culture obtained within 48 hours of admission.

In the second stage of this study, all adult patients (≥16 years of age) who stayed at the ED Observation and Extended Care Area awaiting admission to the medical wards were evaluated for the risk of developing an MDR-GNB infection using the COP model scoring form. This scoring form included different point scores for a range of independent predictors identified in the first stage of this study. Decision-driven clinical cultures were ordered and medications or other treatments were provided by the primary care physicians without any knowledge of the results of the COP model evaluation.

Definition of MDR-GNB

We defined MDR-GNB as *Enterobacteriaceae* or glucose nonfermentative gram-negative bacilli (NFGNB) with resistance to at least 3 different antimicrobial classes. For *Enterobacteriaceae*, MDR was defined as resistance to at least 3 classes of the following agents: third- or fourth-generation cephalosporins, aminoglycosides, fluoroquinolones, ampicillin/sulbactam, and carbapenems (ertapenem was included in the 2015 [second] stage of the study). For NFGNB, MDR was defined as resistance to at least 3 classes of the following agents: antipseudomonal cephalosporins (ceftazidime or cefepime),

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aminoglycosides, fluoroquinolones (levofloxacin or ciprofloxacin), antipseudomonal penicillins (ticarcillin-clavunalic acid or piperacillin-tazobactam), and carbapenems (imipenem or meropenem).[1,23]

Data Collection

For all study patients, the following clinical data were prospectively collected: age, gender, living arrangements prior to the ED visit, pre-existing comorbidities, predisposing factors for infection, and antibiotic exposure history within the 3 months prior to study enrollment. Records of previous microbiological study results for the patient were also reviewed to assess the colonization status of MRSA and/or VRE in the 12 months prior to enrollment. Results of the microbiological assessments performed, including active surveillance cultures and clinical cultures obtained at the ED and after hospitalization, were also recorded.

For all patients in the second stage of the study, the same clinical and previous microbiological data were collected as for the patients in the first stage of the study, with the exception of the active surveillance cultures. Patients were observed for any positive clinical culture of MDR-GNB and the occurrence of culture-confirmed MDR-GNB infection during the hospitalization treatment course. The diagnosis of a MDR-GNB infection of a study patient was independently judged by 2 investigators based on clinical and microbiological findings. A third investigator made the final decision if these 2 investigators did not reach an agreement on the primary site of MDR-GNB infection.

Model Development, Validation, and Usefulness in Clinical Application

The patients in the first stage of the study were randomly assigned to the derivation or validation sets in a 2:1 ratio using a simple randomization method that used computer-generated random numbers. The COP model was developed from the derivation patient set and was tested independently using the validation patient set. We then used the data set collected from the patients in the second stage of the study to evaluate the usefulness of the COP model in stratifying MDR-GNB infection risk among ED patients.

Statistical Analyses

Means (± standard deviation) were calculated for continuous variables, and percentages were used for categorical variables. An independent Student *t* test was used to compare continuous variables, whereas categorical variables were analyzed using a χ^2 test or the Fisher exact test. Because records of previous microbiological test results were not usually available at the time of the initial ED evaluation, only the demographic and clinical variables were included in the logistic regression analysis. Potential predictors for MDR-GNB colonization with $P < .05$ on univariate analysis were investigated using multivariate logistic regression analysis with a backward selection method. The colinearity of the covariates was assessed, and model fitting was explored based on the Hosmer–Lemeshow goodness-of-fit test. The discriminatory ability of each model was assessed using the area under the receiver operating characteristic (ROC) curve method.[24]

To develop an easy-to-use clinical risk score, we assigned a point value to each independent predictor selected by the final logistic regression model by multiplying the value of the corresponding natural logarithm (β-coefficient) of the odds ratio by 2 and rounding to the nearest integer.[25] The overall score was the sum of the individual point values for each predictor. Sensitivity, specificity, positive predictive value, and negative predictive value with an associated 95% confidence interval (CI) for the prediction model at different cutoff values, were evaluated using a standard definition and methods.[26] The best cutoff value for prediction of the final model was chosen based on the Youden index statistics and stratified patients into low and high MDR-GNB colonization risk groups.

For the patients in the second stage of the study, the cumulative probability of developing a MDR-GNB infection, calculated from the date of ED visit, was plotted using the Kaplan-Meier method. Differences between low and high MDR-GNB colonization risk categories were tested using the log-rank test. All statistically analyses were performed using SPSS version 16.0 software (SPSS, Chicago, IL).

RESULTS

Development of the MDR-GNB Colonization Prediction Model

In first stage of this study, 995 patients received active surveillance cultures. Of these patients, 122 (12.3%) were identified as being colonized with MDR-GNB by either the surveillance or clinical cultures. Moreover, the active surveillance cultures detected 95 patients, and the early clinical cultures identified an additional 27 patients. Without considering the surveillance culture results, early clinical cultures identified only 72 of 122 (59.0%) MDR-GNB colonized patients (Online Appendix Figure A). The bacteriological findings and culture sites of the MDR-GNB isolates identified from the 122 MDR-GNB colonized patients are shown in Table 1. *Escherichia coli* was the predominant MDR-GNB species, with the respiratory tract being the most frequent anatomical site with a positive MDR-GNB culture.

Stage 1 patients were randomly assigned to the derivation and validation sets. There were 77 (11.6%) and 45 (13.6%) MDR-GNB colonizers in the derivation and validation sets, respectively ($P = .379$). With the exception of the percentage of patients that resided in a long-term care facility (LTCF) (4.4% vs 7.8%; $P = .024$), the derivation and validation set patients had similar demographic distributions, clinical characteristics, and previous recovery rates of MRSA (Table 2).

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TABLE 1. Bacteriology and Culture Sites of Multidrug-Resistant Gram-Negative Bacteria (MDR-GNB) Isolates

	MDR-GNB Colonization			
	First Stage (n = 122)[a]		Second Stage (n = 47)[b]	
Bacterial isolate	No.	%	No.	%
Escherichia coli	44	36.1	8	17.0
Acinetobacter species	32	26.2[c]	11	23.4[d]
Pseudomonas aeruginosa	22	18.0	8	17.0
Klebsiella pneumoniae	21	17.2	18	38.3
Enterobacter species	14	11.5[e]	1	2.1[f]
Citrobacter species	7	5.7[g]	0	0
Proteus mirabilis	5	4.1	4	8.5
Other bacteria	8	6.6[h]	4	8.5[i]
Clinical culture site				
Sputum	36	29.5	13	27.7
Urine	30	24.6	23	48.9
Blood	8	6.6	7	14.9
Wound	3	2.5	5	10.6
Other site	4	3.3	4	8.5
Surveillance culture site				
Throat swab	50	41.0	…	…
Urine	28	23.0	…	…
Nasal swab	23	18.9	…	…
Wound	11	9.0	…	…

[a]A total of 153 multidrug-resistant isolates were identified.
[b]A total of 54 multidrug-resistant isolates were identified.
[c]Includes *Acinetobacter baumannii* (31) and *A. lwoffii* (1).
[d]All were *Acinetobacter baumannii*.
[e]Includes *Enterobacter cloacae* (10) and *E. aerogenes* (4).
[f]*Enterobacter cloacae*.
[g]Includes *Citrobacter freundii* (4) and *C. koseri* (3).
[h]Includes *Serratia marcescens* (5), *Morganella morganii* (2), and *Providencia stuartii* (1).
[i]Includes *Serratia marcescens* (1), *Morganella morganii* (1), *Chryseobacterium indologenes* (1) and *Elizabethkingia meningoseptica* (1).

Many variables were found to be associated with colonization of patients with MDR-GNB by a univariate analysis of the derivation set data, including patient age >70 years, LTCF residence, hospital discharge in the previous 1 month, intensive care unit admission in the previous 3 months, exposure to any antibiotics for >48 hours in the previous 3 months, a history of cerebrovascular accident (CVA), the presence of pressure sores, and the presence of a Foley catheter. The multivariate logistic regression model, which incorporated all potential predictors from the univariate analysis, identified 5 independent predictors of MDR-GNB colonization: age >70 years, LTCF residence, history of CVA, hospital discharge in the previous month, and recent exposure to any antibiotics for > 48 hours in the previous 3 months (Table 3). The Hosmer–Lemeshow goodness-of-fit statistic was 0.72, and the area under the ROC curve (AUC) of the model was 0.75 (95% confidence interval [CI], 0.69–0.81). When applied to the validation set, the model maintained its predictive performance: AUC, 0.80 (95% CI, 0.73–0.87).

The point values assigned to each predictor within the COP model are shown in Table 3. These point values were used to calculate the overall score of the risk of MDR-GNB colonization for each patient. A complete summary of the diagnostic accuracy of the COP model for the various score cutoffs is detailed in Online Appendix Table A. The Youden index indicated that the COP model performed best at a cutoff of ≥4 points, with an overall diagnostic sensitivity of 0.57 and specificity of 0.85 at this cutoff value. The prevalences of MDR-GNB colonization among the 995 study patients at low risk (score < 4) and high risk (score ≥4) were 6.7% (53 of 794) and 34.3% (69 of 201), respectively (Figure 1).

Usefulness of COP Model in MDR-GNB Infection Risk Stratification

Clinical data of 998 patients enrolled in the second stage of this study were used to evaluate the usefulness of the COP model in stratifying ED patients at risk of subsequent MDR-GNB infection during hospitalization. We identified significant differences in the clinical characteristics of the second-stage study patients compared to those of the first-stage study patients. They were older, had more healthcare-associated or antibiotic

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TABLE 2. Patient Characteristics for the First and Second Stages of the Study

	First Stage					All study patients				
	Derivation (n = 663)		Validation (n = 332)			First Stage (n = 995)		Second Stage (n = 998)		
Patient characteristics	No.	%	No.	%	*P*	No.	%	No.	%	*P*
MDR-GNB culture	77	11.6[a]	45	13.6[a]	.379	122	12.3[a]	47	4.7[b]	<.001
Age in years ± SD	66.0 ± 17.2		64.5 ± 17.5		.202	65.5 ± 17.3		67.9 ± 16.6		.001
Age >70 years	319	48.1	142	42.8	.111	461	46.3	490	49.1	.216
Male gender	385	58.1	192	57.8	.943	577	58.0	533	53.4	.039
LTCF or nursing-home residence	29	4.4	26	7.8	.024	55	5.5	19	1.9	<.001
Long-term hemodialysis	18	2.7	14	4.2	.205	32	3.2	55	5.5	.012
ICU admission in the last 3 mo	52	7.8	19	5.7	.221	71	7.1	71	7.1	.985
Hospital discharge in the last mo	157	23.7	72	21.7	.481	229	23.0	357	35.8	<.001
Antibiotic exposure within 3 mo[c]	154	23.2	68	20.5	.327	222	22.3	394	39.5	<.001
Comorbidities										
Diabetes mellitus	187	28.2	85	25.6	.385	272	27.3	281	28.2	.683
Malignancy	198	29.9	98	29.5	.910	296	29.7	383	38.4	<.001
End stage renal disease	26	3.9	16	4.8	.507	42	4.2	89	8.9	<.001
Liver cirrhosis	73	11.0	37	11.1	.949	110	11.1	47	4.7	<.001
Cerebrovascular accident	105	15.8	52	15.7	.943	157	15.8	99	9.9	<.001
Presence of bedsore	48	7.2	22	6.6	.721	70	7.0	77	7.7	.561
Central vascular catheter[d]	65	9.8	29	8.7	.587	94	9.4	180	18.0	<.001
Foley catheter	52	7.8	26	7.8	.995	78	7.8	40	4.0	<.001
Previous recovery of MRSA[e]	34	5.1	11	3.3	.194	45	4.5	32	3.2	.127
Previous recovery of VRE[e]	6	0.9	4	1.2	.739	10	1.0	111	11.1	<.001

NOTE. MDR-GNB, multidrug-resistant gram-negative bacteria; LTCF, long-term care facility; ICU, intensive care unit; MRSA, methicillin-resistant *Staphylococcus aureus*; VRE, vancomycin-resistant *Enterococcus*.

[a]From initial surveillance culture or clinical culture obtained within 48 hours of hospital visit.

[b]From clinical cultures obtained at the emergency department or during index hospitalization.

[c]Includes oral and intravenous antibiotic exposure for more than 48 hours.

[d]Includes Port-A catheter, Hickman catheter, long-term hemodialysis catheter (permcath), double-lumen catheter, and peripherally inserted central catheter.

[e]Within 1 year prior to the index blood culture.

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TABLE 3. Logistic Regression Analysis for Predictors and the Assigned Point Values associated with the Risk of Multidrug-Resistant Gram-Negative Bacteria (MDR-GNB) Colonization, Using Clinical Data of 663 Study Patients from the Derivation Set

Predictor	MDR-GNB Colonized ($n = 77$)		MDR-GNB Noncolonized ($n = 586$)		Logistic Regression Analysis					
					Univariate		Multivariate			
					OR	95% CI	OR	95% CI	β	Point Value[a]
Age > 70 y	52	67.5	267	45.6	2.49	1.50–4.11[b]	1.84	1.06–3.17	0.61	1
Male sex	46	59.7	339	57.8	1.08	0.66–1.75				
LTCF residence	12	15.6	17	2.9	6.18	2.83–13.51[b]	3.64	1.57–8.43	1.29	3
OPD chemotherapy	3	3.9	50	8.5	0.44	0.13–1.43	...	...	...	...
Long-term hemodialysis	3	3.9	15	2.6	1.54	0.44–5.46	...	...	...	...
Hospital discharge ≤1 mo	39	50.6	118	20.1	4.07	2.49–6.65[b]	2.63	1.39–4.96	0.97	2
Prior ICU admission[c]	14	18.2	38	6.5	3.21	1.65–6.24[b]	...	...	...	...
Antibiotic exposure[c]	39	50.6	115	19.6	4.20	2.57–6.87[b]	2.18	1.16–4.11	0.78	2
Diabetes mellitus	23	29.9	164	28.0	1.10	0.65–1.84	...	...	...	...
Malignancy	21	27.3	177	30.2	0.87	0.51–1.48	...	...	...	...
End-stage renal disease	4	5.2	22	3.8	1.41	0.47–4.19	...	...	...	...
Liver cirrhosis	4	5.2	69	11.8	0.41	0.15–1.16	...	...	...	...
Congestive heart failure	8	10.4	49	8.4	1.27	0.58–2.80	...	...	...	...
Cerebrovascular accident	21	31.2	81	13.8	2.82	1.65–4.83[b]	2.23	1.24–4.01	0.80	2
Presence of pressure sores	14	18.2	34	5.8	3.61	1.84–7.08[b]	...	...	...	...
Presence of Foley catheter	11	14.3	41	7.0	2.22	1.09–4.52[d]	...	...	...	...

NOTE. LTCF, long-term-care facility; OPD, outpatient clinic; ICU, intensive care unit; β, β-coefficient in the multivariate regression model.

[a]Point values assigned in the model to each predictor, determined by doubling the value of the corresponding β-coefficient in final regression model and rounded it to the nearest integer.

[b]$P < .01$.

[c]Within 3 months of prior hospital discharge.

[d]$P < .05$.

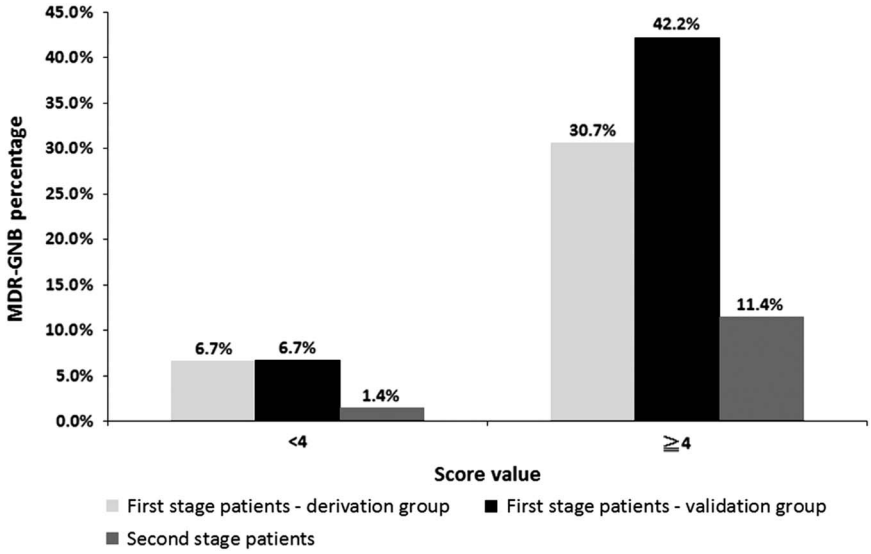


FIGURE 1. Percentage of multidrug-resistant gram-negative bacteria (MDR-GNB) colonization or infection among study patients, according to the score value of the prediction model.

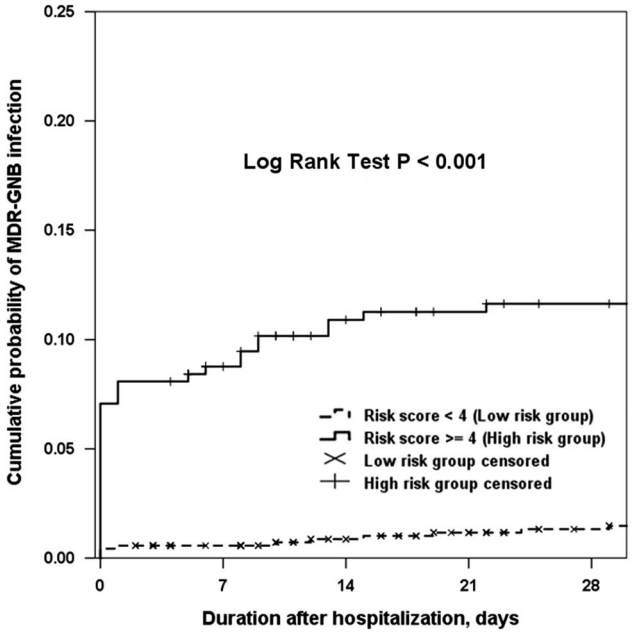


FIGURE 2. Cumulative probability of occurrence of multidrug-resistant gram-negative bacterial (MDR-GNB) infection during hospitalization among 998-second stage study patients.

exposures, had a higher percentage of malignant or end-stage renal disease, and exhibited variation in the positive previous VRE culture history (Table 2). Only 47 (4.7%) patients had at least 1 positive MDR-GNB culture from clinical specimens throughout the entire hospitalization course. *Klebsiella pneumoniae* (18 of 998; 1.8%) and *Acinetobacter baumannii* (11 of 998; 1.1%) were the predominant MDR-GNB isolates among the patients in the second stage of the study (Table 1). Of the 47 patients with positive clinical cultures for MDR-GNB isolates, 44 showed evidence of clinical infection.

When the COP model was applied to the second-stage patient set, the model showed satisfactory predictive performance in stratifying the risk of developing MDR-GNB infection during hospitalization (AUC, 0.80 [95% CI, 0.74–0.87]) (Figure 1). High-risk patients (with scores ≥4 points) had a significantly higher cumulative probability of developing a MDR-GNB infection during hospitalization than low-risk patients (with scores < 4 points) (log-rank test; $P < .001$) (Figure 2).

DISCUSSION

In this study, we developed and validated a scoring system, using clinical variables that were easily obtained upon ED admission to predict patient at risk of MDR-GNB colonization. Our prediction model effectively stratified MDR-GNB colonization risk among patients presenting from the community without requiring prior culture results. In addition, our prediction model further showed a satisfactory degree of discrimination in stratifying patients with differences in the likelihood of contracting a MDR-GNB infection during hospitalization. Therefore, our prediction model is useful for first-line physicians and infection control specialists and can aid in the decision-making process regarding initial antimicrobial therapy or implementation of specific interventions to prevent the spread of antimicrobial-resistant organisms in the hospital.

Antimicrobial-resistant GNB are important in the etiology of nosocomial infections, accounting for a substantial proportion, and they pose important therapeutic challenges for first-line physicians.[27–29] Although community-acquired

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infections in general have a lower degree of antimicrobial resistance than infections acquired in a hospital, there is evidence of an increasing prevalence of MDR-GNB isolates identified in patients in the community.[1,4] Most patients with severe sepsis are rushed into ED,[30] and emergency physicians are confronted with making critical decisions on appropriate initial antibiotic use to lessen the impacts of severe MDR-GNB infection, as highly antimicrobial-resistant GNB have been increasingly recognized as the cause of community-acquired infections. Therefore, it is imperative to provide new tools for these physicians. A useful risk-stratification tool that assists ED physicians in identifying patients presenting from the community at increased risk of MDR-GNB infection would enable better treatment outcomes. Our MDR-GNB COP model, though developed from a surveillance-culture–based cohort, successfully stratified patients with an increased risk of MDR-GNB infection in a separate patient cohort according to distinct demographic and clinical characteristics. Furthermore, of the 998 patients enrolled in the second stage of this study, <30% had a point score ≥4, and >17% (168 of 998) had a score ≥5. Thus, this COP model effectively differentiated high-risk populations for MDR-GNB infection and limited the probability of overuse of antibiotics as the result of arbitrary decisions. Our COP model therefore demonstrated its applicability and broad relevance for first-line physicians in their daily practice.

In addition to decision-making regarding appropriate initial antimicrobial therapy for severe sepsis patents, identification of patients colonized by MDR-GNB with nonsevere infections remains important to the implementation of stringent infection control interventions to contain the spread of MDR-GNB in the hospital setting.[12,31] This finding is supported by the observation that in specific settings, such as intensive care units, active microbiological surveillance combined with other measures such as hand hygiene, contact precautions, and staff education, can reduce the transmission of MRSA.[32–34] However, universal screening of all patients for MDR-GNB upon admission is resource intensive, with a lack of evidence to support the efficacy of such an approach in reducing hospital MDR-GNB burden. A plausible approach to prevent the transmission of or to limit outbreaks of MDR-GNB infections in hospitals is to screen high-risk groups based on known risk factors or prediction systems that aid in the identification of patients in the community harboring MDR-GNB. This strategic approach was supported in this study in the context of MDR-GNB detection by early clinical culture. In the first stage of the study, surveillance cultures on the low-risk population (ie, those with scores < 4) only identified an additional 30 patients with MDR-GNB colonization (30 of 794 or 3.8%). However, surveillance cultures for the 201 high-risk patients (those with scores ≥4) identified an additional 20 MDR-GNB colonized patients who were not detected by decision-driven clinical cultures (20 of 201 or 10.0%). This study provides scientific evaluation of the efficacy of high-risk group surveillance strategies as a recommended infection prevention and control measure.

In contrast to previously reported scoring models for the prediction of antimicrobial-resistant GNB colonization, this COP model is the first scoring system that assists first-line physicians in identifying patients presenting from the community who are likely to be harboring MDR-GNB. The score-based COP model is easy for first-line physicians to use. It may assist them in stratifying MDR-GNB colonization risk among patients presenting from the community using clinical information easily obtained in daily practice. The MDR-GNB colonization group was defined by incorporating the results from both the surveillance and early clinical cultures to avoid MDR-GNB–colonized patients going undetected by microbiological surveillance alone[13] and to lessen the potential bias from study-group misclassification. Prospectively collected clinical data in this study further minimized the threat from information bias. Finally, though the relationship between MDR-GNB colonization and subsequent infection remains to be clarified, the current study demonstrated the usefulness of a prediction system in risk stratification for both initial colonization status and subsequent infection probability.

This study has several limitations. First, we did not obtain perianal swab cultures in the microbiological surveillance performed in the first stage of this study. Previous studies have indicated that the gastrointestinal tract is an important anatomical site harboring antimicrobial-resistant *Enterobacteriaceae*[35,36]; thus, the lack of perianal swab cultures may have caused us to underestimate the MDR-GNB colonization rate and may have introduced an information bias and misclassification of study groups. Second, because our data were derived from a single center, the ability to generalize based on our findings may be limited, due to potential discordance of MDR-GNB prevalence in different hospitals. However, this study still demonstrates the usefulness of a simple decision model in stratifying the risk for MDR-GNB colonization and infection among patients presenting from the community. Finally, in areas where the prevalence of MDR-GNB colonization among patients in the community is lower than the prevalence observed in the current study, the application of our prediction model would result in a lower positive predictive value and a higher negative predictive value. Clinicians should consider this important influential factor when adopting this prediction model in their decision making regarding empirical antibiotic therapy.

In conclusion, a substantial number of ED patients harboring MDR-GNB at hospital admission were observed. The prediction model developed in this well-designed study can be useful for first-line physicians, assisting in the risk stratification not only for initial MDR-GNB colonization status but also the probability of subsequent MDR-GNB infection. Incorporation of the information provided in this prediction tool is crucial for first-line physicians to aid decision making regarding initial antimicrobial therapy and implementation of empirical infection control interventions to mitigate threats from MDR-GNB colonization and infections.

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SUPPLEMENTARY MATERIAL

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