Risk Factors for Mortality in Patients with Urinary and Sterile Site Cultures Positive for Carbapenem-resistant Enterobacteriaceae (CRE) in Atlanta, 2011-2014

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Background

- CRE is emerging as a major problem in the United States
- Prior studies have estimated that the risk of mortality in severe CRE infections ranges from ~30-50%
- Pooled data from 7 EIP sites in 2012-2013 identified a 9% overall mortality rate (including patients with only urine cultures positive), but a 27.5% mortality rate in patients with a positive sterile site culture
- There is limited data on which patients with CRE have the highest risk of mortality, although patient comorbidities appear to contribute in multiple studies
- Identification of risk factors for mortality may have implications for early initiation of empiric therapy and targeting of prevention interventions

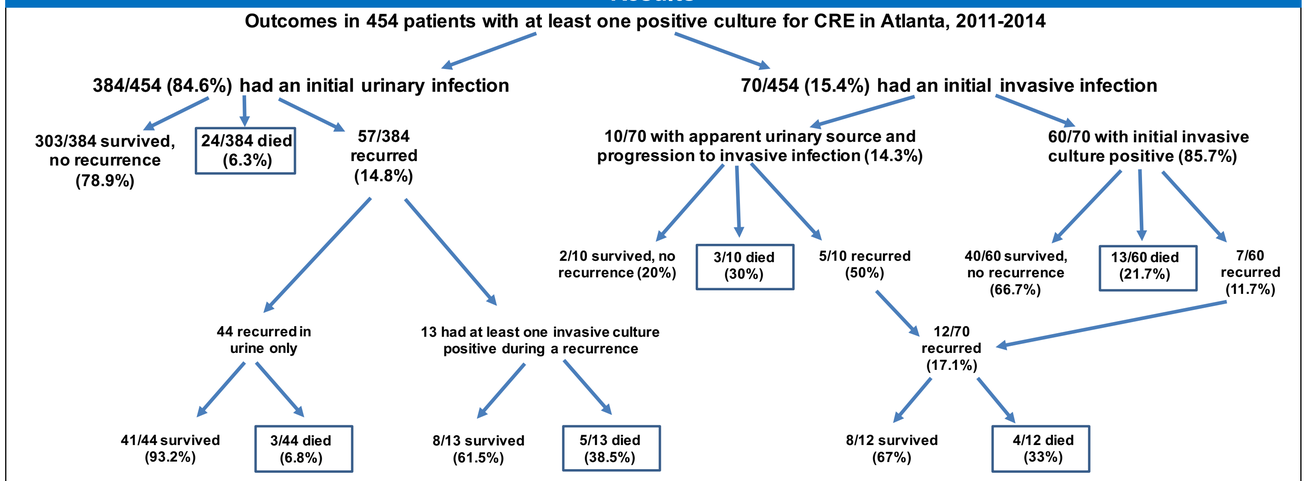
Objectives

1. To compare baseline demographic characteristics of patients with a fatal outcome in the setting of a positive urinary or sterile site culture for CRE to those who survived
2. To evaluate for differences in CRE risk factor prevalence between these two groups
3. To determine if particular risk factors are predictive of mortality in the setting of a positive CRE culture

Methods

- Georgia Emerging Infections Program (EIP) conducts surveillance for CRE cases in the 8-county Atlanta metropolitan area
- CRE defined as nonsusceptible to imipenem, meropenem and doripenem, and resistant to all tested 3rd generation cephalosporins
- Incident case = isolation of CRE from urine or a normally-sterile site with no prior cultures positive for the same organism in the last 30 days
- Data collected on in-hospital mortality (admitted patients) or 30-day mortality (long-term care or dialysis centers)
- Mortality rates compared for patients with a single positive urine or blood culture, those with an apparent urinary source followed by invasive infection within 30 days (progression), and those with multiple positive cultures for the same organism >30 days apart (recurrence)
- Prevalence of demographic and risk factors compared between patients with fatal and non-fatal outcomes, with chi-square analysis for categorical variables and t-tests for continuous variables
- Risk factors assessed with univariable and multivariable logistic regression to evaluate predictors of mortality in the setting of a positive CRE culture

Results



Comparison of Risk Factor Prevalence in CRE Cases with Fatal and Non-Fatal Outcomes, 2011-2014

	Overall Number (%) N = 454	Patient Died At Time of Initial Positive Culture Number (%) N = 40	Patient Survived Initial Infection Number (%) N = 414	p-value*
Location prior to culture:				
Inpatient	73 (16.1)	17 (42.5)	56 (13.5)	<0.0001
Long-Term Acute Care Hospital (LTACH)	31 (6.8)	7 (17.5)	24 (5.8)	0.01
Private Residence	156 (34.4)	6 (15.0)	150 (36.2)	0.01
Long-Term Care Facility (LTCF)	162 (35.7)	9 (22.5)	153 (37.0)	0.07
Hospitalized for ≥3 days	92 (20.3)	18 (45.0)	74 (17.9)	<0.0001
ICU stay	115 (25.3)	26 (65.0)	89 (21.5)	<0.0001
Central venous catheter present	125 (27.5)	27 (67.5)	98 (23.7)	<0.0001
Other indwelling device present	153 (33.7)	27 (67.5)	126 (30.4)	<0.0001
Invasive infection	70 (15.4)	16 (40.0)	54 (13.0)	<0.0001
In an LTACH in the year prior	38 (8.4)	8 (20.0)	30 (7.2)	0.01
Urinary catheter present	215 (47.4)	24 (60.0)	191 (46.1)	0.09
Immunocompromised	262 (57.7)	27 (67.5)	235 (56.8)	0.19
In a LTCF in the year prior	223 (49.1)	16 (40.0)	207 (50.0)	0.23
Hospitalized in the last year	271 (59.7)	27 (67.5)	244 (58.9)	0.29
Surgery within the last year	113 (24.9)	12 (30.0)	101 (24.4)	0.43

Univariable and Multivariable Logistic Regression Analysis of Risk Factors For Mortality in Patients with a Positive CRE Culture

	Crude Odds Ratio+	95% Confidence Interval	Adjusted Odds Ratios+	95% Confidence Interval
ICU stay	6.78	3.40 – 13.53	3.80	1.75 – 8.24
Central venous catheter present	6.70	3.33 – 13.48	2.89	1.26 – 6.61
Other indwelling device present	4.75	2.37 – 9.50	---	---
Invasive infection	4.44	2.22 – 8.90	2.25	1.03 – 4.91
Hospitalized for ≥3 days	3.76	1.92 – 7.36	---	---
In an LTACH in the year prior	3.20	1.36 – 7.56	---	---
Urinary catheter present	1.75	0.90 – 3.39	---	---
Immunocompromised	1.58	0.79 – 3.15	---	---
In a LTCF in the year prior	0.67	0.34 – 1.29	---	---

Immunocompromised = patient history of diabetes, renal failure, cirrhosis or liver failure, hematologic malignancy, solid tumor malignancy, solid organ transplant, AIDS, or connective tissue disorder; Other indwelling device = tracheostomy, gastrostomy or NG tube, or nephrostomy.
*Chi-square tests or Fisher's exact tests performed to calculate p-values for comparisons of fatal and non-fatal outcome groups
+Univariable logistic regression was performed using each risk factor as the sole predictor of mortality for calculation of a crude odds ratio. Multivariable logistic regression was performed with backward selection using a significance level of p<0.05 to identify predictors of mortality that remained significant; only adjusted odds ratios that were significant are reported in the table.

Results (continued)

- Overall mortality rate was 11.7% (53/454), and higher in invasive (22.9%) than urinary infections (6.3%), p<0.0001
- Most deaths (40/53) occurred with initial infection
- More patients died with progression to invasive infection (30%) or recurrent infection (33%), compared to an initial invasive infection (21.7%), although this was not statistically significant (p=0.63)
- In multivariable analysis, death was associated with markers of severe illness (ICU stay, presence of a central venous catheter) and invasive infections

Discussion

- Mortality was significant, but lower than in prior studies
- Early initiation of empiric therapy in high-risk patients may prevent progression to invasive infection and mortality, particularly in the setting of recurrent infection
- These data emphasize the importance of removal of unnecessary central lines, which may reduce mortality
- Other potential risk factors for progression and recurrent infection, such as antibiotic use and changes in the microbiome, warrant further evaluation for possible interventions to decrease mortality

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