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Extended-spectrum beta-lactamase-producing *Enterobacteriaceae* in critically ill patients: impact of carriage and infection on carbapenem consumption, duration of icu stay, and mortality

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Introduction

The spread of extended-spectrum beta-lactamase-producing *Enterobacteriaceae* (ESBL-E) is a major issue in ICU patients. Whether ESBL-E carriage and infection impact the outcome and the use of carbapenems in this population remains scarcely evaluated.

Objectives

We investigated the effects of ESBL-E carriage and infection on carbapenem consumption, ICU length of stay (LOS), and adjusted probability of death at day-28 (D28) in a multicenter cohort of critically ill patients.

Methods

Adult patients admitted between January 1996 and December 2013 in 17 French ICUs contributing to the OUTCOMEREA prospective database were included. Screening for ESBL-E carriage was performed at ICU admission and weekly thereafter. A cause-specific hazard model was built to assess the impact of carriage with and without ICU-acquired infection due to ESBL-E on the likelihood of death or ICU discharge at D28.

Results

Among the 16,734 included patients, 594 (3.5%) were colonized with ESBL-E during their ICU stay (imported carriage, 52.2%). A total of 118 ESBL-E infections occurred in 98 carriers (16.4%). Both ESBL-E infections and ESBL-E carriage without infection increased the use of carbapenems during the ICU stay when compared to non-carriage (627, 241 and 69 treatment days for 1,000 patient-days, respectively, $p < 0.001$ for all comparisons). The ICU LOS was longer in carriers than in non-carriers (median [IQR], 13 [6-26] vs 5 [3-9] days, $p < 0.01$) but similar in carriers with and without ESBL-E infection (13 [6-29] vs 13 [6-26] days, $p = 0.52$). Crude mortality rates at D28 were higher in carriers than in non-carriers (19.7% vs 15.6%, $p < 0.01$), and further differed when comparing carriers with ESBL-E infections and uninfected carriers (30.6% vs 17.5%, $p < 0.01$). After adjustment on baseline (chronic diseases, type of admission, and SAPS II and organ failures at ICU admission) and time-dependent (SOFA score at the time of ESBL-E acquisition, and end-of-life decisions) variables, ESBL-E infections increased the risk of death at D28 [adjusted cause-specific hazard ratio (aCSHR) 1.825, 95% confidence interval (95%CI) 1.235-2.699, $p = 0.003$] and the ICU LOS (aCSHR 0.563, 95%CI 0.432-0.733, $p < 0.001$). ESBL-E carriage without infection prolonged the ICU stay (aCSHR 0.623, 95%CI 0.553-0.702, $p < 0.001$), but had no effect on D28 mortality (aCSHR 0.906, 95%CI 0.722-1.136, $p = 0.4$). When analyzed separately, the effects of carriage and infection did not differ between ESBL-producing *Escherichia coli* (48.7% of carriage isolates) and other ESBL-E.

Conclusions

In this large cohort of critically ill patients, ESBL-E infections increased carbapenem consumption, ICU LOS, and

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D28 mortality. Less than one fifth of carriers developed an ESBL-E infection; however, even ESBL-E carriage without infection increased carbapenem exposure and delayed discharge, thereby amplifying both the selective pressure and the colonization pressure in the ICU.

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