論　文　内　容　要　旨

No improvement in mortality among critically ill patients with carbapenems as initial empirical therapy and more detection of multi-drug resistant pathogens associated with longer use: a post hoc analysis of a prospective cohort study

（初期経験的抗菌治療薬としてのカルバペネムによる重症患者の死亡率改善はなく、その使用期間と関連して多剤耐性菌の同定が増加する：前向きコホート研究の二次解析）

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Whether empirical antimicrobial therapy with carbapenems positively affects the outcomes of critically ill patients with bacterial infections remains unclear. This study aimed to investigate whether the use of carbapenems as the initial antimicrobial administration were associated with lower mortality and whether the duration of carbapenem use was associated with the proportion of subsequent detection of multidrug-resistant (MDR) pathogens.

This was a post-hoc analysis of data acquired from Japanese participating sites from a Determinants of Antimicrobial Use and De-escalation in Critical Care (DIANA) study, which was a multicenter prospective observational study analyzed the data of 1495 critically ill adult patients receiving empirical antimicrobial therapy for suspected or confirmed bacterial infections at 152 intensive care units (ICUs) in 28 countries from October 2016 to May 2018. A total of 268 adult patients with clinically suspected or confirmed bacterial infections from 31 Japanese ICUs were analyzed. The patients were divided into two groups: patients who were administered carbapenems as initial antimicrobials (initial carbapenem group, n = 99) and those who were not administered carbapenems (initial non-carbapenem group, n = 169). The primary outcomes were mortality at day 28 and detection of MDR pathogens. Multivariable logistic regression analysis revealed that mortality at day 28 did not differ between the two groups (18 [18%] vs. 27 [16%], respectively; odds ratio: 1.25 [95% confidence interval (CI): 0.59–2.65], P = 0.564). The subdistribution hazard ratio for detecting MDR pathogens on day 28 per additional day of carbapenem use is 1.08 (95% CI: 1.05–1.13, P < 0.001 using the Fine-Gray model with death regarded as a competing event).

We found no statistical difference in mortality with the empirical use of carbapenems as initial antimicrobial therapy among critically ill patients with bacterial infections. Our study revealed a substantially low proportion of inappropriate initial antimicrobial administrations (6 [6%] vs. 7 (4%), respectively, P = 0.559) compared to those reported in previous studies. This result suggests the importance of appropriate risk assessment for the involvement of MDR pathogens and the selection of suitable antibiotics based on risk.

To the best of our knowledge, this study is the first to demonstrate that a longer duration of carbapenem use as initial therapy is associated with the higher risk of subsequent detection of MDR pathogens. This finding underscores the importance of efforts to minimize the duration of carbapenem use as initial antimicrobial therapy when it is necessary.

In conclusion, in-hospital mortality was similar between the groups with and without initial carbapenems, and a longer duration of carbapenem use as the initial antimicrobial therapy resulted in a higher risk of detection of new MDR pathogens.