中文題目：醫院間篩選病人特徵之不同對Tigecycline治療反應之差異性有相關聯

英文題目：Intra-hospital Different Characteristics in Patient Selection Correlated with Diversity in Therapeutic Response to Tigecycline

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Background: The prevalence of *Enterobacteriaceae* with extended spectrum β-lactamase (ESBL) production or with additional carbapenem resistance (CRE) has been increasing in recent years. However, specific mortality associated with ESBL producers or CRE in patients who suffer from serious infections has not been well demonstrated. Our study assessed the effect of tigecycline and the impact of the ESBL and carbapenem resistance on morbidity and mortality.

Methods: From January 1, 2015 through October 31, 2016, all patients with complicated skin and skin tissue infections (cSSTI), complicated intraabdominal infections (cIAI), and pneumonia caused by ESBL producer or CRE who received tigecycline –based therapy among 3 Taiwan medical centers (NTUH, CMMC and NCKUH) were included in the analysis. Significant differences in variables among 3 hospitals were compared using the chi-square test or Fisher exact test for categorical variables and Student's *t*-test or Mann-Whitney U test for continuous variables as appropriate. A two-tailed p value < 0.05 was considered statistically significant.

Results: A total of 71 patients (NTUH, *n* =16; CMMC, *n* = 17 and NCKUH, *n* =38) were enrolled, including 26 cSSTI, 28cIAI, and 23 pneumonia. Some patients had multiple-site infections. The ESBL-producing pathogens included 39 *K. pneumonie* (with 28 CRE), 30 *E. coli* (with 3 CRE), 2 *Enterobacter cloacae* (with 1 CRE) and 1 *Citrobacter freundii*. One patient had concurrent *E. coli* and *K. pneumoniae* infection. Tigecycline-based therapy was moderate effective (about 50~60% success rate) for treating cIAI, regardless of *E. coli* or *K. pneumoniae* as well as ESBL producer or CRE, but was highly active against *E. coli* pneumonia and cSSTI with 90% clinical success rate. In particular, microbiological eradication of *K. pneumoniae* CRE group was difficult to achieve for pneumonia. Most patients had multiple comorbidities with a mean Charlson score more than 5, including cardiovascular disease (64.8%), metabolic disease (57.8%), genitourinary disease (50.7%), and malignancy (42.3%). The demographic data revealed patients from NTUH were significantly older in mean age (mean age, 72.1 years) than those from other two hospitals ($p = 0.019$). The comorbidity of patients from NTUH had significantly more proportions in respiratory disease, gastrointestinal disease, malignancy, using immunosuppressant agents, and higher Charlson score (mean, 9.5) than those from other hospitals. The infection-related basic information revealed patients from NTUH had significantly

higher respiratory symptoms (dyspnea and cough) at onset of infection, higher proportion of pneumonia and UTI, higher post-operation status and need of surgical intervention, and higher complications of septic shock, prolonged prothrombin time, and ARDS. The SOFA score was higher in the NCKUH group (mean, 9.3) and NTUH (mean, 7.8) than CMMC (mean, 6.2) that reached statistical significance ($p = 0.033$). The proportions of carbapenem-resistant *E. coli* and *K. pneumonia*e as well as resistance to ertapenem or imipenem were significantly higher in the population from NTUH and lowest in the CMMC group. The inappropriateness of empirical antimicrobial coverage was highly distributed among 3 hospitals without statistically significant difference (mean, 80.5%). The outcome revealed that patients from NTUH had significantly lower rates of clinical success (43.8%, $p = 0.020$) and microbiological eradication (0%, $p < 0.0001$) at the end of therapy as well as lower survival rate by 30 days after the end of therapy (37.5%, $p = 0.045$).
Conclusion: These results focusing on ESBL producer or CRE suggest that the tigecycline-based therapy is highly active against *E. coli* pneumonia and cSSTI, only moderate effective for treating cIAI, but *K. pneumoniae* (CRE group) was difficult to eradication in pneumonia. Patients from various hospitals had heterogenous demographics, severity status, resistance mechanism of pathogens and thus correlation with different clinical outcomes.