中文題目：新冠病毒確診病患使用免疫反應蛋白質 IL-6 阻斷劑與續發性感染相關之回溯性研究

英文題目：Association between Tocilizumab and Secondary Bloodstream Infection among Hospitalized COVID-19 Patients : A Retrospective Cohort Study

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Background:

Tocilizumab (TCZ), is an important treatment modality for coronavirus disease 2019 (COVID-19), (figure 2). Nevertheless, growing evidence indicates IL-6 pathway inhibitors may be associated with secondary bloodstream infection(sBSI); Whether IL-6 inhibitor yields additional benefit remains controversial. To investigate whether tocilizumab is associated with sBSI, we report our real-world experience with tocilizumab in a cohort of hospitalized patients with COVID-19 to provide evidence of this vital concern.

Methods :

This multicenter cohort study investigated the association between tocilizumab use and bacterial or fungal sBSIs in hospitalized patients with COVID-19 from 1 May 2021 to 31 August 2021; Baseline characteristics between tocilizumab users and nonusers are shown in table 1. Group comparisons were performed using student t-tests for normally distributed continuous variables and Mann-Whitney U tests for non-normally distributed continuous variables. Differences in proportions were compared using chi-square or Fisher's exact tests. Kaplan-Meier curves was used for time to incident sBSIs among the tocilizumab users and nonusers were compared using the log-rank test. Cox proportional hazard model regression in a backward stepwise algorithm incorporating demographic characteristics, comorbidities, respiratory support, central venous catheter, and medication use was used to calculate hazard ratios (HRs) and 95% confidence intervals (CIs) for associations with risk of sBSIs. The α level was set at .05. Analyses were performed using the R program version 4.1.

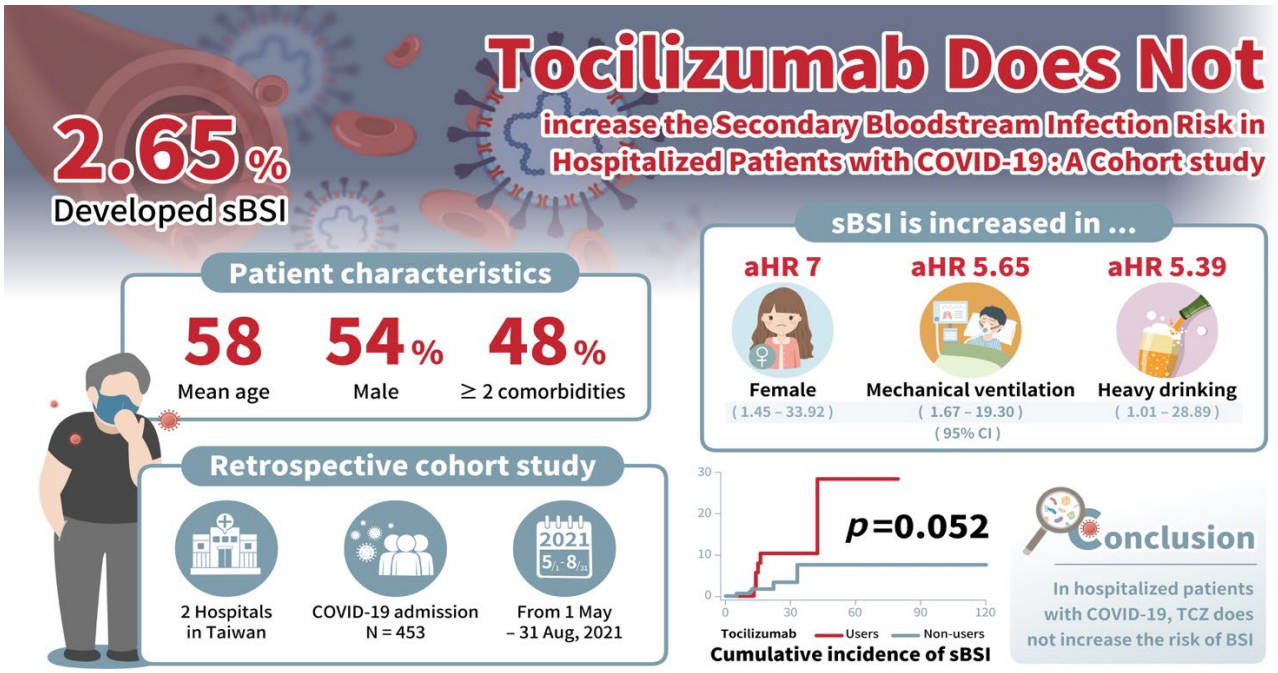
Results :

Our database included 464 patients with COVID-19 who were hospitalized at two hospitals, including 184 (39.7%) in Wang Fang Hospital and 280 (60.3%) in New Taipei City Hospital. After excluding 11 patients aged less than 20 years old, 453 patients were included in the analysis (Figure 1). Eighty-five patients (18.8%) were tocilizumab users. Baseline characteristics between tocilizumab users and nonusers are shown in table 1; Tocilizumab users were significant older ($p < 0.001$), and male predominant (65.9% vs. 51.4%, $p = 0.015$) in comparison with tocilizumab nonusers. Tocilizumab users were more likely to be active smokers (21.2% vs. 11.7%, $p = 0.021$). Tocilizumab users had higher prevalence of comorbidities, including hypertension (67.1% vs. 42.7%, $p < 0.001$), diabetes mellitus (55.3% vs. 23.1%, $p < 0.001$), hyperlipidemia (28.2% vs. 15.2%, $p = 0.005$), coronary artery disease (25.9% vs. 15.8%, $p = 0.027$), chronic kidney disease (24.7% vs. 10.6%, $p = 0.001$) and chronic viral hepatitis (27.1% vs. 8.4%, $p <0.001$).

Interestingly, The Kaplan-Meier analysis revealed that tocilizumab use was not associated with sBSIs ($p = 0.052$ by log-rank test; Figure 3). Both univariate and multivariate Cox proportional hazard regression showed no significant association between tocilizumab use and the risk of sBSIs (Table 2). In the univariate Cox regression analysis, patients with hyperlipidemia [HR 3.29 (95% CI, 1.04–10.40), $p = 0.042$], chronic kidney disease [HR 3.24 (95% CI, 1.02–10.30), $p = 0.046$] and central venous catheters [HR 3.68 (95% CI, 1.13–11.97), $p = 0.030$] were associated with a higher risk of sBSIs, which however became insignificant in multivariate analysis. In the multivariate Cox proportional regression by using backward stepwise algorithm, female sex [aHR 7.00 (95% CI, 1.45–33.92), $p = 0.016$], patients with heavy alcohol uses [aHR 5.39 (95% CI, 1.01–28.89), $p = 0.049$] and patients with mechanical ventilation [aHR 5.65 (95% CI, 1.67–19.30), $p = 0.006$] had a higher risk of sBSIs. Nevertheless, if we retained tocilizumab use, female sex, heavy alcohol use and mechanical ventilation in the multivariate model, tocilizumab and heavy alcohol uses were both insignificant.

Conclusion :

Using tocilizumab for hospitalized patients with COVID-19 is not associated with secondary bloodstream infections. Nevertheless, it could still be related to other risk factors and severity of COVID-19.


Tocilizumab Does Not
increase the Secondary Bloodstream Infection Risk in Hospitalized Patients with COVID-19 : A Cohort study
2.65%
Developed sBSI
Patient characteristics
58
Mean age
54%
Male
48%
≥ 2 comorbidities
Retrospective cohort study
2 Hospitals in Taiwan
COVID-19 admission N = 453
From 1 May – 31 Aug, 2021
sBSI is increased in ...
aHR 7
Female
(1.45 – 33.92)
aHR 5.65
Mechanical ventilation
(1.67 – 19.30)
aHR 5.39
Heavy drinking
(1.01 – 28.89)
(95% CI)
p=0.052
Tocilizumab Users Non-users
Cumulative incidence of sBSI
Conclusion
In hospitalized patients with COVID-19, TCZ does not increase the risk of BSI