Subject: Submission of our manuscript WJCC-56620 entitled “Predictive factors for early clinical response in community-onset E. coli urinary tract infection and effects of initial antibiotic treatment on early clinical response”

Dear Editor,

We have revised our manuscript to incorporate the reviewer’s comments. The revisions are highlighted in red font. We have also provided detailed answers to the reviewers’ questions and concerns. We hope that the revised version of the manuscript is suitable for publication in World Journal of Clinical Cases

We hope to hear from you soon.

Sincerely,

Jae Hoon Lee

Review 1 Specific Comments to Authors: In this study, Young Jun Kim aimed to evaluate the clinical significance of early clinical response and the impact of severe presentations and initial antibiotic therapy on early clinical response in community-onset E. coli UTIs. The results suggested initial appropriate antibiotic therapy was good predictive factor for an early clinical response. However, the initial broad-spectrum antibiotic therapy or initial severe presentations didn’t impact on an early clinical response. This study has provided the helpful information that physicians should restrictively use initial broad-spectrum antimicrobials to treat patient suspected of having multi-drug resistant pathogens. The manuscript might be accepted after a moderate revision.

Major comments: 1.One of major conclusions of this study is “severe presentations in community-onset UTIs were not poor predictive factors for an early clinical response”. However, “Initial septic shock more frequently occurred in patients without an early clinical response than in patients with an early clinical response (28.3% [49/173] vs. 20.4% [69/338], p = 0.045). Concurrent bacteremia was observed in 45% (230/511) of patients. The patients without an early clinical response more frequently had concurrent bacteremia than the patients with early clinical response (51.4% [89/173] vs. 41.7% [141/338], p = 0.039).(lines 119-124)”, so among severe presentations in community-onset UTIs, both “initial septic shock” and “concurrent bacteremia” seemed to be good predictive factors for an early clinical response while “acute renal injury” and “renal and perirenal abscesses” were

potentially not predictive factors for an early clinical response (lines 124-127). The conclusion "severe presentations in community-onset UTIs were not poor predictive factors for an early clinical response" might be defined separately, other than concluded ambiguously.

Response: In univariate analysis, initial septic shock, concurrent bacteremia and acute renal failure occurred more frequently in patients without an early clinical response than in patients with an early clinical response (Table 1). However, results of a multiple logistic regression analysis showed that severe presentations such as initial septic shock, concurrent bacteremia, and acute renal failure, were not associated with an early clinical response. Initially, we described these results in the conclusion section as follows: "severe presentations in community-onset UTIs were not poor predictive factors for an early clinical response." We have corrected this part in the manuscript by inserting the following sentence: "Severe presentations such as initial septic shock, concurrent bacteremia, and acute renal failure were not associated with an early clinical response in community-onset UTIs".

2.As to the definitions of severe presentations in community-onset UTIs , "Septic shock was defined as sepsis with hypotension (systolic blood pressure less than 90 mmHg or 40 mmHg less than the patient's baseline blood pressure) for at least 1 hr despite adequate fluid resuscitation (lines 90-92)", and "Acute renal failure was defined as an increase of more than 300% in serum creatinine levels from baseline (or serum creatinine ≥ 4.0 mg/L with an acute increase of at least 0.5 mg/dl) (lines 92-94)", for UTI patients enrolled in this study, what are the levels of hypotension and serum creatinine of patients with severe presentations, are they presented in a table or a figure?

Response: We agree with the reviewer's comment**.** We have added the following definitions of septic shock and acute renal failure in the table.

1. Septic shock was defined as sepsis with hypotension (systolic blood pressure less than 90 mmHg or 40 mmHg less than the patient's baseline blood pressure) for at least 1 hour despite adequate fluid resuscitation. 2. Acute renal failure was defined as an increase in the serum creatinine levels by more than 300% than the baseline values or serum creatinine ≥ 4.0 mg/L with an acute increase of at least 0.5 mg/dL.

3. For "Concurrent bacteremia", which pathogens were involved except for E. coli? What is the prevalence of these pathogens? Authors might provide some information.

Minor comments: 1.In lines 39 and 58, "……for an an early clinical response" should be "……for an early clinical response".

Response: In this study, blood and urines culture were performed simultaneously for all patients.

A concurrent bacteremia was defined as the isolation of *E. coli* with identical antibiotic

Susceptibility-patterns from both urine and blood cultures simultaneously. We have added the

following definition of concurrent bacteremia in the manuscript.

"A concurrent bacteremia was defined as the isolation of E. coli with identical antibiotic susceptibility patterns from both urine and blood cultures simultaneously."

Review 2 Specific Comments to Authors: The purpose and significance of the experiment were good. This experiment found that initial appropriate antibiotic therapy was good predictive factor for an early clinical response, and the initial broad-spectrum antibiotic therapy or initial severe presentations didn't impact on an early clinical response. But, it didn't achieved the research objectives. The manuscript not good in language, for example, " 72 hr " and " 72 h " , " a stay in a healthcare facility before admission " not in community, et al. The figures and tables not good quality illustrative of the paper contents.

Patients with an early clinical response had a shorter length of stay and an earlier defervescence.

Appropriate initial antibiotic therapy was a good predictive factor for an early clinical response. Severe

Presentations such as initial septic shock, concurrent bacteremia, and acute renal failure were not poor predictive factors for an early clinical response in patients with community-onset UTIs. Initial broad-spectrum antibiotic therapy or improper use of broad-spectrum antimicrobials was not associated with an early clinical response. Our results have been described in the Results, Conclusion, and

Tables.

Community-onset UTI was defined as an infection that was diagnosed within 48 hours of admission into the hospital. Healthcare-associated community acquired (HCA) infection could be included under

community onset infections (Friedman ND, et al. *2002*) Patients with HCA infection were defined as having any of the following criteria: hospitalized in an acute-care hospital for 2 or more days within the last 90 days, attending a hospital for hemodialysis or receiving intravenous chemotherapy within the last 30 days, or residing in a nursing home or long-term care facility.

In this study, we included hospitalized patients (aged ≥ 18 years) who were diagnosed with community-onset *E.coli UTI.* Therefore, we enrolled the patients who resided in a healthcare facility before admission into a hospital.

Science Editor 1 Scientific quality: The manuscript describes a retrospective study of Predictive factors for early clinical response in community-onset E. coli urinary tract infection and effects of initial antibiotic treatment on early clinical response. The topic is within the scope of the WJCC. (1) Classification: Grade B and Grade D; (2) Summary of the Peer-Review Report: The purpose and significance of the experiment were good. This experiment found that initial appropriate antibiotic therapy was good predictive factor for an early clinical response, and the initial broad-spectrum antibiotic therapy or initial severe presentations didn't impact on an early clinical response. But, it didn't achieved the research objectives. The manuscript is not good in language. The figures and tables are not good quality illustrative of the paper contents. (3) Format: There are 2 tables. A total of 15 references are cited, including 4 references published in the last 3 years. There are no self-citations. 2 Language evaluation: Classification: Grade B and Grade C. A language editing certificate issued by editage was provided. 3 Academic norms and rules: The authors provided the Biostatistics Review Certificate, the signed Conflict-of-Interest Disclosure Form and Copyright License Agreement, and the Institutional Review Board Approval Form was provided. Written informed consent was waived. No academic misconduct was found in the CrossCheck detection and Bing search. 4 Supplementary comments: This is an unsolicited manuscript. The study was without financial support. The topic has not previously been published in the WJCC. 5 Issues raised: (1) The title is too long, and it should be no more than 12 words; (2) The "Author Contributions" section is missing. Please provide the author contributions; (3) The "Article Highlights" section is missing. Please add the "Article Highlights" section at the end of the main text; and (9) The "core tip" section is missing, please add the "core tip" section in front of the main text. 6 Re-Review: Required. 7 Recommendation: Conditional acceptance.

Response: The revised title does not have no more than 12 words: "Impact of severe presentations and initial antibiotic therapy on early clinical response"

We have added the “Author contributions” section to the manuscript. The “Core tip” section has been placed before the main text, and the “Article Highlights” section has been placed at the end of the main

text.