

## Peer Review File

Article information: <https://dx.doi.org/10.21037/jeccm-21-117>

Comment 1: "mortality rates remain as high as fifty percent in parts of the country"--this mortality rate is too high even for septic shock, sepsis have much lower than this.

**Reply 1: Thank you for your comment. We have removed this statement from the introduction and have replaced it with more general terminology. On line 104-108 there is a similar quote, reinforced with citations. In the rural counties of Kansas and Missouri, it is estimated that mortality due to septicemia approaches half of all patients. Our reference for this is a 2016 report from the Hospital Industry Data Institute (reference #9) on lines 103-110.**

Comment 2: The statistical analysis is too simple: I suggest to add more comorbidities beyond AKI, because many complications can confound the independent effect of AKI. For such an observational study, multivariable regression analysis is mandatory to control for confounders.

**Reply 2: Thank you for your comment. The study was limited to categorical data usage; quantitative analysis such as multivariable regression analysis could not be used due to our small sample size and inability to isolate comparison groups. Larger sample groups collected from multiple centers could have accounted for additional confounding variables. Data was insufficient in number for quantitative comparisons, hence mortality was used and defined as the proportion of patients that expired. We did our best to explain this limitation to the reader and how all these things should be considered and worked into future studies on lines 256-264.**

Comment 3: Tables are too redundant that can be simplified and two tables be combined into one.

**Reply 3: Great advice- we combined Table 2 and Table 3 into a single table, now called Table 2.**

Comment 4: Due to the low resolution of the variables, I suggest to reduce this article to a research letter.

**Reply 4: Thank you for your comment and review of our paper. We addressed this point in our reply to comment #2. In short, we were limited in this analysis because of how the data was collected. Sample size allowing only categorical data limited the number of compounding variables that could be looked at. However, our population and timing are quite unique. Few publications have focused on elucidating factors that are leading to the high mortality rate due to sepsis in the rural Midwest. Because of our focus on this important sample population, we hope that our paper will be considered for publication in JECCM.**

Comment 5: "Acute Kidney NOS are at a higher risk of mortality than those without Acute Kidney NOS"--this major finding of the study is a well known linkage in the literature, the study lacks novelty.

**Reply 5:** Thank you for your comment. We appreciate your time and feedback. While the linkage between acute kidney injury and mortality in sepsis is well established, other studies have not (to our knowledge) been performed in rural settings. Our data come from the Freeman Health System, serving southwest Missouri and parts of Kansas, Arkansas, and Oklahoma. Patients living in rural settings like this one often lack access to healthcare, predisposing them to comorbidities and poorer outcomes in sepsis. We added reinforcement of this idea throughout the paper (lines 76-77, 112-119, 202-203).

Comment 6: "Further studies are warranted into individual comorbidities affecting sepsis patient outcomes. "--why do you need further studies to do this work, current EHR can be employed to do this work with complete ICD code.

**Reply 6:** Thank you for your comment, and time spent reviewing our paper. It is important to note secondary comorbidities were not considered in the study but are likely affecting patient health and mortality outcomes in our sample. The focus of the study was mortality which is a categorical variable. Therefore, a quantitative analysis such as multivariable regression could not be performed. Sample groups were insufficient in size to isolate the patients with multiple comorbidities. To address this in future studies, multicenter analysis, larger hospitals, or combined health care systems that treat a greater number of patients could be used. Finally, EMRs collected via sepsis ICD10 codes that also had ICD10 codes for AKI diagnosis are assumed to have occurred on that visit. Our data set did not allow us to define personal history of AKI since records obtained was from one visit to Freeman Health System, and not their entire electronic health record (EHR). Thus, we assumed all patients isolated using ICD10 codes for AKI received their diagnosis at the time of sepsis diagnosis. The only way to definitively know would be to refer to the physical patient charts or EHRs, but our access to hospital campuses has been limited following the onset of COVID-19. We added lines 202-207 and 256-264 to discuss this in the paper.