Validation of a simplified comorbidity evaluation predicting clinical outcomes among patients with coronavirus disease 2019 – A multicenter retrospective observation study

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ABSTRACT

Objectives: We compared and validated the performance accuracy of simplified comorbidity evaluation compared to the Charlson Comorbidity Index (CCI) predicting COVID-19 severity. In addition, we also determined whether risk prediction of COVID-19 severity changed during different COVID-19 pandemic outbreaks.
Methods: We enrolled all patients whose SARS-CoV-2 PCR tests were performed at six different hospital Emergency Departments in 2020. Patients were divided into three groups based on the various COVID-19 outbreaks in the US (first wave: March–May 2020, second wave: June–September 2020, and third wave: October–December 2020). A simplified comorbidity evaluation was used as an independent risk factor to predict clinical outcomes using multivariate logistic regressions.
Results: A total of 22,248 patients were included, for which 7023 (32%) patients tested COVID-19 positive. Higher percentages of COVID-19 patients with more than three chronic conditions had worse clinical outcomes (i.e., hospital and intensive care unit admissions, receiving invasive mechanical ventilations, and in-hospital mortality) during all three COVID-19 outbreak waves.
Conclusions: This simplified comorbidity evaluation was validated to be associated with COVID clinical outcomes. Such evaluation did not perform worse when compared with CCI to predict in-hospital mortality.

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1. Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that causes coronavirus disease 2019 (COVID-19) is a worldwide pandemic. Due to its variant strains, the prevalence and mortality of COVID-19 vary across different geographic locations at different time points (waves/outbreaks) [1-3]. Among all COVID-19 patients, risk factors predicting the severity of COVID-19 were reported during the early phase of COVID pandemics in many studies [4-9]. The most commonly reported risk factors of mortality include age (≥65), gender (male), patients with lower socioeconomic status (SES), and patients having different comorbidities [4-9]. Together, these risk factors predict mortality and worse clinical outcomes [7,10].

As an independent risk, patient comorbidity was reported to predict patient clinical outcomes [11,12]. These outcomes range from requiring hospitalization, intensive care unit (ICU) admission, invasive mechanical ventilation (IMV), to all-cause in-hospital mortality. However, previous studies showed inconsistent findings for patients with different chronic conditions in terms of clinical outcome predictions [4,13,14]. The inconsistent results made the investigators consider using an established disease index for overall comorbidity assessment. The two most common comorbidity indexes, the Charlson Comorbidity Index (CCI) and Elixhauser Comorbidity Index (ECI), have been used to determine COVID severity [15,16]. Although the CCI and ECI were not initially designed for COVID severity prediction, their overall COVID severity outcome predictions were fairly consistent [15,17,18]. However, calculating these two comorbidity indexes is complicated. Many chronic diseases were not reported to be directly associated with COVID severity (i.e., peptic ulcer disease). As such, a novel simplified comorbidity

index (CCC: COVID-related high-risk Chronic Conditions) was reported recently [19]. This simple comorbidity index first screened all potential chronic diseases associated with COVID severity cited in previous reports, then used the number of chronic diseases patients suffered as a possible indicator for clinical outcome predictions [19]. The study showed that its performance accuracy was not inferior to those of the CCI or ECI, [19] meaning it did not perform worse than the CCI or ECI. However, this was a single-center study without larger-scale external validations.

During the COVID pandemic in the US (though its prevalence varied at different time-points in different geographic locations), there were several waves of COVID outbreaks in 2020 [20,21]. In the state of Texas, the first wave (1st wave) was defined as patients presented at EDs from March 1st to May 31st, 2020. The second wave (2nd wave) was defined as patients presented at EDs from June 1st to September 30th, 2020. The third wave (3rd wave) was defined as patients presented at EDs from October 1st to December 31st, 2020. These outbreak waves are based on local COVID statistics [22-24], epidemiological and mathematical analysis, [20,21,25] and Texas COVID case statistic reports [26]. Though the etiologies of these outbreaks are still not fully understood, it may, in part, be associated with certain SARS-CoV-2 variant strains [1,3,27]. We understand we are still in the process of learning COVID-19 management, especially as different SARS-CoV-2 variant strains present themselves. During the early COVID-19 pandemic (i.e., first wave), few effective treatments were available, and most patients received only supportive care. However, novel medications and treatments became available during the third pandemic wave [34,35]. Therefore, some risk factors initially used to predict clinical outcomes during the early phase of the COVID-19 pandemic may no longer be risk factors with the improvement of COVID-19 management.

It is essential to understand the role of comorbidity during different outbreak waves in predicting COVID-19 disease severity. At ED, with surges of COVID-positive patients, determining an appropriate disposition becomes challenging. With limited hospital and intensive care unit beds, not every patient can be admitted to the hospital. ED physicians have to decide which patients get the most benefit from hospital admission. The proper outcome predictions by prediction models, will allow ED physicians to recognize the disease progress earlier, thus making appropriate patient dispositions and treatments, and further advocating the necessity of receiving vaccinations. In addition, with likely SARS-CoV-2 variant strains and many COVID outbreaks, it is also important to understand further potential risk changes for COVID-19 severity predictions. Therefore, in this study, we aim to 1) externally validate a novel comorbidity evaluation (CCC) compared to the Charlson Comorbidity Index to predict COVID-19 clinical outcomes in a multi-center setting; and 2) determine the changes of comorbidity risk predicting patient in-hospital mortality during different COVID-19 pandemic waves.

2. Methods

2.1. Study design and setting

This is a multi-center retrospective observational study. We enrolled patients from Emergency Departments (ED) of six different hospitals, including one urban publicly funded hospital and other urban/suburban community hospitals. Among all six hospitals, two are tertiary referral centers and level one trauma centers located in North Texas, USA. The study procedure was designed in compliance with the Declaration of Helsinki. This study was approved by each institution's respective Institutional Review Board, with waived informed consent (No. 1614030–1 & 344,143).

2.2. Study participants

From March 1 to December 31, 2020, we included all patients who presented to EDs with positive SARS-CoV-2 polymerase chain reaction (PCR) tests indicating COVID-19 infections. We exclude ones with unknown dates/times of ED visits and exclude missing information from key variables (i.e., age).

2.3. Data retrieval

Study data were retrieved from the electronic medical record (EMR) by dedicated persons from the Department of Information Technology. They received sufficient data management training and were initially blinded to this study (i.e., before the aggregated data was open to all participants in this project). We also randomly selected 60 patient data three times from the entire dataset to manually check and validate the accuracy of data retrieval.

2.4. Outcome measures

Our primary outcome was to validate the accuracy of using CCC to predict clinical outcomes during different COVID pandemic outbreaks. Four clinical outcomes measured were: 1) hospital admissions; 2) intensive care unit (ICU) admissions; 3) patients who received invasive mechanical ventilation (IMV) during the hospitalizations; and 4) in-hospital all-cause mortality. Our secondary outcome was to determine the changes of such risks predicting clinical outcomes during different pandemic outbreaks.

2.5. Key variables

One Key study variable included CCC (COVID-related high risk chronic conditions) as reported before. These chronic conditions were determined based upon 1) chronic conditions associated with COVID-19 severity from previous studies (e.g., ICU admissions, mortalities, etc.) [5,7,12,28-31], and 2) experts' opinions using a modified Delphi's technique [32]. These chronic conditions are included in Supplementary Table-1.

General patient characteristics (age, gender, race/ethnicity) were also analyzed in this study. We divided age into three groups: 1) <40; 2) 40–65; 3) ≥65 years old. Race/ethnicity is categorized based on the Federal Statistics and Program administrative reporting of basic racial and ethnic categories. We divided the patients into four groups: 1) Non-Hispanic White (NHW); 2) Non-Hispanic Black (NHB); 3) Hispanic/Latino (Hispanic), and 4) others. Due to the relatively small sample size of "other" race/ethnicities (including American Indian, Alaska Native, Asian, Native Hawaiian, or other Pacific Islanders, unknown, or patient refusal), we categorized these patients into one group.

We divided COVID-19 pandemic outbursts of 2020 into three different waves based upon US national trends, Texas COVID case report statistics, and local reports. [22,23,26] These three waves were: the first wave (March 1st to May 31st, 2020), the second wave (June 1st to September 30th, 2020), and the third wave (October 1st to December 31st, 2020).

2.6. Study protocol

First, among the patients who tested positive for SARS-CoV-2-PCR, we determined the association between several chronic conditions that patients reported and patient clinical outcomes. We classified patients with chronic conditions into four categories: 1) patients with no chronic condition; 2) patients with one chronic condition; 3) patients with two chronic conditions; and 4) patients with three or more chronic conditions. We used the same comorbidity classification as previously reported and refer to it as the *simplified comorbidity evaluation (CCC)* [19]. Second, to better determine if these chronic conditions predict severity of clinical outcomes, multivariate logistic regression was performed with the adjustments for other potential independent risks predicting clinical outcomes (i.e., age, sex, and race/ethnicity). Third, we measured the performance accuracy of the simplified comorbidity

evaluation (CCC) in comparison to the CCI. The CCI has been previously used to predict severity of disease and patient in-hospital mortality [33].

2.7. Data analysis

Analysis of variance (ANOVA) was used to compare clinical outcomes of different groups (e.g., different COVID-19 outburst waves). We used multivariate logistic regression analyses to identify patients with chronic condition(s) associated with four clinical outcomes by adjusting other variables (age, gender, race/ethnicity). Adjusted Odds Ratios (AOR) were reported with 95% confidence intervals (CI). AUC (area under the curve) was used to measure the performance accuracy of different comorbidity evaluations (i.e., simplified comorbidity evaluation and CCI) predicting in-hospital mortality. Investigators used STATA 16.0 (College Station, TX) for all statistical study analyses, with $p < 0.05$ considered statistically significant.

3. Results

From March 1 to December 31, 2020, we screened 22,299 ED patients who had SARS-CoV-2-PCR tests performed due to suspicion of COVID-19. We excluded 46 patients who had missing information on the date/time of ED admission among these patients. We further excluded five patients who had missing age information. Among these 22,248 patients, a total of 7023 patients were COVID-19 positive and placed in the final analysis.

Table 1 lists patient general demographic characteristics and clinical metrics. We found that among all COVID-positive patients, Hispanics had the highest SARS-CoV-2-PCR positivity rate during all three COVID-19 pandemic waves. We also discovered fewer patients were admitted to the hospital ($p < 0.001$) during the third wave. However, among those who were admitted to the hospital, they tended to be severe, with more patients requiring Intensive Care Unit (ICU) care ($p = 0.014$) and Invasive Mechanical Ventilation (IMV, $p < 0.001$) in comparison to the first two waves. All-cause in-hospital mortality shows no differences among the three pandemic waves ($p = 0.144$, Table 1).

In this cohort, clinical outcomes worsened among COVID-19 positive patients with an increasing number of chronic conditions (CC). Patients with multiple CCs tended to be admitted to the hospital more, received ICU care and IMV, and yielded higher in-hospital mortality (Table 2, $p < 0.001$). However, certain changes occurred during the different COVID-19 pandemic waves. For example, ED physicians tended to admit more patients during pandemic waves 1 and 2 compared to the third wave regardless of patient comorbidity statuses. With fewer patients admitted to the hospital during the third pandemic wave, this might subsequently result in relatively higher rates of ICU admissions, received IMV, and in-hospital mortality (Table 2).

Multivariate logistic regression was performed to further determine the relationship between the number of chronic conditions and the severity of in-hospital mortality, adjusting for all potential independent risks predicting clinical disease outcomes in previous reports (e.g., age, sex, race/ethnicity, and comorbidities). We found that age is one independent risk predicting in-hospital mortality during all three pandemic waves. In addition, though the Adjusted Odds Ratio (AOR) of chronic conditions predicting in-hospital mortality decreased from the first wave to the third wave, it still acted as one independent risk to predict mortality (Table 3). Male acting as an independent risk to predict mortality occurred only during the second pandemic wave but not during the first and third waves. In general, race/ethnicity had no association with in-hospital mortality, especially during the third pandemic wave (Table 3).

Finally, the Area Under the Curve (AUC) of simplified comorbidity evaluation (CCC) and CCI (Charlson Comorbidity Index) were compared to determine their performance accuracy on in-hospital mortality prediction. Results indicated similar performance accuracies for predicting in-hospital mortality during the 1st and 2nd COVID-19 pandemic waves. Interestingly, during the 3rd COVID-19 pandemic wave, we found better performance accuracy on mortality prediction using simplified comorbidity evaluation than CCI ($p = 0.033$, Table 4).

4. Discussion

This study focused on validating a simplified comorbidity evaluation (CCC) to predict COVID-19 clinical outcomes among ED COVID-19 patients. A previous study showed that COVID-19 patients with fewer comorbidities had better clinical outcomes, including lower hospital general admissions, ICU admissions, requiring IMV, and in-hospital all-cause mortality [19]. Our study has validated these findings in a multi-center setting with different COVID-19 pandemic waves. More importantly, compared with the original tool, we found that the accurate prediction of COVID-19 severity gradually subsided among patients with only one or two chronic conditions. However, the accurate prediction of COVID-19 severity among patients with three or more chronic conditions remains unchanged, regardless of different pandemic waves [1]. Therefore, though more efficient COVID-19 managements emerged with the ongoing COVID-19 pandemic, the number of patients' comorbidities could still act as risk factors to predict clinical outcomes. In addition, the simplified comorbidity evaluation (CCC) is not inferior in predicting in-hospital mortality during different pandemic waves than the CCI. These findings indicate that when managing COVID-19 patients, special attention should be paid to those patients with three or more chronic conditions.

Apart from this, our study reexamined the potential risk factors affecting clinical outcomes among COVID-19 patients during different

Table 1
General Characteristics and Clinical Metrics of Study Patient Population from Six North Texas Emergency Departments during Different COVID-19 Pandemic Outbreaks

	1st Wave	2nd Wave	3rd Wave	P value
Number of COVID positive (n, %)*	1280 (33)	4170 (35)	1573 (24)	
Age year --- year				
(mean, SD)	50 (16)	51 (17)	53 (17)	<0.001
(median, IQR) *	50 (38,61)	51 (38,64)	53(40,64)	
Sex --- male (n, %)	649 (51)	2005 (48)	781 (50)	0.208
Female (n, %)	631 (49)	2165 (52)	792 (50)	
Race/ethnicity--- NHW (n, %)	282 (22)	875 (21)	382 (24)	<0.001
NHB (n, %)	419 (33)	1004 (24)	441 (28)	
Hispanic/Latino (n, %)	499 (39)	2096 (50)	656 (42)	
Others (n, %)	80 (6.3)	195 (4.7)	94 (6.0)	
Hospital admissions in COVID patients (n, %)	787 (62)	3307 (79)	800 (51)	<0.001
ICU admissions among COVID patients (n, %)	224 (18)	646 (16)	291 (19)	0.014
COVID-19 patients receiving IMV (n, %)	81 (6.3)	155 (3.7)	79 (5.0)	<0.001
In-hospital all-cause mortality --- (n, %)	70 (5.5)	229 (5.5)	107 (6.8)	0.144

*$P = 0.029$ age (1st wave vs. 2nd wave), $p < 0.001$ age (1st wave vs. 3rd wave), $p = 0.0026$ age (2nd wave vs. 3rd wave). NHW: non-Hispanic White; NHB: non-Hispanic Black; [a] Others refer to American Indian, Alaska Native, Asian, Native Hawaiian or other Pacific Islander, unknown or patient refusal; COVID-19: coronavirus disease 2019; ED: emergency department; SD: standard deviation; IQR: interquartile range.

Table 2
Association between Different Clinical Outcomes and Number of Chronic Conditions among COVID-19 Patients in Six North Texas Emergency Departments during Different Pandemic Waves

	No CC	One CC	Two CCs	≥Three CCs	P value
1st wave					
Number of Patients (n, %)	380 (30)	285 (22)	233 (18)	382 (30)	<0.001
Hospital Admission (n, %)	185 (49)	176 (62)	144 (62)	282 (74)	<0.001
Intensive Care Unit Admission (n, %)	26 (6.8)	47 (17)	56 (24)	95 (25)	<0.001
Receiving Mechanical Ventilation (n, %)	9 (2.4)	15 (5.3)	22 (9.4)	35 (9.2)	<0.001
All-cause In-hospital Mortality (n, %)	5 (1.3)	10 (3.5)	17 (7.3)	38 (10)	<0.001
2nd Wave					
Number of Patients (n, %)	1276 (31)	1090 (26)	703 (17)	1101 (26)	<0.001
Hospital Admission (n, %)	881 (69)	899 (83)	584 (83)	943 (86)	<0.001
Intensive Care Unit Admission (n, %)	74 (5.8)	123 (11)	135 (19)	314 (29)	<0.001
Receiving Mechanical Ventilation (n, %)	21 (1.7)	27 (2.5)	33 (4.7)	74 (6.7)	<0.001
All-cause In-hospital Mortality (n, %)	22 (1.7)	40 (3.7)	38 (5.4)	129 (12)	<0.001
3rd Wave					
Number of Patients (n, %)	571 (36)	327 (21)	214 (14)	461 (29)	<0.001
Hospital Admission (n, %)	202 (35)	175 (54)	134 (63)	289 (63)	<0.001
Intensive Care Unit Admission (n, %)	39 (6.8)	76 (23)	54 (25)	122 (27)	<0.001
Receiving Mechanical Ventilation (n, %)	14 (2.5)	15 (4.6)	14 (6.5)	36 (7.8)	<0.001
All-cause In-hospital Mortality (n, %)	18 (3.2)	19 (5.8)	15 (7.0)	55 (12)	<0.001
Total					
Number of Patients (n, %)	2227 (32)	1702 (24)	1150 (16)	1944 (28)	
Hospital Admission (n, %)	1268 (57)	1250 (73)	862 (75)	1514 (78)	<0.001
Intensive Care Unit Admission (n, %)	139 (6.2)	246 (14)	245 (21)	531 (27)	<0.001
Receiving Mechanical Ventilation (n, %)	44 (2.0)	57 (3.4)	69 (6.0)	145 (7.5)	<0.001
All-cause In-hospital Mortality (n, %)	45 (2.0)	69 (4.1)	70 (6.1)	222 (11)	<0.001

COVID-19: coronavirus disease 2019; CC: Chronic Condition.

pandemic outbreaks. We found certain changes occurred on these risk factors predicting clinical outcomes. Some risks remained (e.g., elderly and comorbidity), while others no longer considered risks (e.g., sex and race/ethnicity). Such changes might be, in part, due to different SARS-CoV-2 variants, the emergence of novel management, or with the more understanding of COVID-19 by ED physicians. Therefore, some risk prediction tools that could predict COVID-19 severity under certain phases might not be reliable when the COVID-19 pandemic extended to other phases. A validation of this simplified comorbidity index (CCC) thus added its value when evaluated during different pandemic outbreaks among different EDs with diverse patient populations. We understand our findings only reflect the history. However, this study may serve as a foundation for validating COVID-19 severity predictions dynamically during different pandemic phases.

Although our study mainly focuses on comorbidity, other risk factors predicting clinical outcomes were investigated. Race/ethnicity has been

considered one of the risks to predict COVID-19 severity in some studies during the early COVID-19 pandemic [37,38]. When adjusted for other variables such as age and sex, our findings showed that race/ethnicity was no longer considered an independent risk predicting COVID-19 severity [39,40]. Advanced age is reported to be one of the risks predicting COVID-19 severity in many studies [5,11]. Our study had similar findings. . In some studies, the male gender was considered another risk predicting COVID-19 severity [5,7], while others did not [11,41]. Our study showed variations during different waves. Its mechanism(s) are still unclear. We recommend that future larger-scale studies be performed to validate the patients' biographic features related to clinical outcomes.

This study has several strengths: 1) This is a multi-site study. We enrolled ED COVID-19 patients at different ED settings (i.e., a public-funded hospital ED and urban/suburban community EDs); 2) Different comorbidities were analyzed. This study included 12 common

Table 3
The Adjusted Odds Ratios (AOR) of Chronic Conditions Predicting All-cause In-hospital Mortality with Age, Gender, and Racial/Ethical Adjustments among COVID-19 Positive Patients in Six North Texas Emergency Departments during Different COVID-19 Pandemic Waves

	Mortality (1st Wave) aOR (95% CI), P value	Mortality (2nd wave) aOR (95% CI), P value	Mortality (3rd wave) aOR (95% CI), P value
Number of CCs			
None	Reference	Reference	Reference
One	2.24[0.74–6.80] p = 0.155	1.88[1.10–3.21] p = 0.022	1.38[0.70–2.72] p = 0.355
Two	3.73[4.30–10.69] p = 0.014	2.13[1.23–3.71] p = 0.007	1.45[0.70–3.04] p = 0.319
≥Three	4.74[1.75–12.81] p = 0.002	3.86[2.36–6.30] p < 0.001	2.06[1.13–3.74] p = 0.018
Age			
<40 year	Reference	Reference	Reference
40–65 year	3.10[0.91–10.63 p = 0.072	2.52[1.34–4.72] p = 0.004	2.46[1.01–6.03] p = 0.048
65- year	10.73[3.09–37.28] p < 0.001	8.52[4.54–16.00] p < 0.001	8.15[3.30–20.13] p < 0.001
Sex			
Female	Reference	Reference	Reference
Male	1.62[0.96–2.75] p = 0.071	1.94[1.46–2.59] p < 0.001	1.45[0.96–2.19] p = 0.077
Populations			
NHW	Reference	Reference	Reference
NHB	0.45[0.23–0.87] p = 0.017	1.37[0.91–2.05] p = 0.132	1.18[0.69–2.00] p = 0.549
Hispanic	0.58[0.31–1.09] p = 0.092	1.20[0.83–1.73] p = 0.336	0.97[0.57–1.63] p = 0.902
Others	1.46[0.54–3.91] p = 0.453	2.51[1.41–4.47] p = 0.002	0.61[0.20–1.85] p = 0.384

CI: Confidence interval; CC: Chronic Condition; ICU: Intensive Care Unit; IMV: invasive mechanical ventilation; NHW: non-Hispanic White; NHB: non-Hispanic Black;[a] Others refer to American Indian, Alaska Native, Asian, Native Hawaiian, or Other Pacific Islander, unknown or patient refusal; COVID-19: coronavirus disease 2019.

Table 4
Using C-Statistics to Compare Performance Accuracy of Simplified Comorbidity Evaluation and CCI Predicative of All-cause In-hospital Mortality in Six North Texas Emergency Departments during Different COVID-19 Pandemic Waves

	Simplified Comorbidity Evaluation	Charlson Comorbidity Index	P value
1st Wave	0.69[0.64–0.74]	0.70[0.64–0.75]	0.699
2nd Wave	0.70[0.67–0.73]	0.71[0.67–0.74]	0.312
3rd Wave	0.65[0.60–0.70]	0.63[0.58–0.68]	0.033

comorbidities, which account for the most common comorbidities affecting COVID-19 severity in the current literature; and 3) a simplified comorbidity evaluation is compared with Charlson comorbidity index, which has been used and validated to determine disease severity during hospitalization. With these strengths, this study's findings could guide ED physicians in predicting disease severity and determining appropriate dispositions.

This study has its limitations. First, this is a retrospective study. Given the nature of the study design, we cannot avoid missing, incomplete, and incorrect information. Second, though this study enrolled over 22,000 patients, it may not have a large enough sample size in each group when investigators further divided into subgroups. In addition, this study only included data from March 1 to December 31, 2020, when the third pandemic was ongoing, and data might not reflect the actual conditions of the third pandemic wave. Our future study will perform an extended analysis to include all patients through 2021. Third, we only had age, sex, race/ethnicity into our multivariate logistic regression model for clinical outcome prediction analysis. Other variables that could also affect clinical outcomes, such as socioeconomic statuses, household living conditions, were not analyzed. Fourth, this study enrolled only ED patients in North Texas. This might not reflect the COVID-19 patients' status in other geographic locations or different hospital settings. Last, this study only included patients with certain chronic conditions. We intended to validate an existing tool to predict clinical outcomes. However, we did not examine the potential impact of each chronic condition in relation to patients' clinical outcomes. Therefore, our findings should be interpreted with these considerations in mind. A large-scale multicenter prospective study is warranted for further validation.

5. Conclusion

A simplified comorbidity evaluation to predict COVID-19 severity has been validated. Its use to predict COVID-19 clinical outcomes has not changed significantly during different COVID-19 pandemic waves.

Author contributions

J.P.D., N.A., H.W. Research idea, Tables, Manuscript writing. N.A., E.C., J.S.G, J.J.K., D.P.B. H.W. Research conduct, Manuscript revising/editing. S.S., H.W. Statistical analysis, Tables. E.C., J.J.K, S.S., C.D.S. Data harvesting and validation, Manuscript revising/editing.

Data availability

The study data are available upon reasonable requesting to the corresponding author.

Approval for human study

This study was approved by University of North Texas Health Science Center regional and Baylor Scott & Write Health System Institutional Review Board, with waived informed consent (No. 1614030–1 & 344,143).

CRediT authorship contribution statement

James P. d'Etienne: Writing – review & editing, Writing – original draft, Validation, Supervision, Project administration, Methodology, Investigation, Formal analysis, Conceptualization. **Naomi Alanis:** Writing – review & editing, Validation, Resources, Investigation, Conceptualization. **Eric Chou:** Writing – review & editing, Validation, Investigation, Data curation. **John S. Garrett:** Writing – review & editing, Supervision, Resources, Investigation, Data curation. **Jessica J. Kirby:** Writing – review & editing, Validation, Supervision, Project administration, Investigation. **David P. Bryant:** Writing – review & editing, Supervision, Investigation. **Sajid Shaikh:** Writing – review & editing, Software, Resources, Data curation. **Chet D. Schrader:** Writing – review & editing, Supervision, Resources, Investigation, Conceptualization. **Hao Wang:** Writing – review & editing, Writing – original draft, Validation, Supervision, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

Declaration of Competing Interest

The author(s) declare no competing interests.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ajem.2022.03.011.

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