RECLASSIFYING SEVERITY AFTER 48 HOURS COULD BETTER PREDICT MORTALITY IN ACUTE RESPIRATORY DISTRESS SYNDROME

LC. Chiu (1) ; SW. Lin, (1) ; PH. Liu, (2) ; LP. Chuang, (1) ; CH. Chang (1) ; CY. Hung, (1) ; SH. Li, (1) ; CS. Lee, (1) ; HP. Wu, (3) ; CC. Huang, (1) ; HH. Li (4) ; KC. Kao, (1) ; HC. Hu, (1)
(1) Thoracic medicine, Linkou Chang Gung Memorial Hospital, Taoyuan, Taiwan; (2) Clinical informatics and medical statistics research center, College of Medicine, Chang Gung University, Taoyuan, Taiwan; (3) Division of pulmonary, critical care and sleep medicine, Keelung Chang Gung Memorial Hospital, Keelung, Taiwan; (4) Department of respiratory therapy, College of Medicine, Chang Gung University, Taoyuan, Taiwan

INTRODUCTION

The disease severity may change in the first week after ARDS onset. The aim of this study was to evaluate whether the reclassification of disease severity after 48 hours (i.e., day 3) of ARDS onset could help in predicting mortality and determine factors associated with ARDS persistence and mortality.

METHODS

We performed a secondary analysis of a three-year prospective, observational cohort study of ARDS in a tertiary care referral center. Disease severity was reclassified after 48 hours of enrollment, and cases that still fulfilled the Berlin criteria were regarded as nonresolving ARDS.

RESULTS

A total of 1,034 ARDS patients were analyzed. Overall hospital mortality was 57.7 % (56.7 %, 57.5 %, and 58.6 % for patients with initial mild, moderate, and severe ARDS, respectively, \( p = 0.189 \)). On day 3 reclassification, the hospital mortality rates were as follows: resolved (42.1 %), mild (47.9 %), moderate (62.4 %), and severe ARDS (76.1 %) \( (p < 0.001) \). Patients with improving severity on day 3 had lower mortality (48.8 %), whereas patients with the same or worsening severity on day 3 had higher mortality (62.7 % and 76.3 %, respectively). Patients who were older, had lower PaO2/FiO2, or higher PEEP on day 1 were significantly associated with nonresolving ARDS on day 3. Cox regression model with ARDS severity as a time-dependent covariate and competing risk analysis demonstrated that ARDS severity was independently associated with hospital mortality, and nonresolving ARDS had significantly increased hazard of death than resolved ARDS \( (p < 0.0001) \). Cumulative mortality curve for ARDS severity comparisons demonstrated significantly different (overall comparison, \( p < 0.001 \)).

CONCLUSION

Reclassification of disease severity after 48 hours of ARDS onset could help to divide patients into subgroups with greater separation in terms of mortality.
THE IMPACT OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE AND INHALED BRONCHODILATORS ON PATIENTS OUTCOME IN PATIENTS AFTER ACUTE MYOCARDIAL INFARCTION

YC. Jiang (1) ; SH. Kuo (2) ; KC. Lin (1) ; TH. TAI (3) ; HL. Liang (1) ; WC. Huang (4)
(1) Critical care medicine, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan;
(2) Department of Critical Care Medicine, Kaohsiung Veterans General Hospital, Kaohsiung City, Taiwan; (3) Critical care medicine, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan; (4) Critical care medicine and cardiovascular center, Kaohsiung Veterans General Hospital, Taipei, Taiwan

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) in Asia was different from Europe in higher cigarette smoking rate and more severe air pollution. Varies inhaled COPD medications had safety concern in acute myocardial infarction (AMI). The aim of this study was to investigate the effect of COPD in Asia AMI patients and real world safety of COPD medications in AMI patients

METHODS

We conducted a nationwide cohort study extracted data from the Taiwan National Health Insurance Research Database. Patients who hospitalized between 2000 and 2012 with a primary diagnosis of first AMI were included. Among the 186,112 prospective AMI patients, COPD was diagnosed in 13,065 (7.0%) patients. AMI patients without COPD were 1:1 matched by propensity score matching. AMI cohort was further divided to STEMI and NSTEMI cohort. STEMI without COPD was matched by propensity score. Cox proportional hazards regression model was used to estimate adjusted hazard ratios (HR) with 95% confidence intervals (95% CI)

RESULTS

During 12 years follow up, there were 18405 (77.65%) and 16093 (67.89%) deaths in AMI with COPD and without COPD group, respectively. The adjusted hazard ratio (aHR) of mortality in AMI with COPD group was 1.12 (95% CI 1.09 to 1.14). In STEMI with COPD group, aHR was 1.20 (95% CI 1.14 to 1.25). NSTEMI with COPD, aHR was 1.07 (95% CI 1.04 to 1.10). Using short-acting inhaled bronchodilators in AMI patients increased mortality (short acting beta-agonist: aHR 1.2, 95% CI 1.16 to 1.23, short acting muscarinic antagonist: aHR 1.3, 95% CI 1.26 to 1.34). Corticosteroids using also increased 10% mortality (aHR 1.10 , 95% CI 1.07 to 1.14). However, long acting inhaled bronchodilators reduced mortality (long acting beta-agonist: aHR 0.87, 95% CI 0.81 to 0.94, long acting muscarinic antagonist: aHR 0.82, 95% CI 0.69 to 0.96)

CONCLUSION

In Asia, AMI patient with COPD was associated with higher mortality compared with those without COPD. Guideline recommended AMI medications decreased mortality in patient with or without COPD, but they were underused in Taiwan. Using inhaled short-acting bronchodilators and
corticosteroids in AMI patient reduced survival. On the contrary, long acting inhaled bronchodilators were associated with survival benefit. Appropriate COPD medications and adequate standard AMI medications in AMI patient were equal crucial in improving long term survival
THE EFFECTS OF HYDROXYCHLOROQUINE IN HOSPITALIZED PATIENTS WITH COVID-19: UPDATED META-ANALYSIS WITH TRIAL SEQUENTIAL ANALYSIS

HJ. Jhou (1) ; PH. Chen (2) ; LJ. Ou-Yang (3) ; CH. Lee (4)
(1) Department of Neurology, Changhua Christian Hospital, Changhua, Taiwan; (2) Department of internal medicine, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan; (3) Department of physical medicine and rehabilitation, Chang Gung Memorial Hospital, Linkou, Taoyuan, Taiwan; (4) Division of hematology and oncology medicine, department of internal medicine, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan

INTRODUCTION

The coronavirus disease 2019 (COVID-19) outbreak had caused a global health and financial crisis. Until June, 2020, more than ten million people worldwide have been infected; however, the specific treatments remains investigational. Hydroxychloroquine, a classic agent derived from chloroquine to treat rheumatological diseases, expressed activity against the novel coronaviruses in vitro [1]. The aim of study using meta-analysis with trial sequential analysis is to evaluate the effects of hydroxychloroquine in overall mortality among patients with COVID-19.

OBJECTIVES

To compare overall mortality in patients with COVID-19 taking hydroxychloroquine alone, or with a macrolide versus conventional therapy.

METHODS

Comprehensive searches of Pubmed, Google scholar, MedRxiv, PrePrints and grey literature was performed until June 30, 2020 to identify all relevant trials with screening the titles and reviewing the abstracts. Odds ratio (OR) with 95% confidence intervals (CI) was estimated using random-effects model. A relative risk reduction was calculated according to the mean of the event proportions for both intervention and control arms. Trial sequential analysis (TSA) software was used to conduct random-effect TSA.

RESULTS

Meta-analysis of 15 studies (n = 18,869) showed there was no difference regarding overall mortality in patients with COVID-19 received hydroxychloroquine compared with the control (OR 1.07; 95% CI 0.80–1.43; I² = 82%, Cochran Q p-value < 0.01). TSA of overall mortality demonstrated intervention event proportion of 13.96%, control event proportion of 18.99%, and diversity of 89%. The adjusted TSA OR with 95% CI was 1.05 with 0.74–1.48. The cumulative Z-curve did not crossed the conventional boundary, and the required information size of 15,525 (vertical solid red line) has been excessed, confirming the hydroxychloroquine has no difference compared with the control, the current meta-analysis is robust and authentic.

CONCLUSION
This study demonstrates use of hydroxychloroquine among patients with COVID-19 has no benefit in reducing overall mortality.

1. Wang, M., Cao, R., Zhang, L. et al. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. Cell Res 30, 269–271 (2020).
2. None to declare
RISK-STANDARDIZED SEPSIS MORTALITY MAP OF THE UNITED STATES

CC. Lee (1) ; JR. Hu (2) ; CH. Yo (3) ; HY. Lee (4) ; KY. Su (5) ; YC. Chen (6) ; MY. Su (7) ; M. Lee (8) ; WT. Hsu (9)

(1) Department of emergency medicine, National Taiwan University Hospital, Taipei, Taiwan; (2) Department of medicine, Vanderbilt University Medical Center, Nashville, United States of America; (3) Department of emergency medicine, Far Eastern Memorial Hospital, Taipei, Taiwan; (4) Department of medicine, National Taiwan University, Taipei, Taiwan; (5) Health data science research group, National Taiwan University Hospital, Taipei, Taiwan; (6) Department of internal medicine, National Taiwan University Hospital, Taipei, Taiwan; (7) Department of medicine, National Cheng Kung University, Taipei, Taiwan; (8) Medical wizdom, LLC, Brookline, Boston, United States of America; (9) Department of epidemiology, Harvard T.H. Chan School of Public Health, Boston, United States of America

INTRODUCTION

Sepsis is the leading cause of in-hospital mortality in the United States (U.S.). Quality improvement initiatives for improving sepsis care depend on accurate estimates of sepsis mortality. While hospital 30-day risk-standardized mortality rates (RSMRs) have been published for patients hospitalized with acute myocardial infarction (AMI), heart failure (HF), and pneumonia, RSMRs for sepsis have not been well-characterized.

OBJECTIVES

To construct a sepsis RSMR map for the US and to illustrate disparities in sepsis care quality across the country.

METHODS

In this cross-sectional analysis, data from the 2010 and 2011 years of the U.S. Nationwide Inpatient Sample (NIS) were extracted. Hospital-level RSMRs were calculated using hierarchical logistic modeling, and were risk-adjusted with predicted mortality derived from (1) the Sepsis Risk Prediction Score (SRS), a logistic regression model, and (2) gradient-boosted decision trees, a supervised machine learning algorithm.

RESULTS

Among 1,739,033 inpatients with sepsis, mortality increased with age, (aOR:4.17 in 80-89-year-olds compared to <40 year-olds). Mortality was slightly higher in women than men (aOR 1.07), and in African-American than White (aOR 1.05). Mortality was higher in patients requiring early and late mechanical ventilation (aOR: 4.63 and 5.72) than patients not requiring ventilation. Mortality was also higher in patients with shock (aOR 2.06) or required hemodialysis (aOR 1.43).
Using the variables above, we constructed a reference model using SRS logistic regression, and an alternative model using boosted tree to predict mortality for estimating 30-day RSMR of sepsis. In the SRS model, median RSMR was 18.5% (IQR: 17.1-20.6%). In the boosted tree model, median RSMR was 18.4% (IQR 17.0-21.0%). RMSRs higher than 18.5% and 18.4% in the respective models indicate that the mortality from sepsis is higher than expected after risk adjustment. The boosted tree model demonstrated better calibration and discrimination than the SRS model. (C-statistic 0.87 and 0.78, respectively).

Next, we calculated median 30-day RSMR at the state level using both the SRS model and the boosted tree model. The highest RMSRs were found in Wyoming, North Dakota, and Mississippi, while the lowest RMSRs were found in Arizona, Colorado, and Michigan.

**CONCLUSION**

To our knowledge, this is the first description of state-level variation in RSMR of sepsis patients. Most importantly, we constructed a national map of sepsis RSMR, using a dashboard which we are making freely available to any investigator and clinician. We hope that identification of these high-RMSR hotspots will facilitate investment and innovation in sepsis mortality-reduction strategies, diminishing sepsis mortality and healthcare expenditures.

1. This work was supported by Taiwan Ministry of Science and Technology Grant 105-2811-B-002-031. No funding bodies had any role in the study design, analysis, decision to publish, or writing
2. Suter LG, Li S-X, Grady JN, et al. National Patterns of Risk-Standardized Mortality and Readmission After Hospitalization for Acute Myocardial Infarction, Heart Failure, and Pneumonia: Update on Publicly Reported Outcomes Measures Based on the 2013 Release. J GEN INTERN MED. 2014;29(10):1333-1340. doi:10.1007/s11606-014-2862-5
3. Liu V, Escobar GJ, Greene JD, et al. Hospital Deaths in Patients With Sepsis From 2 Independent Cohorts. JAMA. 2014;312(1):90-92. doi:10.1001/jama.2014.5804
4. Lee M-T, Lin F-C, Chen S-T, et al. Web-Based Dashboard for the Interactive Visualization and Analysis of National Risk-Standardized Mortality Rates of Sepsis in the US. J Med Syst. 2020;44(2):54. doi:10.1007/s10916-019-1509-9
5. Ford DW, Goodwin AJ, Simpson AN, Johnson E, Nadig N, Simpson KN. A Severe Sepsis Mortality Prediction Model and Score for Use With Administrative Data: Critical Care Medicine. 2016;44(2):319-327. doi:10.1097/CCM.0000000000001392

6. Gagne JJ, Glynn RJ, Avorn J, Levin R, Schneeweiss S. A combined comorbidity score predicted mortality in elderly patients better than existing scores. J Clin Epidemiol. 2011;64(7):749-759. doi:10.1016/j.jclinepi.2010.10.004

7. Martin GS, Moss M. The Epidemiology of Sepsis in the United States from 1979 through 2000. The New England Journal of Medicine. Published online 2003:9.

8. Singer M, Deutschman CS, Seymour CW, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA. 2016;315(8):801. doi:10.1001/jama.2016.0287