ISARIC (International Severe Acute Respiratory and Emerging Infections Consortium)

A global federation of clinical research networks, providing a proficient, coordinated, and agile research response to outbreak-prone infectious disease

Analysis Plan for ISARIC International COVID-19 Patients

Please complete the following sections:

Title of proposed research
Risk to admission of COVID19 patients from the Emergency Department
Version: (Date: Day/Month/Year)
23/10/2020
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Final draft SAPs will be circulated to all ISARIC partners for their input with an invitation to participate. ISARIC can help to set up collaborator meetings; form a working group; support communications; and accessing data. Please note that the details of all approved applications will be made publicly available on the ISARIC website. Please complete all sections of this form fully and return to **ncov@isaric.org**

Introduction

SARS-CoV-2 is challenging the Health Systems around the whole world. Patients are going to the Emergency Departments (ED) requiring for assistance. Based on lab test and first Chest X-Ray or thoracic CT-scan, clinicians decided to admit patients, frequently despite clinical status of patients is not bad. These patients are admitted in the hospitals to control their clinical evolution and sometimes their course is benign and the only reason to admit is the abnormal radiology or previous conditions considered for high risk for complications. The International Severe Acute Respiratory and emerging Infection Consortium (ISARIC) is collecting data from COVID19 patients from more than 30 countries. With this huge number of patients recruited we can offer a accurate description of patients who would benefit to be admitted based in objective risk from those who would be able to be discharge.

This document details the initial analysis plan for publication on a subset of COVID-19 patients in the global cohort in the ISARIC database, as of 20 Aug 2020. There are currently 44 countries (as of 20 AUG 2020) contributing data and these have so far contributed data on 102,038 patients. This data will represent the global experience of the first 6 months of this pandemic.

Participatory Approach

All contributors to the ISARIC database are invited to participate in this analysis through review and input on the statistical analysis plan and resulting publication. The outputs of this work will be disseminated as widely as possible to inform patient care and public health policy, this will include submission for publication in an international, peer-reviewed journal. ISARIC aims to include the names of all those who contribute data in the cited authorship of this publication, subject to the submission of contact details and confirmation of acceptance of the final manuscript within the required timelines, per ICMJE policies and the ISARIC publication policy.

Research Plan

Summary of Research Objectives

1. To compare those COVID19 patients who are admitted from those who are early discharged.
2. To describe those patients in high risk for complications.

Proposed Target Population

To answer the main objectives, we will include all patients included in the ISARIC and split them in 3 cohorts:

A. Patients admitted in the hospital who do not require specific treatment or supplemental oxygen.
B. Patients admitted in the hospital who require specific treatment or supplemental oxygen.
C. Patients discharged in the first 72 hours.
D. Patients discharged after 72 hours.

Clinical Questions/Descriptive Analyses

1. What are the characteristics of patients admitted for more than 72 hours vs those discharged before 72 hours?
2. What are the characteristics of patients admitted in risk for complications due to COVID19?
3. What are the COVID19 patients admitted in the hospital that could have been discharged without admission?

Planned Statistical Analyses, Methodology and Representation

1. Overall frequencies of key demographic variables and frequencies stratified in general and by cohorts described (A,B,C,D).
2. To answer the question planned, we will make 3 comparisons between laboratory test, signs and symptoms, radiology findings, previous conditions, timing of disease:
- Cohort A and B.
- Cohort C and D.
- Cohorts A+C and B+D (patients admitted less than 72 hours without specific treatment or supplemental oxygen vs. patients admitted more than 72 hours that required specific treatment or supplemental oxygen).

3. After univariate analysis, variables with statistical significance ($p<0,05$) will be included in the multivariate analysis, also respecting the comparisons described in point 2.
4. Results will be displayed:
- In general, all of them will be shown in a table with several columns: all patients, patients discharged, patients admitted and them a second table with comparison between groups.
- Results considered relevant will be shown also by graphs:
- Quantitative analysis: histograms comparing groups.
- Qualitative analysis: Bar diagrams and pie charts.

Handling of Missing Data

Preliminary analysis would be performed to ascertain a detailed overview of the extent of missingness in the data. This should enable the identification of variables which lack sufficient data to allow for any useful analysis to performed on them. Type of missingness shall be considered including whether data are not missing at random and follow-up with sites will be conducted if appropriate. Variables with greater than 30% missingness will be excluded from analysis. Where appropriate, imputation will be performed using Multiple Imputation by Chained Equations (MICE).

Other Information

Outputs

This proposal could be published in one or probably two per review journals (admitted patients by one side and ED patients by the other), both of them according to the ISARIC publication policy. We estimate to have the results of analysis and a paper written in 4 months after receiving the data.

References

- Giamello JD, Abram S, Bernardi S, Lauria G. The emergency department in the COVID-19 era. Who are we missing? Eur J Emerg Med. 2020 Aug;27(4):305-306. doi: 10.1097/MEJ.0000000000000718. PMID: 32345851; PMCID: PMC7202118.
- Hartnett KP, Kite-Powell A, DeVies J, Coletta MA, Boehmer TK, Adjemian J, Gundlapalli AV; National Syndromic Surveillance Program Community of Practice. Impact of the COVID-19

Pandemic on Emergency Department Visits - United States, January 1, 2019-May 30, 2020. MMWR Morb Mortal Wkly Rep. 2020 Jun 12;69(23):699-704. doi: 10.15585/mmwr.mm6923e1. PMID: 32525856; PMCID: PMC7315789.

- Leibner ES, Stokes S, Ahmad D, Legome E. Emergency department COVID management policies: one institution's experience and lessons learned. Emerg Med Pract. 2020 May 4;22(5 Suppl):1. PMID: 32365287.
- Argenziano MG, Bruce SL, Slater CL, Tiao JR, Baldwin MR, Barr RG, Chang BP, Chau KH, Choi JJ, Gavin N, Goyal P, Mills AM, Patel AA, Romney MS, Safford MM, Schluger NW, Sengupta S, Sobieszczyk ME, Zucker JE, Asadourian PA, Bell FM, Boyd R, Cohen MF, Colquhoun MI, Colville LA, de Jonge JH, Dershowitz LB, Dey SA, Eiseman KA, Girvin ZP, Goni DT, Harb AA, Herzik N, Householder S, Karaaslan LE, Lee H, Lieberman E, Ling A, Lu R, Shou AY, Sisti AC, Snow ZE, Sperring CP, Xiong Y, Zhou HW, Natarajan K, Hripcsak G, Chen R. Characterization and clinical course of 1000 patients with coronavirus disease 2019 in New York: retrospective case series. BMJ. 2020 May 29;369:m1996. doi: 10.1136/bmj.m1996. PMID: 32471884; PMCID: PMC7256651.
- Pascual Gómez NF, Monge Lobo I, Granero Cremades I, Figuerola Tejerina A, Ramasco Rueda F, von Wernitz Teleki A, Arrabal Campos FM, Sanz de Benito MA. Potenciales biomarcadores predictores de mortalidad en pacientes COVID-19 en el Servicio de Urgencias [Potential biomarkers predictors of mortality in COVID-19 patients in the Emergency Department]. Rev Esp Quimioter. 2020 Aug;33(4):267-273. Spanish. doi: 10.37201/req/060.2020. Epub 2020 Jul 13. PMID: 32657550; PMCID: PMC7374038.
- Wang S, Ma P, Zhang S, Song S, Wang Z, Ma Y, Xu J, Wu F, Duan L, Yin Z, Luo H, Xiong N, Xu M, Zeng T, Jin Y. Fasting blood glucose at admission is an independent predictor for 28-day mortality in patients with COVID-19 without previous diagnosis of diabetes: a multi-centre retrospective study. Diabetologia. 2020 Oct;63(10):2102-2111. doi: 10.1007/s00125-020-05209-1. Epub 2020 Jul 10. PMID: 32647915; PMCID: PMC7347402.
- Martín-Sánchez FJ, González Del Castillo J, Valls Carbó A, López Picado A, Martínez-Valero C, D Miranda J, Chacón A, López-Ayala P, Chaparro D, Cozar López G, Suárez-Cadenas MDM, Jerez Fernández P, Del Toro E, Cardassay E, Angós B, Díaz Del Arco C, Rodríguez Adrada E, Montalvo Moraleda MT, Espejo Paeres C, Elvira C, García Briñón MÁ, Leal Pozuelo JM, Ortega L, Fernández Pérez C, González Armengol JJ. Diagnostic groups and short-term outcomes in suspected COVID-19 cases treated in an emergency department. Emergencias. 2020 Ago;32(4):242-252. English, Spanish. PMID: 32692001.
- Henry BM, de Oliveira MHS, Benoit S, Plebani M, Lippi G. Hematologic, biochemical and immune biomarker abnormalities associated with severe illness and mortality in coronavirus disease 2019 (COVID-19): a meta-analysis. Clin Chem Lab Med. 2020 Jun 25;58(7):1021-1028. doi: 10.1515/cclm-2020-0369. PMID: 32286245.
- Qin ZJ, Liu L, Sun Q, Li X, Luo JF, Liu JS, Liu D. Impaired immune and coagulation systems may be early risk factors for COVID-19 patients: A retrospective study of 118 inpatients from Wuhan, China. Medicine (Baltimore). 2020 Aug 28;99(35):e21700. doi: 10.1097/MD.0000000000021700. PMID: 32871887; PMCID: PMC7458161.