Microbes, Infection and Chemotherapy

ORIGINAL RESEARCH

https://doi.org/10.54034/mic.e1940

Relationship of troponins with in-hospital mortality in adults with covid-19 in a colombian caribbean city: a nested case-control study

Authors: Maria C. Ospino-Guerra[I,a,*], Carlos H. Murgas-Cañas[I,b], Jessica L. Ospino-Guzman[I,c], Lourdes Varela-Prieto[I,d], Rodolfo Cano-Rivera[I,e], Rusvelt Vargas-Moranth[I,f]

Abstract

Background: myocardial injury, characterized by elevated cardiac troponin levels, is a common finding in severe COVID-19 cases, occurring in up to 38% of patients. It has been identified as an independent predictor of mortality. **Objective**: our aim is to assess the predictive value of cardiac troponin levels for in-hospital mortality among adults hospitalized with COVID-19 in Barranquilla, Colombia, during the period from January to June 2021.**Methods**: this study is a nested case-control analysis within a retrospective cohort. It encompasses individuals aged 18 and older with a confirmed diagnosis of COVID-19 who were hospitalized between January and June 2021 (n = 358). We describe the demographic and paraclinical characteristics of the patients and their association with outcomes at the time of discharge. We also estimate the diagnostic accuracy, including sensitivity, specificity, and predictive values, of elevated troponin levels in predicting in-hospital mortality. **Results**: patients with elevated troponin levels demonstrated a significantly increased risk of in-hospital mortality (OR: 9.4; 95% CI: 5.5-16.0; p < 0.05) and had a notably higher in-hospital mortality rate (55.6%) compared to those with non-elevated troponin levels (11.7%). The troponin biomarker exhibited a sensitivity of 77.9% and specificity of 72.7%, with positive and negative predictive values of 55.6% and 88.3%, respectively, for in-hospital mortality. **Conclusion**: troponin elevation in subjects with COVID-19 is positively related to in-hospital mortality, independently of other conditions such as age group, comorbidities, or oxygen therapy requirement.

Keyword: COVID-19, mortality, troponins, predictive value, myocardial injury.

[I]Universidad Libre seccional Barranquilla, Colombia.
[a]https://orcid.org/0000-0003-1457-6038
[b]carlosmurgasunal@gmail.com; https://orcid.org/0000-0002-6542-0597
[c]jessicaospinog@gmail.com; https://orcid.org/0000-0002-1021-8287
[d]lourdes.varelap@unilibre.edu.co; https://orcid.org/0000-0001-6000-3113
[e]rocanori@gmail.com; https://orcid.org/0000-0003-4938-3789
[f]rusvelt.vargas7@outlook.com; https://orcid.org/0000-0002-1014-0969

Corresponding author:
*Maria Clara Ospino Guerra
Address: Universidad Libre. Km. 7 Via Antigua Puerto Colombia, Atlantico. Colombia.
E-mail: mariaospinog31@gmail.com

Submitted: August 09, 2023
Reviewed : October 20, 2023
Approved: November 06, 2023

How to cite:
Ospino-Guerra MC, Murgas-Cañas CH, Ospino-Guzmán JL, Varela-Prieto L, Cano-Rivera R, Vargas-Moranth R. Relationship of troponins with in-hospital mortality in adults with covid-19 in a colombian caribbean city: a nested case-control study. Microbes Infect Chemother. 2023; 3: e1940

Introduction

The year 2019 marked a milestone in modern history with the emergence of Coronavirus disease, COVID-19, a highly contagious respiratory illness caused by the SARS-CoV-2 virus (severe acute respiratory syndrome coronavirus 2) (1). Since the onset of the pandemic, cardiovascular risk factors and chronic diseases have been shown to play a significant role in the development of severe and fatal forms of COVID-19 (2). Factors such as diabetes, hypertension, respiratory diseases, being male, over 65 years of age, and being an active smoker have been associated with an increased risk of disease progression (3,4).

Likewise, various multicenter studies have observed that an increase in biomarkers such as leukocytes, creatinine, procalcitonin, C-reactive protein (CRP), MB fraction of creatine kinase, myoglobin, high-sensitivity troponin T, N-terminal pro-B-type natriuretic peptide (NT-proBNP), and aspartate aminotransferase are associated, with varying statistical significance, with increased morbidity and fatal outcomes in ARDS-CoV-2 disease (3–5).

Myocardial injury, defined as an elevation of cardiac troponins, occurs in up to 38% of patients with severe forms of COVID-19, and its occurrence has been described as an independent marker of mortality (51.2% vs. 4.5%) (6). A study conducted in Wuhan, China (7), linked troponin elevation and in-hospital mortality with a sensitivity of 67.3% and a specificity of 88.7%. This reiterated that the cutoff points are approximately 40% lower than those typically defined for traditional cardiac pathology. The study also demonstrated that this is independent of previous cardiovascular pathology, as patients with a history of heart disease who did not present elevated troponins had a lower mortality rate compared to those who did, even without prior cardiovascular disease (8). Taking this into account, the aim of this study is to determine

the predictive value of troponins for in-hospital mortality in adults with COVID-19.

Methods

Study design and participants

A case-control study was conducted, nested within a retrospective cohort, which included subjects diagnosed with SARS-CoV-2/COVID-19 infection and treated at the Organización Clínica General del Norte in Barranquilla, Colombia, between January 1, 2021, and June 30, 2021.

The inclusion criteria were individuals aged 18 years or older, with a confirmed diagnosis of COVID-19, and a record of ultrasensitive troponin T measurements in their clinical history. Subjects diagnosed based solely on clinical findings, radiological findings, or antibody measurements were excluded. Patients with acute myocardial injury who showed clinical evidence of acute myocardial ischemia, with a rise and/or fall of cardiac troponin (cTn) values, with at least one value exceeding the 99th percentile URL, and meeting at least one of the following criteria were also excluded: Symptoms of myocardial ischemia, new ischemic ECG changes, development of pathological Q waves, imaging evidence of new loss of viable myocardium or new regional wall motion abnormality consistent with an ischemic etiology, or identification of a coronary thrombus by angiography or autopsy, in accordance with the fourth universal definition of acute myocardial infarction (9).

Demographic variables included age (defined as the time elapsed from birth to inclusion in the study) and sex, categorized as male or female. Clinical variables, known to influence the prognosis of the disease based on the literature, were included: the presence of comorbidities such as arterial hypertension, diabetes mellitus, and/or lung diseases (bronchial asthma, COPD) (2–4). Additionally, the values of the following biomarkers taken within the first 24 hours of admission were considered: total leukocyte count, ferritin, lactate dehydrogenase (LDH), ultrasensitive troponin T, C-reactive protein, D-dimer, and the final dichotomous condition of being alive or deceased. Non-probabilistic convenience sampling was conducted. The sample size was calculated using Epidat 4.2 with a power of 80% and a confidence level of 95%.

Data Collection

After obtaining the necessary approvals from the relevant authorities, medical records were identified by filtering participants' diagnoses recorded under the codes U071 (COVID-19 identified virus) and U072 (COVID-19 unidentified virus) as per ICD-10 (International Classification of Diseases - 10). Subsequently, a database was created to record the study data abstracted from the medical records. Information extracted from clinical histories was systematized into an Excel table, tabulating each variable based on the established treatment criteria for operationalization. A table was designed to relate patient identification data (masked for privacy), demographic and clinical variables, based on the defined treatment for each variable's operationalization and their respective categories. Each independent row corresponded to a single study subject.

Statistical Analysis

For data analysis, the SPSS V23 program was employed. Qualitative variables were presented as frequencies, and quantitative variables were described using mean, standard deviation, and range. Bivariate analysis utilized the chi-square test (with p-value) to determine the presence of statistically significant differences ($p<0.05$). The Mantel-Haenszel formula was used for dichotomous variables to calculate odds ratios (ORs) and their 95% confidence intervals (95% CI) to describe the relationship between elevated cardiac troponin and COVID-19 patient outcomes. Receiver Operating Characteristic (ROC) curve analysis was applied to calculate the sensitivity, specificity, and predictive values of elevated troponins and specific variables in relation to mortality, with their corresponding level of statistical significance ($p<0.05$).

Ethical Considerations

To conduct this study, it underwent evaluation by the ethics committee of the healthcare provider institution (Organización Clínica General del Norte) and was approved with filing number T.I-448, considering it as posing no risk to the patients. It was also evaluated by the research bioethics committee of Universidad Libre, which verified that the study was conducted in accordance with current scientific, methodological, and ethical principles.

Results

Characterization of the Population

Out of the 358 participants, just over half were male (52.2%). The average age was 65.1 years with a standard deviation of 14.9, and 70.4% fell within the age range of 50 to 79 years. The primary method of detecting COVID-19 cases was through antigen testing (60.6%), and 61.5% required oxygen upon admission. Approximately two-thirds of the participants had at least one comorbidity, with 53.1% suffering from arterial hypertension, 31.6% from obesity, and 21.5% from Diabetes Mellitus among those (n=245).

Inflammatory Markers

The averages of the inflammatory markers are presented in Table 1. It's worth noting that not all cases had the opportunity to undergo all five markers, but all had troponin measurements. CRP had the highest percentage of cases with elevated values (91.8%), followed by D-dimer (83.1%). Notably, 42.7% of the participants exhibited elevated troponin levels. Just under a third (30.4%) of the subjects did not survive.

Table 1

Inflammatory Markers

	Mean	SD+/-	Range
Troponins	0,1	0,2	0-1,38
Ferritin*¶	1910,6	5873,3	12-81094
LDH*¶	467,0	362,1	140-3603
D Dimer **¶	3160,6	8135,8	100-99000
Lymphocytes***¶	1040,5	1286,5	84-21400

*n=344; **n=345; ***n=348 SD: Standard deviation
LDH: Lactate Dehydrogenase
¶: Some participants did not have all the biomarkers measured but all had troponin measurements, so they were included in the study.

Relationship between Clinical Variables and Mortality

When examining the relationship between sociodemographic and clinical variables with mortality, statistically significant differences ($p<0.05$) were observed in all the variables studied, except for sex (Table 2). Regarding troponin levels, their elevation represented statistically significant differences ($p<0.05$) in terms of vital status, with an OR of 9.4 (95% CI: 5.5-16.0) (Figure 1).

Table 2

Relationship between sociodemographic and clinical variables with mortality in the participants

		%Deceased	%Alive	Chi2; p
Sex	Male (n=187)	32,1	67,9	0,496; 0,481
	Female (n=171)	28,7	71,3	
Age (years)	≥60 (n=242)	39,3	60,7	27,3; 0,000*
	20-59 (n=116)	12,1	87,9	
Oxygen requirement at admission	Yes (n=220)	40,0	60,0	24,6; 0,000*
	No (n=138)	15,2	84,8	
Comorbidities	Yes (n=245)	36,7	63,3	14,9; 0,000*
	No (n=113)	16,8	83,2	
Number of comorbidities	>1(n=125)	44,0	56,0	5,79; 0,016*
	1(n=120)	29,2	70,8	
Troponins	Increased (n=153)	55,6	44,4	79,54; 0,000*
	Normal (n=205)	11,7	88,3	
Lymphocytes	Altered (n=198	41,9	58,1	24,3; 0,000*
	Normal (n=147)	17,0	83,0	
LDH	Increased (n=313)	33,5	66,5	Fisher: 0,001*
	Normal (n=31)	6,5	93,5	
D Dimer	Increased (n=287)	34,5	65,5	9,66; 0,002*
	Normal (n=58)	13,8	86,2	
CRP	Increased (n=329)	32,5	67,5	Fisher: 0,0027*
	Normal (n=9)	6,9	93,1	
Ferritin	Increased (n=268)	35,4	64,6	12,21; 0,000*
	Normal (n=76)	14,5	85,5	

*Statistically significant differences ($p<0.05$)
LDH: Lactate dehydrogenase; CRP: C reactive protein

Predictive Values of Cardiac Troponins vs. Mortality

An analysis of the overall relationship between troponin levels and in-hospital mortality revealed a significant increase in mortality among those with elevated troponins (55.6%), compared to the group without elevated troponins (11.7%). When stratified by subgroups, a consistent increase in mortality was observed in participants with elevated troponins, irrespective of age group, oxygen requirement upon admission, or presence of comorbidities (Table 3).

Figure 1

Forest Plot for variables related to mortality

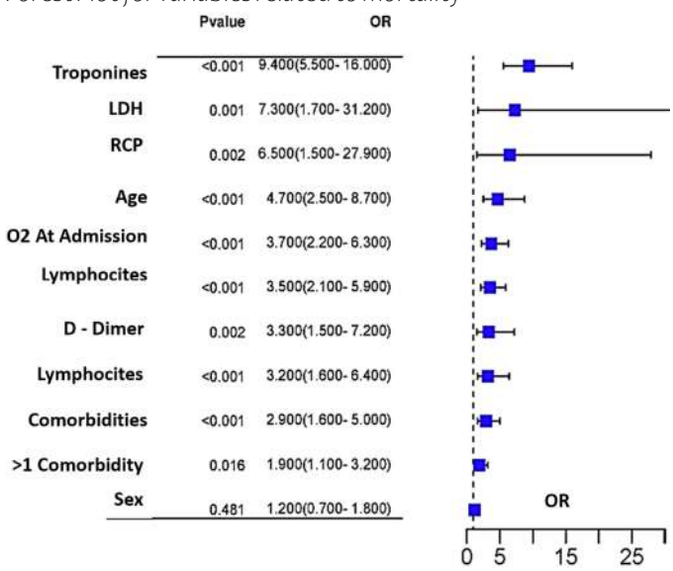


Table 3

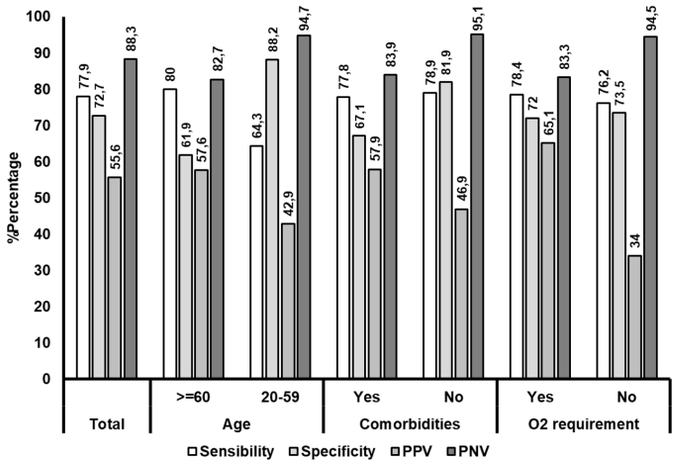
Relationship between having elevated troponins or not and vital status at discharge, in general and according to age, oxygen need at admission and presence of comorbidities

		Troponins	Deceased	
			%Yes	%No
	Total	Increased (n=153)	55,6	44,4
		Normal (n=205)	11,7	88,3
Age	≥60	Increased (n=132)	57,6	42,4
		Normal (n=110)	17,3	82,7
	20-59	Increased (n=21)	42,9	57,1
		Normal (n=95)	5,3	94,7
Oxygen requirement at admission	Yes	Increased (n=106)	65,1	34,9
		Normal (n=114)	16,7	83,3
	No	Increased (n=47)	34,0	66,0
		Normal (n=91)	5,5	94,5
Comorbidities	Yes	Increased (n=121)	57,9	42,1
		Normal (n=124)	16,1	83,9
	No	Increased (n=32)	46,9	53,1
		Normal (n=153)	4,9	95,1

The sensitivity and specificity of troponin elevation in predicting in-hospital mortality were 77.9% and 72.7%, respectively. These values increased when troponin elevation occurred in patients without other comorbidities, with sensitivity at 78.9% and specificity at 81.1%. The positive predictive value of troponin elevation was 55.6%, while the negative predictive value was 88.3%, rising to 95.1% in the absence of other comorbidities (Figure 2).

Figure 2

Sensitivity, Specificity and Predictive Values of elevated Troponins versus mortality, in general (total) and according to age, oxygen need at admission and presence of comorbidities



PPV: Predictive positive value; PNV: Predictive negative value

Discussion

The COVID-19 pandemic has been a challenge for healthcare workers worldwide. Since its onset in 2019, it became evident that the presence of chronic diseases and cardiovascular risk factors plays a significant role in the development of fatal forms of this disease (2). In the present study, it was observed that the sociodemographic groups at the highest risk are adults over 60 years of age, with a mortality rate of 39.3% compared to 12.1%, and there were no significant differences based on sex.

The presence of at least one of the comorbidities studied, which include arterial hypertension, diabetes mellitus, obesity, and chronic lung disease, increased the probability of death by 44% compared to patients without these conditions. Although this study did not find a significant relationship between male sex and mortality, as reported in a recent meta-analysis (3), the results align with other investigations where the group at the highest risk for mortality consists of older patients over 60 years of age with comorbidities such as primary arterial hypertension, type 2 diabetes mellitus, and chronic obstructive pulmonary disease (COPD), which are significantly associated with an increased risk of mortality (OR: 5.15; 95% CI: 2.51–10.57; p<0.00001) (2).

Changes in paraclinical parameters have been linked, with varying statistical significance, to in-hospital and medium-term mortality in SARS-CoV-2 infection. When comparing the paraclinical results of patients with mild and critical forms of COVID-19, a higher frequency of neutrophilia, lymphopenia, and significant elevations in CRP and troponins were found in the latter (11,12).

The results of this investigation reveal that C-reactive protein (CRP) was the most frequently elevated marker in patients, although it is not the one with the strongest association with their condition at discharge. Similar findings were reported in the Asian population, where CRP elevation was the most common alteration, but lymphopenia was the main negative predictor of mortality (13). Consistently, this study found a statistically significant relationship between lymphopenia, elevated lactate dehydrogenase (LDH), ferritin, and D-dimer with in-hospital mortality in patients with COVID-19.

Previous studies have also described the elevation of LDH as one of the parameters with the strongest correlation, and within coagulation studies, the elevation of D-dimer was significantly related to the same outcome, likely associated with the cytokine storm described in the pathophysiology of this disease (14,15).

In the investigated population, troponins were elevated in only 42.7% of the participants, and despite this, they proved to be the primary potential marker of mortality, with an OR of 9.4 (95% CI: 5.5-16.0). When comparing by subgroups, a consistent increase in this outcome was observed in patients with elevated troponins regardless of other conditions such as the need for supplemental oxygen, age group, or the presence of comorbidities. Even the specificity of troponins against mortality increased considerably when this elevation occurred in the absence of the studied comorbidities, with no significant differences in terms of their sensitivity. Likewise, its negative predictive value increased from 88.3% to 95.1% in the absence of other comorbidities.

Myocardial injury, defined as the elevation of cardiac troponins above the reference value, occurs in up to 38% of patients with COVID-19 (6), raising concerns about its association with increased mortality. Previous studies conducted between 2020 and 2021 have shown a strong relationship between the elevation of cardiac biomarkers and mortality, with an increase of up to 7.9 times compared to the group that does not elevate this cardiac enzyme (16,17).

In this study, similar results were found, with a 9.4 times higher risk of death in the group with elevated troponin levels, regardless of other factors such as age, the presence of comorbidities, or the need for supplemental oxygen upon admission. Similarly, a Brazilian study (8) reported the use of troponins as a marker with special impact during the first 7 days of hospitalization, with an independent correlation to the presence of previous heart disease.

Another important element is the timing of troponin measurement, as demonstrated in a study conducted in Italy (18), where early detections within the first 24 hours of admission can discriminate patients with worse outcomes. The results of this study show that mortality was higher (22.5%; OR: 4.35; 95% CI: 1.72-11.04) in people with elevated troponin levels on admission compared to those who did not have such elevation (6.25%).

Additionally, the prognostic value of troponins for the prediction of mortality has been compared in patients with adult respiratory distress syndrome (ARDS) due to COVID-19 and ARDS due to other causes, with favorable results for troponins, taking into account potential biases, as

the patients in the group with ARDS and COVID-19 were older and had a greater number of comorbidities compared to the patients with ARDS due to other causes (19).

On the other hand, some studies report different findings from this investigation, where the main predictor of mortality is established as the ratio between arterial oxygen pressure and the inspired fraction (PaO2/FiO2), (HR: 0.901; 95% CI: 0.829–0.978; P<0.0133), with no statistically significant findings for troponin elevation (20).

Other results suggest the superiority of myoglobin over troponin as a predictor (21), and that troponin alone is not statistically significant in predicting outcomes (HR: 0.98; 95% CI: 0.92–1.03; p: 0.507), while myoglobin was superior to troponin as an independent factor in predicting mortality (HR: 1.001; 95% CI: 1.001–1.002; p < 0.001). However, the low availability of myoglobin makes it impractical for use (21).

In this investigation, a sensitivity for the elevation of troponins against mortality of 77.9% and a specificity of 72.7% was obtained. The total positive predictive value was 55.6%, while the negative predictive value for the elevation of troponins against this same outcome was 88.3% in general. These results confirm previous findings in similar studies, where the relationship between elevated troponin and in-hospital mortality was established with a sensitivity of 67.3% and a specificity of 88.7% (7), a positive predictive value of 51.9%, and an 89.7% negative predictive value for all-cause in-hospital mortality in patients with COVID-19 (22).

It is clear that this research has certain limitations since the information on the study population was obtained from a secondary source of information and was limited to a single healthcare center that serves patients from the contributory and special regime in Colombia, which may represent a better chance of access to some services and a different social vulnerability. Additionally, these results are only applicable to patients who were hospitalized for COVID-19 and do not represent the situation of patients who did not require hospitalization.

Furthermore, several parameters described in the literature with varying relationships between their alteration and the development of more severe forms of the disease were not evaluated in this study. Thrombocytopenia has been recognized as a partial predictor of disease severity, as have elevations in aminotransferases and bilirubin (23). It is essential to consider that due to logistical and safety limitations, it was not possible to perform echocardiographic or cardiac magnetic resonance studies to assess myocardial involvement, as recommended in the literature (24), and to rule out differential diagnoses such as myocarditis and stress cardiomyopathy, which may introduce bias into the results.

Conclusion

This study determined the predictive value of cardiac troponins for in-hospital mortality in adults with COVID-19. Despite not being the most frequently altered marker, there is a positive correlation between troponin elevation and this outcome, independent of the presence of other conditions such as age group, comorbidities, or the need for supplemental oxygen therapy. One of the most significant findings of this study was the predictive value of cardiac enzymes for mortality, which becomes even more valuable in patients without associated pathologies. Normal values of this biomarker in patients infected with SARS-CoV-2 substantially reduce the probability of a fatal outcome.

Authors' contributions

The authors confirm their contribution to the paper as follows: study conception and design: Ospino Maria, Murgas Carlos, Cano Rodolfo; data collection: Ospino María, Murgas Carlos; analysis and interpretation of results: Vargas Rusvelt, Varela Lourdes; draft manuscript preparation: Ospino Maria, Murgas Carlos, Ospino Jessica. All authors reviewed the results and approved the final version of the manuscript. All authors agreed to be responsible for all aspects of the work to ensure the accuracy and integrity of the published manuscript.

Ethics statement

The authors declare that the published work reflects an investigation and analysis carried out truthfully and completely.

Conflict of Interest

The authors declare no conflict of interest.

Funding

None.

Data availability statement

The data of this study are available from the corresponding author upon reasonable request.

References

1. Woodall MNJ, Masonou T, Case KM, Smith CM. Human models for COVID-19 research. J Physiol. 2021; 599(18): 4255–67.
2. Gautret P, Million M, Jarrot PA, Camoin-Jau L, Colson P, Fenollar F, et al. Natural history of COVID-19 and therapeutic options. Expert Rev Clin Immunol. 2020; 16(12): 1159–84.
3. Zheng Z, Peng F, Xu B, Zhao J, Liu H, Peng J. Risk factors of critical & mortal COVID-19 cases: A systematic literature review and meta-analysis. J Infect. 2020;81(2):e16–25.
4. Tian W, Jiang W, Yao J, Nicholson CJ, Li RH, Sigurslid HH, et al. Predictors of mortality in hospitalized COVID-19 patients: A systematic review and meta-analysis. J Med Virol. 2020;92(10):1875–83.
5. Zinellu A, Sotgia S, Fois AG, Mangoni AA. Serum CK-MB, COVID-19 severity and mortality: An updated systematic review and meta-analysis with meta-regression. Adv Med

Sci. 2020;66(2):304–14.
6. McKinney J, Connelly KA, Dorian P, Fournier A, Goodman JM, Grubic N, et al. COVID-19–Myocarditis and Return to Play: Reflections and Recommendations From a Canadian Working Group. Can J Cardiol. 2021;37(8):1165–74.
7. Deng P, Ke Z, Ying B, Qiao B, Yuan L. The diagnostic and prognostic role of myocardial injury biomarkers in hospitalized patients with COVID-19. Clin Chim Acta [Internet]. 2020;510:186–90. Available from: https://doi.org/10.1016/j.cca.2020.07.018
8. Junior GLG de A, Braga F, Jorge JK, Nobre GF, Kalichsztein M, de Faria P de MP, et al. Prognostic value of troponin-t and b-type natriuretic peptide in patients hospitalized for covid-19. Arq Bras Cardiol. 2020;115(4):660–6.
9. Thygesen K, Jaffe AS, Chaitman BR, White HD, Zealand N, Canada PJD. Fourth Universal Definition of Myocardial Infarction (2018). J Am Coll Cardiol. 2018;72(18):2231–64.
10. Vélez M, Velásquez P, Acosta J, Vera C, Santiago J, Jimenez C, et al. Factores clínicos pronósticos de enfermedad grave y mortalidad en pacientes con COVID-19. Univ Antioquia [Internet]. 2020;1(1):57. Available from: http://fi-admin.bvsalud.org/document/view/rpncv NS -
11. Mesas AE, Cavero-Redondo I, Álvarez-Bueno C, Cabrera MAS, de Andrade SM, Sequí-Dominguez I, et al. Predictors of in-hospital COVID-19 mortality: A comprehensive systematic review and meta-analysis exploring differences by age, sex and health conditions. PLoS One. 2020;15(11 November):1–23.
12. Moutchia J, Pokharel P, Kerri A, McGaw K, Uchai S, Nji M, et al. Clinical laboratory parameters associated with severe or critical novel coronavirus disease 2019 (COVID-19): A systematic review and meta-analysis. PLoS One [Internet]. 2020; 15(10 October): 1–25. Available from: http://dx.doi.org/10.1371/journal.pone.0239802
13. Ghahramani S, Tabrizi R, Lankarani KB, Kashani SMA, Rezaei S, Zeidi N, et al. Laboratory features of severe vs. non-severe COVID-19 patients in Asian populations: A systematic review and meta-analysis. Eur J Med Res [Internet]. 2020;25(1):1–10. Available from: https://doi.org/10.1186/s40001-020-00432-3
14. Ali AM, Rostam HM, Fatah MH, Noori CM, Ali KM, Tawfeeq HM. Serum troponin, D-dimer, and CRP level in severe coronavirus (COVID-19) patients. Immunity, Inflamm Dis. 2022;10(3):1–10.
15. Velavan TP, Meyer CG. Mild versus severe COVID-19: Laboratory markers. Int J Infect Dis. 2020; 95(January): 304–7.
16. Malik P, Patel U, Patel NH, Somi S, Singh J. Elevated cardiac troponin i as a predictor of outcomes in covid-19 hospitalizations: A meta-analysis. Infez Med. 2020; 28(4): 500–6.
17. Papageorgiou N, Sohrabi C, Prieto Merino D, Tyrlis A, Atieh AE, Saberwal B, et al. High sensitivity troponin and COVID-19 outcomes. Acta Cardiol [Internet]. 2022;77(1):81–8. Available from: https://doi.org/10.1080/00015385.2021.1887586
18. Stefanini GG, Chiarito M, Ferrante G, Cannata F, Azzolini E, Viggiani G, et al. Early detection of elevated cardiac biomarkers to optimise risk stratification in patients with COVID-19. Heart. 2020;106(19):1512–8.
19. Metkus TS, Sokoll LJ, Barth AS, Czarny MJ, Hays AG, Lowenstein CJ, et al. Myocardial Injury in Severe COVID-19 Compared with Non-COVID-19 Acute Respiratory Distress Syndrome. Circulation. 2021;553–65.
20. Ghio S, Montalto C, Pagnesi M, Lupi L, Cappelletti A, Baldetti L, et al. High troponin levels in patients hospitalized for coronavirus disease 2019: a maker or a marker of prognosis? J Cardiovasc Med (Hagerstown). 2021; 22(11): 828–31.
21. Zhu F, Li W, Lin Q, Xu M, Du J, Li H. Myoglobin and troponin as prognostic factors in patients with COVID-19 pneumonia. Med Clin (Barc). 2021;157(January):164–71.
22. Al B, Torres P, Ramos-tuarez F, Dewaswala N, Abdallah A. Cardiac Troponin-I and COVID-19 : A Prognostic Tool for In-Hospital Mortality. 2020;11(6):398–404.
23. Ponti G, Maccaferri M, Ruini C, Tomasi A, Ozben T. Biomarkers associated with COVID-19 disease progression. Crit Rev Clin Lab Sci [Internet]. 2020;0(0):389–99. Available from: https://doi.org/10.1080/10408363.2020.1770685
24. Imazio M, Klingel K, Kindermann I, Brucato A, De Rosa FG, Adler Y, et al. COVID-19 pandemic and troponin: Indirect myocardial injury, myocardial inflammation or myocarditis? Heart. 2020;106(15):1127–31.