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Analysis of some cardiac markers in patients recovered from COVID-19 Suspected of heart failure

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Abstract

Objective: This study aimed to compare the levels of CRP, ferritin, D-dimer, IgG, IgM, Subfatin, Asprosin, and NT Pro-BNP in four groups: control, heart failure, heart failure with corona, and heart failure after recovery from corona. **Materials and Methods:** Patients from 1st July 2021 until 4th January 2022 were carried on in the isolation wards in Balad Ruz General Hospital and Baqubah Teaching Hospital/Diyala Province/IRAQ, with 89 Participants enrolled in the study, the patients were diagnosed according to the World Health Organization (WHO) guidance for COVID-19. This study included 4 groups as follows: **Group 1(G1):** Healthy individual, their number 20, **Group 2(G2):** heart failure patients, their number 25, **Group 3(G3):** heart failure patients with covid-19, their number 25. **Group 4(G4):** heart failure patients after recovery from COVID-19, for group 3 and 6 patients died with coronavirus, their number 19. **Results:** The result showed significant differences in the levels of IgG, IgM, Ferritin, D-dimer, and CRP which highly increased in G3 and decreased in G4. As for ferritin, it increased in heart G3 at a p-value <0.001. This study also showed decreased levels of Subfatin in G2 and G4, with an increase in G3. As for asprosin increased in G2, G3, and G4 compared with G1.NT Pro-BNP highly increased in G3, followed by G4, then G2 as compared with G1(67.19±18.44) at p-value <0.01.

Keywords: Covid-19, Heart failure, Mortality

INTRODUCTION

COVID-19 is a novel viral infectious disease caused by the SARS-CoV2 infection. It was initially identified in Wuhan, China, towards the end of 2019 [1]. Signs and Symptoms of COVID-19 include fever, muscle pain cough, diarrhea, lethargy, and pneumonia, which can lead to acute respiratory distress syndrome (ARDS), and possibly kidney, liver, or heart failure [2, 3]. COVID-19 in patients with hypertension, diabetes mellitus, coronary artery disease, and renal is responsible for excessive clinical mortality. COVID-19 infection can be exacerbated by the presence of cardiovascular disease as a comorbidity[4]. The increased morbidity noted in persons with pre-existing cardiovascular conditions stems from the interaction between COVID-19 and the circulatory system, resulting in myocardial injury and dysfunction. Approximately 8 - 12% of all cases of COVID-19 have acute heart injury, making it the most often observed cardiac

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anomaly. The primary mechanisms of cardiac injury include direct damage to the heart muscle cells caused by viral infection and the systemic inflammatory response[5]. These mechanisms, along with others such as acute myocardial infarction (MI), viral inflammation, viral myocarditis, and myocardial damage (MI) induced by oxidative stress, contribute to cardiovascular injury. The presence of Asprosin and N-terminal-pro hormone BNP (NT-proBNP) in COVID-19 patients has been observed to serve as a means of predicting cardiac risk and determining the prognosis of severe COVID-19 patients[6]. Increased levels of NT-proBNP have also been linked to the severity of COVID-19. Hence, it is crucial to closely monitor cardiac biomarkers to decrease the occurrence of morbidity and death associated with COVID-19 [6].

An important parameter that indicates the severity of infection with Covid-19 is the D-dimer [7]. D- dimer is an important marker of thrombus formation that is increased in early myocardial infarction (MI)[8, 9].

In order to achieve more compelling findings, a meta-analysis was conducted on cardiac biomarkers to ascertain the elevated titer of various cardiac markers in COVID-19 cases: CRP, ferritin, D-dimer, IgG, IgM, Subfatin, Asprosin, and NT Pro-BNP. The results were anticipated to serve as prognostic indicators of the severity and fatality rates in patients with COVID-19.

MATERIALS AND METHODS

Patients. From 1st July 2021 until 4th January 2022 was carried out in the isolation wards in Balad Ruz General Hospital and Baqubah Teaching Hospital/Diyala province / IRAQ, 19 patients who recovered from COVID-19 were gradually enrolled in our study. All patients were diagnosed according to the World Health Organization (WHO) guidance for COVID-19(10). The inclusion criteria were the following: positive nasal swab for COVID-19, admission due to suspected symptoms in the Balad Ruz General Hospital, or transfer from other health centers with a COVID-19 diagnosis. Patients with an absence of blood samples or inpatients for surgical purposes were excluded.

This study included 4 groups as follows:

Group 1(G1): The first group for a healthy individual, their number 20

Group 2(G2): The second group for heart failure patients, their number 25

Group 3(G3): The third group for heart failure patients with COVID-19, their number 25.

Group 4(G4): The fourth group for heart failure patients after recovery from COVID-19, group 3 but 6 patients died with coronavirus, their number 19.

Routine blood tests

C-reactive protein (CRP) and ferritin were measured using Cobas C-111 automated biochemistry analyzer. Related Coagulation functions (D-dimer and troponin) were determined using AFIS 6 - Biotech using the corresponding reagent. IgG, IgM, Subfatin, Asprosin, and NT Pro-BNP were examined by sandwich ELISA by using (Sunlong).

Statistical Analysis

The program SAS (Statistical Analysis System) version 2018 was applied to determine the influence that a number of different elements have on the parameters of the study, For the purpose of determining whether or not the comparison of percentages at a probability level of 0.05 and 0.01 can be considered statistically significant, the chi-square test was utilized in this investigation.

3. Result

This study showed an **increased** incidence of coronavirus in males than in females that were 72%, and 28% respectively, at a p-value <0.05 in Table 1.

Table 2 shows a total of 25 patients infected with coronavirus were separated into 2 groups according to ages that were 20(80%) in age between 35 – 50 years, and 5(20%) patients in age between 50 – 65 years, at p-value ≤0.01

As shown in Table (3), there was significant differences in the level of IgG, IgM, Ferritin, D-dimer, and CRP which highly increased in G3(7.573±1.231, 0.931 ± 0.103, 400 ± 137**,** 2596 ± 2397, 96.80 ± 18.33) and decreased in G4(2.550±0.776, 0.782±0.097, 65.09 ± 9.58, 460.45 ± 155.13, 22.57± 11.2). As for ferritin increased in heart G3, at p-value <0.001

As shown in Table 4, the result of this study shows a decreased level of Subfatin in G2 and G4(20.34±2.07, 23.39±1.86), while an increase in G3(36.12±3.91). The asprosin increase in G2, G3 and G4 compared to G1 (3.906±1.04, 4.102±0.851, 3.797±1.12, 1.681±0.15).

NT Pro-BNP highly increased in G3, followed by G4, then G2 (134.85± 26.05, 123.88± 22.73, 107.86±20.15) as compared with G1(67.19±18.44) at p-value <0.01.

Table 1: Distribution of sample study according to Sex

Sex	**No**	**Percentage (%)**
Male	18	72%
Female	7	28%
Total	25	100%
Chi-Square	6.0308 *	
P-value	0.0141	
* (P≤0.05).		

Table 2: Distribution of sample study according to Age groups

Age groups (year)	**No.**	**Percentage [%]**
35 – 50 yr.	20	80%
50 – 65 yr.	5	20%
Total	25	100%
Chi-Square	20.800 **	
P-value	0.0001	
** (P≤0.01).		

Table (3): Distribution of the study group according to the level of IgG, IgM, Ferritin, D-dimer, and C-RP

Factors	**Control(G1) 20**	**Heart failure patients(G2) 25**	**Heart failure with Covid-19(G3) 25**	**After 2 months of recovery(G4) 19**	**P-value**
IgG	1.669 ± 0.638 c	1.713± 0.579c	7.573± 1.231a	2.550± 0.776 b	<0.001 **
IgM	0.629± 0.121b	0.678± 0.063b	0.931 ± 0.103a	0.782 ± 0.097 ab	<0.001 *
Ferritin	69.09±16.8 b	43.37±12.7c	400 ± 137 a	65.09 ± 9.58 b	<0.001 *
D-dimer	208 ± 72.5 c	1029 ± 1319 b	2596 ± 2397 a	460.45 ± 155.13 b	<0.001**
CRP	19.13 ± 8.205 b	26.37 ± 9.761 b	96.80 ± 18.33 a	22.57± 11.2 b	0.001*

Table (4): Distribution of the study group according to the level of Subfatin, Asprosin, and **NT Pro-BNP**

Factors	**Healthy individual G1**	**Heart failure patients G2**	**Heart failure Patients with Covid-19 G3**	**After 3 months of recovery G4**	**P-value**
Subfatin ng/ml	**29.36±3.14** b	**20.34±2.07 c**	**36.12±3.91** A	**23.39±1.86** c	0.001
Asprosin	1.681±0.15 **b**	3.906±1.04 **a**	**4.102±0.851 A**	**3.797±1.12 a**	<0.05
NT Pro-BNP	67.19± 18.44 c	107.86± 20.15 b	134.85± 26.05 a	123.88± 22.73 ab	0.001

Discussion

Patients with heart failure are particularly susceptible to an elevated risk of severe infections due to their compromised immune system, overall weakness, and decreased ability to handle more severe illnesses[11].

This study shows an increased incidence of COVID-19 in heart failure males than females, which agrees with [12], which showed a higher incidence and mortality in males, while pulmonary disease was higher in females. Research has demonstrated that testosterone has a suppressive influence on the immune system in males, whereas estrogen has an augmenting effect on the immune system. Testosterone has been discovered to hinder the process of T helper cell differentiation [13] and shows a favorable relationship with the amount of Venezuelan equine encephalitis virus in macaques (VEEV) [14]. Examination of testosterone levels in females revealed that females with autoimmune disease generally have lower levels of testosterone compared to healthy females [15]. Estrogen possesses antiviral characteristics and offers protection against several viral diseases, such as HIV, Ebola, hepatitis C virus, and human cytomegalovirus (CMV) [16]. Due to its preference for replicating in airways, SARS is more likely to infect individuals with greater amounts of estrogen, particularly females [17].

Our study investigates the titer of anti-SARS-CoV-2 IgM and IgG antibodies in hospitalized COVID-19 patients, specifically focusing on one month after the onset of sickness. In general, the levels of IgM and IgG decreased during the second or third month following the commencement of sickness. The antibody response is crucial for the elimination of the virus and the prevention of further infections. This study supports the findings of [18], which demonstrates an initial increase in IgG and IgM levels in COVID patients compared to the control group, followed by a reduction after 4 and 8 weeks post-recovery. Prior research has documented the swift generation of particular IgM and IgG antibodies against SARS-CoV-2 within the initial week, with antibody levels reaching their highest point between 2 to 3 weeks following the commencement of the disease [19, 20]. The highest concentration of antibodies may not endure for extended periods. The decrease in serum IgM levels after reaching its highest point primarily occurred during the second month following the beginning. The virological assessment results showed that the SARS-CoV-2 nucleic acid of most patients became negative between the fourth and seventh week after the onset of sickness[21].

Further analysis of paired data demonstrated a considerable decrease in IgM levels after eradicating the virus. Therefore, it can be inferred that the IgM titer experiences a rapid increase during the initial two weeks, remains present for the subsequent one to two weeks as the virus is being eliminated, and then decreases by the fourth week after the onset of illness as the virus nucleic acid becomes negative [22]. Hence, the decrease in IgM levels can serve as a marker for eliminating the virus, aiding in identifying the actual absence of nucleic acid conversion when combined with RT-PCR testing. It could be used as a standard for determining when someone can be released from the hospital or when quarantine can be lifted, particularly for individuals with weak or no symptoms. Maintaining a consistent level of IgG is essential for developing long-lasting immunological memory and preventing reinfection. Previous research has shown that measurable antibodies remained present for over two years in patients infected with SARS-CoV and MERS-CoV [23].

This study demonstrated a decrease of ferritin in heart failure, while an increase in heart injury patients with COVID-19, but declined after recovery and reached to normal level. Anemia may contribute to the connection between iron shortage and the development of heart failure. The link between low ferritin levels and incident HF can be explained by various pathophysiological processes. Iron

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deficiency leads to a decrease in the levels and functioning of muscular oxidative enzymes and respiratory proteins, resulting in a disruption of cellular energy production [24]. Simultaneously, changes in structure such as enlargement of mitochondria and abnormalities in the arrangement of sarcomeres may occur. Regardless of the presence of anemia, it can potentially elevate catecholamine levels, which in turn contributes to heart hypertrophy. Collectively, these disruptions within the cells and neurohormonal systems may have a role in the progression of heart failure. A study conducted in Najaf, Iraq, demonstrated that individuals with COVID-19 exhibit elevated levels of WBCs, CRP, ALT, and AST in their serum, as compared to healthy volunteers [25]. Ferritin level serves as a predictive indicator and predicts the advancement to severe disease types [26, 27]. Severe COVID-19 complications are characterized by a hyperinflammatory state, which is marked by elevated levels of ferritin. This condition is linked to higher death rates, multiple organ failure, and the requirement for an intensive care unit (ICU) [28,29].

The current study also shows an increase in D-dimer in heart failure, but a 2-fold increase in its level when infected with coronavirus, which is an indicator of the patient's status. D-dimer functions as a byproduct of fibrin degradation and is therefore increased in situations where there is the formation or dissolution of blood clots across the entire circulatory system [30,31].

The concentration of C-reactive protein served as a moderately accurate predictor of the risk of heart disease and made only a little contribution to the predictive value of well-known risk factors for heart disease. COVID-19 infection leads to a hyperinflammatory state, which causes an elevation in C-reactive protein levels[32,33].

The present study showed a decrease of subfatin in heart failure patients, while an increase in covid patients with heart failure as compared with control. subfatin (also known as Meteorin-like (Metrnl), is a newly discovered adipokine that was decreased in heart disease patients. Subfatin is produced by monocytes, adipocytes, and skeletal muscle [34]. Severe muscle damage occurs in COVID-19 disease [35]. This muscle damage may have caused excessive subfatin release and thus subfatin accumulation in the circulation. In addition, subfatin may have increased in circulation as a result of a compensatory mechanism to reduce inflammation that occurred in the skeletal muscle due to COVID-19. Another reason for the increase in subfatin values due to the decrease in oxygen saturations may have been the increase in monocyte values due to COVID-19 infection since monocytes are an important subfatin production factory [34].

The current study found that circulating levels of asprosin are significantly elevated in heart failure patients when compared to controls, This study agrees with [36]. AL-hadidi and al-obaidi. demonstrated increased asprosin levels in atherosclerosis and myocardial infarction patients in comparison to controls [36].

In this study, asprosin values were found to increase in heart failure patients with COVID-19. Karagoz, Z. Karaca; AYDIN showed increased asprosin level as oxygen saturation decreased in patients with coronavirus [37]. In a study [38] conducted on patients with COVID-19, the asprosin values were reported to have decreased, which was contradictory to the results of the current study.

The current study demonstrates an elevation in NT Pro-BNP levels in individuals with heart failure disease compared to the control group. The rise in the NT-proBNP level was caused by reduced renal clearance rather than increased cardiac production, which is a subject of debate. This finding is consistent with the study conducted by [39], which demonstrated a rise in heart failure among patients with chronic kidney disease (CKD) as well as those without CKD. Prior evaluations have determined that heart disease is the main cause of an elevation in the

NT-proBNP level. Higher levels of NT-proBNP upon admission were linked to increased mortality and a higher likelihood of death or the need for mechanical ventilation in hospitalized COVID-19 patients who did not have a previous history of heart failure or cardiomyopathy [40]. Prior research has demonstrated that increases in cardiac biomarkers such as troponin and NT-proBNP are indicative of poorer outcomes in individuals with COVID-19[40].

CONCLUSION

Finally, there were notable disparities in the levels of CRP, ferritin, D-dimer, IgG, IgM, Subfatin, Asprosin, and NT Pro-BNP between heart failure patients, heart failure patients with Corona, and post-recovery heart failure patients with Corona. Significant variations in CRP, ferritin, D-dimer, IgG, IgM, Subfatin, Asprosin, and NT Pro-BNP levels were observed between individuals who experienced mortality and those who survived. Cardiac indicators such as IgG, IgM, NT-proBNP, Asprosin, and d-dimer levels are crucial laboratory measures for diagnosing and predicting the severity and mortality of COVID-19. The d-dimer has been identified as the most reliable indicator of the severity and fatality rates associated with COVID-19. This conclusion is based on numerous studies that have studied the d-dimer and found a high level of statistical significance ($P < 0.00001$). Additional investigation is necessary to ascertain the function of additional cardiac indicators in forecasting the prognosis of patients with COVID-19.

Conflict of interest: NIL

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REFERENCES

1. Jin, Y.-H., et al., *A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version).* Military medical research, 2020. **7**: p. 1-23.
2. Chen, N., et al., *Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study.* The Lancet, 2020. **395**(10223): p. 507-513.
3. Huang, C., et al., *Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China.* The Lancet, 2020. **395**(10223): p. 497-506.
4. Ji, H.-L., et al., *Elevated plasmin (ogen) as a common risk factor for COVID-19 susceptibility.* Physiological reviews, 2020.
5. Bansal, M., *Cardiovascular disease and COVID-19.* Diabetes & Metabolic Syndrome: Clinical Research & Reviews, 2020. **14**(3): p. 247-250.
6. Han, H., et al., *Analysis of heart injury laboratory parameters in 273 COVID-19 patients in one hospital in Wuhan, China.* Journal of Medical Virology, 2020. **92**(7): p. 819-823.
7. Yao, Y., et al., *D-dimer as a biomarker for disease severity and mortality in COVID-19 patients: a case control study.* Journal of Intensive Care, 2020. **8**: p. 1-11.
8. Mansour, H.M. and Y.N. El-Sakhawy, *Initially presented acute coronary syndrome: does D-dimer imply any clinical significance?* The Egyptian Journal of Haematology, 2020. **45**(1): p. 23-27.
9. Reihani, H., A.S. Shamloo, and A. Keshmiri, *Diagnostic value of D-dimer in acute myocardial infarction among patients with suspected acute coronary syndrome.* Cardiology research, 2018. **9**(1): p. 17.
10. Yameny, A. COVID-19 Laboratory diagnosis methods. *Journal of Bioscience and Applied Research*, 2023; 9(2): 94-101. doi: 10.21608/jbaar.2023.311827
11. Bischof, E., J. Wolfe, and S.L. Klein, *Clinical trials for COVID-19 should include sex as a variable.* The Journal of Clinical Investigation, 2020. **130**(7): p. 3350-3352.
12. Nguyen, N.T., et al., *Male gender is a predictor*

of higher mortality in hospitalized adults with COVID-19. PloS One, 2021. **16**(7): p. e0254066.

13. Kissick, H.T., et al., *Androgens alter T-cell immunity by inhibiting T-helper 1 differentiation.* Proceedings of the National Academy of Sciences, 2014. **111**(27): p. 9887-9892.
14. Muehlenbein, M.P., et al., *Testosterone correlates with Venezuelan equine encephalitis virus infection in macaques.* Virology Journal, 2006. **3**: p. 1-5.
15. Singh, A., R. Singh, and M.K. Tripathi, *Evaluation of the sex steroids mediated modulation of leucocyte immune responses in an ophidian Natrix piscator.* Current Research in Physiology, 2022. **5**: p. 355-360.
16. Suba, Z., *Prevention and therapy of COVID-19 via exogenous estrogen treatment for both male and female patients: Prevention and therapy of COVID-19.* Journal of Pharmacy & Pharmaceutical Sciences, 2020. **23**: p. 75-85.
17. Pradhan, A. and P.-E. Olsson, *Sex differences in severity and mortality from COVID-19: are males more vulnerable?* Biology of Sex Differences, 2020. **11**(1): p. 53.
18. Zhou, W., et al., *The dynamic changes of serum IgM and IgG against SARS-CoV-2 in patients with COVID-19.* Journal of Medical Virology, 2021. **93**(2): p. 924-933.
19. Lou, B., et al., *Serology characteristics of SARS-CoV-2 infection after exposure and post-symptom onset.* European Respiratory Journal, 2020. **56**(2).
20. Long, Q.-X., et al., *Antibody responses to SARS-CoV-2 in patients with COVID-19.* Nature Medicine, 2020. **26**(6): p. 845-848.
21. Zhao, J., et al., *Antibody responses to SARS-CoV-2 in patients with novel coronavirus disease 2019.* Clinical infectious diseases, 2020. **71**(16): p. 2027-2034.
22. Wang, Y., et al., *A polymeric solid-phase microextraction fiber for the detection of pharmaceuticals in water samples.* Journal of Chromatography A, 2020. **1623**: p. 461171.
23. Payne, D.C., et al., *Persistence of antibodies against Middle East respiratory syndrome coronavirus.* Emerging infectious diseases, 2016. **22**(10): p. 1824.
24. Brownlie IV, T., et al., *Tissue iron deficiency without anemia impairs adaptation in endurance capacity after aerobic training in previously untrained women.* The American journal of clinical nutrition, 2004. **79**(3): p. 437-443.
25. Abd, M.A.A., *The C-Reactive Protein to Albumin Ratio as a predictive factor in a sample of COVID-19 patients admitted to the hospital.* Journal of Kufa for Chemical Sciences, 2022. **2**(8): p. 262-275.
26. Henry, B.M., et al., *Hematologic, biochemical and immune biomarker abnormalities associated with severe illness and mortality in coronavirus disease 2019 (COVID-19): a meta-analysis.* Clinical Chemistry and Laboratory Medicine (CCLM), 2020. **58**(7): p. 1021-1028.

27 Yameny, A. Ferritin as a biomarker of infection in COVID-19 non-hospitalized patients. *Journal of Bioscience and Applied Research*, 2021; 7(1): 23-28. doi: 10.21608/jbaar.2021.172371

28. Gómez-Pastora, J., et al., *Hyperferritinemia in critically ill COVID-19 patients–is ferritin the product of inflammation or a pathogenic mediator?* Clinica chimica acta; International Journal of clinical chemistry, 2020. **509**: p. 249.
29. Pérez-García, N., et al., *Comparison of analytical values D-Dimer, glucose, ferritin and C-reactive protein of symptomatic and asymptomatic COVID-19 patients.* International Journal of Environmental Research and Public Health, 2022. **19**(9): p. 5354.
30. Koracevic, G.P., *Pragmatic classification of the causes of high D-dimer.* The American journal of emergency medicine, 2009. **27**(8): p. 1016. e5-7.

31 Yameny, A. D-dimer levels in COVID-19 out-hospitalized patients in Egypt. *Journal of*

Medical and Life Science, 2021; 3(1): 19-24. doi: 10.21608/jmals.2021.200216

32. Dadmanesh, M., et al., *Lower serum levels of Meteorin-like/Subfatin in patients with coronary artery disease and type 2 diabetes mellitus are negatively associated with insulin resistance and inflammatory cytokines.* PloS one, 2018. **13**(9): p. e0204180.
33 Alabd, S., Yameny, A. C-Reactive Protein as a Prognostic Indicator in COVID-19 Mild Infection Patients. *Journal of Medical and Life Science*, 2021; 3(2): 38-43. doi: 10.21608/jmals.2021.240126
34. Jung, T.W., et al., *METRNL attenuates lipid-induced inflammation and insulin resistance via AMPK or PPARδ-dependent pathways in skeletal muscle of mice.* Experimental & molecular medicine, 2018. **50**(9): p. 1-11.
35. Ali, A.M. and H. Kunugi, *Skeletal muscle damage in COVID-19: a call for action.* Medicina, 2021. **57**(4): p. 372.
36. Al-Hadidi, E.E.K. and W.M.L. Al-Obaidi, *Assessment of asprosin level and some of physiological variables in patients with cardiovascular diseases in Kirkuk city, Iraq.* Biomedicine, 2022. **42**(5): p. 973-977.
37. Karagoz, Z.K. and S. Aydin, *Effects of oxygen saturation on the hypoxia-inducible factor-1α, subfatin, asprosin, irisin, c-reactive protein, maresin-1, and diamine oxidase in diabetic patients with COVID-19.* Eur Rev Med Pharmacol Sci, 2022. **26**(24): p. 9489-9501.
38. Seyhanli, E.S., et al., *Asprosin and Oxidative Stress Level in COVID-19 Patients.* Clinical Laboratory, 2022. **68**(1).
39. Fu, S., et al., *The ability of NT-proBNP to detect chronic heart failure and predict all-cause mortality is higher in elderly Chinese coronary artery disease patients with chronic kidney disease.* Clinical interventions in aging, 2013: p. 409-417.
40. Guo, T., et al., *Cardiovascular implications of fatal outcomes of patients with coronavirus disease 2019 (COVID-19).* JAMA cardiology, 2020. **5**(7): p. 811-818.