SHORT COMMUNICATION

The independent prediction study of the effect of heart-type fatty acid binding protein on the severity and long-term cardiac function in Covid-19 patients

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Abstract

The study was conducted to assess the predictive ability of the heart-type fatty acid binding protein (HFABP) on the severity and long-term cardiac function of Covid-19 infected persons. In the case of negative HsTn-T, we determined whether HFABP was related to the severity of Covid-19 or it was the long-term impact of cardiac function. Chi-square test and t-test were used to evaluate whether HFABP level was an independent predictor of myocardial injury and whether it was related to the severity of Covid-19 and the long-term impact of cardiac function. Among the 20 patients in each of the two groups (mild and severe), 27.5% of all had elevated HFABP. Two were HFABP positive in the mild group, and nine were HFABP positive in the severe group, with a significant difference between the two groups (P=0.013). The mean serum level of HFABP in the mild group was 3.96 ±1.80, compared with 6.70±3.77 in the severe group, with a significant difference between the two groups (P=0.003). In addition, after two years of follow-up, there was a statistically significant difference in the changes of cardiac function between the HFABP-positive group and the HFABP-negative group (P=0.037). These data indicate that among HsTn-T-negative Covid-19 patients, HFABP is a more sensitive and independent predictor of myocardial damage, and it is useful for distinguishing mild and severe Covid-19. The level of HFABP has a significant effect on the long-term changes of heart function in Covid-19 patients.

Keywords: Heart-type fatty acid binding protein (HFABP), Covid-19, severity, cardiac function.

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Introduction

Currently, there is an outbreak all over the world, and a new type of coronavirus named 2019 new coronavirus (2019-nCoV) is circulating.[1-5] At present, many countries in the world are reporting an increasing number of cases. Although a variety of vaccines against this virus have been developed, in the face of such a rapid outbreak and epidemic, the progress of vaccine promotion is too weak.[6,7]

HFABP is an early biomarker of myocardial injury and has a high degree of cardiac specificity.[6, 8] Our study focussed on the relationship between HFABP level and the severity of the disease in HsTn-T-negative Covid-19 patients.

Patients and Methods

With the approval from the Ethics Committee of Chongqing University Three Gorges Hospital, Wanzhou District, Chongqing, China, 40 Covid-19 patients admitted to Chongqing University Three Gorges Hospital from January 1 to April 30, 2020 and their outpatient follow-up medical records within 2 years (before May 1, 2022) were retrospectively enrolled in this study. The inclusion criteria were: patients diagnosed with Covid-19 (diagnosis based on Chinese guidelines);[7] age > 14 years; negative serum HsTn-T; and serum HFABP concentration monitored during hospitalisation. The exclusion criteria were: age < 14 years; elevated serum HsTn-T; and lack of serum HFABP test. Currently, the diagnostic guidelines for Covid-19 in China are based on a pooled analysis of clinical manifestations, physical signs, and laboratory characteristics.[7] The patients were divided into two groups: mild and severe. Their serum HFABP levels were followed-up during hospitalisation. These patients were followed-up for a two-year period after discharge and their heart function was assessed using the New York Heart Association functional class (NYHA).[9]

The categorical variables were represented by numbers (%). The normality or skewness of the data distribution was analysed by the Shapiro-Wilk (S-W) test. For the presentation of the continuous data with the normal distribution, mean and the standard deviation were used, while for the continuous data with the skewed distribution, Median and Inter-Quartile Range (IQR) were used. The chi-square test or Wilcoxon rank sum test was used to compare mild and severe Covid-19 patients, and the chi-square test or t-test was used to analyse the

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clinical features and clinical outcomes.

IBM SPSS Statistics version 23 was used for statistical analysis, and statistical significance was defined as a P value lower than 0.05.

Results

In our study, all patients diagnosed with Covid-19 at the Chongqing University Three Gorges Hospital between January 1 and April 30, 2020 were screened. Finally, 40 patients (20 with severe disease and 20 with mild disease) were included in this study. The disease characteristics and demographic characteristics of 40 Covid-19 patients (20 with mild Covid-19 and 20 with severe Covid-19) are shown in Table 1. Nine (45.0%) out of the 20 patients in the severe group had an elevated serum level of HFABP, and 2 (10.0%) of the 20 patients in the mild group had an elevated serum level of HFABP. The analysis of serum HFABP levels showed a non-normal distribution; HFABP level in the mild group was between 1.76 ng/mL and 9.80 ng/mL (mean 3.96 ±0.28, 95% CI 0.89–4.57), while in the severe group it was between 2.90 ng/mL and 18.52ng/mL (mean 6.70 ±0.84, 95% CI 1.30–4.16).

Table-1: Demographic and disease characteristics of enrolled patients

Characteristics	Group; no. (%) of the patients*		
	All (n =40)	Mild Covid-19 (n =20)	Severe Covid-19 (n=20)
Male/Female sex	22	14 (70.0)/ 6 (30.0)	11(55.0)/9 (45.0)
MeanAge,(years)	50.2	58.8 (±16.7)	41.9 (±10.5)
Tobacco smoking	3	2 (10.0)	1 (5.0)
Fever	8	6 (30.0)	2 (10.0)
Any comorbidity			
Diabetes	7	0 (0)	7 (35.5)
Hypertension	4	2 (10.0)	2 (10.0)
Cardiovascular disease	2	0 (0)	2 (10.0)
Malignancy	0	0 (0)	0 (0)
COPD	4	0 (0)	4 (20.0)
CLD	0	0 (0)	0 (0)
CKD	0	0 (0)	0 (0)

Chronic obstructive pulmonary disease=COPD, Chronic liver disease=CLD, Chronic kidney disease=CKD. Note: All differences were statistically non-significant. SD = standard deviation *Except as indicated for Age

Table 2 shows the relationship between the levels of HFABP and the severity of Covid-19. Among Covid-19 patients, the positive rate of HFABP in the severe group was significantly higher than that in the mild group (45.0% vs 10.0%, P = 0.013). There was a significant difference in the mean HFABP level between the severe group and the mild group (3.97 ±1.80 vs 7.53 ±4.76, P = 0.003) (Table 2). In addition, after two years of follow-up, six patients in each of the HFABP positive and HFABP negative groups had a decline in NYHA, and there was a significant difference between the two groups (54.5% vs 20.7%, P = 0.037)) (Table 3).

Table-2: Clinical outcomes of the matched study population of Covid-19 with HFABP levels

Clinical outcomes	Mild COVID-19 group N=20	Severe COVID-19 group N=20	P value
HFABP positive (%)	2 (10.0)	9(45.0)	0.013*
HFABP (ng/mL, ±SD)	3.97 (±1.80)	7.53 (±4.76)	0.001#

HFABP, heart fatty acid-binding protein; P<0.05; *Chi-Square test; #, Wilcoxon rank sum test.

Table-3: NYHA outcomes of the matched study population of Covid-19 with HFABP two years after discharge

Clinical outcomes	HFABP positive group N=11	HFABP negative group N=29	P value
NYHA Decreased	6	6	0.037*

NYHA, New York Heart Association functional class; P<0.05; *Chi-Square test.

Discussion

Covid-19 has caused a global pandemic, and in-depth research is underway to assist global anti-epidemic efforts. Reliable and rapid diagnosis of the disease and early vaccination are the key to the treatment and control of the epidemic.[3-5, 10, 11] Studies by Hailong Wang et al have confirmed that HFABP levels are related to the severity of Covid-19,[12] however, whether there is still a correlation in patients without myocardial injury (HsTn-T negative) remains to be further studied. Therefore, in this study, we performed an analysis of HsTn-T-negative patients. This study included 40 confirmed Covid-19 patients, and all of them had normal HsTn-T monitoring. The serum HFABP level may be more sensitive and allow earlier prediction of myocardial injury than HsTn-T. Moreover, the serum HFABP concentration showed a more stable performance than HsTn-T. This happens because, like other viruses, the new coronavirus also induces the secretion of a large number of inflammatory factors after infecting the human body.[13-16] thereby leading to inflammatory lung injury and myocardial damage. In a state of insufficient oxygen concentration in the blood, tissues such as the heart and blood vessels secrete more HFABP into the blood, which leads to an increase in the concentration of serum HFABP. 45% of severely ill persons were serum HFABP positive, with the mean serum level of HFABP being 6.70 ng/mL, while only 10% of patients in the mild group were serum HFABP positive, with the mean serum HFABP level of only 3.96 ng/mL. There were significant differences in the positive rate of serum HFABP and in the mean serum concentration of HFABP between the two groups.

Therefore, serum HFABP has important clinical value for the diagnosis and prediction of patients with mild or severe Covid-19. More laboratory indicators are needed to assess the severity of Covid-19, so serum HFABP monitoring can be used as a very valuable biomarker. HFABP level can guide clinicians to distinguish the mild form from the severe form of Covid-19 in a short time, while serum HFABP concentration may also reflect the severity and prognosis of Covid-19 patients.

Two years later, NYHA was used to assess heart function in these discharged patients.[9] The study revealed that these HFABP-positive patients had significantly decreased heart function. Therefore, we believe that these patients with elevated HFABP on admission are at risk of worsening long-term heart function.

In addition, there were two deaths among the 40 HsTn-T-negative Covid-19 patients included in the study, and both of these had severe Covid-19; one patient had an elevated serum HFABP level and one had a normal serum HFABP level. The expired cases were included in the statistical analysis, and there was no statistically significant difference in mortality between the elevated serum HFABP level group (positive) and the normal group (negative). However, the sensitivity and specificity of the included cases was not analysed because the number of cases that met the inclusion criteria was very small, and the results had selection bias. These conclusions need to be further proved with a larger number of cases.

Conclusion

In summary, in Covid-19 patients who are negative for HsTn-T, there was a significant difference in the positive rate of serum HFABP and in the mean HFABP between the mild and the severe groups. Therefore, for HsTn-T-negative Covid-19 sick persons, serum HFABP level has good clinical value for distinguishing mild and severe Covid-19 cases, and for predicting the conversion of mild to severe disease. In terms of affecting the mortality of Covid-19 sick persons, due to the small number of cases that met the selection criteria, there was a lack of significant predictive value.

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