Analysis of Risk Factors for Adverse Cardiovascular Events in Elderly Patients with Acute Myocardial Infarction and Non-Alcoholic Fatty Liver Disease (NAFLD)

Authors' Contribution:
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Background: The present research aimed to explore the risk factors for adverse cardiovascular events in elderly patients with acute myocardial infarction (AMI) combined with NAFLD.

Material/Methods: We included 325 AMI patients hospitalized in the Department of Cardiology. AMI patients underwent emergency thrombolysis or percutaneous coronary intervention (PCI). AMI patients were classified into NAFLD group and non-NAFLD group. General clinical data, creatinine and myocardial enzyme, GRACE scores of AMI patients were evaluated and compared between two groups. Incidence of adverse cardiovascular events, including ECG instability, hemodynamic instability and death were evaluated.

Results: Compared to patients in the non-NAFLD group, patients in the NAFLD group had remarkably lower proportions of diabetic patients (p=0.001), coronary heart disease (CHD) patients (p=0.027), and CABG/PCI patients (p<0.001), and had significantly higher EF values (p=0.042). Meanwhile, the proportion of adverse cardiovascular events (ECG instability (p<0.001), hemodynamic instability (p=0.033), and deaths (p=0.016)) in patients in the NAFLD group was significantly higher compared to patients in the non-NAFLD group. Multivariate logistic regression analysis showed that GRACE score >140 (OR: 3.005, 95% CI: 1.504–6.032), EF <35% (OR: 2.649, 95% CI: 1.364-4.346), diabetes (OR: 1.308, 95% CI: 1.072–1.589), and NAFLD (OR: 1.112, 95% CI: 1.043–1.324) were independent predictors for elderly AMI patients' adverse cardiovascular events.

Conclusions: The risk for adverse cardiovascular events in elderly acute myocardial infarction patients who also had NAFLD was significantly higher. Therefore, strengthening monitoring and active treatment for elderly AMI patients who also have NAFLD could reduce the incidence of adverse cardiovascular events and improve survival rate prognosis.

MeSH Keywords: **Cardiovascular Abnormalities • Fatty Liver, Alcoholic • Hepatitis, Alcoholic • Myocardial Infarction • Risk Factors**

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Background

Acute myocardial infarction (AMI) is a critical emergency endangering human health, with high mortality and disability rates [1,2]. Although drug therapy and interventional therapy for AMI have been significantly improved, occurrence of adverse cardiovascular events is also higher in elderly AMI patients [3]. With the development of society in China, the number of elderly patients experiencing AMI is steadily increasing [4]. Clinically, the disease condition is serious, the mortality rate is high, and prognosis is poor.

Non-alcoholic fatty liver disease (NAFLD) is a hepatic disorder triggered by alcohol abuse and the other factors [5,6]. NAFLD is clinicopathologically characterized by diffuse hepatocyte bullous steatosis. NAFLD mainly includes simple fatty liver disease and cirrhosis from simple fatty liver and non-alcoholic steatohepatitis (NASH) [7,8]. The prevalence for NAFLD has been remarkably increased year by year and also demonstrates an especially higher prevalence in elderly, which seriously affects the health and life of elderly patients [9]. A previous study [10] focusing on NAFLD patients showed that cardiovascular disease is an important cause of death. Additionally, there is a relationship between NAFLD and metabolic syndrome [11,12], which greatly promotes the risk of recurrence of cardiovascular disorders.

The present study explored risk factors for adverse cardiovascular events in elderly AMI patients with NAFLD. Our results may improve clinical treatment for elderly AMI patients with NAFLD.

Material and Methods

Patients and grouping

We enrolled AMI patients hospitalized in the Department of Cardiology from June 2015 to June 2018. We mainly included AMI patients over the age of 60 years undergoing emergency thrombolysis or percutaneous coronary intervention (PCI). WE excluded patients with history of myocardial infarction and bundle branch block on electrocardiogram (EEG). The sample size was also evaluated using Epitools software. This study finally included 325 AMI patients, including 182 (56%) males and 143 (44%) females, and the sample size of which was sufficient. Table 1 displays the age and disease types of AMI. According to the results of abdominal ultrasound and whether a patient had NAFLD, AMI patients were classified into the NAFLD group (n=111) and non-NAFLD group (n=214).

This study was approved by Ethics Committee of Tianjin First Central Hospital, Tianjin, China. All patients involved in this study provided written informed consent.

Table 1. Basic characteristics for the 325 AMI patients.

	Values
Gender	
Males (n)	182
Females (n)	143
Age (years)	70.24±9.46
Disease types (n)	
Acute anterior myocardial infarction	98
Acute inferior myocardial infarction	88
Acute non ST segment elevation myocardial infarction	72
Acute inferior and right ventricular myocardial infarction	43
Acute anterior and inferior myocardial infarction	17
Myocardial infarction in other parts	7

AMI-related inspection and laboratory inspection

We determined whether the AMI patients were complicated with other diseases and had a smoking history. Using methods described in a previous study [13], we recorded data on blood pressure, heart rate, time from onset to visit, electrocardiogram, type of acute myocardial infarction, abdominal ultrasound, cardiac ultrasound, and coronary angiography. The creatinine and myocardial enzyme levels were assessed as in a previous study [14]. The GRACE scores of the AMI patients were also evaluated based on a previous report [15].

Adverse cardiovascular events and evaluations

Adverse cardiovascular events included ECG instability (ventricular tachycardia or ventricular fibrillation or atrioventricular block), hemodynamic instability (systolic blood pressure <90 mmHg caused by heart failure or shock or non-drug reasons), and death during hospitalization. ECG instability of the patients was defined based on a previous study [16], and hemodynamic instability was defined according to a previously published study [17].

Statistical analysis

Count data were represented as number of positive cases or positive rate and analyzed using the chi-square test. Measurement data were defined as the mean value±standard deviation (SD) were analyzed using Tukey's post hoc validated ANOVA test. The multivariate logistic regression analysis was performed to evaluate risks for adverse cardiovascular events during hospitalization in patients in the NAFLD and non-NAFLD

Table 2. Comparison of baseline data between NAFLD group and non-NAFLD group.

Parameters	NAFLD group (n=111)		Non-NAFLD group (n=214)		χ^2/t value	p value
Male [cases (%)]	62	(56)	128	(60)	0.471	0.492
Age (years)	69.3±9.18		71.1±8.82		1.262	0.208
Hypertension [cases (%)]	60	(54)	122	(57)	0.259	0.611
Diabetes [cases (%)]	73	(66)	101	(47)	10.132	0.001
Coronary heart disease [cases (%)]	84	(76)	136	(64)	4.913	0.027
CABG/PCI [cases (%)]	38	(34)	34	(16)	14.265	<0.001
Smoking [cases (%)]	80	(72)	158	(74)	0.115	0.734
Anterior wall myocardial infarction [cases (%)]	65	(59)	128	(60)	0.048	0.827
Inferior wall myocardial infarction [cases (%)]	39	(35)	71	(33)	0.125	0.724
Right ventricular infarction [cases (%)]	7	(6)	15	(7)	0.057	0.811
EF (%)	40±12		51±13		2.500	0.042
EF <35% [cases (%)]	50	(45)	45	(21)	20.38	<0.001
Time from onset to visit <8 h [cases (%)]	91	(82)	183	(86)	0.689	0.406
Time from onset to visit <12 h [cases (%)]	101	(91)	200	(93)	0.65	0.420
Aspirin [cases (%)]	111	(100)	212	(99)	1.044	0.307
Clopidogrel [cases (%)]	109	(98)	212	(99)	0.452	0.501
β-blocker [cases (%)]	65	(59)	128	(60)	0.048	0.827
ACEI [cases (%)]	98	(88)	199	(93)	2.053	0.152
Statin [cases (%)]	110	(99)	212	(99)	0.001	0.976
Thrombolytic therapy [cases (%)]	39	(35)	91	(43)	1.662	0.197
Emergency PCI treatment [cases (%)]	72	(65)	123	(57)	1.662	0.197

CABG – coronary artery bypass grafting; PCI – percutaneous coronary intervention; EF – ejection fraction in heart; ACEI – angiotensin-converting enzyme inhibitor.

group. SPSS Statistical Software (version: 21.0, SPSS, Inc., Chicago, IL, USA) was used for data analyses, and *p* value less than 0.05 was defined as a statistically significant difference.

Results

AMI patients complicated with NAFLD were more likely to have diabetes and heart disease

Basic clinical data for the NAFLD group and non-NAFLD group showed that compared to patients in the non-NAFLD group (66%), those patients in the NAFLD group (47%) were more likely to also have diabetes (Table 2, *p*=0.001). The incidence rate of coronary heart disease in the NAFLD group (76%) was significantly higher than in the non-NAFLD group (64%) (Table 2, *p*=0.027).

AMI patients complicated with NAFLD were more likely to receive CABG/PCI treatment

The results demonstrated that compared with the AMI patients in the non-NAFLD group, the proportion of AMI patients undergoing CAGB/PCI treatment was remarkably higher than in the NAFLD group (Table 2, *p*<0.001).

AMI patients complicated with NAFLD had lower ejection fraction

The heart ejection fraction was analyzed in AMI patients both groups. Our results indicated that EF values of AMI patients in the NAFLD group were obviously lower compared to that of AMI patients in the non-NAFLD group (Table 2, *p*=0.042). Moreover, the proportion of AMI patients with EF <35% values

Table 3. Comparison of adverse cardiovascular events observed during hospitalization between NAFLD group and non-NAFLD group.

Adverse events	NAFLD group (n=111)	Non-NAFLD group (n=214)	χ^2 value	p value
Hemodynamic instability	26 (33)	30 (14)	4.533	0.033
ECG instability [cases (%)]	29 (26)	12 (15)	27.914	<0.001
Death [cases (%)]	8 (7)	4 (5)	5.857	0.016

Table 4. Multivariate logistic regression analysis of early adverse events.

Predictors	OR (95% CI)	p values
GRACE score >140	3.005 (1.504–6.032)	0.002
EF <35%	2.649 (1.364–4.346)	0.009
Diabetes	1.308 (1.072–1.589)	0.015
NAFLD	1.112 (1.043–1.324)	0.024

EF – ejection fraction in heart.

in the NAFLD group were significantly higher than in AMI patients in the non-NAFLD group (Table 2, *p*<0.001).

AMI patients complicated with NAFLD had higher rates of adverse cardiovascular events

We studied the adverse cardiovascular events, including ECG instability, hemodynamic instability, and death, in patients of both groups. Our results indicated that the incidence of ECG instability in the NAFLD group (26%) was remarkably higher than in the non-NAFLD group (15%) (Table 3, *p*<0.001). The incidence of hemodynamic instability in AMI patients in the NAFLD group (23%) was also remarkably higher than in the non-NAFLD group (14%) (Table 3, *p*=0.033). Furthermore, compared with AMI patients in the NAFLD group (7%), the mortality rate of AMI patients in the non-NAFLD group (5%) was remarkably higher (Table 3, *p*=0.016).

Independent predictors for adverse cardiovascular events of elderly AMI patients complicated with NAFLD

To analyze independent predictors for adverse cardiovascular events of AMI patients complicated with NAFLD, we conducted multivariate logistic regression analysis of the data, showing that GRACE scores >140 (OR: 3.005, 95% CI: 1.504–6.032, *p*=0.002), EF <35% (OR: 2.649, 95% CI: 1.364–4.346, *p*=0.009), diabetes (OR: 1.308, 95% CI: 1.072–1.589, *p*=0.015), and NAFLD (OR: 1.112, 95% CI: 1.043–1.324, *p*=0.024) were independent predictors for adverse cardiovascular events in elderly patients with AMI combined with NAFLD (Table 4).

Discussion

The mortality and disability rates of AMI patients are very high, making AMI a serious threat to human health [18]. The physiology and structure of the cardiovascular system of elderly people usually exhibit many changes [19,20], including endothelial dysfunction, decreased vascular compliance, structural changes in the left ventricle, abnormalities of left-ventricular systolic functions, abnormalities of diastolic functions, and changes in autonomic nerve regulation and neurohumoral function. Moreover, the occurrence of adverse cardiovascular events in elderly AMI patients appears to be increased by many factors [21,22], including comorbidity with other disorders, poor response to pain, and the delayed treatment. Therefore, we high-risk elderly AMI patients should be identified to strengthen monitoring and provide prompt treatment, which would help reduce the incidence of adverse cardiovascular events.

NAFLD is a metabolic stress-induced liver disorder that is associated with insulin resistance and genetic susceptibility [23]. With improved living standards, the aging of society, the wide application of ultrasound technology, and improvement of diagnosis, the incidence of NAFLD has been increasing in recent years [24]. The prevalence of NAFLD is steadily increasing as the population ages [25]. The prevalence of clinically diagnosed NAFLD in adults ranges from 17% to 33% [26]. In this study, we assessed 325 elderly patients with acute myocardial infarction, including 111 patients with NAFLD (34.15%).

NAFLD is considered to be a risk factor for cardiovascular diseases [27]. The intima-media thickness (IMT) is an early indicator of atherosclerosis [28]. A study [29] reported that NAFLD is correlated with increased carotid IMT. A previous study [30] investigated the correlation between CIMT and NAFLD, showing that the CIMT of NAFLD patients was significantly greater. Additionally, other studies [31,32] also demonstrated that the incidence rates of cardiovascular disease, diabetes, hypertension, and metabolic syndrome in NAFLD patients are remarkably higher than in in patients without NAFLD. The present study also demonstrated that the incidence rates of coronary heart disease and diabetes in AMI patients with NAFLD were significantly higher than in AMI patients without NAFLD.

Cardiovascular disease is an important cause of death among NAFLD patients [27]. In the past, fatty liver was considered to be a benign manifestation of liver disease; however, in recent years, coronary heart disease has been recognized as an important cause of premature death in NAFLD patients [33]. We found that the incidence of adverse cardiovascular events such as ECG instability, hemodynamic instability, and death in elderly AMI patients complicated with NAFLD were remarkably higher compared to the non-NAFLD group, which may be due to the high prevalence of diabetes mellitus, serious coronary artery disease, and the poor cardiac function. Our results also confirmed that the proportions of AMI patients undergoing CABG and PCI in the NAFLD group were significantly higher than in the non-NAFLD group. We also found that the EF values of hearts in AMI patients in the NAFLD group were significantly lower than in AMI patients in the non-NAFLD group. The multivariate logistic regression findings demonstrated that GRACE scores more than 140, EF <35%, diabetes mellitus, and NAFLD were the independent predictors for adverse cardiovascular events in elderly AMI patients. A previous study [34] also demonstrated that the proportion of AMI patients with coronary multi-vessel disorder in the NAFLD group was remarkably higher compared to the non-NAFLD group, which suggests that NAFLD is related to the severity of coronary artery disease.

The present investigation has some limitations. First, it was a single-center investigation with a small sample size. Second, the severity of NAFLD patients was not graded. Third, long-term follow-up was not performed in NAFLD patients. Fourth, the relationship between improvement/aggravation of NAFLD and the adverse cardiovascular events in AMI patients was not assessed. Therefore, the long-term prognosis for elderly AMI patients with NAFLD needs to be further studied.

Conclusions

NAFLD, as a risk factor for cardiovascular disease, is associated with the severity of coronary artery disease. NAFLD is an independent predictor of adverse cardiovascular events in elderly acute myocardial infarction patients. NAFLD can be an early warning sign in elderly acute myocardial infarction patients. Therefore, strengthening monitoring and enhancing treatment for elderly AMI patients complicated with NAFLD could reduce the incidence of adverse events during hospitalization, promote survival, and improve prognosis.

Conflict of interest

None.

References:

1. You L, Pan YY, An MY et al: The cardioprotective effects of remote ischemic conditioning in a rat model of acute myocardial infarction. Med Sci Monit, 2019; 25: 1769–79

2. Vogel B, Claessen BE, Arnold SV et al: ST-segment elevation myocardial infarction. Nat Rev Dis Primers, 2019; 5: 39

3. Andrechuk CR, Ceolim MF: Sleep quality and adverse outcomes for patients with acute myocardial infarction. J Clin Nurs, 2016; 25: 223–30

4. Jiang Z, Dreyer RP, Spertus JA et al: Factors associated with return to work after acute myocardial infarction in China. JAMA Netw Open, 2018; 1: e184831

5. Alswat KA, Fallatah HI, Al-Judaibi B et al: Position statement on the diagnosis and management of non-alcoholic fatty liver disease. Saudi Med J, 2019; 40: 531–40

6. Jennison E, Patel J, Scorletti E et al: Diagnosis and management of non-alcoholic fatty liver disease. Postgrad Med J, 2019; 95: 314–22

7. Tacke F: Cenicriviroc for the treatment of non-alcoholic steatohepatitis and liver fibrosis. Expert Opin Investig Drugs, 2018; 27: 301–11

8. Buzzetti E, Pinzani M, Tsochatzis EA: The multiple-hit pathogenesis of non-alcoholic fatty liver disease (NAFLD). Metabolism, 2016; 65: 1038–48

9. Zhang Z, Qi Y, Kong W et al: Efficacy and clinical value of liraglutide for treatment of diabetes mellitus complicated by non-alcoholic fatty liver disease. Med Sci Monit, 2018; 24: 7399–404

10. Adams LA, Anstee QM, Tilg H et al: Non-alcoholic fatty liver disease and its relationship with cardiovascular disease and other extrahepatic diseases. Gut, 2017; 66: 1138–53

11. Kim D, Touros A, Kim WR: Nonalcoholic fatty liver disease and metabolic syndrome. Clin Liver Dis, 2018; 22: 133–40

12. Sookoian S, Pirola CJ: Nonalcoholic fatty liver disease and metabolic syndrome: Shared genetic basis of pathogenesis. Hepatology, 2016; 64: 1417–20

13. Alexander M, Loomis AK, van der Lei J et al: Non-alcoholic fatty liver disease and risk of incident acute myocardial infarction and stroke: Findings from matched cohort study of 18 million European adults. BMJ, 2019; 367: l5367

14. Sodoh WE, Eregie CO, Nwaneri DU et al: The diagnostic value of both troponin T and creatinine kinase isoenzyme (CK-MB) in detecting combined renal and myocardial injuries in asphyxiated infants. PLoS One, 2014; 9: e91338

15. Chen YH, Huang SS, Lin SJ: TIMI and GRACE risk scores predict both short-term and long-term outcomes in Chinese patients with acute myocardial infarction. Acta Cardiol Sin, 2018; 34: 4–12

16. Vu EL, Rusin CG, Penny DJ et al: A novel electrocardiogram algorithm utilizing ST-segment instability for detection of cardiopulmonary arrest in single ventricle physiology: A retrospective study. Pediatr Crit Care Med, 2017; 18: 44–53

17. Belle A, Ansari S, Spadafore M et al: A signal processing approach for detection of hemodynamic instability before decompensation. PLoS One, 2016; 11: e0148544

18. Huang J, Zhang Q, Wang R et al: Systemic immune-inflammatory index predicts clinical outcomes for elderly patients with acute myocardial infarction receiving percutaneous coronary intervention. Med Sci Monit, 2019; 25: 9690–701

19. Horn MA: Cardiac physiology of aging: Extracellular considerations. Compr Physiol, 2015; 5: 1069–121

20. Meschiari CA, Ero OK, Pan H et al: The impact of aging on cardiac extracellular matrix. Geroscience, 2017; 39: 7–18

21. Xu Q, Zhang M, Abeysekera IR et al: High serum uric acid levels may increase mortality and major adverse cardiovascular events in patients with acute myocaridal infarction. Saudi Med J, 2017; 38: 577–85

22. Mosleh W, Elango K, Shah T et al: Elevated end-diastolic wall stress after acute myocardial infarction predicts adverse cardiovascular outcomes and longer hospital length of stay. Echocardiography, 2018; 35: 1721–28

23. Rausch JC, Lavine JE, Chalasani N et al: Genetic variants associated with obesity and insulin resistance in Hispanic boys with nonalcoholic fatty liver disease. J Pediatr Gastroenterol Nutr, 2018; 66: 789–96

24. Perumpail BJ, Khan MA, Yoo ER et al: Clinical epidemiology and disease burden of nonalcoholic fatty liver disease. World J Gastroenterol, 2017; 23: 8263–76

25. Weinstein G, Zelber-Sagi S, Preis SR et al: Association of nonalcoholic fatty liver disease with lower brain volume in healthy middle-aged adults in the Framingham study. JAMA Neurol, 2018; 75: 97–104

26. Patil R, Sood GK: Non-alcoholic fatty liver disease and cardiovascular risk. World J Gastrointest Pathophysiol, 2017; 8: 51–58

27. Wu J, Zhang R, Shen F et al: Altered DNA methylation sites in peripheral blood leukocytes from patients with simple steatosis and nonalcoholic steatochepatitis (NASH). Med Sci Monit, 2018; 24: 6946–67

28. Keskin M, Hayıroğlu Mİ, Uzun AO et al: Effect of nonalcoholic fatty liver disease on in-hospital and long-term outcomes in patients with ST-segment elevation myocardial infarction. Am J Cardiol, 2017; 120: 1720–26

29. Darabian S, Hormuz M, Latif MA et al: The role of carotid intimal thickness testing and risk prediction in the development of coronary atherosclerosis. Curr Atheroscler Rep, 2013; 15: 306

30. Sao R, Aronow WS: Association of non-alcoholic fatty liver disease with cardiovascular disease and subclinical atherosclerosis. Arch Med Sci, 2018; 14: 1233–44

31. Nestel PJ, Mensink RP: Perspective: Nonalcoholic fatty liver disease and cardiovascular risk. Curr Opin Lipidol, 2013; 24: 1–3

32. Wójcik-Cichy K, Koślińska-Berkan E, Piekarska A: The influence of NAFLD on the risk of atherosclerosis and cardiovascular diseases. Clin Exp Hepatol, 2018; 4: 1–6

33. Gaggini M, Morelli M, Buzzigoli E et al: Non-alcoholic fatty liver disease (NAFLD) and its connection with insulin resistance, dyslipidemia, atherosclerosis and coronary heart disease. Nutrients, 2013; 5: 1544–60

34. Buckley AJ, Thomas EL, Lessan N et al: Non-alcoholic fatty liver disease: Relationship with cardiovascular risk markers and clinical endpoints. Diabetes Res Clin Pract, 2018; 144: 144–52