Analysis of Risk Factors for Adverse Events Associated with Cardiogenic Syncope Due to Coronary Artery Disease in the Elderly

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Introduction. To analyze risk factors for adverse events associated with syncope due to coronary artery disease (CAD) in the elderly.

Methods. 208 patients with CAD who were hospitalized for cardiogenic syncope in our hospital from September 2022 to September 2023 were included in this study.Based on the follow-up results, 208 patients with cardiogenic syncope due to geriatric coronary artery disease were classified into into the no-adverse group (n=171) and the adverse group (n=37), and the risk factors for the occurrence of adverse events in cardiogenic syncope in both groups were analyzed.

Results. The differences in age, history of heart failure, cardiac troponin I (hs-TnT) level, N-terminal B-type natriuretic peptide proteins (NT-proBNP) level, heart rate, left ventricular ejection fraction (LVEF), and QTC abnormality between the two groups were statistically significant ($P<0.05$). The COX multifactorial regression analysis revealed that hs-TnT, NT-proBNP, QTC abnormality prolongation, and LVEF were all identified as risk factors for poor prognosis in elderly CAD patients ($P<0.05$). proBNP, abnormal prolongation of QTC, and LVEF were identified as risk factors for cardiogenic syncope in elderly CAD patients, leading to a poor prognosis ($P<0.05$). ROC curve analysis demonstrated that combining hs-TnT, NT-proBNP, QTC, and LVEF tests resulted in a higher diagnostic accuracy compared to using a single test alone, significantly improving the diagnostic accuracy ($P<0.05$).

Conclusion. High hs-TnT and NT-proBNP levels, abnormally prolonged QTC, and LVEF>50% are risk factors for cardiogenic syncope leading to adverse events in elderly CAD patients.

Keywords. Coronary artery disease in the elderly; Cardiogenic syncope; Prognosis; Risk

factors

INTRODUCTION

Syncope is a frequently observed medical condition characterized by a temporary loss of consciousness caused by insufficient blood flow to the brain. It can be caused by a variety of different conditions, ranging from harmless to potentially fatal diseases. This wide range of potential causes makes it challenging to assess the risk for patients experiencing syncope. By utilizing standardized diagnostic approaches, it is possible to ascertain the underlying cause in the majority of patients. The clinical management of syncope can be quite challenging, and healthcare providers and patients are particularly worried about the possibility of future adverse clinical events[1], such as cardiac arrest. Cardiogenic syncope refers to syncope that occurs due to bradycardia, tachycardia, or hypotension caused by a low cardiac index, obstruction of blood flow, vasodilatation, or acute vascular entrapment[2]. According to the 2017 ACC/AHA/HRS guidelines, syncope is caused by neurally mediated syncope in 16.8% of cases and cardiac syncope in 52.2% of cases, making cardiac syncope the second most frequent cause of syncope[3]. The outcome of syncope varies significantly based on the underlying cause. Prior research has indicated[4] that individuals experiencing syncope due to a cardiac cause are at a greater risk of being hospitalized and dying compared to those with non-cardiac syncope. Additionally, individuals with syncope are more prone to experiencing cardiac arrest and subsequent sudden cardiac death if they have heart failure with reduced left ventricular function, hypertrophic cardiomyopathy, or primary electrical disease. Coronary artery disease (CAD) is the main reason for heart attacks and the most frequent cause of cardiac arrest. However, there is a significant lack of information regarding the risk of sudden cardiac death related to syncope in a wider range of patients with heart disease. Therefore, this study aims to examine the clinical risk factors for adverse events of syncope caused by annual coronary artery disease. The study is conducted at a single center in order to enhance the risk stratification for sudden cardiac death in elderly CAD patients who experience cardiogenic syncope.

INFORMATION AND METHODS

General information

This study was a prospective, single-center cohort study that enrolled 208 patients with CAD who were admitted to our institution due to cardiogenic syncope between September 2022 and September 2023. The study adhered to the principles outlined in the Declaration of Helsinki and received approval from the relevant ethical committees. Prior to participating, all patients gave their informed consent.

Inclusion criteria and exclusion criteria

The inclusion criteria consisted of patients with CAD who were 18 years of age or older and were hospitalized for cardiogenic syncope. Syncope is a temporary loss of consciousness caused by inadequate blood flow to the brain. It is characterized by sudden onset, brief duration, and spontaneous full recovery. To obtain a conclusive diagnosis of the cause of syncope, see the Guidelines for ST-segment Elevation Myocardial Infarction[5]. Confirmed CAD is defined as a major coronary artery having a ≥50% narrowing or a history of myocardial infarction or coronary artery revascularization. (2) Comprehensive clinical information. The exclusion criteria included the following: (1) confusion caused by factors such as poisoning, seizure, stroke, transient ischemic attack, head trauma, or metabolic disorders like hypoglycemia, as well as presyncope that did not lead to complete loss of consciousness; (2) new or worsening confusion; (3) patients unable to participate in the screening for the cause of syncope; (4) pregnant or breastfeeding patients; and (5) patients with a history of drug or alcohol abuse.

Data acquisition

All patients underwent a comprehensive evaluation, which included a thorough assessment of their medical history (including conditions such as hypertension and

diabetes), general information (such as age, sex, and blood pressure), cardiac biomarker tests (specifically cardiac troponin I and N-terminal B-type natriuretic peptide proteins), markers related to metabolism (such as triglyceride, cholesterol, creatinine, and alanine aminotransferase), a 12-lead electrocardiogram (specifically measuring QTC), echocardiography (specifically assessing left ventricular ejection fraction), coronary CTA, and chest CT. The results of these evaluations were documented. Cardiac electrophysiology and coronary angiography are conducted when needed. The Evaluation of Syncope Study Guidelines (EGSYS) incorporated five predictors for syncope: abnormal electrocardiogram and/or cardiac disease (3 points), presyncopal palpitations (4 points), syncope during exertion (3 points) or while in a supine position (2 points), autonomic symptoms (-1 point), and predisposing and/or precipitating factors (-1). Cardiogenic syncope is determined by a score of ≥3 on the European Syncope Guidelines Evaluation Study (EGSYS) scale[6].

FOLLOW UP

All patients were followed up by outpatient follow-up and telephone after discharge. The primary outcome measure was the occurrence of adverse events within 1 year following an episode of cardiogenic syncope. These adverse events included all-cause mortality, recurrent syncope, and readmission for cardiogenic diseases such as severe structural heart disease, aortic coarctation, acute pulmonary embolism, severe pulmonary hypertension, cardiac interventions, and cardiac surgery. Participants were categorized into two groups: a no-adverse group and an adverse group, based on the presence or absence of adverse events and their impact on prognosis.

STATISTICAL PROCESSING

The statistical analysis was conducted using SPSS 22.0 software. The measurement data were represented as the mean value plus or minus the standard deviation ($x \pm s$). The independent t-test was used to compare the means between groups. The count data were converted into rates and the rates were compared using the chi-square test.

The study utilized univariate analysis and multivariate COX proportional risk models to examine the variables linked to the prognosis of cardiogenic syncope. Receiver Operating Characteristic (ROC) analysis was conducted on variables discovered using multivariate Cox analysis to evaluate the diagnostic precision of prognosis for cardiogenic syncope. A P-value less than 0.05 was deemed to be statistically significant.

RESULTS

General Information Analysis

According to the follow-up results, 37 patients experienced adverse events during the mean follow-up time (369.20±172) days, and the other 171 CAD patients did not experience any adverse events, and the differences between the two groups were significant when comparing the patients in terms of age, history of heart failure, hs-TnT levels, NT-proBNP levels, heart rate, LVEF, and QTC abnormalities (P<0.05), while the differences were not significant when compared in other aspects (P>0.05), as shown in Table 1.

Table 1 Comparison of general information of the two groups of patients

Variable	No adverse group (n=171)	Adverse group (n=37)	t	*P*
Age(years)	66.75±9.93	71.74±9.06	2.813	0.005
Sex (m/f)	92 (53.80)/79 (46.20)	26 (70.27)/11 (29.73)	3.361	0.067
Systolic blood pressure (mmHg)	139.41±15.41	143.95±16.77	1.599	0.111
Heart rate (beats/min)	70.74±16.79	77.41±15.82	2.191	0.030
Heart failure	99 (57.89)	31 (83.78)	8.699	0.003
Diabetes	35 (20.47)	8 (21.62)	0.025	0.875
High blood pressure	47 (27.49)	9 (24.32)	0.155	0.694

hs-TnT (ug/L)	30.98±4.51	35.61±6.71	5.143	<0.001
NT-proBNP (ng/L)	245.81±73.96	312.93±88.67	4.824	<0.001
D -dimer (ng/mL)	596.94±141.01	643.59±157.10	1.787	0.075
CK (U/L)	12.1 (7.4, 18.2)	13.5 (8.8, 23.8)	1.634	0.096
CK-MB (U/L)	10.7 (5.2, 15.6)	11.2 (6.3, 16.9)	1.212	0.147
Creatinine (umol/L)	67.89±6.36	69.15±7.33	1.063	0.289
ALT (U/L)	34.36±8.12	35.39±6.78	0.719	0.473
AST (U/L)	19.57±4.12	21.01±5.35	1.822	0.070
Hemoglobin (g/L)	135.36±14.41	131.95±15.63	1.285	0.200
Hematocrit value (%)	38.99±2.61	38.12±2.04	1.904	0.058
LVEF (%)	47.52±3.60	68.71±3.92	1.794	0.074
TC (mmol/L)	4.74±0.69	4.91±1.24	1.153	0.250
TG (mmol/L)	2.51±1.03	2.73±1.09	1.166	0.245
QTC>450ms	100 (58.48)	29 (78.38)	5.113	0.024

CoX regression analysis

The COX multifactorial regression analysis revealed that hs-TnT, NT-proBNP, excessively extended QTC, and LVEF were identified as risk variables for the development of cardiogenic syncope in elderly patients with CAD. These factors were found to be associated with a poor prognosis (P<0.05), as indicated in Table 2.

Table 2 COX multifactorial regression analysis of risk factors for cardiogenic syncope leading to poor prognosis in elderly CAD patients

Variable	regression coefficient	standard error	Vardø (city in Finnmark, Norway)	*P*	OR	95% CI
Pulse rate	0.243	0.343	0.423	0.515	1.275	0.613-2.649
Age	1.051	0.591	3.169	0.075	2.862	0.899-9.107

Heart failure	0.110	0.483	0.052	0.819	1.117	0.433-2.877
hs-TnT	0.053	0.024	4.735	0.030	1.055	1.005-1.106
NT-proBNP	0.404	0.144	7.907	0.005	1.497	1.130-1.984
QTC>450ms	1.561	0.37	17.83	0.000	4.766	2.309-9.838
LVEF	0.094	0.04	5.62	0.018	1.098	1.016-1.187

Predictive value of adverse events in patients with syncope

The ROC curves showed that the combined diagnostic AUC of hs-TnT, NT-proBNP, QTC, and LVEF was higher than that of the single test, which could significantly improve the diagnostic accuracy, as shown in Table 3 and Figure 1.

Table 3 Efficacy of hs-TnT, NT-proBNP, Abnormal QTC Prolongation, and LVEF in Predicting the Occurrence of Cardiogenic Syncope Resulting in a Poor Prognosis in Elderly CAD Patients

Variable	AUC	Standard error	*P*	Sensitivity	Specificity	Accuracy
hs-TnT	0.688	0.055	0.001	51.20	84.70	78.74
NT-proBNP	0.656	0.055	0.013	70.70	59.30	61.33
QT Extension	0.764	0.051	0.000	73.20	79.70	78.54
LVEF	0.758	0.049	0.000	65.90	76.30	74.45
Joint test	0.878	0.035	0.000	68.3	94.90	90.17

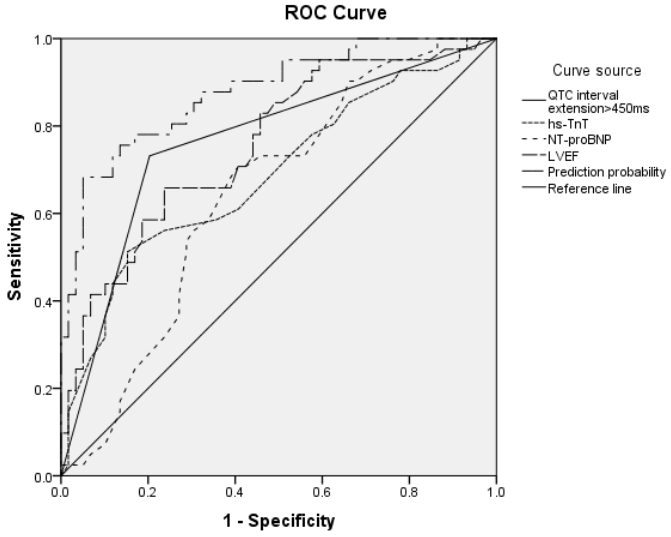

Figure 1 ROC curve analysis graph

DISCUSSION

Syncope is an important public health problem, often incapacitating the patient and may be the only warning before sudden cardiac death.Cardiac syncope is mainly caused by cardiac disease.The diagnosis of cardiac causes of syncope has important prognostic significance. Research comparing mortality rates after syncope based on potential processes consistently demonstrates[7] that individuals with cardiac reasons have a greater mortality rate compared to those with non-cardiac causes. A study with 433 patients[8] and a follow-up period of over 60 months found that patients with cardiac reasons had a mortality rate of 50%, whereas patients with non-cardiac or unexplained causes had mortality rates of 31% and 24% respectively. Coronary artery disease is a common heart disease in which atherosclerosis occurs in the coronary arteries causing narrowing of the coronary arterial lumens, which leads to ischemia in the myocardium, and in the elderly patients due to senility and frailty. Older patients are a group with a high occurrence of coronary artery disease due to the process of aging, frailty, and having several health conditions. However, it is uncertain if fainting

in all older patients with coronary artery disease is linked to a negative outlook. Hence, the objective of this research is to examine the characteristics that increase the likelihood of a negative outcome in older patients with coronary artery disease who have syncope. The goal is to promptly identify high-risk individuals and provide appropriate treatment in order to mitigate the potential effects of life-threatening situations.

The study's findings revealed that patients in the poor prognosis group were characterized by advanced age, concomitant heart failure disease, elevated levels of hs-TnT and NT-proBNP, LVEF more than 50%, and abnormally prolonged QTCs, as compared to the good prognosis group.When analyzing the reasons for this, the increased risk of cardiogenic syncope and the ensuing serious adverse events in the elderly is paralleled by the inevitable progression with age to potentially of severe structural heart disease is parallel. In individuals with heart failure and decreased left ventricular systolic function, syncope is linked to a higher likelihood of sudden death, regardless of the cause of syncope. However, this study shows that the connection between syncope and unfavorable prognosis is specifically related to a prior history of comorbid heart failure in patients with coronary heart disease (CHD). CTnI and NT-proBNP are frequently employed for diagnosing and evaluating the prognosis of heart failure disease[10]. Consequently, they tend to be elevated in the adverse group. This study is the first to establish a link between cardiac syncope and an unfavorable prognosis.

The current study has shown, for the first time, that the link between syncope and negative prognosis is not influenced by left ventricular (LV) systolic function. However, it was observed that patients in the poor prognosis group had a higher LV ejection fraction, which aligns with previous research indicating that sudden cardiac arrest (SCA) events are more frequent in patients with LV ejection fraction greater than 50%[11]. Previous research conducted a small case-control study[12] and found that QTc prolongation was identified as a predictor for the occurrence of sudden cardiac death (SCD) in patients with coronary heart disease (CHD). The study also

revealed that the risk of SCD doubled when QTc abnormalities were prolonged, which aligns with the findings of the current study. The results of this study indicate that there was a twofold increase in ECG abnormalities among the group of individuals with low socioeconomic status.

The COX multifactorial analysis revealed that elevated levels of cTnI, QTc anomalies, and LEVF >50% were separately linked to the prognosis of mortality resulting from syncope. The biomarkers cTnI and NT-proBNP were previously studied to determine the existence and severity of cardiac disease, as well as to assess the risk of adverse events in syncope patients. These biomarkers have also been suggested as a means of identifying syncope patients who are at risk for negative outcomes[13,14]. Probst MA et al.[15] found that high-sensitivity cardiac troponin T and NT-proBNP showed a high level of sensitivity in effectively ruling out death and significant cardiac outcomes in older persons experiencing syncope caused by cardiac issues. Gibson TA et al.[16] Elevated troponin (LR+ 2.49, 95% CI [1.36, 4.10]), B-type natriuretic peptide (LR+ 2.19, 95% CI [1.15, 5.42]) were all risk factors for poor syncope prognosis, which is generally consistent with the present study, and CHD patients with LEVF >50% had a significantly increased risk of poor prognosis for cardiogenic syncope, which is consistent with the Aro AL et al.[17] study (LR+ 3.1, 95% CI [1.68, 5.79]), which is generally consistent with the present study, and these findings may be useful in improving the risk stratification process in SCA patients with preserved LVEF. Nevertheless, the existing guidelines lack a specific approach for categorizing the risk of this significant minority. Patients with coronary artery disease and syncope are a distinct group, and it is important to investigate the potential relevance of syncope as a clinical risk signal in patients with intact LVEF and coronary artery disease.There is a clear connection between QTc prolongation and sudden cardiac arrest (SCA) in older patients with coronary heart disease (CHD) who have syncope. This shows that including QTc intervals in risk assessment algorithms could be useful, and that prolonged QT intervals may indicate an underlying heart condition. ROC curve analysis demonstrated that the diagnostic accuracy was

enhanced by combining hs-TnT, NT-proBNP, QTC prolongation, and LVEF. However, additional validation is required to confirm the inclusion of these indicators in risk stratification. This validation should involve several centers, a bigger sample size, and a longer follow-up period.

CONCLUSION

This study found that elevated levels of hs-TnT and NT-proBNP, along with abnormally prolonged QTC and LVEF >50%, were linked to the occurrence of cardiogenic syncope in elderly CAD patients. These factors may serve as specific risk factors for clinical judgment and should be taken into account when developing future risk prediction tools for serious clinical events following syncopal emergency room visits.

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