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Original Article

Clinical features in adult patients with in-hospital cardiovascular events with confirmed 2009 Influenza A (H1N1) virus infection: Comparison with those without in-hospital cardiovascular events

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Abstract

Background: Comprehensive data regarding in-hospital cardiovascular events of adults with confirmed 2009 influenza A (H1N1) (2009 H1N1) infections are limited. The aim of this study was to determine the clinical characteristics, laboratory parameters, and electrocardiographic (ECG) findings for adults with 2009 H1N1 infections and to assess the differences in these parameters among adult patients with and without in-hospital cardiovascular events.

Methods: Seventy-one patients were enrolled from the 2009 H1N1 registry database (our hospital registry of confirmed 2009 H1N1 infection during the year 2009) and divided according to the presence of in-hospital cardiovascular events. Six patients had cardiovascular events (CV group) and 65 did not (NCV group).

Results: The CV group was more likely to be old ($p = 0.023$). Regarding co-morbidities, underlying coronary heart disease ($p = 0.001$), congestive heart failure ($p = 0.001$), diabetes ($p = 0.001$), and hypertension ($p = 0.014$) had significant influences on cardiovascular events. The CV group was also more likely to have chest pain ($p = 0.034$), dyspnea ($p = 0.045$), higher leukocyte count ($p = 0.014$), higher C-reactive protein ($p = 0.010$), higher glucose level ($p = 0.001$), and higher N-terminal probrain natriuretic peptide level ($p = 0.010$) than the NCV group. In addition, the CV group had a significantly higher in-hospital mortality rate ($p = 0.010$) and cardiac mortality rate ($p = 0.001$) than the NCV group. However, there were no significant differences in ECG findings between the two groups.

Conclusion: Our study demonstrated that the CV group had higher in-hospital and cardiac mortality rates than the NCV group. A meticulous therapeutic approach should be considered for elderly patients with 2009 H1N1 infections having coronary heart disease, congestive heart failure, diabetes, hypertension, and high levels of leukocyte count, hs-CRP, glucose, and NT-proBNP at the time of admission.

Keywords: cardiovascular disease; cardiovascular mortality; influenza A

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1. Introduction

During periods of epidemic influenza, numerous deaths and serious complications occur frequently in vulnerable populations with underlying chronic medical disorders such as cardiovascular diseases.[1–4] Although some reports suggest links between the 2009 influenza A (H1N1) (2009 H1N1) infection and cardiovascular deaths, data describing cardiovascular complications of the 2009 H1N1 infection are limited.[5,6] Moreover, a dearth of literature exists about the role of influenza as a trigger of in-hospital cardiovascular events in adult patients with the 2009 H1N1 infection.[7]

The aim of this study was to determine the clinical characteristics, laboratory parameters, and electrocardiographic (ECG) findings for adults with 2009 H1N1 infections; to assess the differences in these parameters among adult patients who had in-hospital cardiovascular events (CV group) and those who did not (NCV group); and to assess the in-hospital courses and mortality in the two groups.

2. Methods

2.1. Study participants

Study data were obtained from the 2009 H1N1 Samsung Changwon Hospital registry database. We approached 71 consecutive patients >15 years of age who were admitted to our hospital, a 720-bed referral center, for confirmed 2009 H1N1 infection between August 1 and December 31, 2009. A total of 5805 patients visited our center during the study period, and 2436 patients (42%) were tested positive for 2009 H1N1. Out of 850 adult patients who were >15 years of age, 71 (8.4%) were admitted to our hospital because of severe symptoms of H1N1 infection. Among 71 enrolled patients, six (8.3%) had cardiovascular events during index hospitalization and 65 did not. Out of the six patients in the CV group, acute myocardial infarction occurred in three patients (on the 5th, 4th, and 5th day after admission, respectively), paroxysmal atrial fibrillation in two patients (on the 4th and 6th day after admission, respectively), and acute myocarditis in one patient (on the 6th day after admission) during index hospitalization. Acute myocardial infarction was diagnosed according to the American College of Cardiology and the American Heart Association guidelines (patients with acute myocardial infarction presented with typical chest pain with ST elevation on ECG and elevated cardiac enzymes and significant narrowing or plaque rupture on coronary angiogram), and acute myocarditis was diagnosed by myocardial biopsy performed in patients with acute chest pain, ECG changes, and elevation of cardiac enzymes.

One patient with acute myocardial infarction died of cardiac arrest with intractable ventricular tachycardia. Medical records of patients with confirmed 2009 H1N1 infections were retrospectively reviewed, including demographic information, clinical manifestations, and laboratory and ECG findings. In all patients, ECGs and laboratory studies were performed on the first hospital day.

Obese patients were defined as those with a body mass index (BMI) of >30 kg/m^2. Diabetes mellitus was defined as a serum fasting glucose level ≥126 mg/dL, a history of diabetes mellitus, or current use of antidiabetic medications. Hypertension was defined as repeated measurement of systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg, or previous antihypertensive medication treatment. Current smoking was defined as having smoked cigarettes <1 year prior to admission. To determine the severity of illness, the Acute Physiology and Chronic Health Evaluation (APACHE) II score and Charlson comorbidity index were determined in all patients within 24 hours of admission. The protocol was approved by the Institutional Review Board of the Samsung Changwon Hospital. The recommendations of the revised version of the Declaration of Helsinki were met.

2.2. Microbiological studies

Nasopharyngeal swab specimens or transtracheal secretions were collected from each patient at the time of admission and tested for the 2009 H1N1 infection, which was confirmed with real-time reverse-transcriptase polymerase chain reaction analysis (Bioneer Corp., Daejeon, Korea). Laboratory technicians were blinded to patient identity and characteristics.

2.3. ECG

Initially, ECGs were read by two cardiologists who were masked with respect to the status of patient illness. Two additional cardiologists, each with 10 years of experience in their field, reviewed the ECGs to determine the clinical significance of the findings.

2.4. N-terminal probrain natriuretic peptide assay

Blood samples were obtained from the antecubital vein and put into tubes containing lithium heparin, and then centrifuged. These samples were stored at −70°C until further analysis. Plasma N-terminal probrain natriuretic peptide (NT-proBNP) levels were measured using an Elecsys proBNP reagent kit (Roche Diagnostics, Indianapolis, IN, USA) and an Elecsys 2010 (Roche Diagnostics, Indianapolis, IN, USA). Laboratory technicians were blinded to patient identities and characteristics.

2.5. Statistical analysis

Statistical analysis was performed using SPSS Pc + 12.0 software (SPSS Inc., Chicago, IL, USA). Data for continuous variables were given in terms of the median and interquartile range (IQR). The Mann–Whitney nonparametric U test was used to compare continuous variables between the two groups because of wide standard deviation, and a chi-square test was used to compare the categorical variables. Differences were considered statistically significant when $p < 0.05$.

3. Results

3.1. Clinical characteristics

The clinical characteristics and initial presentations of the CV and NCV groups are compared in Table 1. There were no significant differences in gender, BMI, obesity, and current smoker status, underlying cerebrovascular disease, chronic obstructive pulmonary disease, liver cirrhosis, and chronic renal disease between the two groups. The CV group consisted of older patients (median age, 64.5 vs. 50 years; $p = 0.023$) and had a significantly higher prevalence of coronary heart disease (33% vs. 2%; $p = 0.001$), congestive heart failure (33% vs. 2%; $p = 0.001$), diabetes mellitus (100% vs. 15%; $p = 0.001$), and hypertension (67% vs. 22%; $p = 0.014$). Most initial presentations of the CV and NCV groups were similar between the two groups. However, there was a significantly higher incidence of chest pain (50% vs. 15%; $p = 0.034$) and dyspnea (83% vs. 40%; $p = 0.045$) in the CV group than in the NCV group. There were no significant differences in systolic and diastolic blood pressures and heart rate.

3.2. Laboratory and ECG findings

The laboratory and ECG findings for the CV and NCV groups are compared in Table 2. There were no significant differences in ECG findings such as PR interval, QRS duration, or corrected QT interval. Also, there were no significant differences in the prevalence of ST elevation, Q-wave, T-wave inversion, first atrioventricular block, bundle branch block, and atrial and ventricular premature beats.

The CV group had significantly higher blood levels of leukocyte count (median, 15.1 $\times$ 10^3vs. 7.8 $\times$ 10^3/μL; $p = 0.014$), high sensitive C-reactive protein (hs-CRP) (median, 153.4 vs. 54.5 mg/mL; $p = 0.010$), and glucose (median, 310.0 vs. 117.5 mg/dL; $p = 0.001$) than the NCV group. In addition, the CV group had significantly higher NT-proBNP levels (median, 4756.0 vs. 480.0 pg/mL; $p = 0.010$) than the NCV group. However, there were no significant differences in the leukocyte count, hemoglobin level, platelet count, creatinine phosphokinase (CPK), lactate dehydrogenase (LDH), albumin, blood urea nitrogen (BUN), creatinine, creatinine phosphokinase-MB (CK-MB), and troponin-I blood levels between the two groups.

3.3. APACHE II score and Charlson comorbidity index

The CV group had significantly higher APACHE II score [median, 20.0 (IQR, 16.0–32.0) vs. 10.0 (IQR, 5.5–17.5); $p = 0.001$] and Charlson comorbidity index [median, 3 (IQR, 2–4) vs. 1 (IQR, 0–3); $p = 0.035$] than the NCV group (Fig. 1).

Table 1
Comparison of clinical characteristics between CV and NCV groups.

	CV group ($n = 6$)	NCV group ($n = 65$)	p
Age (y)[a]	64.5 (57.5–84.0)	50.0 (28.5–66.0)	0.023*
Male gender, *n* (%)	5 (83)	31 (48)	0.102
Body mass index (kg/m^2)[a]	21.3 (20.1–24.8)	22.4 (19.3–25.0)	0.950
Obesity, *n* (%)	3 (50)	17 (26)	0.204
Diabetes mellitus, *n* (%)	6 (100)	10 (15)	0.001*
Hypertension, *n* (%)	4 (67)	14 (22)	0.014*
Current smoker, *n* (%)	1 (17)	15 (23)	0.719
Coronary heart disease, *n* (%)	2 (33)	1 (2)	0.001*
Congestive heart failure, *n* (%)	2 (33)	1 (2)	0.001*
Cerebrovascular disease, *n* (%)	0 (0)	16 (25)	0.237
COPD, *n* (%)	0 (0)	5 (8)	0.485
Liver cirrhosis, *n* (%)	0 (0)	2 (3)	0.665
Chronic renal disease, *n* (%)	2 (33)	5 (8)	0.041*
Clinical presentation			
Chest pain, *n* (%)	3 (50)	10 (15)	0.034*
Dyspnea, *n* (%)	5 (83)	26 (40)	0.045*
Fever/chills, *n* (%)	5 (83)	54 (83)	0.926
Cough/sputum, *n* (%)	6 (100)	49 (75)	0.171
Sore throat, *n* (%)	0 (0)	15 (23)	0.189
Nausea/vomiting, *n* (%)	1 (17)	8 (12)	0.793
Abdominal pain/diarrhea, *n* (%)	2 (33)	8 (12)	0.337
Headache, *n* (%)	0 (0)	18 (28)	0.140
Fatigue/myalgia, *n* (%)	3 (50)	23 (35)	0.322
Hemodynamic parameters			
SBP (mmHg)[a]	145 (110–150)	120 (105–140)	0.869
DBP (mmHg)[a]	91 (62–103)	80 (60–90)	0.893
Heart rate (beats/min)[a]	101 (85–135)	88 (76–109)	0.557

*Significant finding.
COPD = chronic obstructive pulmonary disease; CV group = patients with cardiovascular events; DBP = Diastolic blood pressure; NCV group = patients with no cardiovascular events; SBP = systolic blood pressure.
[a] Presented as median (interquartile range).

Table 2
Comparison of electrocardiographic and laboratory findings between CV and NCV groups.

	CV group ($n = 6$)	NCV group ($n = 65$)	p
Electrocardiographic changes			
PR interval (ms)[a]	131.0 (118.0−196)	156.0 (144.0−176.0)	0.286
QRS duration (ms)	96.0 (91.0−132.0)	91.5 (86.0−99.0)	0.080
Corrected QT interval (ms)	461.0 (442.0−4932.0)	441.0 (424.0−468.8)	0.352
ST-segment elevation, *n* (%)	3 (50)	20 (31)	0.322
Q-wave, *n* (%)	1 (17)	2 (3)	0.110
T-wave inversion, *n* (%)	4 (67)	19 (29)	0.070
First AV block, *n* (%)	0 (0)	1 (2)	0.761
Bundle branch block, *n* (%)	1 (17)	2 (3)	0.110
Atrial premature beats, *n* (%)	1 (17)	2 (3)	0.110
Ventricular premature beats, *n* (%)	1 (17)	3 (5)	0.215
Laboratory findings			
Leukocyte count ($\times 10^3/\mu L$)[a]	15.1 (8.8−17.4)	7.8 (6.3−10.1)	0.032*
Lymphocyte count (%)[a]	11.2 (7.6−17.8)	12.7 (6.1−20.4)	0.854
Hemoglobin (g/dL)[a]	12.4 (9.5−14.9)	12.5 (11.1−14.4)	0.846
Platelet count ($\times 10^3/\mu L$)[a]	194 (171−209.5)	182 (127.5−244)	0.575
hs-CRP (mg/mL)[a]	153.4 (71.2−259.3)	54.5 (15.5−120.4)	0.010*
CPK (ng/mL)[a]	143.0 (42.0−189.0)	98.0 (41.3−244.5)	0.665
LDH (ng/mL)[a]	322.0 (267.0−432.0)	226.0 (176.0−322.0)	0.102
Albumin (g/dL)[a]	3.0 (2.5−3.5)	3.1 (2.5−3.7)	0.721
Glucose (mg/dL)[a]	310.0 (210.0−420.0)	117.5 (106.3−135.5)	0.001*
BUN (mg/dL)[a]	15.7 (12.3−27.4)	10.0 (7.2−20.4)	0.082
Creatinine (mg/dL)[a]	1.5 (0.9−1.9)	0.9 (0.7−1.2)	0.081
CK-MB (ng/mL)[a]	3.5 (1.5−5.3)	2.6 (1.7−4.1)	0.821
Troponin-I (ng/mL)[a]	0.02 (0.01−0.08)	0.02 (0.01−0.04)	0.640
NT-proBNP (pg/mL)[a]	4756.0 (2405.0−13210.0)	480.0 (54.5−6704.3)	0.010*

* Significant finding.
AV = atrioventricular; BUN = blood urea nitrogen; CK-MB = creatinine phosphokinase-MB; CPK = creatinine phosphokinase; CV group = patients with cardiovascular events; hs-CRP = high sensitive C-reactive protein; LDH = lactate dehydrogenase; NCV group = patients with no cardiovascular events; NT-proBNP = N-terminal probrain natriuretic peptide.
[a] Presented as median (interquartile range).

3.4. Clinical course and treatment

The clinical courses and treatment for the CV and NCV groups are compared in Table 3. There were no significant differences in the time intervals between the two groups, from the duration of symptoms to the time of admission [median, 2.5 days (IQR, 1.0−5.0 days) in the CV group vs. median, 2.0 days (IQR, 0−4 days) in the NCV group; $p = 0.467$] to the time of antiviral therapy [median, 2.5 days (IQR, 2.0−6.0 days)] in the CV group vs. median, 3.0 days (IQR, 1.0−5.0 days) in the NCV group; $p = 0.814$].

Also, there were no significant differences in the use of inotropics and renal replacement therapy, and in the use and duration of antiviral and antibiotic therapies between the two groups. The CV group had a significantly higher prevalence of ventilator use (33% vs. 8%; $p = 0.041$), and a significantly higher duration of ICU stay (median, 15 vs. 2 days; $p = 0.001$) and length of hospitalization (median, 23 vs. 6 days;

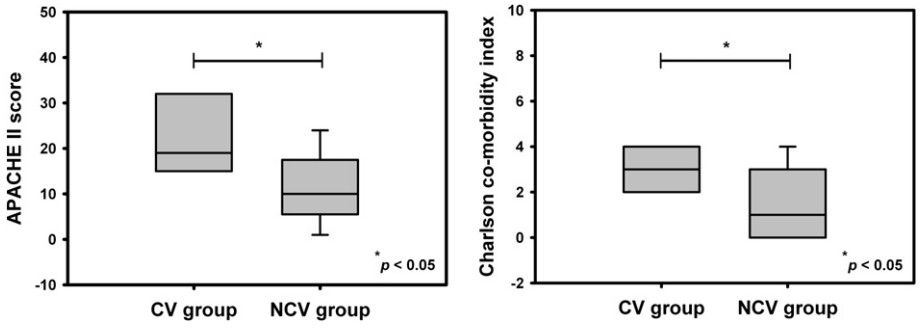

Fig. 1. The APACHE II score and Charlson comorbidity index in the CV and NCV groups. The CV group had significantly higher APACHE II score [median, 20.0 (IQR, 16.0−32.0) vs. 10.0 (IQR, 5.5−17.5); $p = 0.001$] and Charlson comorbidity index [median, 3 (IQR, 2−4) vs. 1 (IQR, 0−3); $p = 0.035$] than the NCV group. APACHE = Acute Physiology and Chronic Health Evaluation; CV group = patients with cardiovascular events; IQR = interquartile range; NCV group = patients with no cardiovascular events.

Table 3
Comparison of clinical courses and management between CV and NCV groups.

	CV group ($n = 6$)	NCV group ($n = 65$)	p
Use of antiviral therapy, n (%)	100 (0)	100 (0)	—
Duration of antiviral therapy (d)[a]	5.0 (5.0−5.0)	5.0 (5.0−5.0)	0.880
Combined bacterial pneumonia, n (%)	3 (50)	35 (54)	0.831
Use of antibiotic therapy, n (%)	6 (100)	54 (84)	0.665
Duration of antibiotic therapy (d)[a]	10.0 (10.0−14.0)	7.0 (5.0−10.0)	0.118
Use of inotropics, n (%)	3 (50)	16 (25)	0.171
Use of renal replacement therapy, n (%)	0 (0)	2 (3)	0.748
Use of ventilator, n (%)	2 (33)	5 (8)	0.041*
ICU stay, n (%)	5 (83)	14 (22)	0.002*
ICU duration (d)[a]	15.0 (4.5−26.8)	2.0 (0.0−4.0)	0.001*
Hospitalization (d)[a]	23.0 (9.8−38.8)	6.0 (3.0−10.5)	0.025*
In-hospital mortality, n (%)	2 (33)	3 (5)	0.010*
In-hospital cardiac mortality, n (%)	1 (17)	0 (0)	0.001*

* Significant finding.
CV group = patients with cardiovascular events; ICU = intensive care unit; NCV group = patients with no cardiovascular events.
[a] Presented as median (interquartile range).

$p = 0.025$) than the NCV group. In addition, the CV group had significantly higher in-hospital mortality rate (33% vs. 5%; $p = 0.010$) and in-hospital cardiac mortality rate (17% vs. 0%; $p = 0.001$) than the NCV group.

During hospitalization (median, 7.5 days; IQR, 3.5−11.8 days), five of 72 patients (6.9%) died; patient death was caused by cardiac arrest with ventricular tachycardia, diabetic ketoacidosis, massive gastrointestinal bleeding, hypoxemia, and septic shock, respectively.

4. Discussion

The main findings of this study were as follows. First, the CV group consisted of older patients; had a higher prevalence of underlying coronary heart disease, congestive heart failure, diabetes mellitus, and hypertension; and had higher blood levels of leukocyte count, hs-CRP, glucose, and NT-proBNP than the NCV group. Second, the CV group had significantly higher in-hospital and cardiac mortalities than the NCV group.

To the best of our knowledge, this is the first study to investigate in detail the clinical characteristics, laboratory parameters, and ECG findings of adult patients with 2009 H1N1 infections in South Korea.[6,7]

Overall, some clinical features of our study were similar to those of earlier published studies in the literature.[8−10] Most cases presented with clinical features of acute respiratory illnesses and radiographic confirmation of pneumonia.[10−12] In comparison with previous studies showing greater than one-third of cases presenting with gastrointestinal symptoms,[8−10] 19 (27%) of our 71 cases presented with gastrointestinal symptoms such as nausea, vomiting, abdominal pain, or diarrhea. In our study, 18% of patients presented with chest pain or discomfort. Bandt et al[13] reported that 5−10% of their patients experienced cardiac symptoms during acute influenza infection.

A remarkable finding in our study was that a significant proportion (69%) of adult patients with 2009 H1N1 infections had abnormal ECG findings in the early stages after symptoms showed up, although serum CK-MB and troponin-I blood levels were normal. According to previous studies, ECG abnormalities have been recorded in up to 81% of patients hospitalized with influenza[14−17] and in 43% of cases in the community where patients were not hospitalized.[18] The possible explanation of any discrepancies between ECG changes and cardiac enzymes in the early stages after symptoms occurred is that the nonspecific nature of the origin of many of the ECG changes may be influenced by respiratory alkalosis or fever, but not by the 2009 H1N1 virus itself.

In our study, there were no significant associations between abnormal initial ECG findings and cardiovascular events during index hospitalization. Previously published studies found that ECG abnormalities were not associated with cardiac injury markers or echocardiographic contractile abnormalities.[16,17,19,20] Our study confirms this finding, and together, these observations suggest that ECG changes during the early stages of 2009 H1N1 infections may not predict the cardiovascular events during index hospitalization and hence are clinically insignificant.

A study of previously healthy military recruits found that six (15%) of 40 patients with influenza had abnormal ECG findings, and all had regional myocardial dysfunction confirmed by echocardiography.[19] The CK-MB levels were elevated in three of the patients. Such findings are consistent with acute myocarditis and suggest a much higher risk than observed in our study. In contrast, other recent studies[17,20,21] found that most increases in CK levels seen during influenza in ambulatory adults were likely of skeletal muscle origin and acute viral myocarditis secondary to influenza was a very uncommon complication, which are consistent with the findings of the present study. According to the recently published reports, adverse cardiovascular events occur in patients with influenza through a number of mechanisms, including fever, vasodilatation, hypovolemia, hypoxia, proinflammatory cytokine elaboration, and procoagulant effects, as well as direct cardiac injury such as myocarditis.[2,20]

In the present study, it is unclear how common asymptomatic cardiac involvement of influenza infection is, because we did not perform systemic investigations such as

echocardiogram, cardiac magnetic resonance imaging, or cardiac biopsy in all patients. However, the prevalence of such cardiac involvement has been reported to range from 0% to 53% of cases.[22]

In the present study, the incidence rate of cardiovascular events during index hospitalization is 8.5%. According to previous studies, cardiac changes associated with acute influenza virus infection were found in 15−43% of ambulatory patients and 14−75% of hospitalized patients.[16,17,19,20] The possible hypothesis for differences in incidence rate is that our patients received antiviral therapy, which might have reduced the likelihood of cardiac complications. Also, small sample size and retrospective design of our study may further account for those differences.

A recent analysis of individuals with health insurance coverage provided by a large insurance company during a single influenza season in the United States suggested a protective effect of oseltamivir treatment for influenza against adverse cardiac outcomes, such as unstable angina, myocardial infarction, arrhythmia, or congestive heart failure.[23] A recently published study has found that influenza vaccination improves the clinical course of coronary artery disease and reduces the frequency of coronary ischemic events in patients with optimally treated coronary artery disease.[24] Therefore, our results may support the results of these studies, showing the importance of early antiviral treatment in patients with severe 2009 H1N1 infections and the possible potential for influenza vaccinations to reduce the number of cardiac fatalities.

Interestingly, in our study, the CV group had higher blood levels of leukocyte count, hs-CRP, and NT-proBNP than the NCV group. Recent experimental studies in mice demonstrated that inoculation of H1N1 virus into a mouse atherosclerosis model resulted in heavy infiltration of atherosclerotic plaques by inflammatory cells, as well as platelet aggregation and thrombosis, which was an essential step in the evolution of acute coronary syndrome.[25−27] Based on these findings, we reasoned that higher hs-CRP and NT-proBNP blood levels in the CV group might be reflective of the role of influenza in stimulating cardiac remodeling, with acute inflammation altering endothelial function. Therefore, higher leukocyte count, hs-CRP, and NT-proBNP blood levels may be useful in predicting an increased risk of cardiovascular events during hospitalization in adult patients with 2009 H1N1 infections.

In our study, the CV group had significantly higher APACHE II score and Charlson comorbidity index than the NCV group. These findings may support findings of previous studies reporting numerous deaths and complications in vulnerable populations with underlying chronic medical disorders such as cardiovascular diseases.[1−4]

Notably, in the present study, the CV group had higher in-hospital mortality and in-hospital cardiac mortality than the NCV group. According to previously published studies, influenza has historically been linked to cardiovascular disease,[1,2] and, based on epidemiological studies, cardiovascular deaths have increased during influenza epidemics.[3,4] A recent systematic review of 39 studies reported consistent observational evidence of an influenza association with myocardial infarction.[4] Based on the consistent findings of these studies, in addition to the results of the current study, we reasoned that the possibility of influenza myocarditis, exacerbation of pre-existing coronary artery disease, or worsening of congestive heart failure is associated with increased cardiovascular mortalities in patients with 2009 H1N1 infections.

In the current study, the overall mortality rate (7%) was similar to that in previous studies, which reported a mortality rate of 7% in a US cohort of 272 hospitalized patients.[9] In our study, mortality associated with 2009 H1N1 infection itself was 3%: one patient died of uncontrolled hypoxemia and the other died of uncontrolled septic shock. Causes of deaths in most patients were associated with underlying diseases. Therefore, we suggest that meticulous medical care, including cardiovascular and pulmonary support, as well as antiviral and antibiotic therapy for infections is critical for controlling the mortality and morbidity associated with 2009 H1N1 infections.

4.1. Study limitations

There were some limitations in the current study. First, this was a retrospective design. The use of a retrospective medical record review may have contributed to information bias. However, to the best of our knowledge, this is the first study investigating in detail the clinical characteristics, laboratory parameters, and ECG findings in adult patients with 2009 H1N1 infections who had in-hospital cardiovascular events. Second, because a small number of case patients may not represent the full 2009 H1N1 influenza clinical spectrum, our study may have lacked a sufficient number of participants to compare the differences between the two groups, and so these comparisons should be interpreted with caution. Third, in most cases, we did not perform systemic investigations such as echocardiogram, cardiac magnetic resonance imaging, or pathology examination. Finally, we could not investigate asymptomatic cardiac involvement in adult patients with 2009 H1N1 infections due to the study's retrospective design.

In conclusion, the CV group had higher in-hospital mortality rate than the NCV group. Old age, underlying coronary heart disease, congestive heart failure, diabetes, and hypertension; and high blood levels of hs CRP, glucose, and NT proBNP were significantly common in the CV group. Based on these findings, a meticulous therapeutic approach should be considered for patients with 2009 H1N1 infections with these risk factors at the time of admission.

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