Appendix

**Association between cardiac injury and mortality in hospital patients infected with avian influenza A (H7N9) virus**



**Figure S1. Schematic of study design**

1. 17 provinces where patients with laboratory-confirmed avian influenza A (H7N9) viral infection were hospitalized.
2. Copies from the original medical records of 338 patients hospitalized with laboratory-confirmed avian influenza A (H7N9) viral infection were compiled. Patients were followed-up until death or hospital discharge. The final analysis included 321 patients, excluding 14 who were lost to follow-up and 3 whose laboratory examination results were missing

**Table S1. Comparison of results of cardiac examinations of influenza A (H7N9) infected hospitalized patients in different outcomes.**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Examinations** | | **All patients** | | **Died during hospitalization** | | |
| **Yes** | **No** | ***P*** |
| **TNI, median (IQR)*****a*** |  | | |  |  |  |
| First day of admission*b* | | 0.5 ( 0.2-2.1) | | 1.2 (0.5-4.8) | 0.3 (0.1-0.7) | <0.001 |
| Maximum during hospitalization | | 1.1 (0.3-5.1) | | 3.3 (0.9-12.4) | 0.4 (0.1-1.2) | <0.001 |
| **CK-MB, median (IQR)** | | |  |  |  |  |
| First day of admission*b* | | 0.9 (0.5-1.5) | | 1.1 (0.7-1.6) | 0.7 (0.4-1.4) | 0.001 |
| Maximum during hospitalization | | 1.3 (0.8-2.4) | | 1.6 (1.0-3.1) | 1.0 (0.6-1.6) | <0.001 |
| **EF, median (IQR)*c*** | | 0.5 (0.4-0.5) | | 0.5 (0.3-0.5) | 0.5 (0.4-0.5) | 0.520 |

*a* The ratio of the detected value to the upper limit of the normal range was used as a unified evaluation index.

*b* If a patient has more than one result, the maximum value was chosen.

*c* Calculated among patients with decreased EF. If a patient has more than one result, the minimum value was chosen.

Abbreviations: TNI, troponin I; IQR, interquartile range; CK-MB, creatinine kinase MB isoform; EF, ejection fraction; ECHO, echocardiography.

**Table S2. Univariate Cox regression analysis of factors associated with mortality in 321 H7N9-infected hospitalized patients.**

|  |  |  |
| --- | --- | --- |
| **Factor** | **Unadjusted HR (95% CI)** | ***P*** |
| Age ≥ 65yr | 2.34 (1.69-3.24) | <0.001 |
| Cardiovascular disease*a* | 1.68 (1.00-2.83) | 0.049 |
| Cerebrovascular [disease](javascript:;)*a* | 2.23 (1.26-3.95) | 0.006 |
| APACHE II ≥ 21*b* | 3.27 (2.37-4.51) | <0.001 |
| PaO2/FiO2 ≤ 200 mmHg*c* | 6.79 (3.14-14.51) | <0.001 |
| WBC count > 10 × 109/L | 1.82 (1.13-2.95) | 0.015 |
| Cardiac injury | 3.08 (1.99-4.77) | <0.001 |
| Acute kidney injury | 4.04 (2.77-5.89) | <0.001 |
| Antiviral treatment after symptom onset ≤ 2 days | 2.26 (0.92-5.56) | 0.075 |
| Use of corticosteroid*d* | 1.42 (0.92-2.18) | 0.110 |

*a* Pre-existing conditions.

*b*APACHE II score was assessed within 24 hours of admission to hospital.

*c*Laboratory findings on admission.

*d* Corticosteroid treatment was defined as administration of at least a dose equivalent to ≥ 0.5 mg∙kg-1 of methylprednisolone during hospitalization.

Abbreviations: APACHE II, Acute Physiology and Chronic Health Evaluation II; WBC, white blood cell; HR, hazard ratio.

**Table S3. Multivariate Cox regression analysis of factors associated with mortality in H7N9-infected hospital patients.**

|  |  |  |
| --- | --- | --- |
| **Factor** | **Adjusted HR (95% CI)** | ***P*** |
| Age ≥ 65yr | 1.87 (1.33-2.62) | <0.001 |
| APACHE II ≥ 21*a* | 1.91 (1.35-2.71) | <0.001 |
| PaO2/FiO2 ≤ 200 mm Hg*b* | 5.43 (2.52-11.71) | <0.001 |
| AKI | 2.08 (1.37-3.16) | 0.001 |
| Pre-existing cardiac conditions | 1.21 (0.71-2.05) | 0.480 |

*a* APACHE II score was assessed within 24 hours of admission to hospital.

*b*Laboratory findings on admission.

The Cox regression analysis included the variables listed in Table S2.

Result of cardiac injury associated with mortality was shown in figure 2.

Abbreviations: HR, hazard ratio; APACHE II, Acute Physiology and Chronic Health Evaluation II; AKI, acute kidney injury.

**Table S4. Subgroup analysis of factors associated with mortality in H7N9-infected hospitalized patients using multivariate Cox regression.**

|  |  |  |
| --- | --- | --- |
| **Subgroup** | **Adjusted HR (95% CI)** | ***P*** |
| Patients with moderate-to-severe ARDS (n = 250) |  |  |
| Age ≥ 65yr | 1.89 (1.33-2.67) | <0.001 |
| APACHE II ≥ 21*a* | 1.98 (1.39-2.83) | <0.001 |
| AKI | 1.84 (1.21-2.79) | 0.004 |
| Pre-existing cardiac conditions | 1.26 (0.74-2.14) | 0.395 |
| Age < 65yr (n = 230) |  |  |
| APACHE II ≥ 21*a* | 1.90 (1.22-2.96) | 0.005 |
| PaO2/FiO2 ≤ 200 mm Hg*b* | 5.43 (1.97-14.95) | 0.001 |
| AKI | 2.37 (1.39-4.06) | 0.002 |
| Pre-existing cardiac conditions | 1.25 (0.54-2.89) | 0.605 |
| Age ≥ 65yr (n = 91) |  |  |
| APACHE II ≥ 21*a* | 1.94 (1.08-3.49) | 0.026 |
| PaO2/FiO2 ≤ 200 mm Hg*b* | 4.53 (1.41-14.58) | 0.011 |
| AKI | 1.83 (0.94-3.57) | 0.077 |
| Pre-existing cardiac conditions | 1.32 (0.66-2.66) | 0.430 |
| APACHE II < 21*a* (n = 243) |  |  |
| Age ≥ 65yr | 2.26 (1.42-3.61) | 0.001 |
| PaO2/FiO2 ≤ 200 mm Hg*b* | 4.88 (1.77-13.47) | 0.002 |
| AKI | 3.07 (1.89-4.98) | <0.001 |
| Pre-existing cardiac conditions | 0.92 (0.41-2.03) | 0.831 |
| APACHE II ≥ 21*a*(n = 78) |  |  |
| Age ≥ 65yr | 1.80 (1.07-3.03) | 0.028 |
| PaO2/FiO2 ≤ 200 mm Hg*b* | 3.81 (1.15-12.65) | 0.029 |
| AKI | 0.61 (0.31-1.20) | 0.150 |
| Pre-existing cardiac conditions | 1.53 (0.74-3.15) | 0.252 |

*a* APACHE II score was assessed within 24 hours of admission to hospital.

*b*Laboratory findings on admission.

The Cox regression analysis included the potential confounding variables listed in Table S3.

Results of cardiac injury associated with mortality were shown in figure 2.

Abbreviations: HR, hazard ratio; APACHE II, Acute Physiology and Chronic Health Evaluation II; AKI, acute kidney injury; ARDS, acute respiratory distress syndrome.