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#### **Clinical paper**

# Pre-hospital airway management and neurological status of patients with out-of-hospital cardiac arrest: A retrospective cohort study



RESUSCITATION

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#### Abstract

Purpose: Little is known about whether pre-hospital advanced airway management (AAM) under the presence of a physician could improve outcome

of patients with cardiac arrest, compared with pre-hospital AAM under the absence of a physician.

Methods: This retrospective multicentre-cohort study enrolled consecutive patients who were transported to participating hospitals after out-of-hospital

cardiac arrest in Japan between 1 June 2014 and 31 December 2019. We included patients who underwent pre-hospital AAM and

resuscitation after arrival at hospital, and who were  $\geq$ 18 years of age, with medical aetiologies. The primary outcome was favourable neurological survival (Cerebral Performance Category score of 1 or 2) one month after cardiac arrest. The primary outcome was called one-month

favourable neurological survival. The first confirmed cardiac rhythm was defined using 3-lead electrocardiogram monitor or an automated

external defibrillator and by determining whether the carotid artery was pulsating. Previous research found that the presence of a pre-hospital physician was associated with improved patients' outcomes, after the type of first confirmed cardiac rhythm was considered. Therefore, the first confirmed cardiac rhythm in current study was subdivided into non-shockable or shockable groups. A multivariable logistic regression analysis was performed on propensity score-matched patients.

**Results**: We analysed 16,703 patients. Among the 2,346 patients in the non-shockable group, 1.2% (N = 29) achieved the primary outcome. The adjusted odds ratio of pre-hospital AAM with or without a physician for the primary outcome in the results of the non-shockable group was 4.64 (95% confidence interval: 1.81–14.4). Among the 826 patients in the shockable group, 16.9% (N = 140) achieved the primary outcome and the adjusted odds ratio of pre-hospital AAM with or without a physician for the primary outcome in the results of the shockable group was 1.05 (95% confidence interval: 0.67–1.63).

**Conclusions**: This retrospective multicentre-cohort study found that pre-hospital AAM under the presence of a physician was significantly associated with increased neurological outcome in specific patients with cardiac arrest, compared with pre-hospital AAM under the absence of a physician.

Keywords: Airway management, Cardiac arrest, Cardiopulmonary resuscitation, Emergency medical services, Emergency medicine, Resuscitation

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#### Introduction

After the occurrence of out-of-hospital cardiac arrest, the proportion of patients experiencing a favourable neurological survival (defined as a Cerebral Performance Category score of 1 or 2) is less than 10%.<sup>1,2</sup> One major predictor of resuscitation success is the time that elapses between cardiac arrest and commencement of appropriate treatment.<sup>3–5</sup>

Physicians in certain areas can be dispatched to the most severely ill patients, including those with cardiac arrest.<sup>5-11</sup> Japanese law does not allow emergency medical services' personnel to make decisions regarding whether to perform advanced life support procedures. Such procedures include advanced airway management, meaning an endotracheal intubation or a supraglottic airway, and the administration of adrenaline.<sup>5,10</sup> Emergency personnel in Japan must be directed via telephone by an emergency physician at a hospital when performing advanced life support.<sup>5</sup> The presence of a pre-hospital physician has been significantly associated with increased favourable neurological survival of patients who experience an out-of-hospital cardiac arrest.5-8,10 However, previous research did not identify specific factors that explain the benefits of dispatching a physician to patients who have suffered an out-ofhospital cardiac arrest.<sup>5–11</sup> The personnel of emergency medical services in Japan are not trained to perform tracheal intubation in emergency departments and pre-hospital settings. Therefore, the presence of a physician could be associated with successful airway management. In fact, a time-dependent propensity score sequential matching, which controlled for resuscitation time bias,<sup>12</sup> indicated that pre-hospital AAM was beneficial for those patients not in need of immediate electrical defibrillation following cardiac arrest.4 Another study showed that the benefit of having a pre-hospital physician was dependent on the type of first confirmed cardiac rhythm observed in patients with cardiac arrest.5

We designed the current study to test the hypothesis that prehospital AAM carried out in the presence of a physician could improve the neurological survival of patients with a specific type of first confirmed cardiac rhythm following cardiac arrest, compared with pre-hospital AAM carried out in the absence of a physician.

#### Methods

#### Ethical consideration

This study was a retrospective secondary analysis of the Japanese Association for Acute Medicine registry for out-of-hospital cardiac arrests. The procedures described in this registry are performed in routine clinical practice, and the registry presents no additional risks to patients.<sup>5</sup> The requirement to provide individual informed consent was waived by the Act on the Protection of Personal Information and the Ethical Guidelines for Medical and Biological Research Involving Human Subjects of Japan. In addition, this registry excluded patients who refused to participate in it, either personally or through a family member. The registry was approved by the Clinical Research Institutional Review Board of Dokkyo Medical University Saitama Medical Center (22043), and by each participating hospital as necessary. This registry project is registered in the University Hospital Medical Information Network (UMIN) Clinical Trials Registry under number UMIN000007528 before the onset of participant enrollment.

Study design, population, setting, and data quality control The registry is a nationwide multicentre hospital-based prospective observational cohort registry maintained by the Japanese Association for Acute Medicine. Its study profile has previously been described.<sup>5,13</sup> The registry began on 1 June 2014 and remains open, with no end date to the registry period.<sup>5</sup> The registry obtains prehospital resuscitation data about patients with cardiac arrest from forms that are based on the Utstein Style international guideline in reporting out-of-hospital cardiac arrests.<sup>14</sup> This reporting form is managed by the Fire and Disaster Management Agency of Japan. For the registry, anonymized data from hospital records were entered into the web sheet either by the physician or the collaborating medical staff one month after the occurrence of cardiac arrest. The data were then checked to ensure they were free of logical contradictions. Finally, the data were checked by the registry committee. which consisted of experts in emergency medicine and clinical epidemiology. If anything was incomplete on a data sheet, a committee member returned it to the participating hospital for further clarification.<sup>5</sup> This study included all consecutive patients on the registry who were transported to participating hospitals after the occurrence of out-of-hospital cardiac arrest between 1 June 2014 and 31 December 2019 in Japan. We included patients who underwent pre-hospital AAM, with or without a physician present, and who received resuscitation after arrival at hospital, and who were >18 years of age, with cardiac arrest attributed to medical aetiologies. Patients for whom data were missing were excluded from the analysis.

#### Outcomes and definitions in this study

The primary outcome in this study was the neurological status of survivors, as evaluated by the medical staff at each hospital, one month after the occurrence of cardiac arrest. This is called the one-month neurological survival. A favourable neurological survival was designated according to a Cerebral Performance Category score of 1 or 2. Cerebral Performance Category score 1 denotes good cerebral performance; score 2, moderate cerebral disability; score 3, severe cerebral disability; score 4, coma or vegetative state; and score 5, death.<sup>14</sup> The secondary outcome was survival, one month after the occurrence of cardiac arrest. This is called one-month survival in the current study.

Cardiac arrest was defined as the cessation of cardiac mechanical activity, confirmed through the absence of palpable cardiac output.14,15 Cardiac rhythm was confirmed by emergency medical services' personnel who checked whether the carotid artery was pulsating, and by the readings from a 3-lead electrocardiogram monitor or an automated external defibrillator.<sup>15,16</sup> This cardiac rhythm is hereafter called the 'first confirmed cardiac rhythm'. The first confirmed cardiac rhythm of patients with cardiac arrest was further divided into 'first confirmed non-shockable cardiac rhythm' and 'first confirmed shockable cardiac rhythm' groups, based on whether or not the rhythm could be altered using an electrical defibrillation from a defibrillator or automated external defibrillator.<sup>16</sup> In this study, we abbreviate these two divisions as the "non-shockable" and "shockable" groups, respectively. The first confirmed non-shockable cardiac rhythm is asystole or pulseless electrical activity. The first confirmed shockable cardiac rhythm is pulseless ventricular tachycardia or ventricular fibrillation. The presumed cardiac cause category was determined by the means of exclusion of other causes by the physician in charge at the receiving hospital.<sup>5</sup> The aetiology of

cardiac arrest was presumed to be of medical origin unless it was caused by trauma, including a fall, hanging, drowning, drug overdose, or asphyxia.<sup>14</sup>

#### Pre-hospital emergency medical system in Japan

The Japanese emergency medical system has been previously described in detail.5-7,10 Briefly, each ambulance has three personnel, at least one of whom is an emergency life-saving technician who has undertaken advanced training in the provision of prehospital emergency care. All emergency life-saving technicians are allowed to insert an intravenous line and an adjunct airway. The specially trained emergency life-saving technicians are permitted to insert tracheal tubes for patients with cardiac arrest. However, they are not able to insert tracheal tubes after the return of spontaneous circulation. They also are permitted to inject intravenous adrenaline. However, they are not permitted to inject drugs other than adrenaline. The education program for endotracheal intubation requires 30 successful cases in the operating room under the instruction of an anaesthesiologist.<sup>7,17</sup> They are not trained to perform tracheal intubation in emergency departments and pre-hospital settings. In addition, they are legally forbidden from performing tracheal intubation in patients where intubation may be particularly challenging. Specifically, intubation is not permitted in patients with a grade 3 or 4 on the Cormack-Lehane classification system for laryngoscopy.<sup>5,18</sup> Furthermore, according to Japanese law, the emergency life-saving technicians must receive authorisation from a physician via mobile phone when performing advanced life support. Therefore, they must be directed via mobile phone by an emergency physician at a hospital when performing AAM and the administration of adrenaline.<sup>5</sup> The procedures of advanced life support are decided in advanced. The devices for supraglottic airway are laryngeal mask, and esophageal obturator airway. Based on the Japanese Resuscitation Council resuscitation guidelines 2020, pre-hospital medical cares are provided. Once the airway was secured, chest compressions were delivered in 30:2 ration. Additionally, after AAM was performed, chest compressions were delivered independently from ventilations.

A pre-hospital physician travelled by ambulance or helicopter to treat the patient. The definition of 'the presence of a pre-hospital physician' was the application of a physician's technical skills to perform AAM and the use of their non-technical skills, including their support for AAM when it was carried out by personnel of the emergency medical services. The pre-hospital physicians were generally engaged in emergency medicine of each local area. They were able to provide appropriate diagnosis and initial treatment for different emergency patients. There is currently no clearly defined and unified protocol that describes how to dispatch a physician to the location of the occurrence of cardiac arrest, and that outlines the precise roles of the physician at the pre-hospital site.<sup>5</sup> For example, the criteria of dispatching a physician is not standardized. It is based on the contents of talking via the phone or the request from the personnel of emergency medical services on the scene. The system of dispatching a physician in Japan has been employed in only a few areas.<sup>5,11</sup> The registry did not provide detailed information on the areas served by each pre-hospital physician and the number of hospitals related the system of dispatching a physician.

#### Statistical analysis

We then compared the characteristics of patients and their clinical outcomes based on the presence or absence of a physician conducting pre-hospital AAM. A multivariable logistic regression analysis

was carried out using adjusted odds ratios (AORs) and 95% confidence intervals (CIs). We chose biologically relevant factors, such as the patient's age and sex, which must be adjusted in clinical epidemiology studies, as well as other reported factors that could influence the analysis of outcomes.<sup>5-7,10</sup> Specifically, the following factors were potential confounders in the multivariable logistic regression analysis: extracorporeal membrane oxygenation (yes or no); percutaneous coronary intervention (yes or no); intra-aortic balloon pumping (yes or no); and targeted temperature management (yes or no). We adjusted for further potential confounding factors when comparing outcomes in the presence and the absence of a physician in pre-hospital AAM. Therefore, we estimated a propensity score by fitting a logistic regression model used the following factors: the patient's age (one-year increments); the patient's sex (man or woman); witnessing by a bystander (witnessed or not); resuscitation by a bystander (yes or no); dispatcher instruction (yes or no); the elapsed time from the emergency dispatch centre receiving the emergency call to the first contact between the emergency medical service personnel and the patient (minutes), weekday (ves or no). and season of the year: spring (March-May), summer (June-August), autumn (September-November), or winter (December-February). These factors were observed before the completion of pre-hospital AAM. One-to-one pair matching between the presence and the absence of a pre-hospital physician was performed by nearest neighbour matching without replacement, using a caliper width of 0.05 of the standard deviation of the logit of the propensity score. Covariate balances before and after matching were checked by comparing standardised mean differences. A standardised difference of less than 10% was considered to indicate negligible balancing. We analysed the two groups according to first confirmed cardiac rhythm (non-shockable group or shockable group), based on the findings of previous studies.<sup>4,5</sup> In addition, we performed a univariate logistic regression analysis according to the type of device used for AAM. Moreover, we summarized the aetiologies of cardiac arrest based on first confirmed cardiac rhythm. All statistical analyses were performed using R, version 3.6.2 (The R Foundation for Statistical Computing) with associated packages including Matching and tableone.

#### Results

A total of 57,754 patients who had an out-of-hospital cardiac arrest during the study period were documented. After excluding patients who met the inclusion criteria but for whom data were missing, 16,703 patients were eligible for analysis (Fig. 1). Among them, 1,593 (9.5%) had received resuscitation by a pre-hospital physician and 15,110 (90.5%) had not.

Table 1 shows the characteristics of the non-shockable and shockable groups according to the presence or the absence of a pre-hospital physician. Before propensity score matching, treatment by a pre-hospital physician was more likely to be witnessed by a lay person in both non-shockable and shockable groups, and patients in both groups tended to be older when a pre-hospital physician was not present. After propensity score matching in the non-shockable group, 1,173 patients were selected from each group. This matching considerably improved the covariate balance between the groups, with all standardised mean differences being less than 10%. Similarly, after propensity score matching in the shockable group, 413 patients were selected from each group; this also considerably improved the covariate balance between the groups.



Fig. 1 – Patient flowchart from a nationwide multicentre cohort study. Cardiac arrest was attributed to medical aetiologies unless instigated by trauma, including a fall, hanging, drowning, drug overdose, or asphyxia. We evaluated first confirmed cardiac rhythm, defined by 3-lead electrocardiogram monitor or an automated external defibrillator and by determining whether the carotid artery was pulsating when emergency medical services' personnel encounter a patient with cardiac arrest. Based on first confirmed cardiac rhythm, we divided the patients into two groups: first confirmed non-shockable cardiac rhythm (asystole or pulseless electrical activity) group, and first confirmed shockable cardiac rhythm (pulseless ventricular tachycardia or ventricular fibrillation) group.

Table 2 shows the primary and secondary outcomes of patients with out-of-hospital cardiac arrest according to our multivariable analysis in the propensity-matched patients. In the non-shockable group, one-month favourable neurological survival was significantly higher in patients treated by a pre-hospital physician than in patients who were not treated by a pre-hospital physician (AOR: 4.64; 95% CI: 1.81–14.4). Similarly, one-month survival in the non-shockable group was significantly higher in patients treated by a pre-hospital physician (AOR: 4.64; 95% CI: 1.81–14.4). Similarly, one-month survival in the non-shockable group was significantly higher in patients treated by a pre-hospital physician than in patients who were not treated by a pre-hospital physician (AOR: 1.64; 95% CI: 1.02–2.67). However, in the shockable group, the presence of a pre-hospital physician had no effect on either outcome (AOR: 1.05; 95% CI: 0.67–1.63 for neurological survival and AOR: 1.12; 95% CI: 0.78–1.62 for one-month survival, respectively).

Table 3 shows the univariate logistic regression analysis according to the type of device used for AAM. In the non-shockable group, pre-hospital AAM under the presence of a physician was associated with increased one-month favourable neurological survival without adjusting, regardless of the type of device used (crude odds ratios: 4.50; 95% Cl: 1.75–11.0, and crude odds ratios: 4.10; 95% Cl: 2.26–7.01, respectively).

Table 4 shows the aetiologies of cardiac arrest based on first confirmed cardiac rhythm. When compared with the shockable group, arrests in the non-shockable group were more likely to have noncardiac aetiologies, such as respiratory disease.

#### **Discussion**

Using the large-scale Japanese prospective registry, we evaluated the difference in outcomes of adult patients who were given prehospital AAM, with or without a physician present, after the occurrence of cardiac arrest. We found a positive association between the presence of a pre-hospital physician and one-month favourable neurological survival in the non-shockable group. The findings of the current study provide valuable data for pre-hospital AAM strategy development and policymaking for local medical systems.

This study found out that the presence of a pre-hospital physician was significantly associated with one-month favourable neurological survival in the non-shockable group. One of the reasons for this finding may be the difference of aetiologies of cardiac arrests in the non-shockable group and the shockable group. As Table 4 shows, patients in the non-shockable cardiac rhythm group included had more non-cardiac aetiologies (such as respiratory disease) than patients in the shockable cardiac rhythm group. Thus, we infer that hypoxia as an aetiology of cardiac arrest may be critical in the non-shockable group. This could mean that pre-hospital AAM is very important to improve outcomes in the non-shockable group. There are two main factors in the association between pre-hospital AAM and improved outcomes. First, the quality of advice given by a physician will depend on the quality of the information related AAM provided from the scene. The potential advantage of having a

Patients with first confirmed non-shockable cardiae rhythm         With a pre- hospital (n = 1,173)         With a pre- hospital (n = 1,173)         Without a pre-hospital physician (n = 1,173)         Standardised mean (n = 1,173)           Patients' characteristics         Age, year, median (interquartile range) (n = 1,173)         75.0 (64.0. 86.0.         79.0 (68.0. 86.0.         0.24         75.0 (64.0. 83.0.         75.0 (64.0. 75.0 (63.0.         7.0 (2.1)         7.9 (3.8)         0.01           Pasuscatation by a bystander, n (%) Best (95.9.2.         52.6 (54.9.)         7.4 (2.0.1)         7.9 (3.3)         7.9 (3.3)         < 0.01           The elapsed time from the emergency call to contact with the patient by emergency medical services' personnel, wither because (slandard deviation)         815 (69.3)         9.003 (65.9)         0.07         813 (69.3)         794 (67.7)         0.04           Spring: March to May         244 (20.7)         3.002 (22.0)         244 (20.8)         258 (22.0)         244 (20.1)         300 (25.6)         296 (7.1) <th></th> <th colspan="3">All patients</th> <th colspan="3">Propensity score-matched patients</th>		All patients			Propensity score-matched patients		
With a pre- hospital         With a pre- hospital         Without a pre- hospital         Standardised mean (n = 1,173)         Without a pre-hospital physician (n = 1,173)         Standardised mean pre-hospital         Standardised pre-hospital         Standardised mean pre-hospital         Standardised pre-hospital         Without a pre-hospital         Standardised pre-hospital         Without a pre-hospital         Standardised pre-hospital         Standardised pre-hospital	Patients with first confirmed non-shockable cardiac rhvthm						
Patients' characteristics       75.0 (64.0-       75.0 (64.0-       75.0 (64.0-       75.0 (64.0-       83.0)       84.0)       83.0)       83.0)       84.0)       0.02         Men, $n$ (%)       75.0 (64.0-       83.0)       83.0)       83.0)       84.0)       0.03         Witnessed by a bystander, $n$ (%)       532 (45.2)       65.26 (35.1)       0.42       695 (54.2)       65.9 (54.8)       0.01         Dispatcher instruction, $n$ (%)       532 (45.2)       6.589 (44.3)       0.06       530 (45.2)       537 (45.8)       0.01         Dispatcher instruction, $n$ (%)       625 (53.1)       7.49 (54.9)       0.04       623 (53.1)       644 (54.9)       0.04         Time exceiving the emergency call to contact with the patient by emergency medical services' personnel, minutes, mean (standard deviation)       7.3 (2.7)       0.21       7.9 (3.3)       7.9 (67.7)       0.04         Season of the year, $n$ (%)       815 (69.3)       9.003 (65.9)       0.07       813 (69.3)       794 (67.7)       0.04         Summer: June to August       263 (22.4)       2.832 (22.7)       244 (20.8)       256 (22.0)       244 (20.8)       268 (21.0)         Summer: June to August       263 (22.4)       2.332 (72.4)       300 (25.6)       299 (25.5)       248 (21.1)         Autu		With a pre- hospital physician ( <i>n</i> = 1,176)	Without a pre- hospital physician ( <i>n</i> = 13,655)	Standardised mean difference	With a pre- hospital physician ( <i>n</i> = 1,173)	Without a pre-hospital physician ( <i>n</i> = 1,173)	Standardised mean difference
Age, year, median (interquaritie range) 83.075.0 (64.0- 83.0700 (66.0- 80.0700 (66.0- 83.0)75.0 (68.0- 83.0)75.0 (75.0)75.0 (75.0)75.0 (75.0)75.0 (75.0)75.0 (75.0)75.0 (75.0)75.0 (75.0)75.0 (	Patients' characteristics						
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	Men, <i>n</i> (%)	716 (60.9)	8,002 (58.6)	0.05	713 (60.8)	729 (62.1)	0.03
Resuscitation by a bystander, $n$ (%)       532 (45.2)       6,589 (48.3)       0.06       533 (45.2)       537 (45.8)       0.01         Dispathce instruction, $n$ (%)       7,9 (3.6)       7,9 (3.6)       7,9 (3.6)       7,9 (3.7)       0.04         Time       0.04       7,9 (3.6)       7,9 (3.6)       7,9 (3.7)       0.04         Season of the year, $n$ (%)       815 (69.3)       9.003 (65.9)       0.07       813 (69.3)       794 (67.7)       0.04         Season of the year, $n$ (%)       815 (69.3)       0.07       813 (69.3)       794 (67.7)       0.04         Season of the year, $n$ (%)       3.027 (22.0)       244 (20.8)       258 (22.0)         Sammer: June to August       2,327 (24.4)       0.00       0.04         Colspan="6">Sammer: June to August       3,327 (24.4)       306 (55.0       0,00         Colspan="6">Sammer: June to August       Adseg (31.3)       44.494 (32.9)	Witnessed by a bystander, n (%)	698 (59.4)	5,286 (38.7)	0.42	695 (59.2)	690 (58.8)	< 0.01
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$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Dispathcer instruction, n (%)	625 (53.1)	7,499 (54.9)	0.04	623 (53.1)	644 (54.9)	0.04
Time       Weekday, $n$ (%)       815 (69.3)       9,003 (65.9)       0.07       813 (69.3)       794 (67.7)       0.04         Season of the year, $n$ (%)       244 (20.7)       3,002 (22.0)       244 (20.8)       258 (22.0)       0.04         Summer: June to August       263 (22.4)       2,832 (20.7)       262 (22.3)       248 (21.1)       248 (21.1)         Autums: September to November       301 (25.6)       3,327 (24.4)       3000 (25.6)       299 (25.5)       299 (25.5)         Winter: December to February       368 (31.3)       4,494 (32.9)       367 (31.3)       368 (31.4)       368 (31.4)         Patients with first confirmed shockable cardiac rhythm       With a prehospital physician (n = 1477)       Mutiout a prehospital physician (n = 417)       Standardised mean (interquartile range)       Standardised (inference       mean difference       mean dif	The elapsed time from the emergency dispatch centre receiving the emergency call to contact with the patient by emergency medical services' personnel, minutes, mean (standard deviation)	7.9 (3.6)	7.3 (2.7)	0.21	7.9 (3.3)	7.9 (3.3)	< 0.01
Weekday, $n$ (%)815 (69.3)9,003 (65.9)0.07813 (69.3)794 (67.7)0.04Season of the year, $n$ (%)0.040.040.040.04Spring: March to May244 (20.7)3,002 (22.0)244 (20.8)258 (22.0)Summer: June to August263 (22.4)2,832 (20.7)262 (22.3)248 (21.1)Autumn: September to November301 (25.6)3,327 (24.4)300 (25.6)299 (25.5)Winter: December to February368 (31.3)4,494 (32.9)367 (31.3)368 (31.4)Patients with first confirmed shockablewith a pre- hospital physician $(n = 417)$ Kith a pre- hospital physician $(n = 413)$ With a pre- hospital physician $(n = 413)$ Standardised meanPatients with first confirmed shockable cardiac rhythm65.0 (54.0- 74.0)65.0 (56.0- 76.0)0.1565.0 (54.0- 74.0)66.0 (55.0- 76.0)0.07Patients' characteristics Age, year, median (interquartile range) Bystander, $n$ (%)345 (82.7)1,167 (80.2)0.07341 (82.6)346 (83.8)0.03Withessed by a bystander, $n$ (%)315 (75.5)1,027 (70.6)0.11311 (75.3)307 (74.3)0.02The elapsed time from the emergency call to contact with the patient by emergency medical services' personnel, minutes, mean (standard deviation)284 (68.1)964 (66.3)0.04281 (68.0)290 (70.2)0.05Season of the year, $n$ (%)284 (68.1)964 (66.3)0.04281 (68.0)290 (70.2)0.05Season of the year,	Time						
Season of the year, $n$ (%)       0.06       0.04         Spring: March to May       244 (20.7)       3,002 (22.0)       244 (20.8)       258 (22.0)         Summer: June to August       263 (22.4)       2,832 (20.7)       262 (22.3)       248 (21.1)         Autumn: September to November       301 (25.6)       3,327 (24.4)       300 (25.6)       299 (25.5)         Winter: December to February       368 (31.3)       4,494 (32.9)       367 (31.3)       368 (31.4)         Patients with first confirmed shockable       with a pre- hospital physician ( $n = 417$ )       Without a pre- hospital physician ( $n = 417$ )       Without a pre- hospital physician ( $n = 413$ )       Standardised mean ( $n = 413$ )       O.07         Patients' characteristics       65.0 (54.0- f6.0)       65.0 (54.0- f6.0)       65.0 (54.0- f6.0)       66.0 (55.0- f6.0)       0.07         Men, $n$ (%)       345 (82.7)       1,167 (80.2)       0.07       346 (83.8)       0.03         Witnessed by a bystander, $n$ (%)       231 (55.4)       779 (53.5)       0.04       227 (55.0)       226 (54.7)       < 0.01	Weekday, n (%)	815 (69.3)	9,003 (65.9)	0.07	813 (69.3)	794 (67.7)	0.04
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Season of the year, n (%)	. ,		0.06		· · ·	0.04
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Winter: December to February Patients with first confirmed shockable cardiac rhythm368 (31.3)4,494 (32.9)367 (31.3)368 (31.4)Patients with first confirmed shockable cardiac rhythm </td <td>Autumn: September to November</td> <td>301 (25.6)</td> <td>3,327 (24.4)</td> <td></td> <td>300 (25.6)</td> <td>299 (25.5)</td> <td></td>	Autumn: September to November	301 (25.6)	3,327 (24.4)		300 (25.6)	299 (25.5)	
Patients with first confirmed shockable cardiac rhythmWith a pre- hospital physician $(n = 417)$ Standardised mean differenceWithout a pre- hospital physician $(n = 413)$ Standardised mean differenceWithout a pre-hospital physician $(n = 413)$ Standardised mean differencePatients' characteristics65.0 (54.0- 74.0)67.0 (56.0- 76.0)0.15 76.0)65.0 (54.0- 74.0)66.0 (55.0- 76.0)0.07Men, n (%)345 (82.7)1,167 (80.2)0.07341 (82.6)346 (83.8)0.03Witnessed by a bystander, n (%)315 (75.5)1,027 (70.6)0.11311 (75.3)307 (74.3)0.02Resuscitation by a bystander, n (%)231 (55.4)779 (53.5)0.04227 (55.0)226 (54.7)<0.01	Winter: December to February	368 (31.3)	4,494 (32.9)		367 (31.3)	368 (31.4)	
With a pre- hospital physician $(n = 417)$ With a pre- hospital physician $(n = 417)$ Without a pre- hospital physician $(n = 413)$ Without a pre- hospital physician differenceWith a pre- hospital physician $(n = 413)$ Without a pre-hospital physician differenceStandardised mean differenceWith a pre- hospital physician $(n = 413)$ Without a pre-hospital physician differenceStandardised mean differencePatients' characteristics Age, year, median (interquartile range)65.0 (54.0- 74.0)67.0 (56.0- 76.0)0.1565.0 (54.0- 74.0)66.0 (55.0- 76.0)0.07Men, n (%)345 (82.7) 315 (75.5)1,027 (70.6)0.11311 (75.3)307 (74.3)0.02Resuscitation by a bystander, n (%)315 (75.5) 191 (45.8)769 (52.9)0.14191 (46.2)186 (45.0)0.02Dispatcher instruction, n (%)191 (45.8)769 (52.9)0.14191 (46.2)186 (45.0)0.02The elapsed time from the emergency call to contact with the patient by emergency medical services' personnel, minutes, mean (standard deviation)284 (68.1)964 (66.3)0.04281 (68.0)290 (70.2)0.05Season of the year, n (%)284 (68.1)964 (66.3)0.04281 (68.0)290 (70.2)0.05Spring: March to May Summer: June to August95 (22.8)348 (23.9)93 (22.5)87 (21.1)86 (20.8)Summer: Summer: June to August Autum: Sectember to November92 (39 3)346 (26.4)92 (20 3)131 (20 3)	Patients with first confirmed shockable cardiac rhythm						
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Patients' characteristics       Age, year, median (interquartile range) $65.0 (54.0 - 74.0)$ $67.0 (56.0 - 74.0)$ $65.0 (54.0 - 74.0)$ $76.0$ $74.0$ $76.0$ $74.0$ $76.0$ $74.0$ $76.0$ $74.0$ $76.0$ $74.0$ $76.0$ $74.0$ $76.0$ $0.07$ $341 (82.6)$ $346 (83.8)$ $0.03$ Witnessed by a bystander, $n (%)$ $315 (75.5)$ $1.027 (70.6)$ $0.11$ $311 (75.3)$ $307 (74.3)$ $0.02$ Resuscitation by a bystander, $n (%)$ $231 (55.4)$ $779 (53.5)$ $0.04$ $227 (55.0)$ $226 (54.7)$ $< 0.01$ Dispatcher instruction, $n (%)$ $191 (45.8)$ $769 (52.9)$ $0.14$ $191 (46.2)$ $186 (45.0)$ $0.02$ The elapsed time from the emergency $7.6 (3.6)$ $7.1 (2.6)$ $0.16$ $7.4 (2.8)$ $7.4 (2.7)$ $< 0.01$ call to contact with the patient by       emergency medical services' personnel, $minutes$ , mean (standard deviation) $0.07$ $0.07$ $0.07$ $0.05$ $0.09$ $0.09$ $0.09$ $0.09$ $0.09$ $0.09$ $0.09$ $0.09$ $0.09$ $0.09$ $0.09$ $0.09$		hospital physician ( <i>n</i> = 417)	hospital physician ( <i>n</i> = 1,455)	mean difference	hospital physician ( <i>n</i> = 413)	pre-hospital physician ( <i>n</i> = 413)	mean difference
Age, year, median (interquartile range) Men, $n$ (%) $65.0$ ( $54.0-$ $74.0$ ) $67.0$ ( $56.0-$ $76.0$ ) $0.15$ $65.0$ ( $54.0-$ $74.0$ ) $66.0$ ( $55.0-$ $76.0$ ) $0.07$ Men, $n$ (%) $345$ ( $82.7$ ) $1,167$ ( $80.2$ ) $0.07$ $341$ ( $82.6$ ) $346$ ( $83.8$ ) $0.03$ Witnessed by a bystander, $n$ (%) $315$ ( $75.5$ ) $1,027$ ( $70.6$ ) $0.11$ $311$ ( $75.3$ ) $307$ ( $74.3$ ) $0.02$ Resuscitation by a bystander, $n$ (%) $231$ ( $55.4$ ) $779$ ( $53.5$ ) $0.04$ $227$ ( $55.0$ ) $226$ ( $54.7$ ) $< 0.01$ Dispatcher instruction, $n$ (%) $191$ ( $45.8$ ) $769$ ( $52.9$ ) $0.14$ $191$ ( $46.2$ ) $186$ ( $45.0$ ) $0.02$ The elapsed time from the emergency call to contact with the patient by emergency medical services' personnel, minutes, mean (standard deviation) $7.6$ ( $3.6$ ) $7.1$ ( $2.6$ ) $0.16$ $7.4$ ( $2.8$ ) $7.4$ ( $2.7$ ) $< 0.01$ TimeWeekday, $n$ (%) $284$ ( $68.1$ ) $964$ ( $66.3$ ) $0.04$ $281$ ( $68.0$ ) $290$ ( $70.2$ ) $0.05$ Spring: March to May $88$ ( $21.1$ ) $328$ ( $22.5$ ) $87$ ( $21.1$ ) $86$ ( $20.8$ ) $300$ Summer: June to August $95$ ( $22.8$ ) $384$ ( $26.4$ ) $93$ ( $22.5$ ) $83$ ( $20.1$ ) $116$ ( $29.2$ )	Patients' characteristics						
Men, $n$ (%)345 (82.7)1,167 (80.2)0.07341 (82.6)346 (83.8)0.03Witnessed by a bystander, $n$ (%)315 (75.5)1,027 (70.6)0.11311 (75.3)307 (74.3)0.02Resuscitation by a bystander, $n$ (%)231 (55.4)779 (53.5)0.04227 (55.0)226 (54.7)< 0.01	Age, year, median (interquartile range)	65.0 (54.0- 74.0)	67.0 (56.0- 76.0)	0.15	65.0 (54.0- 74.0)	66.0 (55.0- 76.0)	0.07
Witnessed by a bystander, $n$ (%)       315 (75.5)       1,027 (70.6)       0.11       311 (75.3)       307 (74.3)       0.02         Resuscitation by a bystander, $n$ (%)       231 (55.4)       779 (53.5)       0.04       227 (55.0)       226 (54.7)       < 0.01	Men, <i>n</i> (%)	345 (82.7)	1,167 (80.2)	0.07	341 (82.6)	346 (83.8)	0.03
Resuscitation by a bystander, $n$ (%)       231 (55.4)       779 (53.5)       0.04       227 (55.0)       226 (54.7)       < 0.01	Witnessed by a bystander, n (%)	315 (75.5)	1,027 (70.6)	0.11	311 (75.3)	307 (74.3)	0.02
Dispatcher instruction, $n$ (%)191 (45.8)769 (52.9)0.14191 (46.2)186 (45.0)0.02The elapsed time from the emergency dispatch centre receiving the emergency call to contact with the patient by emergency medical services' personnel, minutes, mean (standard deviation)7.1 (2.6)0.167.4 (2.8)7.4 (2.7)< 0.01	Resuscitation by a bystander, n (%)	231 (55.4)	779 (53.5)	0.04	227 (55.0)	226 (54.7)	< 0.01
The elapsed time from the emergency       7.6 (3.6)       7.1 (2.6)       0.16       7.4 (2.8)       7.4 (2.7)       < 0.01         dispatch centre receiving the emergency       call to contact with the patient by       emergency medical services' personnel,	Dispatcher instruction, n (%)	191 (45.8)	769 (52.9)	0.14	191 (46.2)	186 (45.0)	0.02
Time       Weekday, n (%)       284 (68.1)       964 (66.3)       0.04       281 (68.0)       290 (70.2)       0.05         Season of the year, n (%)       0.07       0.07       0.09         Spring: March to May       88 (21.1)       328 (22.5)       87 (21.1)       86 (20.8)         Summer: June to August       95 (22.8)       348 (23.9)       93 (22.5)       83 (20.1)         Autumn: Sentember to November       122 (29.3)       384 (26.4)       121 (20.3)       116 (28.1)	The elapsed time from the emergency dispatch centre receiving the emergency call to contact with the patient by emergency medical services' personnel, minutes man (standard dovision)	7.6 (3.6)	7.1 (2.6)	0.16	7.4 (2.8)	7.4 (2.7)	< 0.01
Weekday, n (%)       284 (68.1)       964 (66.3)       0.04       281 (68.0)       290 (70.2)       0.05         Season of the year, n (%)       0.07       0.07       0.09         Spring: March to May       88 (21.1)       328 (22.5)       87 (21.1)       86 (20.8)         Summer: June to August       95 (22.8)       348 (23.9)       93 (22.5)       83 (20.1)         Autumn: Sentember to November       122 (29.3)       384 (26.4)       121 (29.3)       116 (28.1)	Time						
Weekday, <i>n</i> (%)       254 (65.1)       364 (66.5)       0.04       256 (65.6)       256 (70.2)       0.05         Season of the year, <i>n</i> (%)       0.07       0.09       0.09         Spring: March to May       88 (21.1)       328 (22.5)       87 (21.1)       86 (20.8)         Summer: June to August       95 (22.8)       348 (23.9)       93 (22.5)       83 (20.1)         Autumn: Sentember to November       122 (29.3)       384 (26.4)       121 (29.3)       116 (28.1)	Weekday n (%)	284 (68 1)	964 (66 3)	0.04	281 (68.0)	200 (70 2)	0.05
Spring: March to May         88 (21.1)         328 (22.5)         87 (21.1)         86 (20.8)           Summer: June to August         95 (22.8)         348 (23.9)         93 (22.5)         83 (20.1)           Autumn: Sentember to November         122 (29.3)         384 (26.4)         121 (29.3)         116 (28.1)	Season of the year $n(%)$	204 (00.1)	00.0)	0.04	201 (00.0)	230 (70.2)	0.09
Summer: June to August         95 (22.8)         348 (23.9)         93 (22.5)         83 (20.1)           Autumn: Sentember to November         122 (29.3)         384 (26.4)         121 (29.3)         116 (28.1)	Spring: March to May	88 (21 1)	328 (22 5)	0.07	87 (21 1)	86 (20.8)	0.00
Autum: Sentember to November 122 (20 3) 384 (26 4) 121 (20 3) 116 (28 1)	Summer: June to August	95 (22.8)	348 (23.9)		93 (22.5)	83 (20.1)	
	Autumn: September to November	122 (29.3)	384 (26.4)		121 (29.3)	116 (28.1)	
Winter: December to February 112 (26.9) 395 (27.1) 112 (27.1) 128 (31.0)	Winter: December to February	112 (26.9)	395 (27.1)		112 (27.1)	128 (31.0)	

#### Table 1 - Baseline characteristic of each patient with or without a pre-hospital physician.

pre-hospital physician, therefore, is to reduce frequency in which erroneous information is transferred between the emergency medical services' personnel and a physician working remotely. In addition, the presence of multiple rescuers was known as an independent factor associated with one-year survival.<sup>19</sup> The presence of a pre-hospital physician might lead to a better outcome, by performing sophisticated AAM through increased rescuers on the scene.

There are several limitations to this study. First, we note that there was potential selection and information bias in this study. As mentioned in the Methods section, the system of dispatching a physician in Japan has been employed in only a few areas. This means serious potential selection bias in our analysis. In fact, among analysed patients, the patients of approximately 10% had received resuscitation by a pre-hospital physician and the patients of approximately 90% had not. We should pay attention to this selection bias when interpreting the results of current study. Our study used a hospitalbased registry and does not include all hospitals in Japan. The registry did not indicate the proportion of non-participating hospitals.

	With a pre- hospital physician	Without a pre- hospital physician	Crude odds ratios (95% confidence intervals)	Adjusted odds ratios (95% confidence intervals)
One-month favourable neurological	survival as primary	outcome		
Before propensity score-matched				
	<i>n</i> = 1,176	<i>n</i> = 13,655		
First confirmed non-shockable cardiac rhythm, <i>n</i> (%)	24 (2.0)	67 (0.5)	4.23 (2.59–6.66)	2.11 (1.23–3.50)
	<i>n</i> = 417	<i>n</i> = 1,455		
First confirmed shockable cardiac rhythm, <i>n</i> (%)	78 (18.7)	191 (13.1)	1.52 (1.14–2.03)	1.10 (0.78–1.56)
After propensity score-matched				
	<i>n</i> = 1,173	<i>n</i> = 1,173		
First confirmed non-shockable cardiac rhythm, $n$ (%)	24 (2.0)	5 (0.4)	4.88 (2.01–14.5)	4.64 (1.81–14.4)
	<i>n</i> = 413	<i>n</i> = 413		
First confirmed shockable cardiac rhythm, <i>n</i> (%)	78 (18.9)	62 (15.0)	1.32 (0.92–1.90)	1.05 (0.67–1.63)
One-month survival as secondary of	outcome			
Before propensity score-matched	1			
	<i>n</i> = 1,176	<i>n</i> = 13,655		
First confirmed non-shockable cardiac rhythm, $n$ (%)	64 (5.4)	322 (2.4)	2.38 (1.80–3.12)	1.33 (0.95–1.85)
	<i>n</i> = 417	<i>n</i> = 1,455		
First confirmed shockable cardiac rhythm, <i>n</i> (%)	151 (36.2)	365 (25.1)	1.70 (1.34–2.14)	1.25 (0.93–1.68)
After propensity score-matched				
	<i>n</i> = 1,173	<i>n</i> = 1,173		
First confirmed non-shockable cardiac rhythm, $n$ (%)	64 (5.5)	37 (3.2)	1.77 (1.78–2.70)	1.64 (1.02–2.67)
	<i>n</i> = 413	<i>n</i> = 413		
First confirmed shockable cardiac rhythm, <i>n</i> (%)	150 (36.3)	116 (28.1)	1.46 (1.09–1.96)	1.12 (0.78–1.62)

### Table 2 – Multivariable analysis of primary and secondary outcomes of a patient with out-of-hospital cardiac arrest.

Adjusted odds ratios and 95% confidence intervals are adjusted to extracorporeal membrane oxygenations, percutaneous coronary intervention, intra-aortic balloon pumping, and targeted temperature management in the propensity score-matched patients. The propensity score is calculated using patients' characteristics (the patient's age, the patient's sex, witnessed by a bystander, resuscitation by a bystander, dispatcher instruction, the elapsed time from the emergency dispatch centre receiving the emergency call to contact with the patient by emergency medical services personnel), and the time (weekday, weekend or holiday, season of the year). Favourable neurological survival is defined as Cerebral Performance Category score 1 or 2.

The phrase of "before propensity score-matched" is defined as the full cohort before propensity score matching. The phrase of "after propensity score-matched" is defined as the cohort after propensity score matching.

Based on previous papers that used the registry protocol,<sup>13</sup> the registry is comprised mainly of critical emergency medical centres or tertiary emergency medical facilities. The medical professionals in these facilities can provide sophisticated treatments for severely ill patients (including patients with out-of-hospital cardiac arrest) that may not be available in other types of medical facility.<sup>5</sup> Additionally, there is a significant selection bias in the enrolled patients of both groups of current study. Japanese personnel of emergency medical services do not have the authority to perform intubation for patients with spontaneous circulation after cardiac arrest. This means we were not able to evaluate on the patients, who would be better to perform AAM after return of spontaneous circulation, at pre-hospital settings under the absence of a physician. Moreover, a pre-hospital physician could selectively decide not to perform AAM for patients having prolonged downtime in the non-shockable group. If decided not to complete AAM, the patients were not measured by our study. This is major critical selection bias. We should also pay attention to

this selection bias when interpreting the results of current study. The persons who evaluated patient outcomes in this study were not blinded. However, they evaluated the outcomes based on a Cerebral Performance Category score, using hospital medical records. Thus, we infer that the information bias in our current study is limited. Furthermore, because of its observational nature, there may be additional factors affecting the association between AAM and patient outcomes that were not measured. For example, pre-hospital practice rules such as the criteria for dispatching a physician and the choice of device for AAM are not uniform across Japan. In addition, some information about AAM for each patient, such as the number of attempts and unsuccessful intubation, is not available in the registry. Similarly, the registry did not provide data about the location of occurrence of cardiac arrest. Additionally, we were unable to quantify the technical and non-technical skills of pre-hospital physicians who performed AAM. Moreover, the registry did not provide detailed information on the areas served by each pre-hospital physician and the

Table	3 – Univa	riate logist	ic regressi	on analys	is accord	ing to t	he type o	f device	e used for	advanced	airway
manag	ement in	the pre-ho	spital loca	tion.							

	With a pre-hospital physician	Without a pre-hospital physician	Crude odds ratios (95% confidence intervals)			
One-month favourable neurological survival						
Endotracheal intubation						
	<i>n</i> = 368	n = 2,442				
First confirmed non-shockable cardiac rhythm, <i>n</i> (%)	8 (2.2)	12 (0.5)	4.50 (1.75–11.0)			
	<i>n</i> = 90	n = 249				
First confirmed shockable cardiac rhythm, $n$ (%)	13 (14.4)	29 (11.6)	1.28 (0.62–2.54)			
Supraglottic airway						
	<i>n</i> = 808	<i>n</i> = 11,213				
First confirmed non-shockable cardiac rhythm, <i>n</i> (%)	16 (2.0)	55 (0.5)	4.10 (2.26–7.01)			
	n = 327	<i>n</i> = 1,206				
First confirmed shockable cardiac rhythm, <i>n</i> (%)	65 (19.9)	162 (13.4)	1.60 (1.16–2.19)			
One-month survival						
Endotracheal intubation						
	<i>n</i> = 368	n = 2,442				
First confirmed non-shockable cardiac rhythm, <i>n</i> (%)	21 (5.7)	62 (2.5)	2.32 (1.37–3.80)			
	<i>n</i> = 90	n = 249				
First confirmed shockable cardiac rhythm, <i>n</i> (%)	24 (26.7)	55 (22.1)	1.28 (0.73–2.22)			
Supraglottic airway						
	<i>n</i> = 808	<i>n</i> = 11,213				
First confirmed non-shockable cardiac rhythm, $n$ (%)	43 (5.3)	260 (2.3)	2.37 (1.68–3.26)			
	n = 327	<i>n</i> = 1,206				
First confirmed shockable cardiac rhythm, <i>n</i> (%)	127 (38.8)	310 (25.7)	1.84 (1.42–2.37)			
Favourable neurological survival is defined as Cerebral Performance Category score 1 or 2.						

#### Table 4 - The etiologies of cardiac arrest based on first confirmed cardiac rhythm.

	A pre-hospital physician	Without a pre-hospital physician
Aetiology		
First confirmed non-shockable cardiac rhythm, n (%)	<i>n</i> = 1,176	<i>n</i> = 13,655
Cardiac	896 (76.2)	11,036 (80.8)
Non-cardiac		
Respiratory disease	115 (9.8)	1,317 (9.6)
Cerebrovascular disease	124 (10.5)	865 (6.3)
Malignant tumour	41 (3.5)	437 (3.2)
First confirmed shockable cardiac rhythm, n (%)	<i>n</i> = 417	<i>n</i> = 1,455
Cardiac	411 (98.6)	1,408 (96.8)
Non-cardiac		
Respiratory disease	2 (0.5)	24 (1.6)
Cerebrovascular disease	4 (1.0)	15 (1.0)
Malignant tumour	0 (0.0)	8 (0.5)

number of hospitals related the system of dispatching a physician. Finally, we note that our findings may not be fully applicable in other regions, due to differences in national legislation and in systems of pre-hospital emergency care worldwide. In particular, Japanese emergency medical service personnel cannot legally make decisions to perform advanced life support procedures in real time. This differs from many other regions and most certainly may affect the generalizability of this study.

#### Conclusions

Pre-hospital AAM, in the presence of a physician, was significantly associated with increased favourable neurological survival in nonshockable group of patients after the occurrence of cardiac arrest.

#### **CRediT** authorship contribution statement

Toshihiro Hatakeyama: Conceptualization, Formal analysis, Investigation, Methodology, Project administration, Resources, Software, Validation, Visualization, Writing – original draft, Writing – review & editing. Takeyuki Kiguchi: Conceptualization, Funding acquisition, Investigation, Supervision, Writing – review & editing. Toshiki Sera: Conceptualization, Writing – review & editing. Sho Nachi: Conceptualization, Writing – review & editing. Nao Urushibata: Conceptualization, Data curation, Writing – review & editing. Kanae Ochiai: Conceptualization, Writing – review & editing. Tetsuhisa Kitamura: Supervision, Writing – review & editing. Shinji Ogura: Conceptualization, Writing – review & editing. Yasuhiro Otomo: Conceptualization, Writing – review & editing. Taku Iwami: Conceptualization, Writing – review & editing.

#### **Declaration of Competing Interest**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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