例と非心原性症例で良い傾向がみられ，特に非心原性症例でその傾向が顕著にみられた。一方SOS-KANTOでは，バイスタンダーにより目撃から4分以内に心肺蘇生が実施された症例では，胸骨圧迫のみの予後が従来法よりも良いと報告されており，BMJ研究とは異なる結果であった。この理由は，BMJ研究ではすべての年齢階級を含んでいるのに対して，SOS-KANTOでは成人症例のみによる分析であり，この分析対象群の違いによるものと考えられる。

2010年のAHAガイドライン[17]によれば，心肺蘇生を含むBLS（basic life support）の手順としては，従来のA-B-C（気道，呼吸，胸骨圧迫）から，C-A-B（胸骨圧迫，気道，呼吸）に変更することを勧告している。その理由としては，心停止症例の多くが成人の心室細動（VF）あるいは無脈性心室頻拍（VT）症例であり，これらの症例に対しては迅速な胸骨圧迫と除細動が重要とされているからであり，その観点から気道確保，人工呼吸を優先して実施する従来のBLS手順よりも胸骨圧迫を優先することは適切であると結論づけている。また，心停止傷病者の多くがバイスタンダーによる心肺蘇生を受けてないとの報告もあり，その理由が十分な訓練を受けていないバイスタンダーにとっては気道確保や人工呼吸の実施が困難であることがあげられる。

BMJ研究では，成人症例では胸骨圧迫のみと従来法の予後には差がみられなかったことから，2010年のAHAガイドラインのBLS手順の変更は，成人に対しては問題ないと思われる。しかしながら，BMJ研究により20歳未満の症例に対しては従来法の予後が良いという結果が示されたことで，若年層に対するBLS手順は従来通りのA-B-C（気道，呼吸，胸骨圧迫）を維持することを再検討すべきであると考えられよう。

なお，BMJ研究には以下の課題が存在する。BMJ研究では，「救急蘇生統計」に収載されている院外発生で救急搬送された心停止傷病者のうち，一般市民による目撃症例を用いて分析したが，一般市民にとっては救急の現場で患者の心肺機能が停止したかどうかの判断が難しいため，一部心肺機能が停止しなかった症例が混在している可能性がある。そのためBMJ研究の結果はやや過剰評価の可能性があるが比較研究であることから，これらの非停止症例は両群に均等に存在すると考えられ，両群比較の結果には影響はないと思われる。第二に，年齢別の分析においては，40歳未満の症例数が少ないため，これらの年齢群においては交絡因子の影響が大きいと予想される。第三に，目撃からバイスタンダーによる心肺蘇生実施までの経過時間に関する分析においては，時間情報はバイスタンダーに対する聞き取り調査により把握しており，救急の現場でこれらの時間が正確には把握できていない可能性がある。第四に交絡因子の選択については，医学的な見地から実施したが，必要な交絡因子をすべて選択できたかどうかは十分に検討できない。第五に，心停止傷病者の予後は，実施された心肺蘇生の質に左右されるといわれている[18]が，「救急蘇生統計」においては実施された心肺蘇生の質に関する情報は存在しない。したがって，実施された心肺蘇生はすべて同じ質であったと仮定した。第六に，胸骨圧迫のみと従来法の両群の予後は全症例で差がみられたが，その差は調整前後ともあまり大きくないのが現状で，そのためType 1エラーの危険性が存在する。このためには，さらなるデータ収集と解析が必要であろう。第七に，予後として用いた生存率や脳機能カテゴリー良好割合は発生から1ヶ月後のものであり，本来はより長期の予後について検討すべきと考えられる[19]が，「救急蘇生統計」では1ヶ月後の予後のみが記載されているため，より長期の予後については検討できないのが現状である。最後に，わが国の全国データを用いた分析であったため，他国への適用が可能かどうかについては不透明である。

4．結　論

BMJ研究により，院外発生の心停止傷病者に対してバイスタンダーによる従来法（胸骨圧迫＋人工呼吸）の予後は，胸骨圧迫のみに比べて良いことが示唆された。特に，非心原性の若年層，あるいは非心原性で目撃からある程度経過してから心肺蘇生を実施された症例で，従来法の予後が胸骨圧迫のみに比べて良いことが示唆された。この結果は，今後の

ガイドライン作成等に活用できるものと期待される。

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Selected Topics: Prehospital Care

COMPARISON OF NEUROLOGICAL OUTCOME BETWEEN TRACHEAL INTUBATION AND SUPRAGLOTTIC AIRWAY DEVICE INSERTION OF OUT-OF-HOSPITAL CARDIAC ARREST PATIENTS: A NATIONWIDE, POPULATION-BASED, OBSERVATIONAL STUDY

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☐ **Abstract—Background: The effect of prehospital use of supraglottic airway devices as an alternative to tracheal intubation on long-term outcomes of patients with out-of-hospital cardiac arrest is unclear. Study Objectives: We compared the neurological outcomes of patients who underwent supraglottic airway device insertion with those who underwent tracheal intubation. Methods: We conducted a nationwide population-based observational study using a national database containing all out-of-hospital cardiac arrest cases in Japan over a 3-year period (2005–2007). The rates of neurologically favorable 1-month survival (primary outcome) and of 1-month survival and return of spontaneous circulation before hospital arrival (secondary outcomes) were examined. Multiple logistic regression analyses were performed to adjust for potential confounders. Advanced airway devices were used in 138,248 of 318,141 patients, including an endotracheal tube (ETT) in 16,054 patients (12%), a laryngeal mask airway (LMA) in 34,125 patients (25%), and an esophageal obturator airway (EOA) in 88,069 patients (63%). Results: The overall rate of neurologically favorable 1-month survival was 1.03% (1426/137,880). The rates of neurologically favorable 1-month survival were 1.14% (183/16,028) in the ETT group, 0.98% (333/34,059) in the LMA group, and 1.04% (910/87,793) in the EOA group. Compared with the ETT group, the rates were significantly lower in the LMA group (adjusted odds ratio 0.77, 95% confidence interval [CI] 0.64–0.94) and EOA group (adjusted odds ratio 0.81, 95% CI 0.68–0.96). Conclusions: Prehospital use of supraglottic airway devices was associated with slightly, but significantly, poorer neurological outcomes compared with tracheal intubation, but neurological outcomes remained poor overall.** © 2012 Elsevier Inc.

☐ **Keywords—out-of-hospital cardiac arrest; tracheal intubation; supraglottic airway device; neurological outcome; airway management**

INTRODUCTION

Tracheal intubation has long been considered the gold standard for airway management during resuscitation after cardiac arrest. However, this method is now being

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challenged by some experts, especially when the tracheal intubation is performed by inexperienced providers in prehospital settings (1). Critics of the technique cite incorrect placement of the endotracheal tube (ETT) and unnecessary interruption of chest compressions associated with the lengthy procedure as the major disadvantages of prehospital tracheal intubation (2).

Several supraglottic airway devices are currently in clinical use as alternatives to ETT, including the laryngeal mask airway (LMA) and the laryngeal tube, which can be used without the need for elaborate training for airway management (3–7). However, a systematic comparison of the clinical outcomes of ETT and supraglottic airway devices has not been conducted (8).

The aim of the current study was to compare the effects of tracheal intubation and insertion of supraglottic airway devices on neurological outcomes of patients with out-of-hospital cardiac arrest.

MATERIALS AND METHODS

Study Design

This study was approved by the Ethics Committee of Nara Medical University (Authorization Code: 260). We conducted a nationwide population-based observational study using a Japanese national database containing information about out-of-hospital cardiac arrests over a 3-year period from January 1, 2005 to December 31, 2007. The database was compiled by the Fire and Disaster Management Agency (FDMA) in Japan, and contained all out-of-hospital cardiac arrest cases that were transferred to hospitals by emergency medical service (EMS) personnel (9). The data set included age, sex, whether the collapse was witnessed, whether bystander cardiopulmonary resuscitation (CPR) was performed, cause of cardiac arrest (cardiac or non-cardiac origin), first documented cardiac rhythm, whether the patient was defibrillated by the EMS, whether epinephrine was administered by the EMS, whether advanced airway devices were used by the EMS, and, if so, the type of advanced airway device used, time course of resuscitation, and outcomes (10).

Setting

Japan contains approximately 128 million residents in an area of 377,914 km^2. A total of 807 fire departments with dispatch centers covered the whole nation as of 2007. The most highly trained prehospital emergency care providers are Emergency Life-Saving Technicians. Among ambulance attendants, only Emergency Life-Saving Technicians are authorized to use supraglottic airway devices other than ETT (11). ETT insertion is conducted only by Emergency Life-Saving Technicians who have received specific training, including a minimum of 30 successful attempts at tracheal intubation in elective surgical patients under anesthesia (11).

The National Protocol for Resuscitation stated that bag-valve-mask ventilation (BVM) was to be used as the first choice for resuscitation, and that an advanced airway device should be considered only when the patient's airway could not be sufficiently secured or a long transportation period was expected (12).

Selection of Participants

We included all out-of-hospital cardiac arrest patients aged 15 years or older who were treated by EMS personnel using advanced airway devices. Patients younger than 15 years of age were excluded from this study because the National Protocol for Resuscitation states that tracheal intubation should be used only for patients aged 15 years or older. We also excluded patients for whom the type of advanced airway device was unknown.

Methods of Measurement

Patients were categorized into three groups according to the advanced airway devices used: ETT group; LMA group; and esophageal obturator airway (EOA) group. Any supraglottic airway devices designed to occlude the esophagus using a balloon were classified as EOAs. The EOAs included a laryngeal tube, a Combitube (an esophageal-tracheal twin-lumen airway device; Kendall Inc., Mansfield, MA), and an esophageal gastric tracheal airway. Cases with unsuccessful advanced airway device insertion and subsequent use of BVM were excluded. Cases in which the airway management method was changed midway were classified according to the airway device in use on arrival at the hospital.

Cardiac arrest was defined as the absence of cardiac mechanical activity, as confirmed by the absence of signs of circulation (10,13,14). The etiology of cardiac arrest was determined clinically by the physician in charge, in collaboration with EMS personnel. Cardiac arrest was presumed to be of cardiac origin unless external causes or any other non-cardiac causes (e.g., respiratory diseases, cerebrovascular diseases, or malignant tumors) were obvious (15). The external causes of out-of-hospital cardiac arrest included trauma, drowning, drug overdose, asphyxia, and hanging. Outcome data such as the 1-month survival and neurological status were collected by EMS personnel from the physicians in charge of the patients (16).

Data Collection and Processing

All the information was entered at local fire departments by EMS personnel using an online entry form, which

conformed to the Utstein-style guidelines (10,13,14). The data were verified by EMS personnel and anonymized at the local fire departments, then transferred and stored in the database at the FDMA (17). The data were checked in a logical manner by the computer system at the FDMA. If there were any inconsistencies or missing data, the FDMA consulted the corresponding regional fire department and the data were corrected (9). This is a national database, and the FDMA determines which data are included. There is only one nationwide ambulance service system covering all of Japan, and this service is operated publicly. Thus, the data including the outcome data are collected officially and systematically.

Outcome Measures

The primary outcome measure was the rate of neurologically favorable 1-month survival. Neurologically favorable 1-month survival was defined as Glasgow-Pittsburgh Cerebral Performance Category 1 (good cerebral performance) or 2 (moderate cerebral disability), as evaluated by the physician in charge via a follow-up interview at 1 month after hospital admission (10,13,14). The secondary outcome measures were the return of spontaneous circulation (ROSC) before hospital arrival and 1-month survival.

Statistical Analysis

Patient characteristics were evaluated by analysis of variance (ANOVA) for numerical variables and the chi-squared test for categorical variables. The outcomes were evaluated using the chi-squared test and multiple logistic regression analysis. Multiple logistic regression analyses were performed to compare the effects in the LMA and EOA groups with those in the ETT group as a reference, after controlling for potential confounders. Potential confounders were selected by clinical considerations and included age, sex, first documented cardiac rhythm, time between emergency call and initiation of CPR by EMS personnel, time between initiation of CPR by EMS personnel and hospital arrival, etiology of cardiac arrest, witness status, presence of bystander-initiated CPR, first shock by lay people, shock by EMS personnel, and intravenous administration of fluid and epinephrine.

For post hoc subgroup analyses, we divided the eligible patients into internally caused (endogenous) cardiac arrest cases (e.g., cardiac origin, respiratory diseases, cerebrovascular diseases, malignant tumors) and externally caused (exogenous) cardiac arrest cases (e.g., trauma, drowning, drug overdose, asphyxia, hanging), and separately analyzed the effects in the LMA and EOA groups compared with those in the ETT group. The calculated odds ratio was adjusted for the above confounders, except for omission of the etiologies of cardiac arrest among the independent variables in the analyses for the exogenous cardiac arrest group. In addition, similarly, the eligible patients were divided into ventricular fibrillation and pulseless ventricular tachycardia (VF/VT) cases, pulseless electrical activity (PEA) cases, and asystole cases according to first documented rhythms, and post hoc subgroup analyses were then conducted.

All statistical analyses were conducted using PASW version 17 (SPSS Inc., Chicago, IL). The value of $p < 0.05$ was considered statistically significant. We used 95% confidence intervals in the analysis of odds ratios of the outcomes.

RESULTS

Resuscitation was attempted in a total of 308,710 patients aged 15 years and older. Among these patients, cases in which CPR was performed by BVM without an advanced airway device (n = 167,953), patients in whom it was unclear whether an advanced airway device was used (n = 2169), and patients in whom the type of airway device used was unknown (n = 340) were excluded from the analysis, leaving 138,248 patients eligible for our study. Among these patients, ETT was used in 16,054 (12%), an LMA was used in 34,125 (25%), and an EOA was used in 88,069 (63%) (Figure 1). The neurological status at 1 month was not documented in 368 (<0.3%) patients. These cases were excluded from the primary outcome analysis. Secondary outcome was documented in all eligible patients.

Table 1 shows the background characteristics of the patients. Although the three groups seemed to be homogenous in terms of the background characteristics, ANOVA and chi-squared tests revealed significant differences among the three groups for most characteristics.

The overall rate of neurologically favorable 1-month survival was 1.03% (1426/137,880), survival rate at 1 month was 3.84% (5303/138,248), and the rate of ROSC before hospital arrival was 6.90% (9546/138,248).

Table 2 shows the comparisons of outcome measures in the ETT, LMA, and EOA groups. The rates of neurologically favorable 1-month survival were 1.14% (183/16,028) in the ETT group, 0.98% (333/34,059) in the LMA group, and 1.04% (910/87,793) in the EOA group. There were no significant differences among the three groups (chi-squared test). After adjustment for confounders, the rates of neurologically favorable 1-month survival were significantly lower in the LMA and EOA groups than in the ETT group.

The 1-month survival rates were 4.19% in the ETT group, 3.64% in the LMA group, and 3.85% in the EOA group. The 1-month survival rates were significantly lower in the LMA and EOA groups than in the ETT group in both the chi-squared test and the multivariable logistic regression analysis.

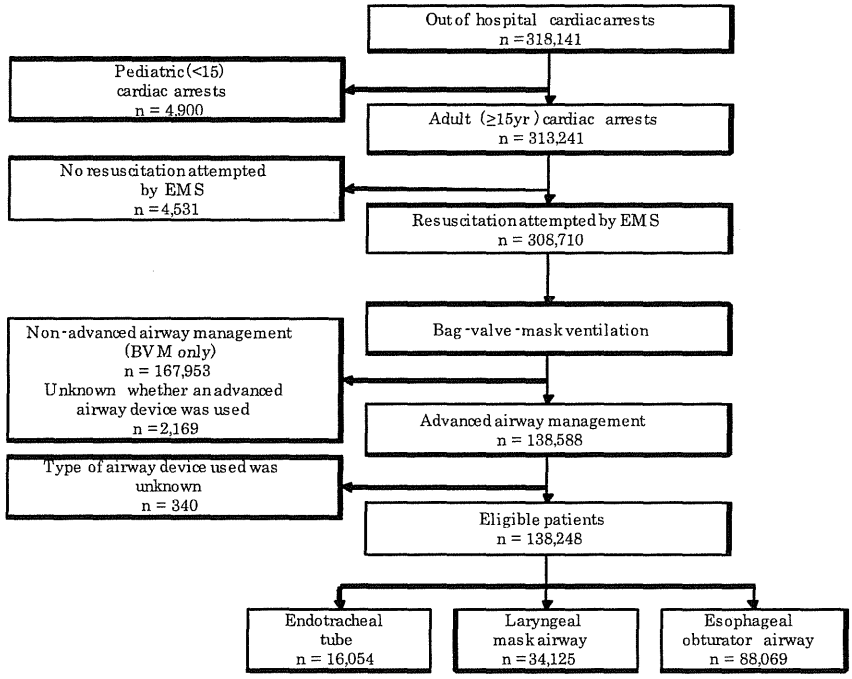

Figure 1. Flow diagram of the patient inclusion procedure. During the 3 years of the study, 318,141 out-of-hospital cardiac arrests were documented, of which 138,248 were treated with endotracheal tube, laryngeal mask, or esophageal obturator airway. EMS = emergency medical service; BVM = bag-valve-mask.

The rates of ROSC before hospital arrival were 7.24% in the ETT group, 4.90% in the LMA group, and 4.41% in the EOA group. The rates were significantly lower in the LMA and EOA groups compared with the ETT group in both the chi-squared test and the multivariable logistic regression analysis.

Table 1. Patient Characteristics of Study Participants According to Type of Advanced Airway Device Used

	Total n = 138,248	Endotracheal Tube n = 16,054 (12%)	Laryngeal Mask Airway n = 34,125 (25%)	Esophageal Obturator Airway n = 88,069 (63%)	*p*-Value
Age, years, mean ± SD	72.3 ± 15.9	73.8 ± 15.3	72.1 ± 15.9	73.8 ± 16.0	< 0.001
Male, n (%)	83,074 (60.1)	9397 (58.5)	20,657 (60.5)	53,020 (60.2)	< 0.001
Witnessed by laypersons, n (%)	55,441 (40.1)	7126 (44.4)	13,413 (39.3)	34,902 (39.6)	< 0.001
Bystander-initiated CPR, n (%)	54,508 (39.4)	6722 (41.9)	12,930 (37.9)	34,856 (39.6)	< 0.001
First shock by PAD - AEDs, n (%)	302 (0.2)	51 (0.3)	77 (0.2)	174 (0.2)	0.09
First documented rhythm, n (%)					< 0.001
VF/pulseless VT	11,241 (8.1)	1201 (7.5)	2943 (9.8)	7097 (8.1)	
PEA	31,581 (22.8)	3858 (24.0)	8224 (27.3)	19,499 (22.1)	
Asystole	92,203 (66.7)	10,659 (66.4)	22,275 (73.9)	59,269 (67.3)	
AED by EMS, n (%)	17,076 (12.5)	1946 (12.4)	4423 (13.0)	10,707 (12.3)	0.02
Intravenous fluid, n (%)	40,798 (29.8)	5836 (36.9)	9083 (26.7)	25,879 (29.6)	< 0.001
Epinephrine, n (%)	5416 (4.0)	1771 (11.3)	851 (2.5)	2794 (3.2)	< 0.001
Call to CPR by EMS, min, mean ± SD	9.4 ± 5.0	9.5 ± 5.2	9.1 ± 4.5	9.5 ± 5.0	< 0.001
CPR by EMS to hospital arrival, min, mean ± SD	23.5 ± 8.8	25.8 ± 9.3	23.9 ± 8.5	22.9 ± 8.7	< 0.001
Type of etiology, n (%)					< 0.001
Endogenous causes	116,071 (84.0)	12,992 (80.9)	29,640 (86.9)	73,439 (83.4)	
Cardiac	80,448 (58.2)	8594 (53.5)	21,561 (63.2)	50,293 (57.1)	
Respiratory diseases	7493 (5.4)	1101 (6.9)	1616 (4.7)	4776 (5.4)	
Cerebrovascular diseases	7272 (5.3)	808 (5.0)	1649 (4.8)	4815 (5.5)	
Malignant tumors	3484 (2.5)	389 (2.4)	894 (2.6)	2201 (2.5)	
Others	17,374 (12.6)	2100 (13.1)	3920 (11.5)	11,354 (12.9)	
Exogenous causes	22,173 (16.0)	3062 (19.1)	4483 (13.1)	14,628 (16.6)	

SD = standard deviation; CPR = cardiopulmonary resuscitation; PAD = public access defibrillation; AED = automated external defibrillator; VF = ventricular fibrillation; VT = ventricular tachycardia; PEA = pulseless electrical activity; EMS = emergency medical services.

Table 2. Outcomes of Out-of-Hospital Cardiac Arrest Patients According to Types of Advanced Airway Devices Used

	Endotracheal Tube	Laryngeal Mask Airway		Esophageal Obturator Airway	
	n = 16,054	n = 34,125	*p*-Value	n = 88,069	*p*-Value
Neurologically favorable 1-month survival, n (%)	183 (1.14)	333 (0.98)		910 (1.04)	
OR (95% CI)	Reference	0.85 (0.71–1.02)	0.09	0.91 (0.78–1.07)	0.23
Adjusted OR (95% CI)	Reference	0.77 (0.64–0.94)	0.010	0.81 (0.68–0.96)	0.014
1-month survival, n (%)	673 (4.19)	1242 (3.64)		3388 (3.85)	
OR (95% CI)	Reference	0.86 (0.78–0.95)	0.003	0.91 (0.84–0.99)	0.038
Adjusted OR (95% CI)	Reference	0.85 (0.77–0.95)	0.003	0.91 (0.83–1.00)	0.043
ROSC before hospital arrival, n (%)	1162 (7.24)	1671 (4.90)		3880 (4.41)	
OR (95% CI)	Reference	0.66 (0.61–0.71)	< 0.001	0.59 (0.55–0.63)	< 0.001
Adjusted OR (95% CI)	Reference	0.86 (0.79–0.93)	<0.001	0.76 (0.70–0.82)	< 0.001

OR = odds ratio; CI = confidence interval; ROSC = return of spontaneous circulation.

Table 3 shows the results of subgroup analyses of the endogenous and exogenous cases. Endogenous cases (n = 116,071) accounted for 84% of the eligible patients. The etiology of cardiac arrest was not documented in 4 patients. These cases were excluded from the analysis. The overall rates of neurologically favorable 1-month survival were 1.13% (1314/115,778) in endogenous cases and 0.51% (112/22,098) in exogenous cases. After adjustment for confounders, in the endogenous subgroup the rates of neurologically favorable 1-month survival were significantly lower in the LMA (1.05%) and EOA (1.15%) groups than in the ETT group (1.25%). In the exogenous subgroup, the neurologically favorable 1-month survival rates did not differ among the three groups.

Table 4 shows the results of subgroup analyses of the VF/VT cases, PEA cases, and asystole cases. The overall rate of neurologically favorable 1-month survival was 6.47% (725/11,213) in VF/VT cases, 1.1% (348/31,512) in PEA cases, and 0.3% (257/91947) in asystole cases. After adjustment for confounders, in the PEA subgroup, the rates of neurologically favorable 1-month survival were significantly lower in the LMA (0.96%) and EOA (1.12%) groups than in the ETT group (1.35%).

DISCUSSION

The current results revealed significantly higher rates of neurologically favorable 1-month survival in the ETT

Table 3. Outcomes of Out-of-Hospital Cardiac Arrest Patients According to Endogenous and Exogenous Causes of Arrest and Types of Advanced Airway Devices Used

	Endotracheal Tube	Laryngeal Mask Airway	*p*-Value	Esophageal Obturator Airway	*p*-Value
Endogenous, n	12,992	29,640		73,439	
Neurologically favorable 1-month survival, n (%)	162 (1.25)	310 (1.05)		842 (1.15)	
OR (95% CI)	Reference	0.84 (0.69–1.02)	0.069	0.92 (0.78–1.09)	0.33
Adjusted OR (95% CI)	Reference	0.77 (0.63–0.94)	0.012	0.81 (0.68–0.97)	0.025
1-month survival, n (%)	474 (3.65)	1060 (3.58)		2822 (3.84)	
OR (95% CI)	Reference	0.98 (0.88–1.09)	0.71	1.06 (0.96–1.17)	0.29
Adjusted OR (95% CI)	Reference	0.96 (0.85–1.08)	0.45	1.04 (0.93–1.16)	0.52
ROSC before hospital arrival, n (%)	853 (6.57)	1386 (4.68)		3193 (4.35)	
OR (95% CI)	Reference	0.70 (0.64–0.76)	< 0.001	0.65 (0.60–0.70)	< 0.001
Adjusted OR (95% CI)	Reference	0.87 (0.79–0.96)	0.004	0.79 (0.73–0.87)	< 0.001
Exogenous, n	3062	4483		14,628	
Neurologically favorable 1-month survival, n (%)	21 (0.69)	23 (0.52)		68 (0.47)	
OR (95% CI)	Reference	0.75 (0.41–1.36)	0.34	0.68 (0.42–1.11)	0.12
Adjusted OR (95% CI)	Reference	0.92 (0.49–1.75)	0.81	0.76 (0.44–1.33)	0.34
1-month survival, n (%)	199 (6.50)	182 (4.06)		566 (3.87)	
OR (95% CI)	Reference	0.61 (0.50–0.75)	< 0.001	0.58 (0.49–0.69)	< 0.001
Adjusted OR (95% CI)	Reference	0.69 (0.55–0.86)	0.001	0.67 (0.56–0.80)	< 0.001
ROSC before hospital arrival, n (%)	309 (10.1)	285 (6.36)		687 (4.70)	
OR (95% CI)	Reference	0.61 (0.51–0.72)	< 0.001	0.44 (0.38–0.51)	< 0.001
Adjusted OR (95% CI)	Reference	0.91 (0.76–1.10)	0.32	0.67 (0.57–0.79)	< 0.001

OR = odds ratio; CI = confidence interval; ROSC = return of spontaneous circulation.

Table 4. Outcomes of Out-of-Hospital Cardiac Arrest Patients According to First Documented Rhythm and Type of Advanced Airway Device Used

	Endotracheal Tube	Laryngeal Mask Airway	*p*-Value	Esophageal Obturator Airway	*p*-Value
VF/pulseless VT, n	1201	2943		7097	
Neurologically favorable 1-month survival, n (%)	86 (7.17)	185 (6.30)		454 (6.42)	
OR (95% CI)	Reference	0.87 (0.67–1.13)	0.31	0.89 (0.70–1.13)	0.33
Adjusted OR (95% CI)	Reference	0.87 (0.65–1.15)	0.33	0.80 (0.61–1.03)	0.09
1-month survival, n (%)	173 (14.40)	444 (15.09)		1047 (14.75)	
OR (95% CI)	Reference	1.06 (0.88–1.28)	0.58	1.03 (0.87–1.23)	0.75
Adjusted OR (95% CI)	Reference	1.05 (0.86–1.29)	0.63	0.96 (0.8–1.16)	0.71
ROSC before hospital arrival, n (%)	214 (17.82)	451 (15.32)		1055 (14.87)	
OR (95% CI)	Reference	0.83 (0.69–0.99)	0.047	0.81 (0.69–0.95)	0.009
Adjusted OR (95% CI)	Reference	0.89 (0.74–1.08)	0.23	0.81 (0.68–0.97)	0.02
PEA, n	3858	8224		19,499	
Neurologically favorable 1-month survival, n (%)	52 (1.35)	79 (0.96)		217 (1.12)	
OR (95% CI)	Reference	0.71 (0.50–1.01)	0.057	0.82 (0.60–1.11)	0.21
Adjusted OR (95% CI)	Reference	0.65 (0.45–0.95)	0.02	0.74 (0.54–1.04)	0.08
1-month survival, n (%)	267 (6.92)	382 (4.65)		1017 (5.22)	
OR (95% CI)	Reference	0.66 (0.56–0.78)	< 0.001	0.74 (0.64–0.85)	< 0.001
Adjusted OR (95% CI)	Reference	0.69 (0.58–0.82)	< 0.001	0.75 (0.64–0.87)	< 0.001
ROSC before hospital arrival, n (%)	483 (12.52)	646 (7.86)		1347 (6.91)	
OR (95% CI)	Reference	0.60 (0.53–0.68)	< 0.001	0.52 (0.47–0.58)	< 0.001
Adjusted OR (95% CI)	Reference	0.83 (0.72–0.95)	0.01	0.69 (0.61–0.78)	< 0.001
Asystole, n	10,659	22,275		59,269	
Neurologically favorable 1-month survival, n (%)	36 (0.34)	50 (0.22)		171 (0.29)	
OR (95% CI)	Reference	0.66 (0.43–1.01)	0.061	0.86 (0.60–1.23)	0.39
Adjusted OR (95% CI)	Reference	0.67 (0.43–1.05)	0.08	0.82 (0.56–1.2)	0.31
1-month survival, n (%)	202 (1.90)	361 (1.62)		1120 (1.89)	
OR (95% CI)	Reference	0.85 (0.71–1.01)	0.072	1.00 (0.86–1.16)	0.97
Adjusted OR (95% CI)	Reference	0.90 (0.75–1.09)	0.28	1.06 (0.9–1.25)	0.46
ROSC before hospital arrival, n (%)	415 (3.89)	482 (2.16)		1164 (1.96)	
OR (95% CI)	Reference	0.55 (0.48–0.63)	< 0.001	0.49 (0.44–0.55)	< 0.001
Adjusted OR (95% CI)	Reference	0.86 (0.74–1.00)	0.05	0.76 (0.67–0.86)	< 0.001

OR = odds ratio; CI = confidence interval; ROSC = return of spontaneous circulation; VF = ventricular fibrillation; VT = ventricular tachycardia; PEA = pulseless electrical activity.

group than in the LMA or EOA groups. However, the differences among the three devices were slight, with rates of neurologically favorable 1-month survival in patients remaining low in all groups, with an overall rate of 1.03% across groups (ETT group, 1.14%; LMA group, 0.98%; EOA group, 1.04%). Accordingly, our study suggests that the choice between ETT, LMA, or EOA as an advanced airway device will not result in major differences in clinical outcomes.

Out-of-hospital endotracheal intubation is a complex procedure with many potential pitfalls, including unrecognized esophageal tube placement that can result in death (1). For this reason, in Japan, when Emergency Life-Saving Technicians perform out-of-hospital tracheal intubation, it is required that they receive specific training, including a minimum of 30 successful tracheal intubations in elective surgical patients under anesthesia. It has been proposed that regular clinical experience is an important element for maintaining tracheal intubation skills and for improved patient survival after out-of-hospital tracheal intubation of cardiac arrest patients (18). According to the *White Book of the Fire Service in Japan*, 7484 cases of out-of-hospital tracheal intubations were performed by 5476 emergency life-saving technicians per annum all over Japan (as of 2007) (19). Thus, the number of cases experienced per capita is only 1.37 per year on average, which is far from sufficient clinical experience. This may have a bearing on the slight improvement in outcome in the ETT group compared with supraglottic airway devices.

A number of previous studies of supraglottic airway devices have examined the rates of successful device insertion, ease of ventilation/oxygenation, and safety issues in comparison with ETTs (2,20–22). However, only a few studies have compared the effects of supraglottic airway devices on clinical outcomes with those of tracheal intubation. In the few studies conducted, no difference in outcome has been reported in patients treated with the Combitube compared with those treated with tracheal intubation (21).

Assuming that outcomes may vary widely among the types of advanced airway devices in limited populations

of out-of-hospital cardiac arrest patients, we divided the patients into endogenous and exogenous cases, and separately analyzed the outcomes in the LMA and EOA groups compared with those in the ETT group. In endogenous cases, the ETT group had significantly better outcomes than the LMA and EOA groups after adjustment (Table 3). However, because the differences among the three devices were slight, future studies may produce variable findings among the types of advanced airway devices in other specific populations of out-of-hospital cardiac arrest patients, for example, subjects with witnessed cardiac arrest.

The question of whether the use of any type of advanced airway device improves outcomes compared with BVM should be examined in future studies. However, the probability of serious confounding by the indications for each procedure prevented us from conducting such an analysis. It is known that patients who regain spontaneous circulation during the initial phase of resuscitative intervention (i.e., at the scene) are the strongest candidates for long-term survival. Because such patients also usually regain spontaneous respiration, advanced airway procedures are not indicated, and they are subsequently managed with BVM. Because there were no data regarding the initial intention-to-treat by the Emergency Life-Saving Technicians, we were unable to adjust for this factor.

We used the time from the start of CPR by EMS personnel to the hospital arrival (CPR–hospital time) as one of the independent variables in the regression analyses. However, it is unclear whether this is the most appropriate measure. The CPR–hospital time was approximately 2 min longer in the ETT group than in the other two groups. The delay in the ETT group may have resulted from the more lengthy procedure for tracheal intubation, including the arrangement of equipment or confirmation of correct placement of the tube. If this is the case, the CPR–hospital time could be considered a consequence of choosing tracheal intubation or an "intermediate variable," meaning that CPR–hospital time is not an appropriate independent variable. As such, we also performed regression analyses that did not include the CPR–hospital time (data not shown). However, there were no clear differences in the recalculated odds ratios.

Limitations

Several limitations were involved in the present study. First, the analyses were not conducted with an intention-to-treat principle. The advanced airway devices were classified based on the devices in use upon arrival at the hospital and were not based on the intention-to-treat in the field. This means that cases with failed tracheal intubation attempts were included in either the BVM category (and therefore excluded from the analysis) or in the LMA and EOA groups. In this case, the overall outcome of the LMA and EOA groups might be worse due to the need of conversion. Conversely, cases in which LMA or EOA insertion was attempted but failed to provide sufficient ventilation would be included in either the BVM category or the ETT group. In this case, the overall outcome in the ETT group might be worse. Unfortunately, there were no data available regarding rates of successful insertion by different devices, rates of conversion from one type of airway device to another, or types of complications. Future studies should collect information about these factors. Second, the selection of confounding factors should be examined in more detail. In the current study, we selected potential confounding factors based on clinical considerations. However, it is unclear whether we included all potential confounding factors in the present analysis. In particular, the database did not include information regarding post-resuscitation care (e.g., therapeutic hypothermia or percutaneous coronary intervention). As such, in our multivariate analyses, we were not able to adjust factors related to post-resuscitation care. However, we assumed that the effects of such factors would be similarly distributed among the three groups (LMA, EOA, and ETT groups) because the current database was nationwide and population based. Therefore, we propose that any differences in post-resuscitation care were unlikely to have substantially affected the results. In addition, the Emergency Life-Saving Technicians authorized to insert an ETT receive additional training over the standard training required for non-tracheal-intubation-authorized Emergency Life-Saving Technicians. Consequently, the patients in the ETT group may have been managed by more proficient Emergency Life-Saving Technicians. We were not able to adjust for this potential confounding factor due to a lack of data on the individual profiles of the Emergency Life-Saving Technicians. Future studies should collect information about these factors to enable more detailed analyses. Third, the database did not include information about the timing of advanced airway placement. Fourth, the laryngeal tube, Combitube, and esophageal gastric tracheal airway were combined into a single category (EOA) in the present study. Because data were not available regarding the specific types of airway devices used, their separate effects remain unclear. Fifth, the generalizability of our findings to other countries and ethnicities remains unclear, because the data were solely derived from a national database in Japan. For example, compared with the United States, our sample included a high number of patients presenting with asystole as the initial rhythm, which may have also contributed to the overall poor outcome compared with American studies (23). In Japan, do-not-resuscitate orders and living wills are not generally accepted, and EMS personnel are not allowed to terminate resuscitation out of hospital. Therefore, most patients experiencing out-of-hospital cardiac arrest who were treated by EMS personnel were

transported to the hospital and registered in this study, excluding those with decapitation, incineration, decomposition, rigor mortis, or dependent cyanosis (24). This is likely to have resulted in the high number of patients presenting with asystole as the initial rhythm in our database, and to the overall poor outcomes in our sample.

However, despite these limitations, we believe that our current findings are valid, utilizing uniform data collection and consistent definitions based on the Utstein guidelines, a large sample size, and a nationwide, population-based design. In addition, because all consecutive cases of out-of-hospital cardiac arrest patients transferred by the EMS in Japan were included in the database, selection bias was minimal. The results of this study, although limited, suggest that the clinical outcomes associated with the different techniques are at least comparable.

CONCLUSION

The current findings among out-of-hospital cardiac arrest patients arriving to the hospital with an advanced airway device in place revealed that those who were treated by more experienced Emergency Life-Saving Technicians and ultimately underwent ETT were associated with significantly better neurologically favorable survival outcomes compared with patients who were treated by any grade of Emergency Life-Saving Technicians and ultimately underwent LMA or EOA. However, given the low overall rate of neurologically favorable 1-month survival across all groups, these differences do not seem to have major clinical consequences.

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ARTICLE SUMMARY

1. Why is this topic important?

Tracheal intubation is traditionally considered the gold standard for airway management during resuscitation after cardiac arrest, but no systematic comparison of the clinical outcomes of intubation or alternative airway devices has been previously reported.

2. What does this study attempt to show?

To the best of our knowledge, this is by far the largest study to examine the impact of airway management on outcomes after cardiac arrest.

3. What are the key findings?

We found that tracheal intubation was associated with significantly better neurological outcomes compared with prehospital use of alternative airway devices.

4. How is patient care impacted?

Although we found that tracheal intubation was associated with significantly better neurological outcomes compared with prehospital use of alternative airway devices, given the overall low rate of neurologically favorable 1-month survival, these differences do not seem to be of major clinical consequence.

Immediate Defibrillation or Defibrillation After Cardiopulmonary Resuscitation

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ABSTRACT

Objectives. This study aimed to determine whether short cardiopulmonary resuscitation (CPR) by emergency medical services before defibrillation (*CPR first*) has a better outcome than immediate defibrillation followed by CPR (*shock first*) in patients with ventricular fibrillation/pulseless ventricular tachycardia (VF/pulseless VT) out-of-hospital cardiac arrest. **Methods.** We analyzed a national database between 2006 and 2008, and included patients aged 18 years or more who had witnessed cardiac arrests and whose first recorded rhythm was VF/pulseless VT. Those study subjects were divided into five groups in accordance with the CPR/defibrillation intervention sequence. Each group was subdivided into call-to-response intervals of <5 minutes and ≥5 minutes. We identified 267 patients in the shock-first group and 6,407 patients in the CPR-first group. One-month survival and neurologically favorable one-month survival rates were used for outcome measures. The association of intervention type on outcomes (one-month survival or neurologically favorable one-month survival) was analyzed using multivariate logistic regression analyses by adjusting potential confounding factors such as survey year, gender, age (years), bystander CPR, intubation, and call-to-response interval (min). **Results.** The overall one-month survival rate was 26.2% (3,125/11,941) and the neurologically favorable one-month survival rate was 16.6% (1,983/11,934). The CPR-first group had a one-month survival rate of 27.8% (1,780/6,407) and a neurologically favorable one-month survival rate of 17.8% (1,140/6,404), and the shock-first group had survival rates of 24.7% (66/267) and 18.4% (49/267), respectively. There were no significant differences in one-month survival and neurologically favorable one-month survival in these two primary comparison groups (odds ratio [95% confidence interval], 0.85 [0.64–1.13] and 1.04 [0.76–1.42], respectively). Logistic regression analysis showed that neither CPR first nor shock first was associated with the rate of one-month survival or neurologically favorable one-month survival, after adjusting for potential confounders. **Conclusions.** In our study, CPR prior to attempted defibrillation did not present a better outcome compared with shock first as measured by either one-month survival or neurologically favorable one-month survival, after adjusting for potential confounders. Further studies are required to determine whether CPR first has an advantage over shock first. **Key words:** cardiopulmonary resuscitation; electric defibrillation; emergency medical services; ventricular fibrillation; survival; cardiac arrest.

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Introduction

Current cardiopulmonary resuscitation (CPR) guidelines recommend that emergency medical services (EMS) system directors consider implementing a protocol that would allow EMS responders to provide approximately five cycles (approximately 2 minutes) of CPR before defibrillation of patients found by EMS personnel to be in ventricular fibrillation (VF), particularly when the EMS system call-to-response interval is greater than 4 to 5 minutes.[1]

These guidelines are supported by some evidence from animal and human studies. Myocardial metabolic degradation may be slowed or partially reversed by increased blood flow generated by CPR.[2] In a study on dogs, after 7.5 minutes of VF, CPR and high-dose epinephrine were given followed by defibrillation, and it was found that there was a higher rate of return of spontaneous circulation than with defibrillation only.[3] In humans, Cobb et al.[4] carried out a population-based study using 42 months of preintervention analysis and 36 months of postintervention analysis, and they showed that 90 seconds of CPR prior to defibrillation improved survival. This improvement was predominantly in the subgroup of a later (≥4 min) response interval. In a randomized study, Wik et al.[5] showed that

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3 minutes of CPR before defibrillation did not show overall improvement compared with shock first, but there was better survival in the subgroup of a later (≥5 min) response. In other randomized trials, Jacobs et al.[6] showed that 90 seconds of CPR before defibrillation does not improve overall survival, and Baker et al.[7] showed that 3 minutes of CPR before defibrillation also does not improve overall survival. The optimal CPR duration prior to defibrillation is unknown. Bradley et al.[8] demonstrated that 46–195 seconds of EMS CPR before defibrillation was weakly associated with a higher survival rate compared with that for ≤45 seconds.

It is still debatable whether shock first or CPR first has the best outcome. The purpose of this study was to determine whether EMS CPR first has a better outcome compared with immediate defibrillation (shock first) in patients with VF/pulseless ventricular tachycardia (pulseless VT) out-of-hospital cardiac arrest (OHCA).

METHODS

Study Design

The present study was a nonrandomized, nationwide, retrospective observational study that analyzed the national OHCA registry of the Fire and Disaster Management Agency between 2006 and 2008. We obtained permission from the Agency to use the data in this study. The national guidelines for epidemiology studies issued by the Ministry of Education, Culture, Sports, Science and Technology and the Ministry of Health, Labour and Welfare state that obtaining individual informed consent from each patient is not required if the study is an analysis of secondary data from a preexisting data set. Therefore, we did not obtain individual consent from the study participants. This study was approved by the Institutional Review Board of Nara Medical University.

Study Setting and Population

In Japan, the emergency network covers the whole country. The universal emergency access number, 1-1-9, is directly connected to a dispatch center located in the regional fire defense headquarters. Upon receiving a call, the nearest available ambulance is dispatched to the site. The OHCA registry of the Fire and Disaster Management Agency comprises almost all cases of OHCA in Japan. The national CPR guidelines are based on the International Liaison Committee on Resuscitation (ILCOR) 2005 guidance. The national guidelines implemented during study period were revised in June 2006 for Basic Life Support (BLS)[9] and in August 2006 for Advanced Life Support (ALS) and published in July 2006 and February 2007,[10] respectively.

Study Subjects

Regional fire defense headquarters identified OHCA patients according to the modified Utstein-style format.[11] Parameters analyzed in the study included survey year, gender, age, estimated time of collapse (the time that sudden falling into unconsciousness was either seen or heard by a bystander), time of the call, bystander CPR, public automated external defibrillator (AED) use, time of arrival of EMS personnel, the first documented cardiac rhythm, presumed etiology, EMS CPR start time, first defibrillation time, intubation, epinephrine, time of return of spontaneous circulation, time of hospital admission, one-month survival rate, and one-month cerebral performance category (CPC) score. Emergency medical services personnel recorded the presumed etiology, one-month survival, and neurologically favorable one-month survival in cooperation with attending physicians at medical institutions.[12]

Out of 329,230 OHCA patients between 2006 and 2008, we included those who were aged 18 years or more, whose arrests were witnessed (but not witnessed by paramedics) and had a presumed cardiac origin, whose first recorded rhythm was VF/pulseless VT, and whose call-to-response interval (interval from call to EMS arrival on site) was shorter than 60 minutes. In this study, *call* time was defined as the time the 1–1-9 call was connected to the dispatch center, and *EMS arrival on site* time was defined as the time when EMS personnel arrived at the building or nearest available location and stopped their vehicle. Those who had public AED use ($n = 745$) were excluded from this study because the time of defibrillation was not recorded in the database. A call-to-response interval longer than 60 minutes ($n = 49$) was excluded to avoid potential outliers. The 11,941 study subjects were divided into five groups in accordance with the CPR/defibrillation intervention sequence. These five groups were also subdivided into call-to-response intervals of <5 minutes and ≥5 minutes. We identified 267 patients in the *shock-first* group (call-to-response interval <5 min, $n = 54$; ≥5 min, $n = 213$) and 6,407 patients in the *CPR-first* group (call-to-response interval <5 min, $n = 1{,}488$; ≥5 min, $n = 4{,}919$) (Fig. 1). Because no data were obtained for neurologically favorable outcome in seven patients (0.06%), these patients were excluded from the analysis of neurologically favorable outcomes.

Measurements

Our primary outcome measure was the one-month survival rate. Our secondary outcome measure was the neurologically favorable one-month survival rate, which was defined as the rate of CPC 1 (good performance) and CPC 2 (moderate disability) over all CPC categories.[13]

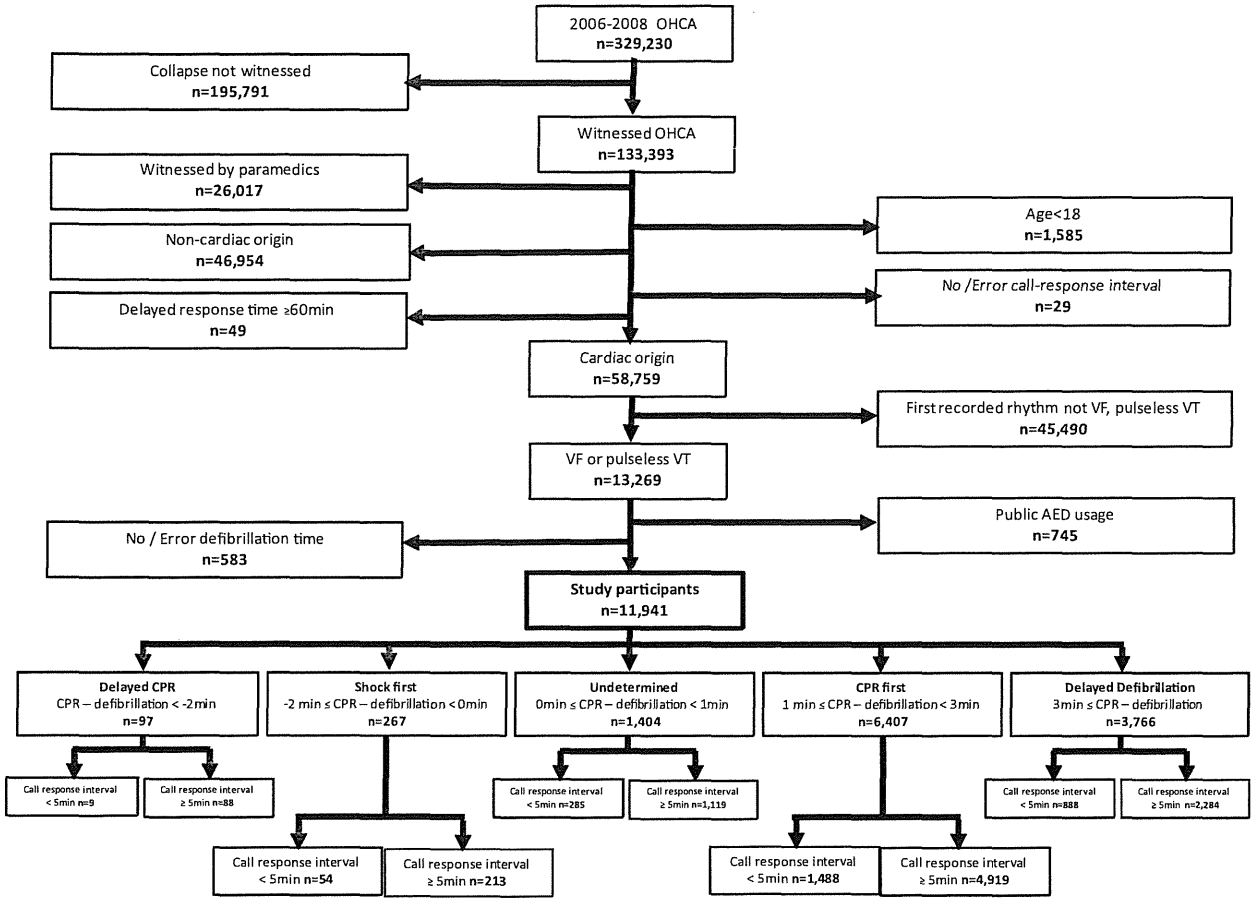

FIGURE 1. Flow diagram of the study participants from 2006 to 2008 from the national out-of-hospital cardiac arrest (OHCA) registry. AED = automated external defibrillator; CPR = cardiopulmonary resuscitation; VF = ventricular fibrillation; VT = ventricular tachycardia.

Data Analysis

We used descriptive statistics to assess characteristics according to the five CPR–defibrillation interval groups. Overall outcome in each intervention group is presented as odds ratios and 95% confidence intervals (CIs). The association of intervention type on outcomes (one-month survival or neurologically favorable one-month survival) was determined using multivariate logistic regression analyses adjusting for potential confounding factors, such as survey year, gender, age (years), bystander CPR, intubation, and call-to-response interval (min). A p-value < 0.05 was considered statistically significant. All statistical analyses were conducted using SPSS 16.0J (SPSS Japan Inc., Tokyo, Japan).

RESULTS

The characteristics of the study subjects, including survey year, gender, age, bystander CPR, intubation, epinephrine, call-to-response interval, and amounts of time defibrillation was attempted, are presented in Table 1.

Call-to-Response Interval and Outcomes

Outcomes, i.e., one-month survival and neurologically favorable one-month survival, were measured for the call-to-response intervals (Fig. 2). The longer the call-to-response interval was, the lower the outcome result was.

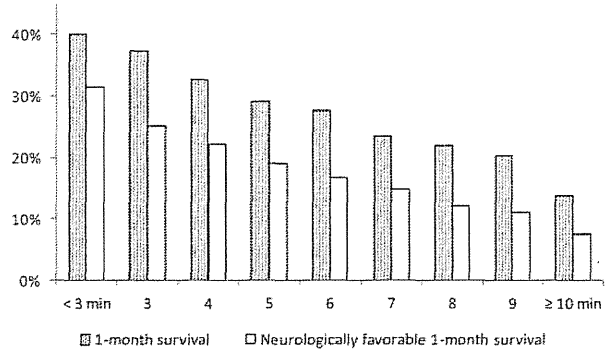

FIGURE 2. One-month survival and neurologically favorable one-month survival rates, presented by the call-to-response time interval.

TABLE 1. Characteristics of the Study Participants

	Total $n = 11,941$		CPR First (≥1 min and <3 min) $n = 6,407$		Shock First (≥1 min and <3 min) $n = 267$		Undetermined (<1 min) $n = 1,404$		Delayed (≥3 min) Defibrillation) $n = 3,766$		Delayed (≥3 min) CPR) $n = 97$	
Survey year												
2006	4,089	(34.2%)	2,226	(34.7%)	156	(58.4%)	642	(45.7%)	1,033	(27.4%)	32	(33.0%)
2007	3,539	(29.6%)	1,898	(29.6%)	54	(20.2%)	331	(23.6%)	1,224	(32.5%)	32	(33.0%)
2008	4,313	(36.1%)	2,283	(35.6%)	57	(21.3%)	431	(30.7%)	1,509	(40.1%)	33	(34.0%)
Gender—male (%)	9,522	(79.7%)	5,152	(80.4%)	232	(86.9%)	1,146	(81.6%)	2,915	(77.4%)	77	(79.4%)
Age—mean (±SD), years	64.6	(± 15.0)	64.4	(± 14.9)	62.7	(± 15.7)	63.8	(± 14.6)	65.4	(± 15.3)	67.1	(± 14.1)
Bystander CPR	6,078	(50.9%)	3,347	(52.2%)	159	(59.6%)	837	(59.6%)	1,674	(44.5%)	61	(62.9%)
Intubation	5,855	(49.1%)	3,220	(50.3%)	138	(51.7%)	674	(48.0%)	1,784	(47.4%)	39	(40.2%)
Epinephrine	1,205	(10.1%)	625	(9.8%)	18	(6.7%)	122	(8.7%)	432	(11.5%)	8	(8.2%)
Call-to-response interval—mean (±SD), min	6.6	(± 3.0)	6.5	(± 2.9)	7.0	(± 3.3)	6.9	(± 3.5)	6.6	(± 3.0)	8.7	(± 4.0)
Time during which defibrillation was attempted—mean (±SD), min	2.4	(± 1.7)	2.4	(± 1.7)	2.6	(± 1.9)	2.5	(± 1.8)	2.3	(± 1.6)	2.6	(± 1.8)

CPR = cardiopulmonary resuscitation; SD = standard deviation.

Overall Outcomes by Intervention Sequence

Overall comparison of the outcomes by CPR/defibrillation sequence and odds ratios with CPR first as a reference value are shown in Table 2. Without adjusting for potential confounders, there were no significant differences in outcome between CPR first and shock first in all call-to-response interval subcategories (≥5 min, <5 min, and total response interval). There was no significant difference between CPR first and the undetermined category in outcome. However, a delayed (CPR/defibrillation interval ≥3 min) defibrillation showed a lower outcome than short CPR followed by defibrillation (CPR first; CPR/defibrillation interval ≥1 min and <3 min).

Cardiopulmonary Resuscitation First versus Shock First by Logistic Regression Analysis

Logistic regression analyses showed that a survey year of 2007 or 2008, being female, a younger age, having bystander CPR, and no intubation were associated with a higher rate of one-month survival (all response time categories). There was no significant difference in the rate of one-month survival between shock first and CPR first ($p = 0.26$ for a call-to-response interval <5 min; $p = 0.84$ for ≥5 min; and $p = 0.68$ for total call-to-response interval) (Table 3).

Regression analysis also showed that in the survey year of 2007 or 2008, a younger age, having bystander CPR, no intubation, and a shorter call-to-response interval were associated with a higher rate of neurologically favorable one-month survival (all response time categories). Being female was associated with a higher neurologically favorable one-month survival in the call-to-response interval total and ≥5 minutes. Shock first was not associated with a higher rate of neurologically favorable one-month survival than CPR first ($p = 0.99$ for a call-to-response interval <5 min; $p = 0.15$ for ≥5 min; and $p = 0.24$ for total call-to-response interval) (Table 4).

DISCUSSION

Call-to-Response Interval and Outcome

Previous studies have shown that with successful defibrillation, survival rates following VF are decreased by approximately 7–10% with every minute that defibrillation is delayed.[14] Survival after sudden cardiac arrest varies as a function of the delay before the onset of critical prehospital interventions such as CPR, defibrillation, and Advanced Cardiac Life Support.[15] Another study reported that the effect of defibrillation response intervals on survival showed a steep decrease in the first 5 minutes, and then leveled off gradually at longer intervals.[16] A study of VF patients proposed that an increasing time interval may decrease survival reciprocally as time proceeds.[17]

In the current study, the shorter the call-to-response interval was, the better the one-month survival and neurologically favorable outcome were. This result reiterates the prognostic importance of early defibrillation, but further studies are required to determine the relationship between response time and outcome of patients with VF/pulseless VT.

Cardiopulmonary Resuscitation First versus Shock First

In the present study, we did not detect any significant difference in either one-month survival or neurologically favorable one-month survival in OHCA patients

TABLE 2. Overall Outcomes by Intervention Sequence

	Call-to-Response Interval, Total				Call-to-Response Interval <5 min				Call-to-Response Interval ≥5 min			
	No. / Total	(%)	OR	(95% CI)	No. / Total	(%)	OR	(95% CI)	No. / Total	%	OR	(95% CI)
One-month survival	3,125 / 11,941	(26.2%)			959 / 2,724	(35.2%)			2,166 / 9,217	(23.5%)		
CPR first (≥1 min and <3 min)	1,780 / 6,407	(27.8%)	*Reference*		555 / 1,488	(37.3%)	*Reference*		1,225 / 4,919	(24.9%)	*Reference*	
Shock first (≥1 min and <3 min)	66 / 267	(24.7%)	0.85	(0.64–1.13)	16 / 54	(29.6%)	0.71	(0.39–1.28)	50 / 213	(23.5%)	0.93	(0.67–1.28)
Undetermined (<1 min)	390 / 1,404	(27.8%)	1.00	(0.88–1.14)	111 / 285	(38.9%)	1.07	(0.83–1.39)	279 / 1,119	(24.9%)	1.00	(0.86–1.16)
Delayed (≥3 min) defibrillation	868 / 3,766	(23.0%)	0.78	(0.71–0.85)	274 / 888	(30.9%)	0.75	(0.63–0.90)	594 / 2,878	(20.6%)	0.78	(0.70–0.88)
Delayed (≥ 3 min) CPR	21 / 97	(21.6%)	0.72	(0.44–1.17)	3 / 9	(33.3%)	0.84	(0.21–3.37)	18 / 88	(20.5%)	0.78	(0.46–1.31)
Neurologically favorable one-month survival	1,983 / 11,934	(16.6%)			666 / 2,724	(24.4%)			1,317 / 9,210	(14.3%)		
CPR first (≥1 min and <3 min)	1,140 / 6,404	(17.8%)	*Reference*		388 / 1,488	(26.1%)	*Reference*		752 / 4,916	(15.3%)	*Reference*	
Shock first (≥1 min and <3 min)	49 / 267	(18.4%)	1.04	(0.76–1.42)	14 / 54	(25.9%)	0.99	(0.53–1.84)	35 / 213	(16.4%)	1.09	(0.75–1.58)
Undetermined (<1 min)	272 / 1,402	(19.4%)	1.11	(0.96–1.29)	85 / 285	(29.8%)	1.20	(0.91–1.59)	187 / 1,117	(16.7%)	1.11	(0.93–1.33)
Delayed (≥ 3 min) defibrillation	512 / 3,764	(13.6%)	0.73	(0.65–0.81)	177 / 888	(19.9%)	0.71	(0.58–0.86)	335 / 2,876	(11.6%)	0.73	(0.64–0.84)
Delayed (≥ 3 min) CPR	10 / 97	(10.3%)	0.53	(0.27–1.02)	2 / 9	(22.2%)	0.81	(0.17–3.92)	8 / 88	(9.1%)	0.55	(0.27–1.15)

CI = confidence interval; CPR = cardiopulmonary resuscitation; OR = odds ratio (unadjusted).

TABLE 3. Logistic Regression Model on One-Month Survival

	Call-to-Response Interval, Total			Call-to-Response Interval <5 min			Call-to-Response Interval ≥5 min		
	OR	(95% CI)	p-Value	OR	(95% CI)	p-Value	OR	(95% CI)	p-Value
Survey year									
2006		*Reference*			*Reference*			*Reference*	
2007	1.24	(1.11-1.38)	<0.001	1.26	(1.03-1.54)	0.02	1.23	(1.08-1.40)	<0.001
2008	1.31	(1.18-1.45)	<0.001	1.37	(1.12-1.67)	<0.001	1.29	(1.14-1.45)	<0.001
Gender									
Male		*Reference*			*Reference*			*Reference*	
Female	1.24	(1.11-1.37)	<0.001	1.25	(1.01-1.53)	0.04	1.23	(1.09-1.40)	<0.001
Age	0.98	(0.98-0.98)	<0.001	0.98	(0.98-0.99)	<0.001	0.98	(0.98-0.98)	<0.001
Bystander CPR									
Without bystander CPR		*Reference*			*Reference*			*Reference*	
With bystander CPR	1.36	(1.25-1.49)	<0.001	1.26	(1.06-1.48)	0.01	1.40	(1.26-1.55)	<0.001
Intubation									
No intubation		*Reference*			*Reference*			*Reference*	
Intubation	0.53	(0.49-0.58)	<001	0.40	(0.34-0.47)	<0.001	0.59	(0.53-0.65)	<0.001
Call-to-response interval	0.87	(0.85-0.88)	<001	0.91	(0.82-0.99)	0.04	0.87	(0.85-0.89)	<0.001
CPR/defibrillation									
CPR first (≥1 min and <3 min)		*Reference*			*Reference*			*Reference*	
Shock first (≥1 min and <3 min)	0.94	(0.70-1.26)	0.68	0.70	(0.38-1.30)	0.26	1.04	(0.74-1.44)	0.84
Undetermined (<1 min)	1.03	(0.90-1.18)	0.63	0.99	(0.76-1.30)	0.96	1.04	(0.89-1.22)	0.60
Delayed (≥ 3 min) defibrillation	0.77	(0.70-0.85)	<0.001	0.73	(0.61-0.88)	<0.001	0.79	(0.71-0.89)	<0.001
Delayed (≥ 3 min) CPR	0.88	(0.53-1.46)	0.63	0.81	(0.19-3.34)	0.77	0.91	(0.53-1.57)	0.74

CI = confidence interval; CPR = cardiopulmonary resuscitation; OR = odds ratio (adjusted).

who received CPR prior to defibrillation. For the total response interval, our results are consistent with the studies of Wik et al.,[5] Jacobs et al.,[6] and Baker et al.[7] In a subgroup analysis, the lack of difference in subgroups was not consistent with Cobb et al.[4] and Wik et al.,[5] who found a better outcome with CPR before defibrillation with response intervals of ≥4 minutes and ≥5 minutes, respectively.

Jacobs et al.[6] pointed out that the study by Cobb et al.[4] had changes in clinical protocol and guidelines that might have influenced their results, and the nonrandomized study design might have overestimated the treatment effect.[18] Jacobs et al.[6] also found that the subgroup analysis by Cobb et al.[4] had wide confidence intervals and no adjustment for three interim analyses. Baker et al.[7] mentioned that in the studies of Cobb

TABLE 4. Logistic Regression Model on Neurologically Favorable One-Month Survival

	Call-to-Response Interval, Total			Call-to-Response Interval <5 min			Call-to-Response Interval ≥5 min		
	OR	(95% CI)	p-Value	OR	(95% CI)	p-Value	OR	(95% CI)	p-Value
Survey year									
2006		*Reference*			*Reference*			*Reference*	
2007	1.51	(1.33-1.73)	< 0.001	1.50	(1.19-1.89)	< 0.001	1.52	(1.30-1.79)	< 0.001
2008	1.60	(1.41-1.82)	< 0.001	1.64	(1.31-2.06)	< 0.001	1.59	(1.37-1.86)	< 0.001
Gender									
Male		*Reference*			*Reference*			*Reference*	
Female	1.22	(1.07-1.38)	< 0.001	1.16	(0.92-1.47)	0.21	1.24	(1.06-1.45)	0.01
Age	0.97	(0.97-0.98)	< 0.001	0.98	(0.97-0.98)	< 0.001	0.97	(0.97-0.98)	< 0.001
Bystander CPR									
Without bystander CPR		*Reference*			*Reference*			*Reference*	
With bystander CPR	1.78	(1.60-1.98)	< 0.001	1.54	(1.28-1.86)	<.001	1.91	(1.68-2.17)	< 0.001
Intubation									
No intubation		*Reference*			*Reference*			*Reference*	
Intubation	0.38	(0.34-0.42)	< 0.001	0.36	(0.30-0.44)	< 0.001	0.38	(0.34-0.44)	< 0.001
Call-to-response interval	0.83	(0.82-0.85)	< 0.001	0.83	(0.75-0.92)	< 0.001	0.84	(0.81-0.86)	< 0.001
CPR/defibrillation									
CPR first (≥1 min and <3 min)		*Reference*			*Reference*			*Reference*	
Shock first (≥1 min and <3 min)	1.22	(0.87-1.71)	0.24	0.99	(0.52-1.92)	0.99	1.33	(0.90-1.95)	0.15
Undetermined (<1 min)	1.15	(0.99-1.35)	0.07	1.11	(0.82-1.48)	0.51	1.17	(0.97-1.41)	0.10
Delayed (≥3 min) defibrillation	0.72	(0.64-0.81)	< 0.001	0.68	(0.55-0.84)	< 0.001	0.74	(0.64-0.85)	< 0.001
Delayed (≥3 min) CPR	0.64	(0.33-1.27)	0.20	0.78	(0.15-3.94)	0.76	0.62	(0.29-1.33)	0.22

CI = confidence interval; CPR = cardiopulmonary resuscitation; OR = odds ratio (adjusted).

et al.[4] and Wik et al.,[5] an extended period of CPR before subsequent defibrillation had the greatest impact on survival. These factors discussed above may have affected the results of our study.

LIMITATIONS AND FUTURE RESEARCH

Our study has several limitations. First, this study was nonrandomized for intervention. In addition, the distribution of the participants receiving CPR first and shock first was not balanced. The allocation criteria were not very clear as to why certain patients received particular interventions (CPR first or shock first). Therefore, even after adjusting for potential confounders in a logistic regression analysis, unpredicted confounding factors may have affected the outcome of the patients. In contrast to the guidelines, 31.5% (3,766/11,941) of the study participants had delayed (>3 min) defibrillation and their prognosis was significantly poorer, which could be an indication of poor compliance with protocol or potential conditions that prevented defibrillation or whatever unknown unpredictable confounders. Second, the database contained no information on the hospitals to which the patients were transferred. Transportation to critical care medical centers results in a better outcome for OHCA patients in Japan[19]; therefore, this may have affected the outcome.

Third, recording an accurate time in the EMS system is still a challenge.[20] In Japan, the proportion of EMS teams whose clocks (control center, emergency medical technician's watch, and emergency transport care and defibrillator) were synchronized every day increased from 39% in December 2005 to 43% in July 2007.[21] In addition, as time is recorded in units of minutes, we could not identify the sequence of CPR and defibrillation in the "undetermined" category, which comprised 11.8% (1,404/11,941) of the study participants. Although an improvement in clock synchronization has been achieved, the quality of the time was still a limitation of this study.

Further studies are required to determine whether CPR prior to attempted defibrillation has a positive outcome. However, the present study, which was a three-year, multicentered, large-scale study, has provided additional evidence regarding effective intervention for shockable OHCA patients.

CONCLUSIONS

In our study, CPR prior to attempted defibrillation did not present a significantly different outcome compared with shock first in either one-month survival or neurologically favorable one-month survival after adjusting for potential confounders. Further studies are needed before consideration is given to revision of the current guidelines, and for evaluation of the advantage of shock first over CPR first.

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Clinical paper

Effect of time and day of admission on 1-month survival and neurologically favourable 1-month survival in out-of-hospital cardiopulmonary arrest patients☆

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ABSTRACT

Aim: We sought to examine whether the outcomes of out-of-hospital cardiopulmonary arrest (OHCA) patients differed between weekday and weekend/holiday admissions, or between daytime and nighttime admissions.

Methods: From a national registry of OHCA events in Japan between 2005 and 2008, 173,137 cases where the call-to-hospital admission interval was shorter than 120 min and collapse was witnessed by a bystander were included in this study. One-month survival rate and neurologically favourable 1-month survival rate were used as outcome measures. Logistic regression was used to adjust for potential confounding factors.

Results: No significant differences in outcome were found between weekday and holiday/weekend admissions in rates of 1-month survival or neurologically favourable 1-month survival ($p = 0.78$ and $p = 0.80$, respectively). In contrast, patients admitted in the daytime exhibited significantly better outcomes than those admitted at night, on both outcome measures ($p < 0.001$ and $p < 0.001$). After adjusting for possible confounding factors, outcomes were significantly better for daytime admissions, with odds ratios of 1.26 (95% confidence interval (CI) 1.22–1.31; $p < 0.001$) for 1-month survival, and 1.26 (95% CI 1.20–1.32; $p < 0.001$) for neurologically favourable 1-month survival. In contrast, no significant differences on either outcome measure were found between weekday and weekend/holiday cases, with odds ratios of 1.00 (95% CI 0.96–1.04; $p = 0.96$) for 1-month survival and 0.99 (95% CI 0.94–1.04; $p = 0.78$) for neurologically favourable 1-month survival.

Conclusions: Even after adjusting for confounding factors, admission day (weekday vs. weekend/holiday) had no effect on 1-month survival or neurologically favourable 1-month survival. In contrast, daytime admission was associated with significantly better outcomes than nighttime admissions.

1. Introduction

Despite recent medical advances, outcomes in cases of out-of-hospital cardiopulmonary arrest (OHCA) remain poor.[1] To address this problem, in addition to improving the treatment at medical institutions, more emphasis has been put on pre-hospital care. The "chain of survival," concept,[2] which involves improvements in immediate resuscitation techniques, including access to cardiopulmonary resuscitation (CPR), defibrillation, and advanced cardiovascular life support, has become widely accepted.[3]

To provide a desirable level of medical care, it is important to establish adequate treatment systems at night as well as during weekends and holidays. Differences in outcomes due to circadian variations and the day of occurrence have been reported. Previous studies have suggested that outcomes in cases of pulmonary embolism,[4] ischaemic cerebral infarction,[5] and ischaemic heart disease[6] are poorer at night and on weekends. There is evidence that outcomes of in-hospital cardiac arrest cases are poorer at night and on weekends, even after adjustment for patient condition and the status of the medical institutions involved.[7,8] On the other hand, some studies have reported that weekend admission is not significantly correlated with mortality, readmission rate, or admission

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