

Timing and sequence of advanced airway interventions in out-of-hospital cardiac arrest

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Airway management during cardiopulmonary resuscitation (CPR) is one of the time-dependent interventions for providing oxygenation and ventilation in patients with cardiac arrest. However, the best strategy for managing the airway after cardiac arrest has yet to be determined. Some observational studies have made objections to the assumption that advanced airway management techniques are necessarily superior to basic airway management techniques (1). In 2015, the International Liaison Committee on Resuscitation Advanced Life Support Task Force suggested the use of either a bag-valve-mask (BVM) or an advanced airway during CPR in both in-hospital and out-of-hospital settings, as there was insufficient evidence to show a difference in the survival or favorable neurological outcome with the use of BVM compared with advanced airway devices (2). Accordingly, a large, prospective study is required to define the benefits of advanced airway management [endotracheal intubation (ETI) or supraglottic airway (SGA)] or more simple technique during resuscitation after cardiac arrest (3). In practice, emergency medical service (EMS) providers must determine the best airway management (BVM device or advanced airway insertion) using their skill or experience in treating patients with out-of-hospital cardiac arrest (OHCA) (4).

Benoit *et al.* (5) showed the concept of the time-dependent benefit of advanced airway management relative to other interventions for cardiac arrest. They postulated that an interaction may exist between the relative timing

of advanced airway management and other interventions for OHCA. Weisfeld *et al.* (6) proposed a three-phase model of CPR to reflect the time-sensitive progression of resuscitation physiology: (I) the electrical phase [within 4 minutes of cardiac arrest with ventricular fibrillation (VF)]; (II) the circulatory phase (from 4 to 10 minutes of VF); and (III) the metabolic phase (after 10 minutes of cardiac arrest). In the very early phase of VF, immediate defibrillation may be preferable over airway management. In the circulatory phase, airway management may have a critical impact on outcomes. Moreover, in the metabolic phase, therapeutic hypothermia (7) may be more critical than airway management. Taken together, the concept of airway timing affecting the outcomes after OHCA is plausible.

SGA and neurological outcomes

Recent research (8) published in *Academic Emergency Medicine* demonstrated that the SGA was associated with a favorable neurological outcome (Cerebral Performance Categories scale 1 or 2) in patients with OHCA, particularly in those who received prolonged CPR after adjusting the post-resuscitation variables. Park and colleagues (8) reported these findings following a retrospective analysis utilizing a multicenter registry in Korea from December 2013 to April 2016. A total of 254 patients with OHCA aged ≥ 18 years were analyzed. Of these, 37 patients (14.6%) survived with favorable neurological outcomes 28 days following OHCA.

Univariate analysis showed that SGA was significantly associated with favorable neurological outcomes [odds ratio (OR), 2.22; 95% confidence interval (CI), 1.07 to 4.59; $P=0.03$]. Multivariate logistic regression analysis showed that SGA had a significant association with favorable neurological outcomes although the 95% CI was very wide: adjusted OR, 7.88; 95% CI, 1.33 to 46.53; $P=0.023$. In this analytic model, they analyzed seven confounding factors including Sequential Organ Failure Assessment (SOFA) score after excluding one insignificant post-resuscitation variable [targeted temperature management (TTM), 19/37 (51.4%) with favorable neurologic outcome versus 94/217 (43.3%) with unfavorable neurologic outcome, $P=0.39$] in the univariate model. Moreover, SGA had a significant association with 28-day favorable neurological outcome in patients with prolonged CPR: adjusted OR, 8.75; 95% CI, 1.06 to 72.54; $P=0.04$.

From the standpoint of a three-phase model of CPR (6), the phase of prolonged CPR (low-flow time >15 minutes) is categorized as metabolic phase. In this phase, organ failure from both global ischemia and reperfusion injury can result in the production of circulating metabolic substances that cause additional injury over the effects of local ischemic events. Therefore, advanced airway management and TTM would be helpful for patients with prolonged ischemic time (7). For both SGA and BVM, descriptions of the following important information were not provided in Park *et al.*'s study: (I) success rates; (II) difficulty rates; (III) complication rates including SGA displacement or regurgitation of gastric content; (IV) number of attempts of SGA associated with hypoxemia; (V) ventilation rates; and (VI) airway insertion or airway management times. All of these variables influence the outcomes after OHCA. As far as analytic model is concerned, more sophisticated statistical methods, such as time-dependent propensity matching, may be useful because an airway management is a time-dependent intervention for OHCA.

The Korean study conducted by Park *et al.* (8) supports the idea that advanced airway management, especially SGA, may improve 28-day functional outcomes after OHCA compared with BVM. However, their results are not consistent with those reported in Kang *et al.*'s study (9), a nationwide population-based study performed using the Korean OHCA cohort database between 2010 and 2013 ($n=32,513$). This study showed that no statistical significances were found in the survival rates between two groups (adjusted OR of SGA, 1.09; 95% CI, 0.82 to 1.44). In Kang's study, 13 prehospital co-variables were included

in the multivariate logistic regression analysis (9). In Park's study (8), seven prehospital variables and one in-hospital [SOFA score upon intensive care unit (ICU) admission] variable were included in the analysis as the previous study (9,10) did not include the adjustment of post-resuscitation variables. Moreover, in Park's study, the use of early coronary angiography (CAG) was not considered as a post-resuscitation confounder for analysis. Early CAG (<24 hours) and percutaneous coronary intervention (PCI) were found to be associated with significantly higher survival and better neurological outcomes (11,12). Therefore, early CAG and PCI should be included as confounding factors for analysis in addition to TTM application and SOFA scores upon admission. Anyhow, this observational study has several limitations: the confounding factors cannot be fully accounted for (13-16). Moreover, studies for medical intervention are subject to confounding by indication, leading to mistaken conclusions (15,16). In addition, the Korean EMS system differs from other countries (10,17), raising concerns about generalizability. The provisions of prehospital advanced airway management are to be performed only by level 1 emergency medical technicians (9). For this reason, the Korean nationwide OHCA registry showed that most patients with OHCA (91.3%) received BVM for initial airway management (9). Prehospital advanced airway management was performed only 5% for SGA and 3.7% for ETI in patients with OHCA of cardiac origin (9). Accordingly, randomized controlled trial (RCT) on advanced airway management is desirable to confirm whether prehospital SGA has beneficial effect on oxygenation in the prolonged ischemic phase compared with BVM.

RCT on airway management for patients with OHCA

Until now, three RCTs on airway management of patients with OHCA have been reported (18-22). Gausche *et al.* (18) demonstrated that prehospital ETI did not improve the survival or neurological outcomes of patients with OHCA aged ≤ 12 years [survival to hospital discharge: 110/416 (26%) with ETI *vs.* 123/404 (30%) with BVM; OR, 0.82 (95% CI, 0.61 to 1.11); favorable neurological outcome at discharge: 85/416 (20%) with ETI *vs.* 92/404 (23%) with BVM].

At the 2017 European Society of Cardiology Congress in Barcelona, Spain, Professor Frederic Adnet reported that, from the RCT of patients with OHCA aged ≥ 18 ,

the two groups had the same 28-day survival rate with favorable neurological outcome: 43/1022 (4.2%) with ETI *vs.* 42/1018 (4.1%) with BVM (19,20). However, failure rates (failure to ventilation or to intubate) were higher in patients with BVM than in those with ETI (6.3% *vs.* 2.3%, $P < 0.0001$) (21). Aspiration or regurgitation of gastric content occurred almost twice as often with BVM compared with ETI (14.9% *vs.* 7.7%, $P < 0.0001$) (21). In this context, the multicenter trial in France and Belgium concluded that BVM appears less safe than ETI as a means of ventilation during CPR in patients with OHCA, and they could not recommend BVM as the standard method to ventilate patients with OHCA during CPR.

Benger *et al.* (22) compared two SGA devices [the i-gel and laryngeal mask airway supreme (LMAS)] to ETI for OHCA in the United Kingdom. The rates of survival to discharge showed no difference: i-gel, 10.3%; LMAS, 8.0%; and ETI, 9.1% ($P = 0.73$). The rates of survival to 90 days also showed no difference: i-gel, 9.5%; LMAS, 6.9%; and ETI, 8.6% ($P = 0.65$). Therefore, a large-scale RCT is underway to compare the effectiveness of i-gel and ETI in the management of patients with OHCA (ISRCTN: 08256118) (23). Other clinical trials comparing ETI with SGA devices in the OHCA settings are also underway in the United States (NCT02419573) (24) and in Taipei city (NCT02967952) (25). These RCTs could define the role of ETI and SGA in OHCA.

Conclusions

A recent observational study conducted in Korea (8) supports the hypothesis that prehospital SGA is associated with good neurological outcome in adult patients with OHCA compared with BVM, after adjusting the prehospital and post-resuscitation covariates including SOFA scores. The RCT conducted in France (19-21) showed that BVM appears less safe than ETI as a means of ventilation during CPR in OHCA. Ongoing several RCTs (23-25) would answer which advanced airway management (ETI or SGA) is preferable as an initial prehospital airway management. Patients with OHCA, EMS providers, and hospital staff all deserve to know what is best.

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Footnote

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