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## Experimental paper

# Effect of endotracheal intubation and supraglottic airway device placement during cardiopulmonary resuscitation on carotid blood flow over resuscitation time: An experimental porcine cardiac arrest study



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## Abstract

**Background:** Supraglottic airway devices (SGDs) are widely used during the resuscitation of out-of-hospital cardiac arrest (OHCA). The effect of SGDs on carotid blood flow (CBF) as resuscitation time passes is controversial. We assessed the effects of endotracheal intubation (ETI) and 3 types of SGD placement on CBF over time in prolonged resuscitation through an experimental porcine cardiac arrest study.

**Methods:** We conducted a randomized crossover study using 12 female pigs. After 4 min of untreated ventricular fibrillation, 3 pairs of ETI for 3 min and each type of SGD placement, including Combitube, I-gel, and laryngeal mask airway, for 3 min were conducted. The order of the 3 pairs of ETI and SGD were randomly assigned for each pig. We measured physiological parameters including CBF and mean arterial pressure (MAP). We compared CBF and MAP between the last 1 min of the insertion period for each of the 3 types of SGD and the preceding ETI period. Trends of CBF and MAP according to ETI and SGD transition were also plotted during the prolonged resuscitation duration.

**Results:** CBF decreased after inserting I-gel and Combitube compared to ETI (mean difference (95% CI): –685 ml (–1052 to –318) for Combitube, –369 ml (–623 to –114) for I-gel). MAP subsequently decreased after transitioning airway devices as resuscitation was prolonged, regardless of the device type. The mean CBF during the transition from ETI to SGD decreased by –480 ml (95% CI: –675 to –286), but the decrease in CBF during the transition from SGD to ETI was only –4 ml (95% CI: –182 to 175).

**Conclusion:** SGD placement was associated with decreased carotid blood flow during cardiopulmonary resuscitation in an experimental porcine model. As time passed during prolonged resuscitation, reduction in CBF was aggravated after the transition to SGD placement compared to the reduction after the transition to ETI. This study was approved by the study institution IACUC 16-0140-S1A0.

**Keywords:** Endotracheal intubation, Supraglottic airway device, Cardiopulmonary resuscitation, Carotid blood flow

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## Introduction

Advanced airway management, including endotracheal intubation (ETI) and supraglottic airway device (SGD) placement, are conducted to protect the airway and improve oxygenation and ventilation during the resuscitation of out-of-hospital cardiac arrest (OHCA).<sup>1,2</sup> Although the treatment of choice for advanced airway placement is ETI, a high level of skill, continuous training and a sufficient volume of clinical experience are required to achieve a high success rate. The insertion of SGDs is widely performed during the prehospital resuscitation of OHCA by emergency medical service (EMS) providers as an alternative to ETI.<sup>3–7</sup> In contrast to ETI, SGDs can be inserted in a blind manner with an easy skill level by EMS providers.<sup>8,9,10</sup>

In spite of the feasibility of SGD insertion, many previous studies have reported that the use of SGDs worsened the clinical outcome for OHCA when compared to ETI.<sup>4–7,11</sup> However, the physiological mechanism of SGDs for the poor outcome of OHCA is unproven. Several studies have indicated that the balloon and fitting part of the device in the supraglottic area could compress vital vascular structures such as the carotid artery and interrupt carotid blood flow (CBF), which could negatively affect the patient outcome.<sup>12,13</sup> Furthermore, the effect of each type of SGD on CBF is unknown.

Prehospital resuscitation for OHCA victims generally includes a long duration of cardiopulmonary resuscitation (CPR) and exposed airway management by SGD placement for more than 10 min.<sup>14–17</sup> During a prolonged duration of resuscitation, hemodynamic function deteriorates. The effect of airway management devices on CBF could be different according to different types of devices, such as ETI or SGDs.

We conducted an experimental porcine cardiac arrest study to assess the effects of SGDs and ETI on CBF for a prolonged duration of CPR. We hypothesized that SGD insertion would be associated with decreased CBF when compared to ETI as time passed during a prolonged duration of resuscitation.

## Methods

### Ethical statement

The protocol of this study was approved by the Institutional Animal Care and Use Committee of the study institution (IACUC No. 16-0140-S1A0). This investigation was supported by the Cooperative Research Program of Basic Medical Science and Clinical Science from the study institution (Grant No. 800-20160091). This study had no conflicts of interest with the manufacturers of the ETI or SGDs.

### Study design and setting

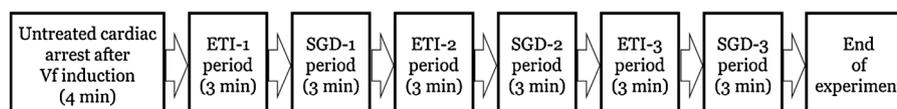
We conducted a randomized, crossover, large-animal experimental study using a porcine ventricular fibrillation cardiac arrest model. The

experimental design of this study was a porcine ventricular fibrillation cardiac arrest model. It was designed to compare the effects of ETI and 3 kinds of SGDs (Combitube™ (Kendall-Sheridan, Argyll, NY), laryngeal mask airway™ (LMA, Windhagen, Germany) and I-Gel™ (Intersurgical, Wokingham, UK)) on CBF. After 4 min of untreated ventricular fibrillation, 3 pairs of ETI and SGD placement were conducted, including ETI-Combitube, ETI-LMA and ETI-I-gel. The order of each pair was subsequently randomized by a computer-generated random order (Fig. 1). For each pair, ETI was performed for 3 min and then each randomly assigned type of SGD was placed for 3 min.

### Experimental procedure

While spontaneously breathing with sedation, each pig was intubated with a size 7.5 endotracheal tube. Positive pressure ventilation was provided by a mechanical ventilator (Aespire 7100, GE Healthcare, USA). An incision smaller than 3 cm was made with the blade on left side of the neck of the pig to measure CBF. After the surgical dissection of soft tissue at the incision site, the common carotid artery was exposed. A Doppler probe (PR-series, Transonic Systems, USA) was placed on the carotid artery to measure CBF. After placement of the flow probe, the soft tissue and skin was sutured with nylon. A burr hole trephination for ICP monitoring was performed in the midline of the left eyebrow and the posterior bony prominence of the skull. A pressure catheter (Millar catheter-SPR-350s, Millar Instruments, Inc., Houston) was inserted and placed through the burr hole for ICP monitoring and recording. The femoral artery was punctured and aortic pressures were measured. Electrocardiography and EtCO<sub>2</sub> were also observed. All physiologic parameters were measured and recorded continuously by a digital recording system (Powerlab, AD instruments, Australia).

Ventricular fibrillation was induced using a pacing catheter placed in the right ventricle. After 4 min of untreated ventricular fibrillation, chest compression was delivered by the mechanical compression device (LUCAS-II, Physio-Control Inc., Sweden) and positive pressure ventilation was provided via an endotracheal tube (ETI-1). After 3 min of the initial CPR period with ETI, extubation of the endotracheal tube and replacement with the first order of a randomly assigned SGD (SGD-1) was conducted within 30 s. Confirmation for correct placement of SGD was done by pulmonary auscultation and EtCO<sub>2</sub> monitoring. Then, we resuscitated with the placement of SGD-1 for 3 min. After 3 min of resuscitation with SGD-1, we removed SGD-1 and reintubated with an endotracheal tube for 30 s. We followed with 3 min of CPR with ETI (ETI-2), and we changed ETI to the second type of SGD (SGD-2) in the same manner. After 3 min of CPR with SGD-2, we reintubated with an endotracheal tube and resuscitated for 3 min (ETI-3). After the ETI-3 period, we finally placed the third type of predetermined SGD and resuscitated for 3 min (SGD-3). After all 3 cycles of randomly paired ETI and SGD, we finished the experimental protocol, and the animal was sacrificed (Fig. 1).



**Fig. 1 – Course of the experimental process.**

### Experimental animals and housing

Twelve female cross-bred 13–15 weeks old pigs with a mean body weight of  $40 \pm 3$  kg were used in the experiment. The pigs were raised and acquired from local farm. Experiments on pig were initiated after a day of fasting. The pigs were initially sedated with an intramuscular injection of tiletamine/zolazepam (Zoletil<sup>®</sup>) 5 cc with xylazine (Rompun<sup>®</sup>) 5 cc followed by isoflurane inhalation.

### Statistical analysis and sample size

We measured profiles of CBF and MAP during the last 1 min of every 3-min period. The profiles were extracted from continuously measured data for the whole experimental duration for the final analysis.<sup>12</sup> The primary outcome was CBF for 1 min of each period including ETI-1, ETI-2, ETI-3, SGD-1, SGD-2, and SGD-3. CBF was calculated automatically using data processing software (Labchart, AD instruments, Australia) by integrating parameters measured from the Doppler flowmeter. MAP was also calculated based on observed parameters. The Wilcoxon signed rank-sum test was used for the paired comparison of parameters recorded during the SGD period and preceding ETI period, such as comparing the SGD-1 and ETI-1 periods. To assess the change in CBF according to the transition of airway devices, a paired t-test was used to calculate mean differences with 95% confidence intervals (CI). Sample size was calculated based on prediction of mean 400 ml difference of cerebral blood flow according to type of airway device during 1 min of resuscitation.

## Results

All experiments were performed with 12 pigs according to a predetermined protocol (Fig. 1). Every pig underwent 3 pairs of an ETI period and every kind of SGD period. Hemodynamic parameters, including carotid blood flow during the SGD period and the preceding ETI period, are shown and compared in Tables 1, 2 and 3 according to the type of SGD. A minimal decrease in SBP, DBP, MAP and ICP was observed between each SGD type and the preceding ETI period.

CBF decreased significantly after Combitube or I-gel insertion compared to each preceding ETI period, (Fig. 2). The mean reduction in carotid blood flow after SGD insertion was 480 ml (95% CI: 286–675) (Fig. 2). During the SGD period using Combitube, CBF decreased by 685 ml (95% CI: –1,052 to –318) compared to the preceding ETI period (Table 1). I-gel also showed a CBF decrease of –369 ml (95% CI: –623 to –114) (Table 3). Mean difference of CBF after Combitube insertion compared to the preceding ETI period was –33.7% of the median CBF value of the preceding ETI period. Mean difference of CBF after LMA and I-gel insertion was –22.3% and –23.2% of the median CBF value of the preceding ETI period.

MAP and CBF during each experimental period are shown in Fig. 3. MAP decreased subsequently after transitioning airway devices regardless of device types as resuscitation was prolonged (mean MAP change (95% CI) in ETI to SGA transition: –2.8 mmHg (–4.6/–0.9), SGA to ETI transition: –3.6 mmHg (–5.6/–1.6)). However reduction of carotid blood flow was relatively spared

**Table 1 – Carotid blood flow and hemodynamic parameters of Combitube insertion compared to the preceding ETI.**

	ETI		Combitube		p-Value	ETI-Combitube		
	Median	IQR	Median	IQR		Mean difference	95% CI	
Total observed N	12		12					
Systolic blood pressure (mmHg)	73.7	51.3–88.6	71.0	46.6–83.7	0.02	–4.8	–8.4	–1.2
Diastolic blood pressure (mmHg)	10.4	7.3–18.9	8.2	6.0–19.9	0.58	–0.9	–3.7	2.0
Mean arterial pressure (mmHg)	32.8	20.9–39.3	28.6	19.2–41.4	0.14	–2.2	–5	0.7
Intracranial pressure (mmHg)	21.3	10.0–23.2	18.3	6.9–21.4	0.02	–2.5	–5.6	0.6
Carotid blood flow rate (ml/s)	33.9	13.2–38.4	14.4	5.4–21.4	<0.01	–11.4	–17.5	–5.3
Carotid blood flow during measurement period <sup>a</sup> (ml)	2031	794–2309	862	325–1288	<0.01	–685	–1052	–318

<sup>a</sup> Carotid blood flow was measured during the last 1 min of a 3-min period with each airway device.

**Table 2 – Carotid blood flow and hemodynamic parameters of LMA insertion compared to the preceding ETI.**

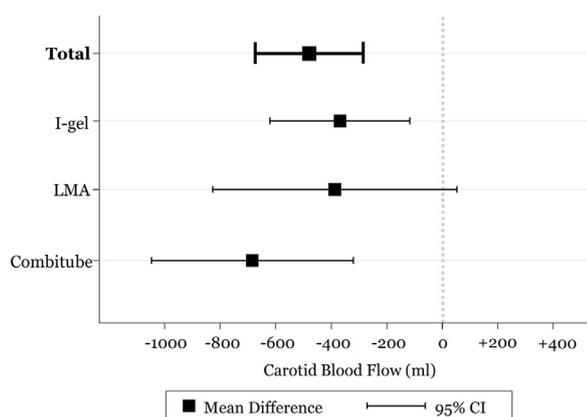
	ETI		LMA		p-Value	ETI-LMA		
	Median	IQR	Median	IQR		Mean difference	95% CI	
Total observed N	12		12					
Systolic blood pressure (mmHg)	70.2	55.1–82.7	65.7	52.6–73.6	0.03	–3.3	–8.2	1.7
Diastolic blood pressure (mmHg)	8.8	5.2–15.4	6.7	1.5–16.2	0.07	–1.5	–4.7	1.7
Mean arterial pressure (mmHg)	30.8	23.0–37.4	23.3	20.0–36.6	0.03	–2.1	–5.8	1.5
Intracranial pressure (mmHg)	17.2	14.0–19.7	16.7	12.6–19.8	0.02	–1.4	–2.7	–0.2
Carotid blood flow rate (ml/s)	31.6	17.7–44.7	22.0	10.5–37.2	0.24	–6.4	–13.8	1.0
Carotid blood flow during measurement period <sup>a</sup> (ml)	1657	1064–2554	1322	630–1668	0.21	–387	–831	58

<sup>a</sup> Carotid blood flow was measured during the last 1 min of a 3-min period with each airway device.

**Table 3 – Carotid blood flow and hemodynamic parameters of I-gel insertion compared to the preceding ETI.**

	ETI		I-gel		p-Value	ETI-I-gel	
	Median	IQR	Median	IQR		Mean difference	95% CI
Total observed N	12		12				
Systolic blood pressure (mmHg)	76.3	47.5–89.1	62.0	44.6–84.2	0.01	–5.7	–9.4 –1.9
Diastolic blood pressure (mmHg)	13.2	5.7–18.0	10.9	3.7–14.3	0.12	–3.2	–7.4 0.9
Mean arterial pressure (mmHg)	36.6	19.9–38.0	29.7	16.6–36.2	0.02	–4.0	–7.9 –0.1
Intracranial pressure (mmHg)	19.6	13.0–23.2	18.6	11.7–20.5	<0.01	–1.7	–2.5 –0.8
Carotid blood flow rate (ml/s)	26.5	18.5–46.4	21.7	9.3–40.0	0.02	–6.2	–10.4 –1.9
Carotid blood flow during measurement period <sup>a</sup> (ml)	1589	1111–2784	1310	560–2400	0.02	–368.7	–623.4 –114

<sup>a</sup> Carotid blood flow was measured during the last 1 min of a 3-min period with each airway device.

**Fig. 2 – Carotid blood flow change from the preceding ETI after SGD insertion.**

when transitioning of airway device was from SGA to ETI (mean carotid blood flow change (95% CI) in ETI to SGA transition: –480 ml (–675/–286), SGA to ETI transition: –4 ml (95% CI –182/175). There was no adverse event during whole course of experiment.

## Discussion

We conducted an experimental porcine model of cardiac arrest, comparing the hemodynamic profile between ETI and insertion with 3 kinds of SGDs including Combitube, LMA and I-gel. In our experiment we observed decreased CBF during SGD insertion compared to the preceding ETI period. Although MAP subsequently decreased as the resuscitation time passed, the reduction in CBF from the SGD to ETI transition was minimal, but the mean reduction in CBF from ETI to SGD was observed as –327.6 ml, –459.8 ml and –652.6 ml at each transition phase, respectively. The results of our study might explain the negative outcome related to SDG insertion compared to ETI reported from previous observational and experimental studies.<sup>7,12,18</sup>

Reduction in CBF was more prominent in prolonged resuscitation over time (Fig. 3). Systemic vascular resistance as well as coronary perfusion pressure decreases gradually during cardiopulmonary resuscitation.<sup>19</sup> In our results, MAP measured from the systemic circulation of the aorta subsequently decreased as resuscitation time

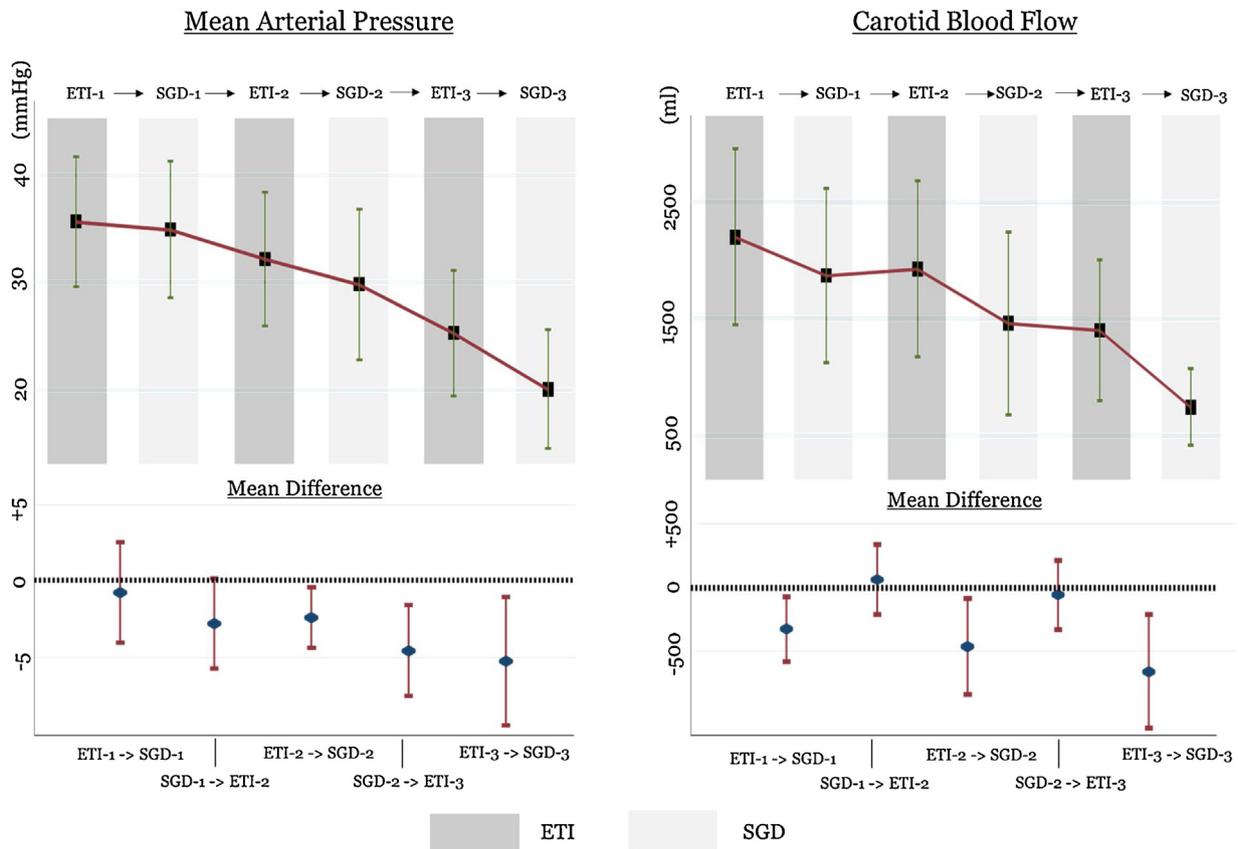
increased. In the carotid artery, blood flow also decreased over time, but the reduction in flow was nonsignificant when the airway was changed from SGD insertion to ETI. Local pressure around the supraglottic area caused by the structure of an inserted SGD in the area could aggravate the decrease in CBF, which was restored to its physiologic status when the transition of the airway from SGD to ETI was performed. This could be a reason why CBF did not decrease significantly after ETI insertion, even though the total resuscitation time had passed.

Prehospital EMS providers should deliver full resuscitative efforts at the scene of OHCA before deciding whether to transport the patient to the hospital or terminate resuscitation. However, as seen in our results, CBF impairment deteriorated as the resuscitation time passed. Including time for a rhythm analysis by AED or manual defibrillator, intravenous line establishment and direct medical direction, field resuscitation time usually exceeds 10 min. Based on our results, the use of an SGD in prolonged prehospital resuscitation could impair CBF in OHCA victims compared to the use of ETI.

Advanced airway placement is recommended during cardiac arrest with minimal interruption of chest compressions. Performing ETI during ongoing chest compressions is difficult and often causes an interruption in chest compressions and other complications.<sup>10,20</sup> In contrast, SGDs have been widely used because they can be inserted successfully with an easy skill level by EMS providers as opposed to health care professionals in hospitals.<sup>8</sup> A recent study reported that SGDs were inserted in approximately 60% of OHCA patients with an advanced airway performed by EMS providers in a prehospital area.<sup>4</sup> Although several randomized trials have been conducted, the optimal choice of advanced airway methods during the prehospital resuscitation of OHCA by EMS providers is still controversial.<sup>21,22</sup>

Good neurological recovery is as important as the clinical outcome after cardiac arrest. A good neurological outcome depends on cerebral perfusion to decrease hypoxic brain damage. Anatomically, CBF is the main route of blood flow to the brain. Therefore, maintaining sufficient CBF is important for preventing hypoxic brain damage during CPR. Impaired CBF by SGD insertion might cause an insufficient supply of oxygenated blood to the brain, which might worsen the neurological outcome.

We observed some differences in the decrease in CBF between the 3 types of SGDs. Combitube decreased –685 ml of CBF during the last 1 min of the SGD period compared to the ETI period, and I-gel also decreased –368.7 ml. The mean decrease in LMA was –387 ml, but the 95% CI was –831 to 58. To obtain more robust evidence, a greater number of experiments is required. Structural size and the



**Fig. 3 – Trend of carotid blood flow and mean arterial pressure according to airway device transition during the course of the experiment.**

hardness of the portion of each device located in the supraglottic area could cause differences in the decrease in CBF. However, the decrease in CBF over time was observed during the transition from ETI to SGD, in contrast to the sparing decrease during the transition from SGD to ETI, regardless of the type of SGD.

### Limitations

Our study has a few limitations. First, it was an experimental animal study and has the limitation of generalizability. And the SGDs used in our experiments were not designed for use in pigs. Although we designed our experiment after reviewing previous articles for porcine experimental model using advanced airway devices, we could not confirm the possibility of over-blocking. However the porcine model would be the most appropriate model to test our theory considering the anatomy. Also we used auscultation and EtCO<sub>2</sub> monitoring for confirmation method, like other previous study using SGD on porcine experiment.<sup>12</sup> A previous study reported decreased carotid blood flow by inserting the LMA in humans,<sup>23</sup> and all 3 SGDs in our experiment use compressive force for the fixation and sealing of the device in the supraglottic area. Therefore, similar physiological changes after SGD insertion in humans might be suggested. Second, although we proved impaired CBF during resuscitation, we did not evaluate the histological extent of hypoxic brain damage. Third, we did not measure neurological or survival outcomes. In our experimental model, all pigs were sacrificed. Fourth, we did not measure cerebral perfusion directly, but CBF could be a

surrogate indicator for measuring cerebral perfusion and could influence cerebral perfusion during resuscitation.

### Conclusions

In a porcine cardiac arrest model of ventricular fibrillation induction, SGD insertion was associated with decreased CBF compared to ETI during cardiopulmonary resuscitation. Impairment of CBF was aggravated during the transition from ETI to SGD as resuscitation time passed, but the decrease in CBF was spared during the transition from SGD to ETI, although MAP subsequently decreased during resuscitation.

### Funding acknowledgement and conflict of interest

This study had no conflict of interest. This study was funded by the Cooperative Research Program of Basic Medical Science and Clinical Science from Seoul National University College of Medicine (Grant No. 800-20160090,800-2016-0091).

### Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.resuscitation.2019.04.020>.

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