

# Endotracheal intubation—still the gold standard in out-of-hospital cardiac arrest airway management?

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Submitted Sep 05, 2021. Accepted for publication Nov 11, 2021. doi: 10.21037/atm-21-4668 View this article at: https://dx.doi.org/10.21037/atm-21-4668

We read with great interest the article written by Yang *et al.* titled "Comparing the efficacy of bag-valve mask, endotracheal intubation, and laryngeal mask airway for subjects with outof-hospital cardiac arrest: an indirect meta-analysis" (1). The authors of the study must be congratulated for their efforts in performing an indirect meta-analysis of 13 studies to compare the outcomes of bag-valve mask (BVM), laryngeal mask airway (LMA), and endotracheal intubation (ETI). Outcome measures used were return of spontaneous circulation (ROSC) and the survival rate to admission or discharge.

Approximately 300,000 persons in the United States alone experience an out-of-hospital cardiac arrest (OHCA) each year with a mortality of approximately 92% (2). This review is made even more timely by the current unprecedented global health crisis caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). A recent systematic review identified that there has been a 120% increase in the incidence of OHCA since the pandemic, with an increase in mortality and supraglottic airway usage (3). Therefore, this article provides invaluable insights in the current conversation for OHCA management during the pandemic.

Despite the importance of effective airway management in the treatment of patients with OHCA, there is a paucity of available data on the topic, including limited high-quality Randomized Controlled Trial (RCT) data comparing the efficacy of various techniques in airway management. Randomized trials have proven to be the gold standard in analysing causal relationships as the act of randomisation and concealment of allocation eradicates inherent biases that might exist in other study designs (4). Equipoise between the various techniques have led to calls for more and larger RCTs comparing the use of BVM, LMA, and ET in the context of OHCA, to determine the most optimal device for airway management.

Of the 13 studies included by Yang *et al.*, three studies were randomized while the rest were observational in nature. We conducted a sensitivity analysis to compare the findings of the randomized studies against the findings by Yang *et al.*, to identify any incongruity in the findings.

Our analysis found that there were differing results for ROSC and survival to discharge when comparing BMV to LMA as compared to the values that were presented by Yang *et al.* On inspection of the randomized studies by Benger *et al.* and Fiala *et al.*, we found no statistically significant difference when comparing BVM and LMA in the outcome of ROSC (RR =1.00, 95% CI, 0.75–1.33;  $I^2$ =0%, P=1.00) (*Figure 1A*) (5,6). Yang *et al.*, however, found that there was a significant difference between LMA and BVM (RR =0.84%, 95% CI, 0.57–1.24;  $I^2$ =94.8%, P<0.001) (1).

Further discrepancies were noted in survival to discharge when comparing BVM with LMA for the randomized studies. Our results revealed no significant difference

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Study or Subaroun	BVN		LMA		Wainht	Risk Ratio	Vers	Risk Ratio
Study or Subgroup 1.2.1 Non-Randomized Studies		Total	Events	Total	weight	M-H, Random, 95% CI	rear	M-H, Random, 95% Cl
		200	67	175	16 704	1 02 (0 00 1 22)	2000	
SOS KANTO Study Group, 2009	80	200	67	173	16.2%	1.03 [0.80, 1.33]		T
Takei et al, 2010		1539	152	660	18.5%	1.03 [0.87, 1.22]		
Chien et al, 2012	32	89 1929	147	309 3110	14.9%	0.76 [0.56, 1.02]		
McMullan et al, 2014					20.0%	1.43 [1.32, 1.56]		
Yeung et al, 2014	8	25 74	6 62	25 395	4.6% 6.1%	1.33 [0.54, 3.29]		
Roth et al, 2015 Subtotal (95% CI)	/	3856	62	4672	80.3%	0.60 [0.29, 1.26] 1.03 [0.80, 1.32]	2015	
	1107	3030	1777	4072	00.3/0	1.05 [0.00, 1.52]		
Total events	1197	df - 5	1227	000010	12 - 0.40	,		
Heterogeneity: $Tau^2 = 0.07$ ; $Chi^2$			(P < 0.0	00001)	; I <sup>=</sup> = 842	, ,		
Test for overall effect: $Z = 0.20$ (	r = 0.84	,						
1.2.2 Randomized Studies								
Benger et al, 2016	67	205	53	170	15.0%	1.05 [0.78, 1.41]	2016	+
Fiala et al, 2017	7	41	9	35	4.8%	0.66 [0.28, 1.60]		
Subtotal (95% CI)		246		205	19.7%	1.00 [0.75, 1.33]		<b>•</b>
Total events	74		62					
Heterogeneity: $Tau^2 = 0.00$ ; $Chi^2$	= 0.93,	df = 1	(P = 0.3)	3);   <sup>2</sup> =	0%			
Test for overall effect: Z = 0.00 (								
Total (05% CI)		4102		4077	100.0%	101 (0 81 1 26)		
Total (95% CI)	45.74	4102	1200	40//	100.0%	1.01 [0.81, 1.26]		T
Total events	1271		1289		2 0.00			n n i i i i i i i i i i i i i i i i i i
Heterogeneity: $Tau^2 = 0.06$ ; $Chi^2$			(P < 0.0	JUU1);	r = 80%			0.01 0.1 1 10 10
Test for overall effect: $Z = 0.10$ (				001 12	00/			Favours [BVM] Favours [LMA]
Test for subgroup differences: Ch	$1^{\circ} = 0.02$	, ar =	I(P = 0.	89), F	= 0%			
В	BVN	4	LM	4		<b>Risk Ratio</b>		Risk Ratio
Study or Subgroup	Events				Weight	Risk Ratio M-H, Random, 95% CI	Year	
and a set of the set o	Events				Weight		Year	
Study or Subgroup	Events				Weight 15.1%			
Study or Subgroup 3.2.1 Non-Randomized Studies	Events	Total	Events	Total		M-H, Random, 95% CI	2009	
Study or Subgroup 3.2.1 Non-Randomized Studies SOS KANTO Study Group, 2009	Events 12 85	Total	Events	Total	15.1%	M-H, Random, 95% Cl 0.46 [0.23, 0.89]	2009 2010	
Study or Subgroup 3.2.1 Non-Randomized Studies SOS KANTO Study Group, 2009 Takei et al, 2010	Events 12 85 323	<b>Total</b> 196 1539	Events	<b>Total</b> 172 660	15.1% 16.6%	M-H, Random, 95% CI 0.46 [0.23, 0.89] 1.74 [1.09, 2.77]	2009 2010 2012	
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Figure 1 Forest plots of BVM and LMA for the outcome of ROSC and for the outcome of survival to discharge. (A) Forest plot comparing BVM and LMA for the outcome of ROSC; (B) Forest plot comparing BVM and LMA for the outcome of survival to discharge. BVM, bag-valve-mask; LMA, laryngeal mask airway; ROSC, return of spontaneous circulation.

between BVM and LMA (RR =1.11, 95% CI, 0.59–2.11;  $I^2$ =0%, P=0.74). (*Figure 1B*) This is contrary to the results in the original study, whereby BVM was shown to be significantly better than LMA (RR =0.61; 95% CI, 0.38–0.98;  $I^2$ =79.4%, P<0.001) (1). The study by Ono *et al.* was intentionally excluded from the results in *Figure 1* as the use of the laryngeal tube, an extra glottic airway device, was classified under ETI instead (7,8).

However, these values should be interpreted with

caution as the two randomized studies listed had relatively smaller sample sizes as compared to the non-randomized counterparts. This can be attributable either to the nature of the study; as a direct consequence of randomization, or due to limitations such as number of eligible participants that fulfil the inclusion criteria, the amount of time available, and the budget allocated for the trial.

Nonetheless, there are benefits to randomized trials as it allows for the comparison of cause and effect relationships

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between interventions and outcomes (9). Randomisation also prevents any priori knowledge of group assignments and balances participant characteristics between the groups, therefore reducing any selection biases that might skew the results and allowing for any attribution of differences in outcomes to the intervention (10).

Besides the aforementioned limitations with RCTs, it is essential to acknowledge the challenges that exist especially in the context of Emergency Medicine, due to the possible ethical implications and the nature of the trial. This is particularly so with OHCA due to its unpredictable nature, making it impossible to gain the consent of patients prior to enrolment and implementation of intervention. Moreover, due to the urgency and variability in the presentation of eligible patients, randomization by patients might lead to delays in care processes and is not only impractical but potentially unethical.

Finally, there also exists a risk of residual confounding bias as numerous compounding variables such as the ventilation rate, duration of chest compression interruption for the insertion of airway adjunct, as well as other interventions that might have been performed either on-site or in-hospital, might have influences on the outcome which cannot be accounted for.

In conclusion, we acknowledge that airway management is of paramount importance in the treatment of OHCA. Although ETI has long been considered the gold standard of airway management, with the advent of alternative airway devices, there has been a recent paradigm shift regarding the most effective device for airway control. Currently, evidence on this matter remains scarce and there is a pertinent need to conduct further large scale RCTs, in order to gather more data on the efficacy of each device on the outcomes of OHCA.

# **Acknowledgments**

Funding: None.

#### Footnote

*Provenance and Peer Review:* This article was a standard submission to the journal. The article did not undergo external peer review.

*Conflicts of Interest:* All authors have completed the ICMJE uniform disclosure form (available at https://dx.doi. org/10.21037/atm-21-4668). The authors have no conflicts

of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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**Cite this article as:** Loke JTF, Teoh SE, Zhang JJY, Masuda Y. Endotracheal intubation—still the gold standard in out-of-hospital cardiac arrest airway management? Ann Transl Med 2021;9(23):1748. doi: 10.21037/atm-21-4668

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