



## Comment on: Letter to the article by Sasaki et al

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To the Editor:

Sasaki et al. recently reported the effect of cuffed endotracheal tubes (ETTs) on postoperative extubation-related respiratory adverse events (RAEs) in pediatric patients with airway hypersensitivity undergoing general anesthesia [1]. The finding of the study indicated that cuffed ETTs were not associated with RAEs, compared to uncuffed ETTs (odds ratio, 1.14; 95% confidence interval, 0.64 to 2.06). Fang et al. raised concern regarding the accuracy of the frequency of RAEs in the study [2]. Sasaki et al. used aggregated data from anesthesia records for intraoperative periods and medical charts for the postoperative course, which were documented by the anesthesiologist and the responsible medical provider, respectively. Laryngospasm was one of the outcomes extracted from the aggregated data and was reported based on the judgment of the responsible anesthesiologist. Sasaki et al. acknowledged that one limitation of their study regarding the reliability of outcome measurement is the inherent nature of a retrospective observational study.

Sasaki et al. defined RAE based on the literature by Von Ungern-Sternberg et al. [3], but further modified the

definition according to available data in their study. The modified definition did not include cough, stridor, bronchospasm, and airway obstruction, while it included laryngospasm and peripheral capillary oxygen saturation <92%. The limited availability of information on outcomes is always one of the limitations of a retrospective observational study. Otherwise, the lack of a gold-standard definition for RAEs poses a challenge for comparisons of any study about RAEs. Due to the absence of a gold-standard definition, it is impossible to compare the outcome across studies employing different definitions for RAEs.

Sasaki et al. included children under eight years of age in their study. While neonates could have been included in the study population, no neonates were enrolled as a result. Fang et al. suggested that laryngospasm is less likely to occur in older children compared to younger ones, referring to the literature by Birlie et al. [4]. Therefore, Fang et al. denoted a selection bias in the study by Sasaki et al., which did not include neonates. However, Birlie et al. did not report the risk of laryngospasm associated with cuffed ETTs in neonates. Furthermore, although Birlie et al. mentioned in their introduction that the risk of laryngospasm increases in younger children, the studies they cited did not report the risk of laryngospasm associated with cuffed ETTs in neonates. To the best of our knowledge, there is no study concluding the risk of RAEs associated with cuffed ETTs in neonates with airway hypersensitivity. Given that neonates could have been included in the study by Sasaki et al. and clear evidence does not exist regarding the risk of RAEs associated with cuffed ETTs in neonates with airway hypersensitivity, we could not determine whether a selection bias affected the study findings by Sasaki et al..

The definition and measurement of outcomes and the potential of selection bias, which Fang et al. pointed out for the study by Sasaki et al., should be carefully considered and addressed in any type of clinical research [5]. On the other hand, there are no randomized controlled trials (RCTs)

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conducted to answer the same research question as Sasaki et al.'s. Therefore, the originality and relevance of the retrospective observational study by Sasaki et al. appear to be sufficient [6]. Further evidence on the risk of RAEs associated with cuffed ETTs in neonates with airway hypersensitivity warrants studies which employ a gold-standard definition of RAEs and minimize a selection bias. In this area of clinical research, we still need to continue accumulating evidence from RCTs or observational studies employing sophisticated methodological and statistical approach to mitigate confounding factors as much as possible [7, 8].

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## Declarations

**Conflict of interest** The authors declare that they have no competing interest related to this publication.

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