Comparison of Anesthetics for Laryngeal Mask Airway Insertion: A Network Meta-Analysis

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Objective: This study aimed to establish which anesthetic agents are associated with minimized adverse outcomes during laryngeal mask airway (LMA) insertion.

Methods: Databases were searched for randomized controlled trials (RCTs) with American Society of Anesthesiologists I or II adult patients (≥15 years of age) receiving general anesthesia (GA) with an LMA. Propofol only was the comparator to other anesthetics used during LMA insertion. The primary outcome was prolonged apnea, and secondary outcomes were adverse airway events, LMA insertion failure, inadequate depth of anesthesia, and hemodynamic events. A network meta-analysis was conducted to estimate the treatment effects (odds ratios, 95% credible intervals, and surface under the cumulative ranking curve [SUCRA]).

Results: A total of 28 anesthetic combinations used on 4695 patients for GA induction and LMA insertion were examined across 53 RCTs. Overall, there was an apnea incidence rate of 33.3% (849 of 2548) with a mean time of 3.74 ± 3.56 minutes (n = 3091). Propofol + dexmedetomidine had the highest overall summed score of SUCRA ranks in reducing adverse outcomes (apnea incidence: SUCRA = 37%, apnea time: SUCRA = 66%, airway adverse event: SUCRA = 67%, insertion failure: SUCRA = 73%, inadequate depth of anesthesia: SUCRA = 84%). In comparison among all propofol combinations, propofol alone ranked lowest for overall summed score of SUCRA in reducing adverse outcomes (apnea incidence: SUCRA = 47%, apnea time: SUCRA = 71%, airway adverse event: SUCRA = 9%, insertion failure: SUCRA = 20%, inadequate depth of anesthesia: SUCRA = 9%).

Conclusion: All anesthetic combinations, other than those with thiopental, reduced adverse outcomes as compared with propofol alone. The combination of propofol and dexmedetomidine infused over 10 minutes ranked as the most effective for reducing adverse outcomes during LMA insertion.

Key Words: Laryngeal mask airway; Propofol; Dexmedetomidine; Systematic review; Network meta-analysis.

The laryngeal mask airway (LMA) is a supraglottic airway device that can be inserted after induction of general anesthesia (GA) using either inhalational or intravenous (IV) agents. Propofol, a short-acting lipophilic agent, is the most widely used IV agent for GA induction because it is able to induce relaxation of the masticatory musculature and depression of the upper airway reflexes, and thus allow LMA insertion.[1,2] When used as the sole anesthetic, high-dose propofol can lead to profound hypotension, cardiorespiratory depression, and prolonged apnea.[3,4] To minimize these undesirable effects, other anesthetic agents such as opioids, benzodiazepines, inhaled anesthetics, and neuromuscular blocking agents have been used to reduce the dose of propofol required. Each anesthetic combination confers different benefits and risks that may improve or impair LMA placement.[5] Despite the use of LMAs for over 4 decades, there is no consensus on which anesthetic combination facilitates the greatest LMA insertion success while minimizing adverse events.

The aim of this study was to examine differences in adverse outcomes between anesthetic agents used during

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LMA insertion following GA induction. We performed a systematic review and network meta-analysis (NMA) comparing propofol as the sole anesthetic for GA induction with other anesthetic combinations used during LMA insertion. Our primary outcome was prolonged apnea, and our secondary outcomes were airway adverse events, LMA insertion failure, inadequate anesthetic depth, adverse hemodynamic events, unanticipated hospital admission, and patient mortality.

Anesthesia practice among clinicians is diverse in their selection of drug combinations and doses, which is challenging when creating evidence-based statements on airway management. The NMA creates a network of interventions with both direct and indirect comparisons.[6] By combining direct and indirect estimates across a network of interventions in a single analysis, a relative ranking of treatments for a given outcome can be made. This study uniquely employs an NMA to compare the variety of induction agents used during LMA insertion to establish which may reduce risks of prolonged apnea and other adverse outcomes the most.

METHODS

This study was registered at PROSPERO (CRD42020202474). The Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension statement for NMA was used to report our methodology and results.[6] Eligibility criteria included the following:

- Population: American Society of Anesthesiologists I or II adult patients (≥15 years of age) receiving GA with an LMA for nonemergency medical or dental surgery in hospital or ambulatory clinical setting who are spontaneously breathing during the procedure
- Interventions: Any anesthetic agent(s) for induction of GA and LMA insertion
- Comparison: Propofol as sole anesthetic for GA induction and LMA insertion
- Outcomes:
  - Primary outcome: prolonged apnea, defined as duration (time from induction until first breath) or incidence (≥15 s without breath after LMA insertion)[7,8]
  - Secondary outcomes[9,10]:
    - Airway adverse event
      - Incidence of coughing or gagging
      - Incidence of breath holding
      - Incidence of laryngospasm
      - Incidence of hypoxia (oxygen saturation as measured by pulse oximetry <96%)[11]
      - Incidence of swallowing
    - Insertion failure of LMA
      - Proportion of LMAs unsuccessful placed on first attempt
      - Inadequate ease of insertion (difficult/impossible)
    - Inadequate depth of anesthesia
      - Incidence of additional/rescue anesthetic required
      - Inadequate jaw relaxation/mouth opening (Young's criteria[12]; full, partial, nil)
      - Incidence of excitatory (head or limb) or nonpurposeful movements
    - Adverse hemodynamic event
      - Bradycardia (<60 beats/min)[13]
      - Tachycardia (>100 beats/min)[13]
      - Hypotension (systolic arterial blood pressure <90 mm Hg[14] or mean arterial pressure decrease >20% of the baseline value)[15]
      - Hypertension (systolic arterial blood pressure >160 mm Hg[16] or mean arterial pressure increase >20% of the baseline value)[16]
    - Unanticipated hospital admission
    - Mortality
- Study design: Randomized controlled trials (RCTs)

Data Sources and Search Strategy

Our search strategy was constructed with the help of 2 medical librarians and was applied to the following electronic databases: Cochrane Library (Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials [CENTRAL], Cochrane Methodology Register), OVID MEDLINE, OVID EMBASE, CINAHL, and SCOPUS (Supplemental Information, Table S1; all supplemental information available online only). The main databases were initially searched on January 9, 2021, and updated on January 19, 2022. A search filter of 1983, the year of the first LMA publication, to present was used for each database.[17] The first 100 hits of Web of Science and ScienceDirect were also searched for additional relevant studies. Completed and ongoing trials were searched through clinicaltrials.gov and World Health Organization International Clinical Trials Registry Platform. Unpublished studies such as dissertations, reports, and conference abstracts were searched for in ProQuest, Google Scholar (the first 100 hits), and the OpenGrey database. Reference lists of previous reviews in the same topic and included studies were searched manually. There were no language or publication date restrictions. We attempted to contact the authors in case of missing information. Search results were imported into EndNote X9 (Clarivate) for duplication screening, then Covidence systematic review software (Veritas Health Innovation) for study screening and selection.[18,19]

Study Selection and Data Collection

Two review authors (C.G. and E.G.) independently reviewed and selected trials from screening. C.G. extracted the data from the selected trials and E.G. reviewed and confirmed all

extracted data. Disagreements were resolved through discussion and consensus or by consulting a third reviewer (M.W.). Reason for study exclusion and included study characteristics are found in the Supplemental Information (Tables S2 and S3).

Risk of Bias Assessment

The 2 review authors, C.G. and E.G., independently used Cochrane's risk of bias assessment tool to evaluate the methodological quality of included trials across 6 domains[20]: selection, performance, detection, attrition, reporting, and other biases. Studies were graded as low risk if all the domains were judged to be of low risk, moderate risk if any domain was judged to be of unclear risk, and high risk if any domain was judged to be of high risk or if all domains were judged to be unclear risk. Disagreements were resolved with discussion or with a third reviewer (M.W.).

NMA and Data Synthesis

The included studies' data were entered into a standardized spreadsheet. If the study contained an intervention with the same anesthetic but different doses, the intervention arms were combined. Anesthetics were grouped together based on related drug class (ie, pharmacodynamic properties) for analysis. Continuous outcome (apnea time) was analyzed with mean and SD. Binary outcomes (presence of an airway adverse event or inadequate depth of anesthesia) were analyzed using the odds ratio (OR). Ordinal outcomes were combined and analyzed as a binary outcome. Missing SDs were calculated from the available CI or standard error and the number of participants.[21] If mean and SD were unavailable, they were estimated using median and range (the formula presented by Hozo and colleagues[22] using median and range) or using range (the formula presented by Walter and Yao[23]). If numerical data were not reported, authors were contacted.

NMA was conducted using the program R (version 3.5.0; R Project for Statistical Computing) with the Gemtc version 0.8.2 and rjags packages, which interface with Just Another Gibbs Sampler software (version 4.0.0; developed by Martyn Plummer) for Markov chain Monte Carlo modeling. A Bayesian NMA was performed under a hierarchical random effects framework and unified generalized linear model. For continuous outcomes, a normal likelihood and identity link function was used. For binary outcomes, a binomial likelihood with logit link function was used.[24,25] The treatment effects were estimated as ORs or mean differences with associated 95% credible intervals (CrIs) and the surface under the cumulative ranking curve (SUCRA). Heterogeneity was assessed using the I^2 statistic. Node-splitting method was used to calculate the inconsistency of the model through direct and indirect evidence with its Bayesian P value.[24] Posterior probabilities were used and scored to rank the interventions for the overall conclusions. Sensitivity analysis was conducted by excluding any high–risk of bias studies. Subgroup analysis was conducted comparing (1) the effect of premedication and (2) the type of LMA.

Quality of Evidence

Two review authors (C.G. and E.G.) used the CINeMA web application (University of Bern) to evaluate the confidence of the main NMA results considering 6 domains: heterogeneity, imprecision, incoherence, indirectness, and within- and across-studies bias.[26] Results were judged as high, moderate, low, or very low confidence.[26] Consensus was reached by consulting the other reviewer or by third reviewer (M.W.) when necessary.

RESULTS

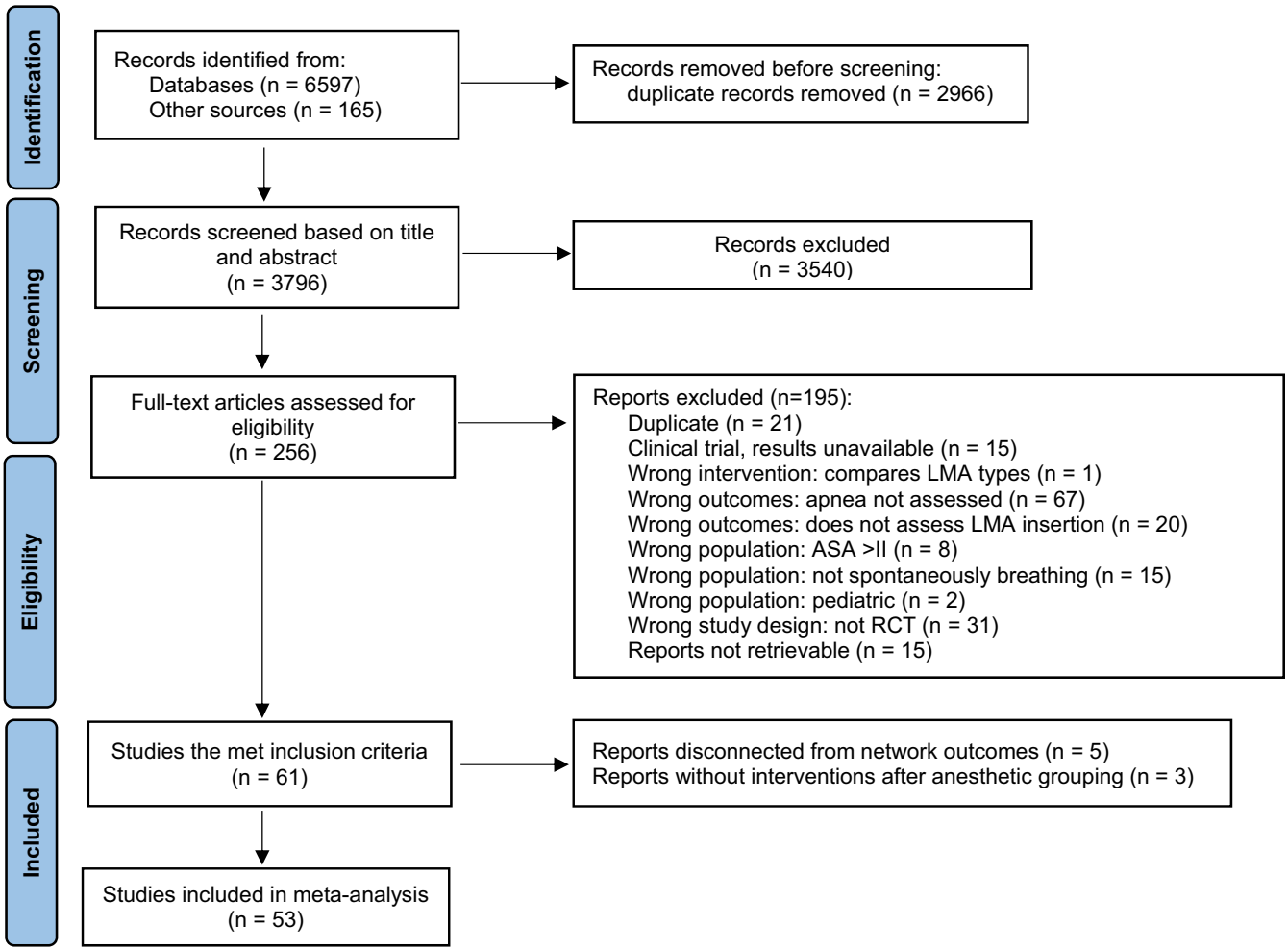
Search Results

In the initial screening stage, 6762 potentially eligible reports were retrieved, 2966 duplicates were removed, and 3540 records were excluded based on title and abstract (Figure 1). A total of 256 full-text trials were assessed for eligibility; 195 studies were excluded, and 61 RCT met the inclusion criteria (Supplemental Information, Tables S2 and S3). The included studies were from India (18), China (8), Turkey (6), Singapore (4), United Kingdom (4), Malaysia (3), South Korea (3), Brazil (2), Iran (2), Taiwan (2), Australia, Canada, Egypt, Ireland, Japan, Lebanon, Poland, Saudi Arabia, and Singapore (Supplemental Information, Table S3).

Study Characteristics

Population. All studies limited their patients to adults, although the minimal age of inclusion ranged from 15 years to 18 years of age (≥15 y, 3 studies; ≥16 y, 4 studies; ≥17 y, 1 study; and ≥18 y, 44 studies; Supplemental Information, Table S3). Nine studies did not specify their adult age range of inclusion. LMA types used were the first-generation LMA Classic (Teleflex; 14 studies) and second-generation ProSeal LMA (Teleflex; 5 studies) and I-gel (Intersurgical; 1 study). Forty-one studies did not specify LMA type used; however, 16 of these studies were conducted before the introduction of second-generation LMAs[27] in 2000. Twenty-nine studies did not use premedication prior to anesthetic induction. Of the 24 studies that reported premedication use, 12 used an anticholinergic (glycopyrrolate or atropine), 10 used an oral benzodiazepine (midazolam, lorazepam, or

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses Flow Diagram



Flow diagram of study inclusion and exclusions. LMA indicates laryngeal mask airway; ASA, American Society of Anesthesiologists; and RCT, randomized controlled trial.

temazepam), and 2 used hydroxyzine. Eight studies did not specify if premedication was utilized. The surgical reasons for GA and LMA placement were elective general surgery, orthopedics, and plastic or gynecologic procedures (17 studies); lower abdominal or urologic operations (7 studies); oncological (4 studies); minor, elective, or short procedures (22 studies); and not specified (11 studies).

Interventions. A total of 48 different anesthetics and anesthetic combinations were identified. Of the 61 studies, 5 had intervention pairings that were disconnected from the comparator network across all outcomes, and were excluded from analysis. An additional 3 trials were excluded from analysis as they became single-arm trials following the anesthetic drug class grouping. In total, 4695 patients and 37 anesthetic treatments were combined into 28 anesthetic drug class groupings for inclusion in the NMA (Table).

Outcome Assessment. Figure 2 demonstrates the networks of each outcome. As reporting of outcomes differed across studies, analysis was completed for 31 studies for apnea incidence (2548 patients, 20 anesthetic combinations), 29 studies for apnea time (3091 patients, 17 anesthetic combinations), 41 studies for airway adverse events (3679 patients, 26 anesthetic combinations), 41 studies for LMA insertion failure (3853 patients, 26 anesthetic combinations), and 36 studies for inadequate depth of anesthesia (3888 patients, 20 anesthetic combinations). Supplemental Information, Figure S1 summarizes relative treatment effects for all possible comparisons as expressed by ORs with 95% CrIs.

In total, there was a 33% (849 of 2548) incidence of prolonged apnea overall (Table). For prolonged apnea, vapor + midazolam + short opioid demonstrated a high SUCRA score (OR, 0.02; 95% CrI, 4.0×10^{-3} to 0.64; SUCRA = 92%; Figure 3), which indicates a higher likelihood that combination is

Table. Anesthetic Interventions and Adverse Outcome Data

		Apnea						*Hemodynamic event*								
		Incidence			*Time*			*Bradycardia*			*Tachycardia*			*Hypotension*		
Anesthetic(s)	*Total patients, No.*	*Observed, No.*	*Patients, No.*	*Percentage*	*Mean time, min*	*SD*	*Patients, No.*	*Observed, No.*	*Patients, No.*	*Percentage*	*Observed, No.*	*Patients, No.*	*Percentage*	*Observed, No.*	*Patients, No.*	*Percentage*
PPF	593	114	249	45.8	2.13	1.52	415	0	208	0.0				4	158	2.5
PPF + AA opioid																
PPF + butorphanol	50				0.96	0.22	50									
PPF + nalbuphine	30	16	30	53.3												
PPF + dexmedetomidine	143	34	143	23.8	3.10	1.63	143	7	103	6.8				1	77	1.3
PPF + ketamine	119	20	60	33.3	2.00	0.60	59	0	30	0.0				0	30	0.0
PPF + LIDO (IV)	48	11	34	32.4	4.20	1.50	10									
PPF + LIDO (topical)	30	1	30	3.3										4	30	13.3
PPF + MDZ	99	28	40	70.0	2.80	0.70	59									
PPF + MDZ + AA opioid																
PPF + MDZ + butorphanol	80	14	60	23.3	1.62	0.12	50	0	30	0.0				0	30	0.0
PPF + MDZ + dexmedetomidine	100	15	100	15.0	3.48	0.26	70	5	70	7.1				3	70	4.3
PPF + MDZ + ketamine	120	30	120	25.0	1.56	0.26	30	0	30	0.0				0	30	0.0
PPF + MDZ + LIDO (IV)	40	23	40	57.5												
PPF + MDZ + short opioid																
PPF + MDZ + fentanyl	270	88	250	35.2	3.11	1.07	120	0	100	0.0				5	130	3.8
PPF + NMBA																
PPF + succinylcholine	60	10	30	33.3												
PPF + mivacurium	109				3.70	1.08	109									
PPF + remifentanil	319	32	61	52.5	3.17	1.82	255	12	256	4.7				7	136	5.1
PPF + short opioid																
PPF + fentanyl	936	275	544	50.6	4.32	3.51	675	2	233	0.9	0	31	0.0	75	308	24.4
PPF + alfentanil	160	19	60	31.7	5.63	3.30	159	7	100	7.0						
PPF + short opioid + ketamine																
PPF + fentanyl + ketamine	40				6.85	2.80	40	0	40	0.0				14	40	35.0
PPF + short opioid + NMBA																
PPF + fentanyl + rocuronium	150				10.60	6.00	150									
PPF + fentanyl + succinylcholine	188				6.65	5.30	185									
PPF + THIO + short opioid																
PPF + THIO + fentanyl	41	17	41	41.5	2.81	0.63	41							21	41	51.2
PPF + vapor																
PPF + sevoflurane + N_2O	61	10	61	16.4	0.88	0.40	61									
PPF + N_2O	25				1.02	0.68	25									
PPF + vapor + short opioid																
PPF + fentanyl + N_2O	30	0	30	0.0												
PPF + sevoflurane + N_2O + fentanyl	40	4	40	10.0												
THIO	30				3.64	3.84	30									
THIO + NMBA																
THIO + succinylcholine	40				3.57	0.78	40									

Table. *(Continued)*

Anesthetic(s)	Total patients, No.	Apnea						Hemodynamic event								
		Incidence			Time			Bradycardia			Tachycardia			Hypotension		
		Observed, No.	Patients, No.	Percentage	Mean time, min	SD	Patients, No.	Observed, No.	Patients, No.	Percentage	Observed, No.	Patients, No.	Percentage	Observed, No.	Patients, No.	Percentage
THIO + short opioid + LIDO (IV)																
THIO + fentanyl + LIDO (IV)	60				1.95	1.15	60									
THIO + short opioid + LIDO (topical)																
THIO + fentanyl + LIDO (topical)	76				1.60	1.09	76									
Vapor																
Sevoflurane	73	27	73	37.0				0	33	0.0				0	33	0.0
Sevoflurane + N_2O	199	8	155	5.2	1.34	1.10	100	0	21	0.0				0	21	0.0
Vapor + MDZ + short opioid																
Sevoflurane + MDZ + fentanyl	40	13	40	32.5												
Vapor + remifentanil																
Sevoflurane + remifentanil	67	16	67	23.9				0	67	0.0				0	68	0.0
Vapor + short opioid																
Sevoflurane + fentanyl	39				4.61	3.52	39									
Sevoflurane + N_2O + fentanyl	150	21	150	14.0							0	30	0.0	16	30	53.3
Desflurane + N_2O + fentanyl	40	3	40	7.5	0.24	0.73	40									
Overall	**4695**	**849**	**2548**	**33.3**	**3.74**	**3.56**	**3091**	**33**	**1321**	**2.5**	**0**	**61**	**0.0**	**150**	**1232**	**12.2**

Anesthetic(s)	Airway adverse event														
	Coughing and/or gagging			Breath holding			Laryngospasm			Hypoxia			Swallowing		
	Observed, No.	Patients, No.	Percentage	Observed, No.	Patients, No.	Percentage	Observed, No.	Patients, No.	Percentage	Observed, No.	Patients, No.	Percentage	Observed, No.	Patients, No.	Percentage
PPF	141	370	38.1				55	369	14.9	0	40	0.0	138	214	64.5
PPF + AA opioid															
PPF + butorphanol															
PPF + nalbuphine	9	30	30.0				0	30	0.0				5	30	16.7
PPF + dexmedetomidine	5	103	4.9	14	77	18.2	0	40	0.0						
PPF + ketamine	15	89	16.9	0	59	0.0	1	119	0.8				4	89	4.5
PPF + LIDO (IV)	11	34	32.4				0	38	0.0						
PPF + LIDO (topical)	3	30	10.0				0	30	0.0						
PPF + MDZ	30	95	31.6	0	59	0.0	3	95	3.2				1	59	1.7
PPF + MDZ + AA opioid															
PPF + MDZ + butorphanol	6	50	12.0				0	80	0.0						
PPF + MDZ + dexmedetomidine	4	100	4.0	12	70	17.1	1	30	3.3						
PPF + MDZ + ketamine	14	30	46.7				7	60	11.7						
PPF + MDZ + LIDO (IV)	10	39	25.6				0	39	0.0						

Table. *(Continued)*

	Airway adverse event														
	Coughing and/or gagging			*Breath holding*			*Laryngospasm*			*Hypoxia*			*Swallowing*		
Anesthetic(s)	*Observed, No.*	*Patients, No.*	*Percentage*	*Observed, No.*	*Patients, No.*	*Percentage*	*Observed, No.*	*Patients, No.*	*Percentage*	*Observed, No.*	*Patients, No.*	*Percentage*	*Observed, No.*	*Patients, No.*	*Percentage*
PPF + MDZ + short opioid															
PPF + MDZ + fentanyl	33	150	22.0	34	70	48.6	5	140	3.6						
PPF + NMBA															
PPF + succinylcholine	12	60	20.0				2	60	3.3				6	60	10.0
PPF + mivacurium	11	109	10.1				4	110	3.6				24	109	22.0
PPF + remifentanil	18	96	18.8				5	75	6.7	2	101	2.0			
PPF + short opioid															
PPF + fentanyl	81	642	12.6	25	77	32.5	10	639	1.6	0	44	0.0	64	270	23.7
PPF + alfentanil	2	59	3.4				4	59	6.8				7	59	11.9
PPF + short opioid + ketamine															
PPF + fentanyl + ketamine	0	40	0.0				2	40	5.0				3	40	7.5
PPF + short opioid + NMBA															
PPF + fentanyl + rocuronium	1	150	0.7												
PPF + fentanyl + succinylcholine	8	188	4.3				0	188	0.0						
PPF + THIO + short opioid															
PPF + THIO + fentanyl	17	41	41.5				0	41	0.0						
PPF + vapor															
PPF + sevoflurane + N_2O	1	31	3.2				0	31	0.0						
PPF + N_2O															
PPF + vapor + short opioid															
PPF + fentanyl + N_2O	0	30	0.0				1	30	3.3						
PPF + sevoflurane + N_2O + fentanyl	2	40	5.0				2	40	5.0	3	40	7.5			
THIO	17	20	85.0				1	20	5.0						
THIO + NMBA															
THIO + succinylcholine	16	40	40.0				0	40	0.0						
THIO + short opioid + LIDO (IV)															
THIO + fentanyl + LIDO (IV)	33	60	55.0				14	60	23.3						
THIO + short opioid + LIDO (topical)															
THIO + fentanyl + LIDO (topical)	23	76					3	76	3.9	0	46	0.0			

Table. *(Continued)*

	Airway adverse event														
	Coughing and/or gagging			*Breath holding*			*Laryngospasm*			*Hypoxia*			*Swallowing*		
Anesthetic(s)	*Observed, No.*	*Patients, No.*	*Percentage*	*Observed, No.*	*Patients, No.*	*Percentage*	*Observed, No.*	*Patients, No.*	*Percentage*	*Observed, No.*	*Patients, No.*	*Percentage*	*Observed, No.*	*Patients, No.*	*Percentage*
Vapor															
Sevoflurane	13	73	17.8							0	73	0.0	2	33	6.1
Sevoflurane + N_2O	34	169	20.1				12	148	8.1	0	61	0.0			
Vapor + MDZ + short opioid															
Sevoflurane + MDZ + fentanyl	3	40	7.5							0	40	0.0			
Vapor + remifentanil															
Sevoflurane + remifentanil	3	67	4.5							0	68	0.0	4	67	6.0
Vapor + short opioid															
Sevoflurane + fentanyl															
Sevoflurane + N_2O + fentanyl	6	70	8.6				4	120	3.3	2	40	5.0			
Desflurane + N_2O + fentanyl	0	40	0.0				1	40	2.5						
Overall	**582**	**3261**	**17.8**	**85**	**412**	**18.2**	**137**	**2887**	**4.7**	**7**	**553**	**1.3**	**258**	**1030**	**25.0**

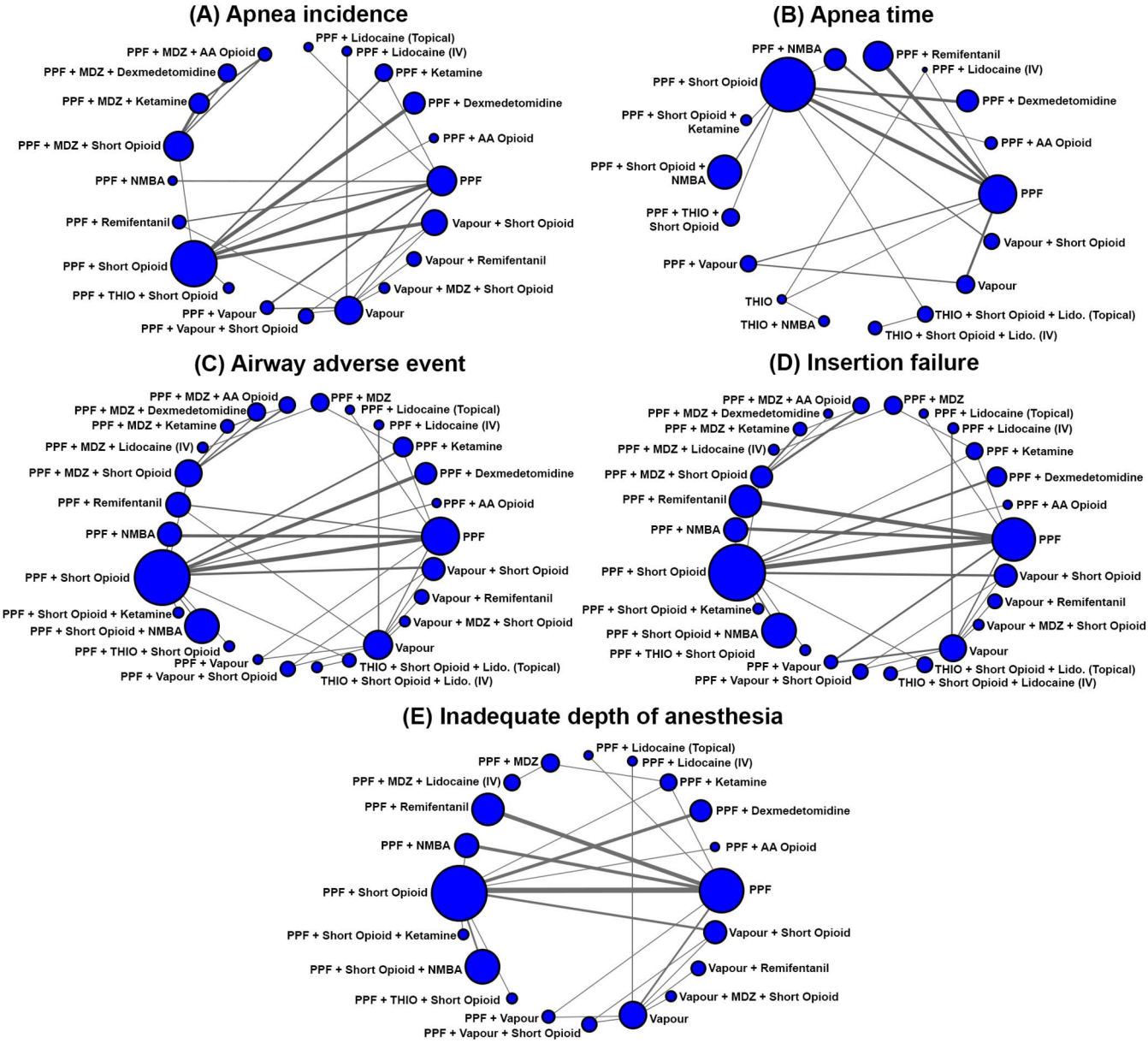
	Insertion failure						*Inadequate depth of anesthesia*								
	Unsuccessful first attempt			*Difficult insertion*			*Additional bolus required*			*Inadequate mouth opening*			*Head or limb movement*		
Anesthetic(s)	*Observed, No.*	*Patients, No.*	*Percentage*	*Observed, No.*	*Patients, No.*	*Percentage*	*Observed, No.*	*Patients, No.*	*Percentage*	*Observed, No.*	*Patients, No.*	*Percentage*	*Observed, No.*	*Patients, No.*	*Percentage*
PPF	145	476	30.5	182	458	39.7	122	300	40.7	168	288	58.3	225	389	57.8
PPF + AA opioid															
PPF + butorphanol															
PPF + nalbuphine	2	30	6.7	1	30	3.3				3	30	10.0	4	30	13.3
PPF + dexmedetomidine	5	77	6.5	3	80	3.8	2	37	5.4	2	143	1.4	0	26	0.0
PPF + ketamine	9	89	10.1	7	89	7.9	5	89	5.6	15	89	16.9	33	89	37.1
PPF + LIDO (IV)	11	38	28.9										18	34	52.9
PPF + LIDO (topical)	2	30	6.7	10	30	33.3	2	30	6.7				5	30	16.7
PPF + MDZ	10	99	10.1	14	99	14.1	9	59	15.3	28	99	28.3	36	99	36.4
PPF + MDZ + AA opioid															
PPF + MDZ + butorphanol	5	60	8.3	0	80	0.0	10	80	12.5	5	80	6.3	6	50	12.0
PPF + MDZ + dexmedetomidine	3	30	10.0	1	30	3.3				7	100	7.0			
PPF + MDZ + ketamine	27	60	45.0	7	60	11.7	35	60	58.3	28	60	46.7	18	30	60.0
PPF + MDZ + LIDO (IV)	1	40	2.5	4	40	10.0				8	40	20.0	19	40	47.5
PPF + MDZ + short opioid															
PPF + MDZ + fentanyl	33	120	27.5	1	110	0.9	31	80	38.8	41	180	22.8	22	50	44.0
PPF + NMBA															
PPF + succinylcholine	3	60	5.0	4	60	6.7				12	60	20.0	12	60	20.0
PPF + mivacurium	10	109	9.2	15	109	13.8				60	109	55.0	51	109	46.8
PPF + remifentanil	28	215	13.0	35	223	15.7	29	180	16.1	44	133	33.1	18	115	15.7
PPF + short opioid															
PPF + fentanyl	71	566	12.5	78	575	13.6	60	317	18.9	179	598	29.9	141	512	27.5
PPF + alfentanil	9	160	5.6	7	159	4.4	19	100	19.0	17	59	28.8	6	59	10.2

Table. *(Continued)*

	Insertion failure						*Inadequate depth of anesthesia*								
	Unsuccessful first attempt			*Difficult insertion*			*Additional bolus required*			*Inadequate mouth opening*			*Head or limb movement*		
Anesthetic(s)	*Observed, No.*	*Patients, No.*	*Percentage*	*Observed, No.*	*Patients, No.*	*Percentage*	*Observed, No.*	*Patients, No.*	*Percentage*	*Observed, No.*	*Patients, No.*	*Percentage*	*Observed, No.*	*Patients, No.*	*Percentage*
PPF + short opioid + ketamine															
PPF + fentanyl + ketamine				3	40	7.5				3	40	7.5	3	40	7.5
PPF + short opioid + NMBA															
PPF + fentanyl + rocuronium				4	150	2.7	5	150	3.3	22	150	14.7	9	150	6.0
PPF + fentanyl + succinylcholine	10	188	5.3	14	188	7.4	16	188	8.5	57	188	30.3	21	188	11.2
PPF + THIO + short opioid															
PPF + THIO + fentanyl				11	41	26.8	5	41	12.2	15	41	36.6			
PPF + vapor															
PPF + sevoflurane + N_2O	5	61	8.2				2	31	6.5				8	31	25.8
PPF + N_2O							4	25	16.0						
PPF + vapor + short opioid															
PPF + fentanyl + N_2O				1	30	3.3	2	30	6.7	3	30	10.0	1	30	3.3
PPF + sevoflurane + N_2O + fentanyl	1	40	2.5										6	40	15.0
THIO				12	20	60.0				18	20	90.0			
THIO + NMBA															
THIO + succinylcholine				9	40	22.5				30	40	75.0			
THIO + short opioid + LIDO (IV)															
THIO + fentanyl + LIDO (IV)	22	60	36.7	25	58	43.1									
THIO + short opioid + LIDO (topical)															
THIO + fentanyl + LIDO (topical)	6	76	7.9	4	30	13.3									
Vapor															
Sevoflurane	7	40	17.5	7	33	21.2				6	33	18.2	32	73	43.8
Sevoflurane + N_2O	54	134	40.3				7	70	10.0				70	148	47.3
Vapor + MDZ + short opioid															
Sevoflurane + MDZ + fentanyl	1	40	2.5										18	40	45.0
Vapor + remifentanil															
Sevoflurane + remifentanil				8	67	11.9				3	67	4.5	4	67	6.0
Vapor + short opioid															
Sevoflurane + fentanyl															
Sevoflurane + N_2O + fentanyl	2	90	2.2	4	30	13.3				7	30	23.3	24	100	24.0
Desflurane + N_2O + fentanyl	8	40	20.0	15	40	37.5	2	40	5.0				1	40	2.5
Overall	**490**	**3028**	**16.2**	**486**	**2999**	**16.2**	**367**	**1907**	**19.2**	**781**	**2707**	**28.9**	**811**	**2669**	**30.4**

* PPF indicates propofol; AA, agonist-antagonist; LIDO, lidocaine; MDZ, midazolam; IV, intravenous; NMBA, neuromuscular blocking agent; THIO, thiopentone; and N_2O, nitrous oxide. Bold type indicates ???

Figure 2. Network Geometries of the Adverse Outcomes



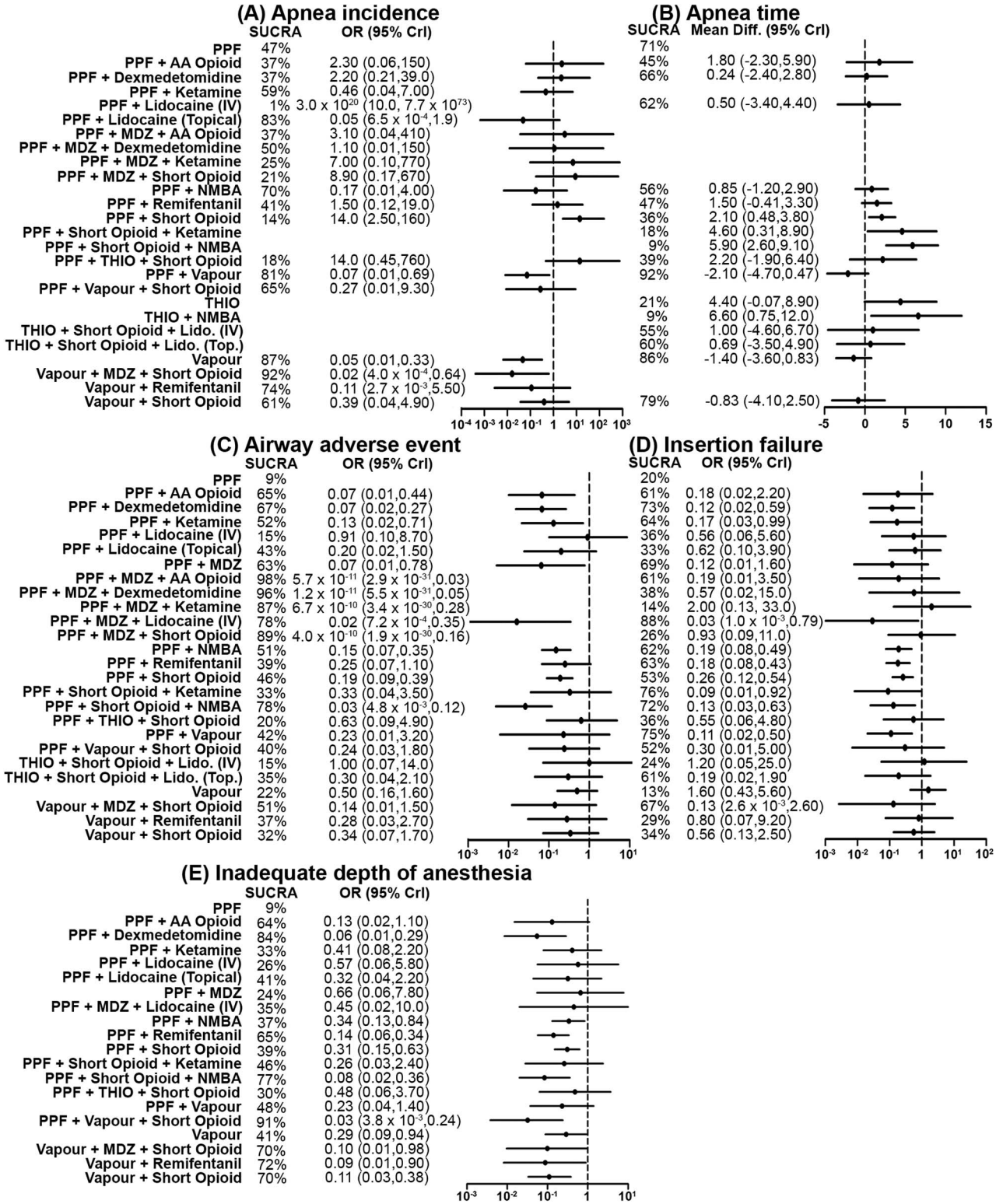
The network geometry of the primary, (A) apnea incidence and (B) apnea time, and secondary, (C) airway adverse events, (D) insertion failure, and (E) inadequate depth of anesthesia, outcomes during LMA placement. Gray connecting lines between circles indicate the direct comparison of interventions and the circle width is proportional to the number of studies evaluating the comparison. The circle volume is proportional to the number of patients who received the intervention. PPF indicates propofol; MDZ, midazolam; AA, agonist-antagonist; IV, intravenous; NMBA, neuromuscular blocking agent; and THIO, thiopentone.

one of the top ranked for reducing the risk of prolonged apnea. For comparison, propofol alone demonstrated a SUCRA score of 47% in this outcome (Figure 3).

Overall, the mean apnea time was 3.74 ± 3.56 minutes (Table). Propofol + vapor (mean difference = −2.10; 95% CrI, −4.70 to 0.47; SUCRA = 92%) ranked the top combination for reducing the risk of apnea time (Figure 3). For comparison, propofol alone demonstrated a SUCRA score of 71% in this outcome (Figure 3).

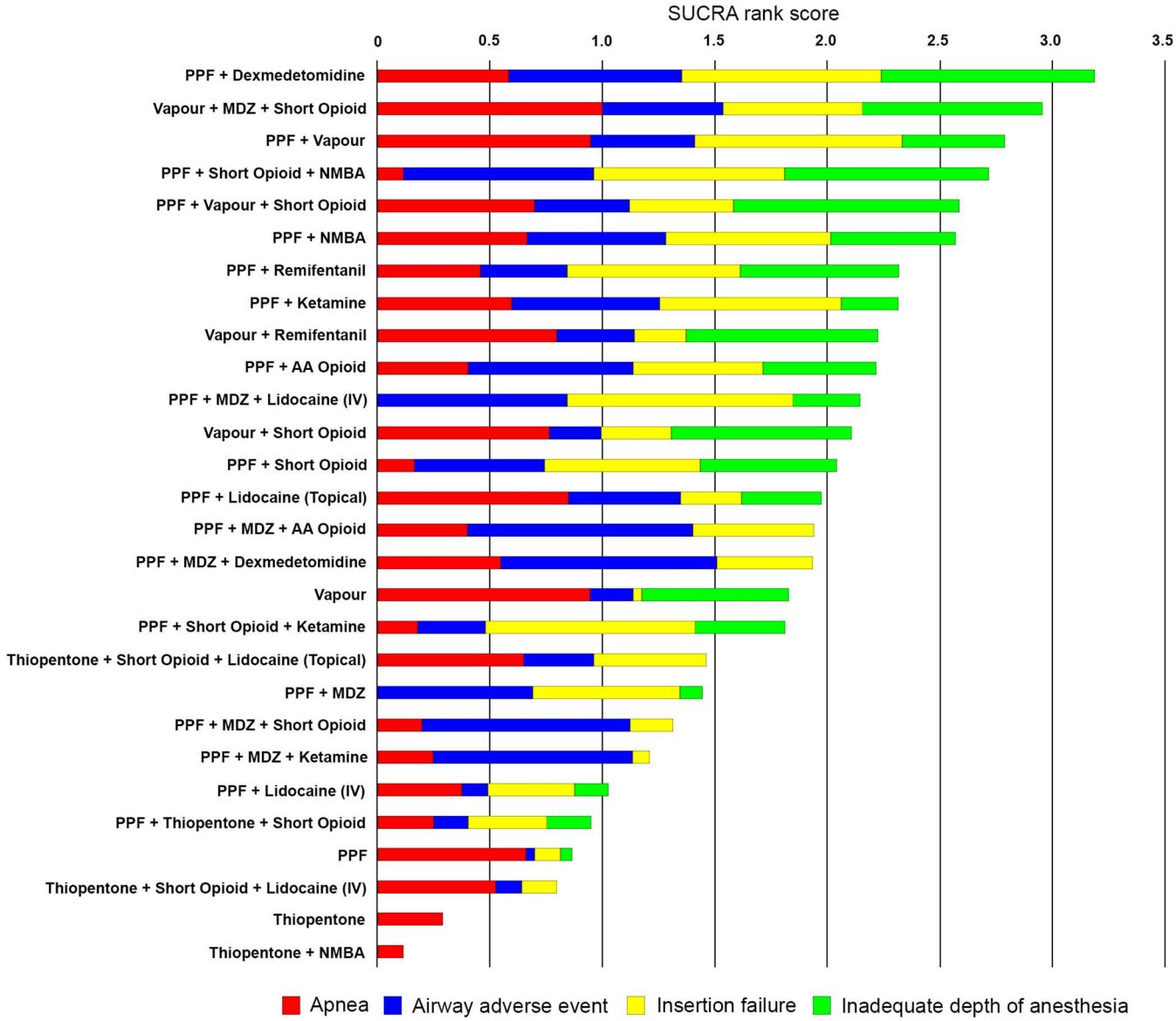
In the airway adverse event outcome, coughing and/or gagging was reported the most and had an incidence of 17.8% (582 of 3261; Table). Laryngospasm was examined among 2887 patients and had an incidence of 4.7%. Propofol + midazolam + agonist-antagonist opioid (OR,

Figure 3. NMA Outcome SUCRA Values and ORs



SUCRA values and forest plots of odds ratios and mean differences of NMA of (A) apnea time, (B) apnea incidence, (C) airway adverse event, (D) insertion failure, and (E) inadequate depth of anesthesia. NMA indicates network meta-analysis; SUCRA, surface under the cumulative ranking curve; OR, odds ratio; CrI, credible interval; PPF, propofol; MDZ, midazolam; AA, agonist-antagonist; IV, intravenous; NMBA, neuromuscular blocking agent; THIO, thiopentone; Lido., lidocaine; and Top., topical.

Figure 4. Cumulative SUCRA Scores of Anesthetic Interventions



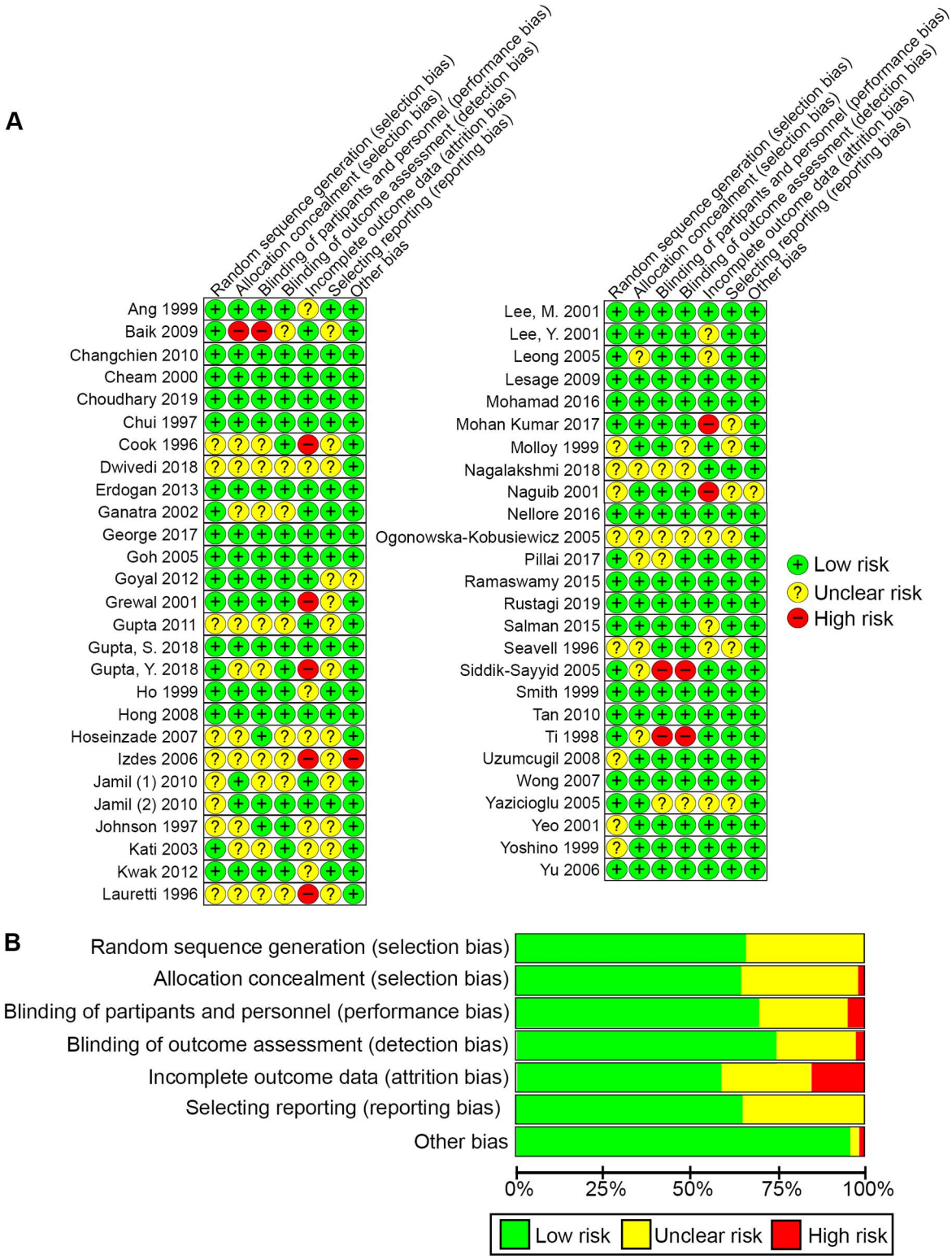
Summed scores of anesthetic intervention SUCRA ranks for apnea (red), airway adverse event (blue), insertion failure (yellow), and inadequate depth of anesthesia (green). SUCRA indicates surface under the cumulative ranking curve; PPF, propofol; MDZ, midazolam; NMBA, neuromuscular blocking agent; AA, agonist-antagonist; and IV, intravenous.

5.7×10^{-11}; 95% CrI, 2.9×10^{-31} to 0.03; SUCRA = 98%) ranked the top intervention for reducing the risk of airway adverse events (Figure 3). For comparison, propofol alone demonstrated a SUCRA score of 9% in this outcome (Figure 3).

Under the insertion failure outcome, failed LMA insertion on the first attempt occurred in 16.2% of patients (490 of 3028; Table). Furthermore, 16.2% (486 of 2999) were reported to have inadequate ease of LMA insertion. Propofol + midazolam + IV lidocaine (OR, 0.03; 95% CrI, 1.0×10^{-3} to 0.79; SUCRA = 88%) ranked the top intervention to reduce risk of insertion failure (Figure 3). For comparison, propofol alone demonstrated a SUCRA score of 20% in this outcome (Figure 3).

Within the inadequate depth of anesthesia outcome, head and/or limb movement had the highest incidence of occurrence and was reported in 30.4% (811 of 2669) of patients (Table). Propofol + vapor + short opioid (OR, 0.03; 95% CrI, 3.8×10^{-3} to 0.24; SUCRA = 91%) ranked the top intervention to reduce the risk of inadequate depth of anesthesia (Figure 3). For comparison, propofol alone demonstrated a SUCRA score of 9% in this outcome (Figure 3).

Figure 5. Risk of Bias Assessment



Each included study assessed by review authors' judgments for risk of bias and deemed as low risk of bias (+, green), unclear risk of bias (?, yellow), or high risk of bias (−, red).

Hemodynamic events (bradycardia, tachycardia, and hypotension) were reported in 19 studies, across 1613 patients and 15 anesthetic interventions. The most reported event was hypotension, which occurred in 12.2% (150 of 1232) of patients. However, 75 of 150 hypotension events occurred in the propofol + short opioid intervention. The OR and CrI demonstrated large variability across all interventions following analysis and was excluded in the summed scores of SUCRA ranks (Supplemental Information, Figure S2).

The SUCRA ranks were scored across all outcomes and summed (Supplemental Information, Table S4). Propofol + dexmedetomidine had the highest summed score (Figure 4), as it ranked among the top interventions across the outcomes for apnea incidence (OR, 2.20; 95% CrI, 0.21-39.0; SUCRA = 37%; rank 13 of 20), apnea time (mean difference 0.24; 95% CrI, −2.40 to 2.80; SUCRA = 66%; rank 5 of 17), airway adverse event (OR, 0.07; 95% CrI, 0.02-0.27; SUCRA = 67%; rank 7 of 26), insertion failure (OR, 0.12; 95% CrI, 0.02-0.59; SUCRA = 73%; rank 4 of 26), and inadequate depth of anesthesia (OR, 0.06; 95% CrI, 0.01-0.29; SUCRA = 84%; rank 2 of 20). Eighteen of 28 anesthetic interventions had scores across all outcomes, of which propofol had the lowest summed SUCRA score.

None of the included studies reported hypertension, unanticipated hospital admission, or mortality.

Risk of Bias

The overall risk of bias was graded as low in 19 studies (36%), moderate in 21 studies (40%), and high in 13 studies (24%) (Figure 5). Overall, high risk of bias was found in the domains of selection bias (1 study), performance bias (3 studies), detection bias (4 studies), and attrition bias (7 studies; Figure 5).

Sensitivity and Subgroup Analysis

When the high–risk of bias studies were removed, propofol + dexmedetomidine remained as having the highest overall cumulative SUCRA rank score in reducing adverse outcomes (Supplemental Information, Table S4). The results of the other subgroup analyses, (1) the effect of premedication and (2) the type of LMA (Supplemental Information, Table S4), were similar to those of the primary analysis. The quality of evidence ranged from very low to moderate (Supplemental Information, Table S5). Heterogeneity analysis demonstrated significant inconsistency (I^2 = 8.9-99.1%) with low to considerable heterogeneity (Supplemental Information, Tables S6 and S7).

DISCUSSION

This NMA attempted to identify the best anesthetic combination to avoid prolonged apnea and the other secondary outcomes of airway adverse events, inadequate anesthetic depth, LMA placement failure, and adverse hemodynamics after LMA insertion. Anesthesiologists often intend to have brief apnea to achieve sufficient anesthetic depth for LMA placement; however, anesthetic overdose during induction has been frequently identified by bispectral index monitoring.[28,29] Avoiding prolonged apnea and promptly resuming spontaneous breathing are desired; hence, prolonged apnea after LMA insertion was selected as the primary outcome for this study. Return of spontaneous breathing can be evaluated along with other physiology- and medication-related parameters to allow anesthesiologists to titrate their anesthetics by monitoring changes in their patients' respiration rates and tidal volumes, thereby decreasing risk of anesthetic overdose.

Preventing overdose may also avoid adverse outcomes such as hemodynamic instability, prolonged recovery time, and increased mortality.[29,30] In our study, it was difficult to determine if prolonged apnea was associated with other adverse outcomes such as hypoxia, as there was a lack of reporting in the included studies. Of the 53 studies included for meta-analysis, only 7 reported hypoxia as an outcome. Lack of reporting of hemodynamic events was also seen across the studies. In contrast, by reducing apnea time, the risk of inadequate depth of anesthesia is increased. In this NMA, 36 studies reported an outcome that suggests the risk of inadequate depth of anesthesia (ie, head or limb movement, inadequate jaw relaxation). Likewise, other more serious outcomes, such as laryngospasm, may be seen with insufficient anesthetic depth. Therefore, a balance exists between preventing anesthesia overdose and providing an adequate depth of anesthesia to reduce the risk of adverse events during LMA insertion.

Propofol as the only anesthetic agent for GA induction ranked near lowest for reducing adverse events during LMA insertion; only thiopental demonstrated a poorer ability to prevent adverse outcomes. The addition of other anesthetics with propofol improved the conditions for GA induction and LMA insertion. The combination of propofol + dexmedetomidine ranked the most effective anesthetic combination for reducing adverse events evidenced by SUCRA scores. This finding is supported by the recent meta-analysis completed by Ju and colleagues,[5] which demonstrated the use of dexmedetomidine in comparison with sedative agents, such as fentanyl or midazolam, improved the success rate of LMA placement, lessened respiratory depression, and reduced adverse events, such as coughing and limb movement. In our NMA study, the benefit of dexmedetomidine was compared with all anesthetic combinations used for LMA placement available in literature.

Dexmedetomidine is an α-2 adrenoreceptor agonist that has several beneficial properties for anesthesia induction that may have helped rank it as the top anesthetic when combined with propofol for LMA insertion.[31] Unlike other anesthetics that provide sedation (eg, opioids), dexmedetomidine has minimal negative effect on respiratory drive.[31] The respiratory-sparing effect makes dexmedetomidine ideally suited for the management of a difficult airway, and it has been used for awake fiberoptic intubation.[32,33] Dexmedetomidine has analgesic, antitussive, and anxiolytic properties that have been demonstrated to reduce patient reactivity during airway-stimulating events (eg, awake intubation), sparing the need for opioids or benzodiazepines.[32,33] Moreover, dexmedetomidine also has antisialagogue properties, potentially reducing the risk for cough and laryngospasm.[32,34]

In our study, the combination of propofol + dexmedetomidine ranked 13 of 20 in apnea incidence and 5 of 17 in apnea time. It is possible that the respiratory-sparing properties of dexmedetomidine were negated by the combined use of propofol. Despite the middle ranking of propofol + dexmedetomidine for apnea, the other desirable properties of dexmedetomidine may have helped it rank higher in the other outcomes of insertion failure, inadequate depth of anesthesia, and airway adverse events. Undesirable effects of dexmedetomidine include the potential for bradycardia and hypotension.[31] Of the 4 studies examining propofol + dexmedetomidine included in our meta-analysis, the incidences of bradycardia and hypotension were 6.8% and 1.3%, respectively. Overall, the quality of evidence of the included studies was low to moderate for propofol + dexmedetomidine, and further, better-quality studies are required to establish the full benefit of that anesthetic combination for LMA insertion.

The implication of this study is that propofol + dexmedetomidine could be seen as more favorable and have increased use among anesthesiologists because of its effectiveness for reducing adverse events during LMA insertion. The use of dexmedetomidine with propofol has clinical and economic considerations that go beyond reducing adverse events and increasing patient safety. First, the use of dexmedetomidine may increase the cost of GA compared with other commonly used anesthetics. Dexmedetomidine may cost twice as much as using propofol alone and as much as 4 times when compared with midazolam.[35] However, considering the total cost of managing some more serious adverse events, dexmedetomidine may prove more favorable. When used in the intensive care unit (ICU) for intubated patients, dexmedetomidine was associated with increased cost savings because of the reduction in ICU length of stay and the degree of monitoring and management.[36] Second, according to the product monograph, dexmedetomidine should be used as a slow induction bolus (1 μg/kg) given over 10 minutes to avoid adverse events such as bradycardia.[37] All studies that were included in this NMA utilized this suggested protocol of slow bolus of dexmedetomidine over 10 minutes for anesthesia induction before LMA placement. This required time for dexmedetomidine delivery compared with faster anesthetics, such as 30 seconds for remifentanil, may increase total anesthesia time and reduce the number of patients who can be seen in a clinical day. However, with optimal case organization and scheduling, the additional time required for dexmedetomidine use may be negated. Overall, the use of propofol + dexmedetomidine for LMA placement may prove to be an effective and efficient anesthetic combination for LMA insertion. Only through increased use and further clinical research can the full benefits of propofol + dexmedetomidine be appreciated.

The large number of included studies from Asia and the few from North America may be indicative of the LMA's popularity in each of the respective regions. In Europe and Asia, the LMA has become highly favored and is used more commonly over tracheal intubation, unlike in the US, where tracheal intubation is still the most used airway device.[38–40] Only 2 studies reported the use of second-generation LMAs. Our subgroup analysis of LMA type did not demonstrate any differences, mainly because of the lack of reporting. It is possible that with increased use of second-generation LMAs, the incidence of adverse events may be reduced.[41,42]

Inconsistency in what outcomes constituted successful LMA placement was notable. The most common reported set of outcomes was that of the modified scheme of Lund and Stovner,[43] examining mouth opening, ease of insertion, swallowing, coughing or gagging, head or limb movement, and laryngospasm. Another set of outcomes reported was those used by Muzi and colleagues,[44] which included jaw mobility, coughing, movement, spontaneous ventilation, breath holding, and lacrimation. Most of the included studies did not cite an existing set of LMA outcomes, and our NMA required grouping of outcomes into similar adverse event categories to permit analysis and comparison. Our study limited outcomes to only those that encompassed LMA insertion after GA induction and not outcomes that followed GA, such as patient satisfaction, sore throat, or incidence of postoperative nausea and vomiting (PONV). The meta-analysis by Joo and Perks[45] suggested that induction of GA with propofol for LMA insertion may be favored over sevoflurane due patient satisfaction and less frequent PONV. Further investigation is required to determine how the choice of anesthetics for LMA insertion may affect patient satisfaction and recovery.

A limitation of this NMA was that combining similar anesthetics into groups resulted in 3 one-arm studies without a comparator, preventing inclusion in the meta-analysis. By grouping anesthetics together, we made robust class comparisons at the expense of interdrug comparisons, such as alfentanil vs fentanyl. The ability to make comparisons is dependent on the sets of interventions being similar enough to be combined.[21] The heterogeneity analysis in this study demonstrated significant inconsistency with low to considerable heterogeneity; hence, caution is required for interpretation of the study's results.

Another limitation of the included studies was the lack of standardized dosing of anesthetics used. Propofol was used in doses that ranged from 1.5 mg/kg to 3.0 mg/kg. Higher doses of propofol are associated with hypotension, cardiorespiratory depression, and prolonged apnea.[5,41,42] Therefore, combining propofol with another anesthetic may be beneficial only if the propofol dose is reduced appropriately. Furthermore, a limitation of the included studies was the lack of preoperative standardization regarding the use of anticholinergics, sedatives, and anxiolytics. Though our subgroup analysis did not show any conclusive influence on the use of premedication with LMA insertion, we were limited by the number of studies that reported their use. The use of a benzodiazepine, such as midazolam, works synergistically with opioids and may potentially prolong apnea time following induction if an opioid is used.[46] Similarly, anticholinergics have been shown to improve the success of tracheal intubation by reducing oral secretions and preserving hemodynamic stability.[47,48] Likewise, antihistamines (eg, hydroxyzine) can be used as premedication to reduce anxiety, pruritus, and PONV as well as reduce oral secretions through their antisialagogue properties.[49] By reducing oral secretions, anticholinergics and antihistamines may potentially reduce the risk of laryngospasm during induction.[50] It is unclear how the role of premedication affects the success rate of LMA insertion, as different types of premedication can provide beneficial or unfavorable conditions for LMA insertion. Our subgroup analysis of premedications did not demonstrate a difference. If further study on anesthetics for LMA insertion is undertaken, we recommend that premedication be omitted for clear, uninfluenced comparison of the anesthetics. Finally, caution should be taken with interpretation of the SUCRA-ranked results. SUCRA does not take into consideration the magnitude of differences in effects between treatments.[51] Differences in top-ranked treatments may not be clinically appreciable. Likewise, this NMA weighed all outcomes equally during the overall SUCRA ranking. Some outcomes may be more relevant for the clinician in their setting and should be considered when selecting an anesthetic for LMA insertion given their respective clinical circumstances.

To the authors' knowledge, a strength of this study is that it is the first NMA to compare and rank all anesthetic combinations used for GA induction. The NMA method allows for direct and indirect comparisons of multiple treatments when head-to-head comparisons are not always available in the literature. In the studies that met our inclusion criteria, 48 different anesthetics and anesthetic combinations were identified. This study demonstrates that the comparison of different anesthetic combinations with an NMA is feasible and effective.

CONCLUSION

Our systematic review and meta-analysis of anesthetics used for GA induction and LMA insertion demonstrated that all anesthetic combinations, except for those used with thiopental, reduced adverse outcomes in comparison with propofol alone. In an NMA using cumulative SUCRA-ranked scoring, very low to moderate quality evidence suggests that the combination of propofol + dexmedetomidine is the most effective anesthetic combination for minimizing adverse outcomes during LMA insertion following GA induction according to the current literature.

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Disclosures

The authors have no interests to declare.

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REFERENCES

1. Aghamohammadi D, Eydi M, Hosseinzadeh H, Amiri Rahimi M, Golzari SE. Assessment of mini-dose succinylcholine effect on facilitating laryngeal mask airway insertion. *J Cardiovasc Thorac Res*. 2013;5(1):17–21.

2. Allsop E, Innes P, Jackson M, Cunliffe M. Dose of propofol required to insert the laryngeal mask airway in children. *Paediatr Anaesth*. 1995;5(1):47–51.

3. Goh PK, Chiu CL, Wang CY, Chan YK, Loo PL. Randomized double-blind comparison of ketamine-propofol, fentanyl-propofol and propofol-saline on haemodynamics and laryngeal mask airway insertion conditions. *Anaesth Intensive Care*. 2005;33-(2):223–228.

4. Lee MP, Kua JS, Chiu WK. The use of remifentanil to facilitate the insertion of the laryngeal mask airway. *Anesth Analg*. 2001;93(2):359–362.

5. Ju Q, Xiao Z, Sun W, Zhu M, Lv P. The anesthesia induction effect of dexmedetomidine in patients undergoing laryngeal mask intubation: a systematic review and meta-analysis of 7 RCTs. *Ann Palliat Med*. 2021;10(12):12358–12366.

6. Hutton B, Salanti G, Caldwell DM, et al. The PRISMA extension statement for reporting of systematic reviews incorporating network meta-analyses of health care interventions: checklist and explanations. *Ann Intern Med*. 2015;162(11):777–784.

7. Saunders R, Struys MMRF, Pollock RF, Mestek M, Lightdale JR. Patient safety during procedural sedation using

capnography monitoring: a systematic review and meta-analysis. *BMJ Open*. 2017;7(6):e013402.

8. Choi GJ, Kang H, Baek CW, Jung YH, Ko JS. Etomidate versus propofol sedation for electrical external cardioversion: a meta-analysis. *Curr Med Res Opin*. 2018;34(11):2023–2029.

9. Boonmak P, Boonmak S, Pattanittum P. High initial concentration versus low initial concentration sevoflurane for inhalational induction of anaesthesia. *Cochrane Database Syst Rev*. 2016;(6):CD006837.

10. Azarpazhooh A, Lawrence HP, Shah PS. Xylitol for preventing acute otitis media in children up to 12 years of age. *Cochrane Database Syst Rev*. 2016;(8):CD007095.

11. Mathew PJ, Mathew JL. Early versus late removal of the laryngeal mask airway (LMA) for general anaesthesia. *Cochrane Database Syst Rev*. 2015;(8):CD007082.

12. Young HSA, Clarke RSJ, Dundee JW. Intubating conditions with AH 8165 and suxamethonium. *Anaesthesia*. 1975;30(1): 30–33.

13. Kwon CH, Kim S-H. Intraoperative management of critical arrhythmia. *Korean J Anesthesiol*. 2017;70(2):120–126.

14. Südfeld S, Brechnitz S, Wagner JY, et al. Post-induction hypotension and early intraoperative hypotension associated with general anaesthesia. *Br J Anaesth*. 2017;119(1):57–64.

15. Bijker Jilles B, van Klei Wilton A, Kappen Teus H, van Wolfswinkel L, Moons Karel GM, Kalkman Cor J. Incidence of intraoperative hypotension as a function of the chosen definition: literature definitions applied to a retrospective cohort using automated data collection. *Anesthesiology*. 2007;107(2):213–220.

16. Varon J, Marik PE. Perioperative hypertension management. *Vasc Health Risk Manag*. 2008;4(3):615–627.

17. Brain AI. The laryngeal mask—a new concept in airway management. *Br J Anaesth*. 1983;55(8):801–805.

18. Bramer W, Bain P. Updating search strategies for systematic reviews using EndNote. *J Med Libr Assoc*. 2017;105(3):285–289.

19. Bramer WM, Giustini D, de Jonge GB, Holland L, Bekhuis T. De-duplication of database search results for systematic reviews in EndNote. *J Med Libr Assoc*. 2016;104(3):240–243.

20. Higgins JP, Altman DG. Assessing risk of bias in included studies. In: Higgins JP, Green S, ed. *Cochrane Handbook for Systematic Reviews of Interventions*. Cochrane; 2008:187–241.

21. Higgins JP, Thomas J, eds. *Cochrane Handbook for Systematic Reviews of Interventions*. Version 6.0. Cochrane; 2019.

22. Hozo SP, Djulbegovic B, Hozo I. Estimating the mean and variance from the median, range, and the size of a sample. *BMC Med Res Methodol*. 2005;5(1):13.

23. Walter SD, Yao X. Effect sizes can be calculated for studies reporting ranges for outcome variables in systematic reviews. *J Clin Epidemiol*. 2007;60(8):849–852.

24. Dias S, Sutton AJ, Ades AE, Welton NJ. Evidence synthesis for decision making 2: a generalized linear modeling framework for pairwise and network meta-analysis of randomized controlled trials. *Med Decis Making*. 2013;33(5):607–617.

25. Lu G, Ades AE. Combination of direct and indirect evidence in mixed treatment comparisons. *Stat Med*. 2004;23(20):3105–3124.

26. Salanti G, Del Giovane C, Chaimani A, Caldwell DM, Higgins JPT. Evaluating the quality of evidence from a network meta-analysis. *PLoS One*. 2014;9(7):e99682.

27. Brain AI, Verghese C, Strube PJ. The LMA "ProSeal"—a laryngeal mask with an oesophageal vent. *Br J Anaesth*. 2000;84(5): 650–654.

28. Giraldo JC, Acosta C, Giraldo-Grueso M. Frequency of anesthetic overdose with mean alveolar concentration-guided anesthesia at high altitude. *Med Gas Res*. 2019;8(4):150–153.

29. Punjasawadwong Y, Phongchiewboon A, Bunchungmongkol N. Bispectral index for improving anaesthetic delivery and postoperative recovery. *Cochrane Database Syst Rev*. 2014;2014(6):CD003843-CD.

30. Monk TG, Saini V, Weldon BC, Sigl JC. Anesthetic management and one-year mortality after noncardiac surgery. *Anesth Analg*. 2005;100(1):4–10.

31. Ebert TJ, Hall JE, Barney JA, Uhrich TD, Colinco MD. The effects of increasing plasma concentrations of dexmedetomidine in humans. *Anesthesiology*. 2000;93(2):382–394.

32. Chopra P, Dixit MB, Dang A, Gupta V. Dexmedetomidine provides optimum conditions during awake fiberoptic intubation in simulated cervical spine injury patients. *J Anaesthesiol Clin Pharmacol*. 2016;32(1):54–58.

33. Bergese SD, Candiotti KA, Bokesch PM, et al. A phase IIIb, randomized, double-blind, placebo-controlled, multicenter study evaluating the safety and efficacy of dexmedetomidine for sedation during awake fiberoptic intubation. *Am J Ther*. 2010;17(6):586–595.

34. Sasaki Y, Kato S, Miura M, Fukayama H. Correlation between body movements and salivary secretion during sedation. *Anesth Prog*. 2016;63(4):185–191.

35. Canadian Agency for Drugs and Technologies in Health. Dexmedetomidine for sedation in the ICU or PICU: a review of cost-effectiveness and guidelines. Publisher; 2014.

36. Aggarwal J, Lustrino J, Stephens J, Morgenstern D, Tang WY. Cost-minimization analysis of dexmedetomidine compared to other sedatives for short-term sedation during mechanical ventilation in the United States. *Clinicoecon Outcomes Res*. 2020;12:389–397.

37. Product monograph—Precedex. Pfizer Canada Inc. December 9, 2009. Updated March 30, 2023. https://www.pfizer.ca/files/Precedex_PM_EN.pdf

38. Woodall NM, Cook TM. National census of airway management techniques used for anaesthesia in the UK: first phase of the Fourth National Audit Project at the Royal College of Anaesthetists. *Br J Anaesth*. 2011;106(2):266–271.

39. Kadar S, Koshy R. Survey of supraglottic airway devices usage in anaesthetic practice in South Indian State. *Indian J Anaesth*. 2015;59:190.

40. Clark HM, Saxen MA, Yepes JF, et al. Comparison of intubated versus nonintubated airway management in children under general anesthesia provided by dentist anesthesiologists. *Pediatr Dent*. 2019;41(1):52–55.

41. Park SK, Choi GJ, Choi YS, Ahn EJ, Kang H. Comparison of the i-gel and the laryngeal mask airway proseal during general anesthesia: a systematic review and meta-analysis. *PLoS One*. 2015;10(3):e0119469.

42. de Montblanc J, Ruscio L, Mazoit JX, Benhamou D. A systematic review and meta-analysis of the i-gel® vs laryngeal mask airway in adults. *Anaesthesia*. 2014;69(10):1151–1162.

43. Lund I, Stovner J. Dose-response curves for tubocurarine, alcuronium and pancuronium. *Acta Anaesthesiol Scand Suppl*. 1969;37:238–242.

44. Muzi M, Robinson BJ, Ebert TJ, O'Brien TJ. Induction of anesthesia and tracheal intubation with sevoflurane in adults. *Anesthesiology*. 1996;85(3):536–543.

45. Joo HS, Perks WJ. Sevoflurane versus propofol for anesthetic induction: a meta-analysis. *Anesth Analg*. 2000;91(1):213–219.

46. Avramov MN, Smith I, White PF. Interactions between midazolam and remifentanil during monitored anesthesia care. *Anesthesiology*. 1996;85(6):1283–1289.

47. Shim JG, Cho EA, Ryu KH, et al. Effects of prophylactic atropine on the time to tracheal intubation with the pre-administration of remifentanil. *Acta Anaesthesiol Scand*. 2021;65(3):335–342.

48. Cho E-A, Hwang S-H, Lee SH, Ryu K-H, Kim Y-H. Does glycopyrrolate premedication facilitate tracheal intubation with a rigid videostylet? a randomized controlled trial. *Medicine*. 2018;97(32):e11834-e.

49. Sheen MJ, Chang F-L, Ho S-T. Anesthetic premedication: new horizons of an old practice. *Acta Anaesthesiol Taiwan*. 2014; 52(3):134–142.

50. Gavel G, Walker RW. Laryngospasm in anaesthesia. *Contin Educ Anaesth Crit Care Pain*. 2013;14(2):47–51.

51. Mbuagbaw L, Rochwerg B, Jaeschke R, et al. Approaches to interpreting and choosing the best treatments in network meta-analyses. *Syst Rev*. 2017;6(1):79.

SUPPLEMENTAL INFORMATION

(available online only)

Figure S1. Relative Treatment Effects of Primary and Secondary Outcomes

Figure S2. Adverse Hemodynamic Event Secondary Outcome

Table S1. NMA Search Strategy

Table S2. Exclusion Study Table

Table S3. Included Studies Table of Characteristics

Table S4. SUCRA Scores for Primary and Secondary Outcomes

Table S5. Grade for Top-Ranked Anesthetic Combinations

Table S6. Heterogeneity Analysis

Table S7. Inconsistency Analysis