Systematic Review and Meta-Analysis

Perioperative adverse cardiac events in maxillofacial surgery: A systematic review and meta-analysis

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ABSTRACT

Background and Aims: Maxillofacial surgeries, including procedures to the face, oral cavity, jaw, and head and neck, are common in adults . However, they impose a risk of adverse cardiac events (ACEs). While ACEs are well understood for other non-cardiac surgeries, there is a paucity of data about maxillofacial surgeries. This systematic review and meta-analysis report the incidence and presentation of perioperative ACEs during maxillofacial surgery. **Methods:** We included primary studies that reported on perioperative ACEs in adults. To standardise reporting, ACEs were categorised as 1. heart rate and rhythm disturbances, 2. blood pressure disturbances, 3. ischaemic heart disease and 4. heart failure and other complications. The primary outcome was ACE presentation and incidence during the perioperative period. Secondary outcomes included the surgical outcome according to the Clavien–Dindo classification and trigeminocardiac reflex involvement. STATA version 17.0 and MetaProp were used to delineate proportion as effect size with a 95% confidence interval (CI). **Results:** Twelve studies (34,227 patients) were included. The incidence of perioperative ACEs was 2.58% (95% CI 1.70, 3.45, I^2 = 96.17%, P = 0.001). Heart rate and rhythm disturbances resulted in the greatest incidence at 3.84% among the four categories. Most commonly, these ACEs resulted in intensive care unit admission (i.e. Clavien–Dindo score of 4). **Conclusion:** Despite an incidence of 2.58%, ACEs can disproportionately impact surgical outcomes. Future research should include large-scale prospective studies that may provide a better understanding of the contributory factors and long-term effects of ACEs in patients during maxillofacial surgery.

Keywords: Adult, arrhythmias, blood pressure, cardiac, heart arrest, heart failure, heart rate, incidence, intraoperative complications, maxillofacial surgeries, myocardial infarction, myocardial ischaemia, perioperative care, perioperative period, reflex, trigeminocardiac

INTRODUCTION

Each year, over 100 million non-cardiac surgeries are performed worldwide, and this value is projected to increase.[1] Although these surgeries can enhance patients' quality and duration of life, the surgical experience may precipitate adverse cardiac events (ACEs), including myocardial infarctions, arrhythmias and cardiac arrest.[2] Unfortunately, ACEs following non-cardiac surgery increase hospitalisation duration and costs and are a leading cause of postoperative mortality and morbidity.[3-5]

Oral and maxillofacial surgery includes procedures within the face, oral cavity, jaw, head, and neck.[6,7] More commonly, oral maxillofacial operations are performed in adults (patients ≥18 years).[8] Currently, various cardiac complications, including dysrhythmias, asystole, hypertensive crises and chest pain, have been reported in patients undergoing maxillofacial

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surgeries.[9-12] While ACEs during other non-cardiac surgeries (i.e. vascular, thoracic, ophthalmological) are well explored, less is understood in the context of maxillofacial surgeries. There is a lack of systematically aggregated evidence on ACEs' incidence, presentation and impact during the maxillofacial perioperative period. This confers challenges to healthcare providers in better understanding their influence on surgical outcomes and management approaches. This systematic review and meta-analysis aims to elucidate the incidence and presentation of ACEs during the perioperative period of maxillofacial surgery. In addition, the review will explore the impact of these cardiac complications on surgical outcomes using the Clavien–Dindo classification system and investigate trigeminocardiac reflex (TCR) involvement.

METHODS

This systematic review and meta-analysis adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[13] The protocol was registered in the International Prospective Registry of Systematic Reviews (PROSPERO) (registration number CRD42022334058).

Search strategy

The search strategy was developed in consultation with an information specialist who conducted a comprehensive systematic search to identify eligible studies. A search was conducted from MEDLINE/PubMed, Embase, Cumulative Index to Nursing and Allied Health (CINAHL), Web of Science and Cochrane Library from inception until 5 May 2023. The search strategy was limited to English. The search strategy combined appropriate controlled vocabulary and keywords: 'maxillofacial surgery', 'perioperative', 'adverse cardiac events', 'reflex' and 'adult'. Full details regarding the search strategy are provided in the Supplementary Material. Reference lists were manually checked for additional publications.

Study selection and screening process

Two independent reviewers assessed each article in the initial stage of title and abstract screening and subsequent stages of full-text screening. Disagreements at either stage were resolved by consulting the principal investigator.

Inclusion and exclusion criteria

We included articles from any type of primary study, including randomised controlled trials (RCTs). Retrospective and prospective observational studies such as cohorts, cross-sectional studies and case–control studies which reported on ACEs in patients aged ≥18 years during the perioperative period of maxillofacial surgery were included. The perioperative period was defined in this review as the time frame from the patient's surgical admission through their intraoperative course and up to final discharge.[14] Maxillofacial surgery includes surgeries on the face, oral cavity, head and neck, mouth and jaws. Non-English articles, animal studies, duplicates, secondary research articles, case series, case reports, conference abstracts, pregnant patients and exclusive ocular surgical patients were excluded from the study.

Outcomes

The primary outcomes were the incidence and presentation of ACEs during the perioperative period of oral and maxillofacial surgery. The secondary outcomes included surgical outcomes as defined by the Clavien–Dindo classification and the involvement of TCR. The following definitions were used:

ACEs – We included ACEs that were described by any of the following: 1. change in heart rate and/or blood pressure 20% or above the baseline; 2. occurrence of heart rhythm abnormalities, such as arrhythmias, atrial fibrillation, atrial flutter, atrioventricular block, etc.; 3. cardiac arrest; 4. cardiac muscle injury and/or ischaemia and 5. requirement of any therapeutic or pharmacological intervention to abort or treat the ACE. Subsequently, all ACEs that were described by the included studies were categorised into one of four broad categories to standardise reporting: 1. blood pressure disturbances, 2. heart rate and rhythm disturbances, 3. ischaemic heart disease (IHD) or 4. heart failure and complications (i.e. cardiac arrest).[15,16]

Clavien–Dindo classification – All ACEs were graded according to the Clavien–Dindo surgical complications classification, with scores ranging from 1 to 5. The Clavien–Dindo system is widely used throughout surgery to grade the severity of adverse events resulting from the procedure. The grading is based on the type of therapeutic management required to correct the complication. A score of 1 refers to any deviation from the normal postoperative course without needing intervention beyond administering antiemetics, antipyretics, analgesics, diuretics, electrolytes and physiotherapy. A score of 2 refers to any other pharmacological intervention. A score of 3

refers to complications that require further surgical, endoscopic or radioscopic intervention. A score of 4 refers to multiorgan dysfunction requiring intensive care unit (ICU) admission. A score of 5 refers to patient death.[17]

TCR was defined as a sudden onset of parasympathetic dysrhythmias, including haemodynamic instability, apnea and gastric hypermobility, that occur secondary to trigeminal nerve [cranial nerve (CN) V] stimulation.[18] Because oral and maxillofacial procedures occur at regions innervated by the trigeminal nerve, it is suggested that these operations may induce this brainstem reflex, manifesting as sudden bradycardia and hypotension.[19,20]

Data extraction and quality assessment

Two independent reviewers performed data extraction. The following data were extracted onto a standardised excel file: author, year of publication, country, study design, sample size, mean age, sex, comorbidities, anaesthetic agents administered, surgical procedures, follow-up period, and primary and secondary outcomes. Two independent reviewers completed the quality assessment for all studies. The principal investigator resolved any disagreement in scoring. We used the Newcastle–Ottawa Scale (NOS) for observational cohorts.[21] NOS evaluates cohort studies according to three domains (selection, comparability and outcome) with eight question items for a maximum score of 9. Studies with a score of 7–9 were considered good quality, studies with a score of 4–6 were considered fair quality and studies with a score of 0–3 were considered poor quality. For RCTs, quality was evaluated in accordance with the Cochrane Risk of Bias 2 (RoB2) revised tool.[22]

Data analysis

Data analyses were performed qualitatively and quantitatively. The demographic and outcome data description was presented using percentages and mean [standard deviation (SD)]. Data were presented in tables and figures as appropriate. Regarding the reporting of incidence, most included studies did not provide a quantitative endpoint for when the ACEs were recorded. As a result, we could not calculate the study-specific incidence rates in person-years format. Hence, we calculated each study's incidence rate as n/N, with n being the number of patients who developed an ACE postoperatively before discharge and N being the total number of patients undergoing oral and maxillofacial surgery.

The pooled incidence rate of ACEs (composite of the four categories) and the incidence rates of each ACE category were determined by a meta-analysis with inverse variance and a random effects model, given the expected heterogeneity between studies. The pooled effect sizes were cross-checked using the Freeman–Tukey double arcsine transformation. In addition, we performed a leave-one-out meta-analysis to identify studies with an exaggerated effect size.

Subgroup analyses were also performed. A subgroup analysis based on sample size (<100, 100–500, >500) and a meta-regression analysis was conducted to evaluate whether the study sample size influenced the effect size (i.e. incidence). Finally, a funnel plot and Egger's test value were determined to illustrate publication bias. All analyses were conducted using the STATA version 17.0 software, and MetaProp was used to delineate the incidence proportion as the effect size with a 95% confidence interval (CI).

RESULTS

Our search strategy yielded 4099 studies. After removing 351 duplicates, 3748 studies progressed to the initial title and abstract screening phase. Of these, 3652 studies were excluded based on the inclusion and exclusion criteria, and 96 full texts further underwent full-text screening. A total of 12 studies were included in the final analysis [Figure 1].[23-34]

Study and patient characteristics

In total, 34,227 patients were included [Table 1]. Men comprised 41.7% of the population (10 studies).[23,24,26-28,30-34] The mean (SD) age was 33.5 (14.9) years.[23,30-33] Eight studies were retrospective cohort studies, three prospective cohort studies and one RCT. Across the 11 non-randomised studies, which included both retrospective and prospective cohort studies, the mean NOS score was 5.8 (range 0–9), indicating that all studies were rated of fair quality according to the NOS criteria (with scores between 4 and 6) [Table 2].[23-31,33-34] The single RCT study was deemed to have a low risk of bias according to the ROB2 scale [Table 3].[32] Seven studies have reported on patient comorbidities, the most common being heart conditions [Table 1].[23,24,26,28,29,32,33]

Four studies reported on the anaesthetic details of the surgery [Table 4].[23,25,29,33] Sedation and general anaesthesia (GA) were the only anaesthetic techniques undertaken; both were used in two

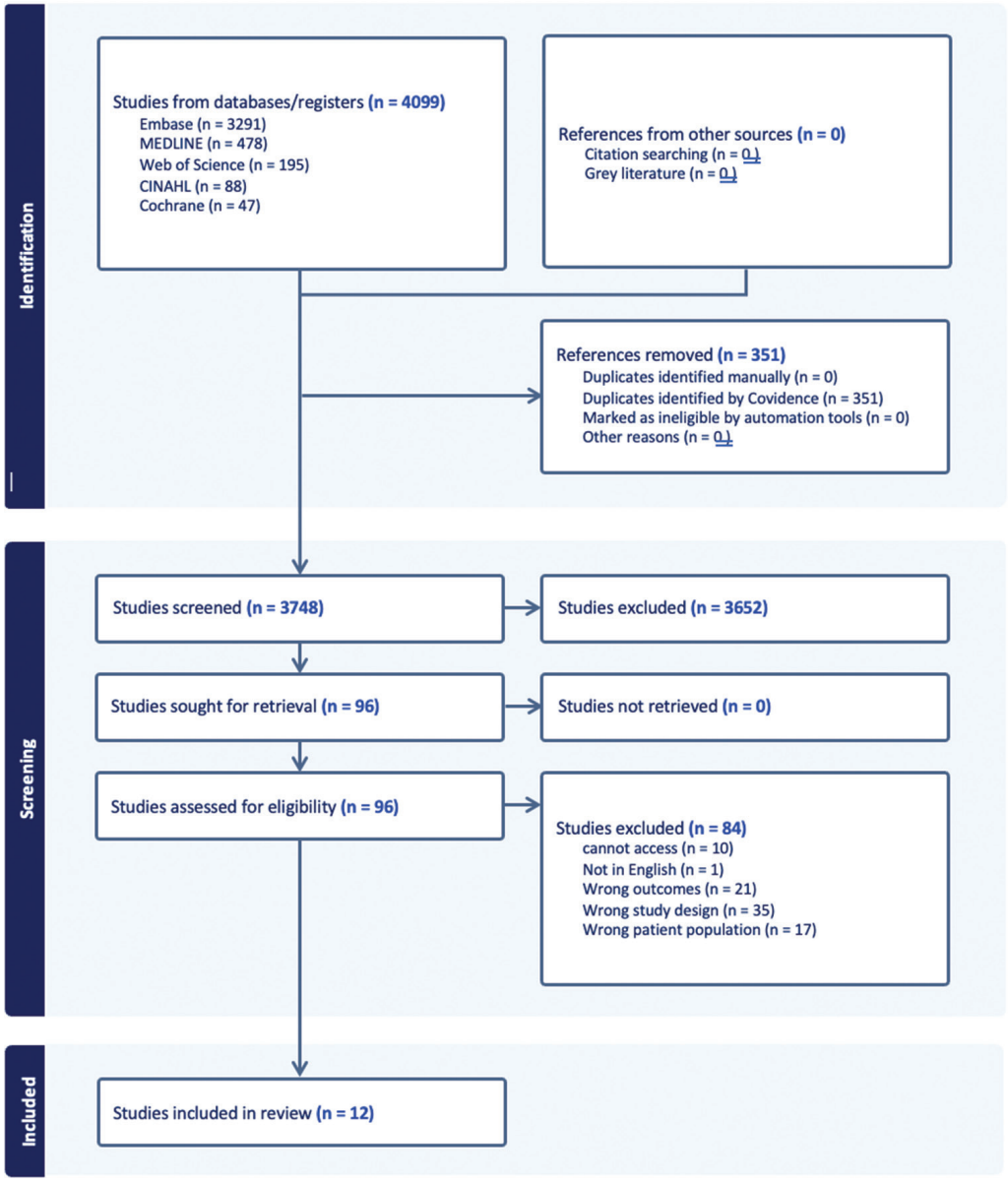

Figure 1: PRISMA flow chart of study selection process. This figure presents the study selection process conducted in accordance with the PRISMA guidelines. After database searching, 4099 studies were retrieved. Finally, 12 studies were included in the review. PRISMA = Preferred Reporting Items for Systematic reviews and Meta-Analyses

studies. Patients receiving only sedation were spontaneously ventilated, while patients undergoing GA were mechanically ventilated with either an endotracheal tube or tracheostomy, and in terms of the anaesthetic agents administered, three of the four studies described the medications given.[23,25,29] In the studies that used sedation, patients were sedated at varying degrees of consciousness with midazolam, fentanyl, and propofol or ketamine infusions.[23,25] For patients undergoing GA, they were premedicated with midazolam, induced with propofol, fentanyl and rocuronium, and maintained with sevoflurane.[29] Three of the four studies reported on analgesia agents, and all included the use of opioids, including fentanyl and remifentanil.[23,25,29] Local anaesthetic was reported in only one study and was used exclusively by the surgeon for infiltration at the surgical site.[23] Regional anaesthesia was not used in any study.

Primary findings

Table 5 displays each study's ACE incidence rate as a proportion (*n*/*N*), their specific presentations as described by the study authors, and the subsequent categorisation (heart rate and rhythm disturbances, blood pressure disturbances, IHDs, and heart failure and complications).

The pooled incidence rate of perioperative ACE (composite of the four categories) was 2.58% (95% CI 1.70, 3.45, $I^2 = 96.17\%$, $P = 0.001$) [Figure 2]. Following the Freeman–Tukey double arcsine transformation, the pooled incidence rate was 4.95% (95% CI 1.94, 9.12). The leave-one-out sensitivity analysis identified one study with an exaggerated effect size of 75%, and once removed, the pooled incidence rate decreased to

Table 1: Study characteristics of the included studies

First author (year)	Country	Study design	Total sample size	Mean age (SD)	Male %	Comorbidities
Braidy (2011)[23]	USA	RC	1167	26.8 (8.2)	45.9	Diabetes mellitus, hypertension, neurological conditions[a], psychiatric conditions[b]
Buitelaar (2006)[24]	The Netherlands	RC	469	NR	64.0	Heart conditions[c], respiratory conditions[d], renal conditions[e], vascular disease, liver impairment, diabetes mellitus, hypertension
Christensen (2019)[25]	USA	PC	642	NR	NR	NR
Cramer (2016)[26]	USA	RC	29,891	NR	39.7	Heart conditions[c], respiratory conditions[d], renal conditions[e], haematological conditions[f], diabetes mellitus, disseminated cancer, ascites, hypertension
Dean NR (2010)[27]	USA	RC	65	65.2 (NR)	77.0	NR
Gates (2021)[28]	USA	RC	1081	42.0 (NR)	73.7	Heart conditions[c], respiratory conditions[d], haematological conditions[f], diabetes mellitus, hypertension
Ivosevic (2017)[29]	Serbia	RC	359	NR	NR	Heart conditions[c], renal conditions[e], diabetes mellitus, hypertension, cerebrovascular conditions[g], hyperlipoproteinemia
Joshi (2017)[30]	India	PC	36	30.1 (8.0)	86.1	NR
Lalabekyan (2021)[31]	UK	PC	187	58.2 (13.7)	63.1	NR
Mackay (2020)[32]	Australia	RCT	51	44.6 (12.8)	82.0	Heart conditions[c], respiratory conditions[d], cerebrovascular conditions[g], diabetes mellitus, hypertension, arthritis, chronic pain syndrome
Riley (1997)[33]	USA	RC	182	48.2 (11.2)	86.0	Heart conditions[c], respiratory conditions[d], hypertension
Spiegel (2005)[34]	USA	RC	117	39.8 (NR)	91.0	NR

NR=Not reported, PC=Prospective cohort, RC=Retrospective cohort, RCT=Randomised controlled trial, SD=Standard deviation. [a]Neurological conditions: seizures. [b]Psychiatric conditions: attention deficit disorder, bipolar disorder, anxiety disorder. [c]Heart conditions include myocardial infarction, arrhythmias, coronary artery disease, congestive heart failure, ischaemic heart disease, angina pectoris. [d]Respiratory conditions include dyspnoea at rest or with exertion, asthma, chronic obstructive pulmonary disorder, obstructive sleep apnoea, obstructive and/or restrictive lung diseases. [e]Renal conditions: renal impairment with creatinine clearance <50 mL/min, renal failure requiring dialysis, chronic kidney disease. [f]Haematological conditions: bleeding disorders, clotting disorders. [g]Cerebrovascular conditions: stroke

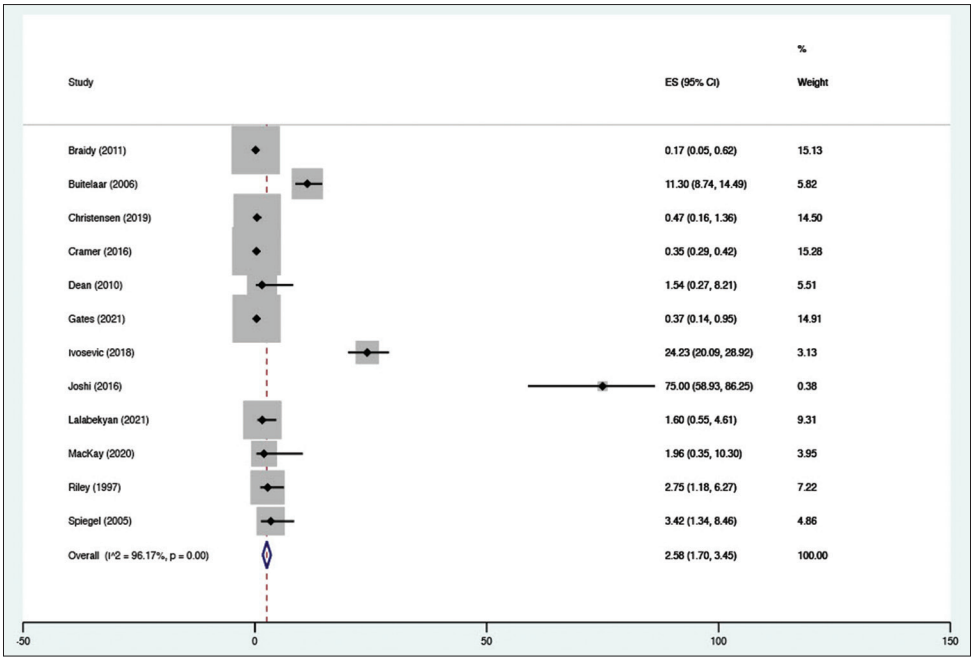

Figure 2: Pooled incidence of perioperative adverse cardiac events in maxillofacial surgeries. The figure presents the pooled incidence of perioperative adverse cardiac events in maxillofacial surgeries, with an incidence of 2.58% (95% CI 1.70, 3.45, $I^2 = 96.17\%$, $P = 0.00$). The analysis was performed on STATA version 17.0, and MetaProp was used to delineate proportion as effect size with a 95% CI. Considering significant heterogeneity due to study design, sampling and reporting outcomes, a random effects model was used. CI = confidence interval

Table 2: Assessment of quality – Newcastle–Ottawa Scale

Author (year)	Cohort selection				Comparability	Outcome ascertainment			Total score	Quality
	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at the start of the study	Comparability of cases and controls based on design or analysis	Assessment of outcome	Was follow-up long enough for outcomes to occur?	Adequacy of follow-up of cohorts		
Braidy (2011)[23]	1	1	1	0	0	1	1	1	6	Fair
Buitelaar (2006)[24]	1	0	1	1	0	1	1	1	6	Fair
Christensen (2019)[25]	1	0	1	1	0	1	1	1	6	Fair
Cramer (2016)[26]	1	0	1	1	0	1	1	1	6	Fair
Dean (2010)[27]	1	0	1	1	0	1	1	1	6	Fair
Gates (2021)[28]	1		1	1	0	1	1	1	6	Fair
Ivosevic (2017)[29]	1	0	1	1	0	1	1	1	6	Fair
Joshi (2017)[30]	1	0	1	1	0	1	1	1	6	Fair
Lalabekyan (2021)[31]	1	0	1	1	0	1	1	1	6	Fair
Riley (1997)[33]	1	0	1	0	0	1	1	1	5	Fair
Spiegel (2005)[34]	1	0	1	0	0	1	1	1	5	Fair

1.25% ($P = 0.045$).[30] The subgroup analysis based on sample size showed that studies with >500 patients had a lower pooled incidence rate of 0.34% and a reduced heterogeneity of 0.00% in comparison to studies with smaller sample sizes (<100 and 100–500 patients) [Figure 3].

Separate analyses for incidence rates were conducted for each ACE category [Table 6]. Heart rate and rhythm disturbances had the greatest incidence among the four ACE categories at 3.84% (95% CI 2.23, 5.45). This was followed by heart failure and complications, IHD and blood pressure disturbances at 0.53%, 0.21% and 0.20%, respectively.

Lastly, the funnel plot of the included 12 studies appeared asymmetrical, with a rightward skew [Figure 4]. This indicates a likely publication bias due to the small sample sizes of the included studies. An Egger's test value for bias confirmed this assumption ($P < 0.01$).

Secondary findings

The most common Clavien–Dindo score was 4, referring to multiorgan dysfunction requiring ICU admission, which was reported in 109 patients (37.1%). The least common Clavien–Dindo score was 3 (i.e. surgical, endoscopic or radioscopic intervention), which was reported in two patients (0.7%) only. Interventions for these patients included coronary artery stent insertion and coronary bypass surgery. Patients with a Clavien–Dindo score of 2 (11.2%) required pharmacological intervention consisting of labetalol, hydralazine, sodium nitroprusside infusion, antiarrhythmics and other antihypertensive medications. Table 7 presents the ACEs, their respective management and the Clavien–Dindo classification score.

The involvement of TCR in ACEs was rare. Only two studies have noted the possible contribution of a vagal brainstem reflex during intraoperative bradycardia.[29,30]

DISCUSSION

In our systematic review of 34,227 patients, the incidence of perioperative ACEs for patients undergoing maxillofacial surgeries was 2.58%, and with the Freeman–Tukey arcsine transformation, it was around 4.95%. Considering the results of the leave-one-out meta-analysis and the subgroup analysis based on sample sizes, it is important to recognise that

Table 3: Assessment of quality – RoB2

Author (year)	Domain 1: Risk of bias due to randomisation process	Domain 2: Risk of bias due to deviations from the intended interventions	Domain 3: Risk of bias due to missing outcome data	Domain 4: Risk of bias due to measurement of the outcome	Domain 5: Risk of bias due to selection of the reported result	Overall risk of bias and quality
MacKay (2020)[32]	Low	Low	Low	Low	Low	Low risk of bias

RoB2=Risk of Bias 2

Table 4: Anaesthetic techniques, agents and ventilation approaches

First author (Year)	Anaesthetic technique	Intravenous agents administered	Volatile agents	Regional anaesthesia	Local anaesthesia	Analgesia	Ventilation
Braidy (2011)[23]	IV sedation	Midazolam, fentanyl, propofol and/or ketamine	No	No	Yes (at the surgical site)	Fentanyl	Spontaneous ventilation
Christensen (2019)[25]	IV sedation	Midazolam, fentanyl, remifentanil, propofol, ketamine	No	No	No	Fentanyl, remifentanil	NR
Ivosevic (2017)[29]	GA	Midazolam, fentanyl, remifentanil, propofol, rocuronium	Yes (sevoflurane)	No	No	Fentanyl, remifentanil	Mechanical ventilation with ETT
Riley (1997)[33]	GA	NR	NR	No	No	NR	Mechanical ventilation with ETT and tracheostomy

ETT=Endotracheal tube, GA=General anaesthesia, IV=Intravenous, NR=Not reported

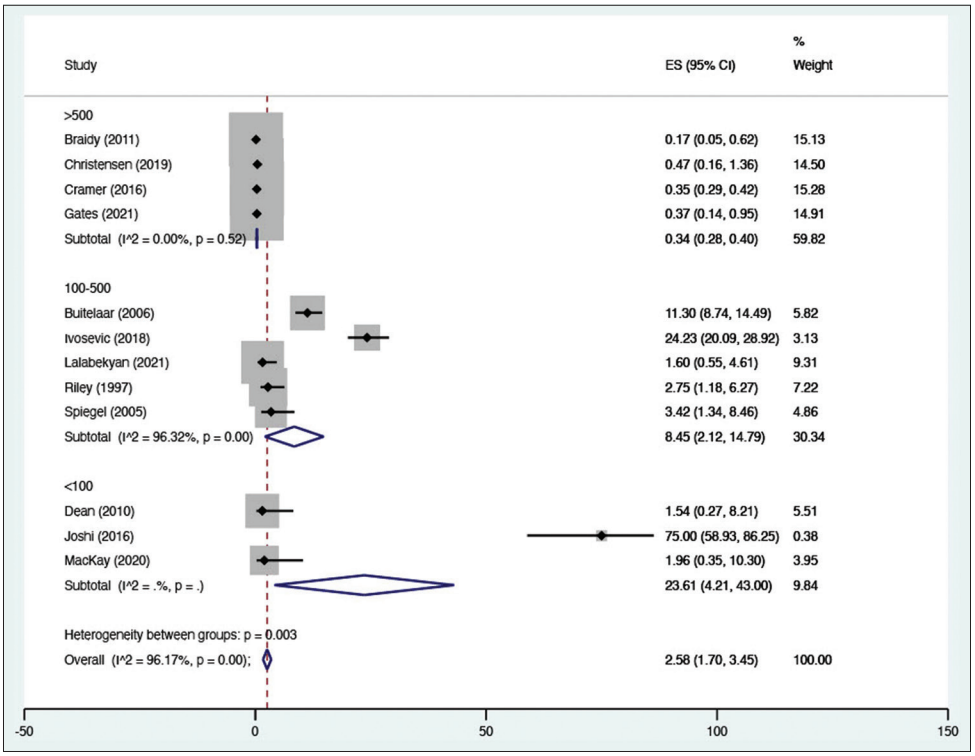

Figure 3: Subgroup analysis of ACE incidence stratified by sample size. The figure shows studies with more than 500 patients had a lower pooled incidence rate (0.34%) and a lower heterogeneity (0.00%). Conversely, studies including lower sample sizes (<100 and 100–500 patients) exhibited more heterogeneity and higher pooled incidence rates. ACE = adverse cardiac event

the incidence of 2.58% and 4.95% may be slightly higher than the true incidence.

Previously, studies have reported similar but slightly higher incidences within non-cardiac surgeries. Smilowitz *et al*.[35] found that perioperative ACE occurred in 3.0% of all hospitalisations for non-cardiac surgery between 2004 and 2013, and Oh *et al*.[36] reported a 30-day postoperative incidence of 3.9%. However, these studies reported ACE incidence across a composite of non-cardiac surgeries and found that the majority were attributed to vascular, thoracic and transplant procedures.[35] In comparison to maxillofacial surgeries, these procedures innately impose a higher

Table 5: Presentation and incidence of ACEs

First author (year)	Surgical procedures	Sample size	No. of patients who developed an ACE, *n* (%)	ACE presentation (*n*)	ACE classification
Braidy (2011)[23]	Dental extractions Preprosthetic surgery Arch bar removal Closed reduction of mandibular fractures Pathology (biopsies, etc.)	1167	2 (0.2%)	Hypertension (1) Tachycardia (1)	Blood pressure disturbances Heart rate and rhythm disturbances
Buitelaar (2006)[24]	Glossectomy Commando procedure Radical neck dissection Parotidectomy Laryngectomy Miscellaneous major tumour resections Thyroidectomy	469	53 (11.3%)	Heart failure (38) Atrial fibrillation (4) Atrial flutter (1) Atrial tachycardia (1) Ventricular fibrillation (1) Premature ventricular contractions (3) Bradycardia (2) MI (3)	Heart rate and rhythm disturbances Ischaemic heart disease Heart failure and complications
Christensen (2019)[25]	Oral and maxillofacial surgeries	642	3 (0.5%)	Hypertension (2) ST elevation (1)	Blood pressure disturbances Ischaemic heart disease
Cramer (2016)[26]	Glossectomy/floor of mouth, lip, palate/alveolar maxilla/mandible, salivary gland excision Tonsillectomy Pharyngectomy Laryngectomy Neck dissection Parotidectomy Thyroidectomy	29,891	104 (0.4%)	MI (NR) Cardiac arrest (NR)	Ischaemic heart disease Heart failure and complications
Dean (2010)[27]	Temporal bone resection	65	1 (1.5%)	MI (1)	Ischaemic heart disease
Gates (2021)[28]	Palatopharyngoplasty	1081	4 (0.4%)	MI (3) Cardiac arrest (1)	Ischaemic heart disease Heart failure and complications
Ivosevic (2017)[29]	Maxillofacial surgery	359	87 (24.2%)	Bradycardia (87)	Heart rate and rhythm disturbances
Joshi (2017)[30]	Mandibular and midface fracture repair	36	27 (75%)	Bradycardia (27)	Heart rate and rhythm disturbances
Lalabekyan (2021)[31]	Major head and neck surgery	187	3 (1.6%)	MI (3)	Ischaemic heart disease
Mackay (2020)[32]a	Uvulopalatopharyngoplasty Tongue volume reduction	51	1 (1.9%)	MI (1) Recurrent angina (1)	Ischaemic heart disease
Riley (1997)[33]b	Mandibular osteotomy Hyoid myotomy Maxillary and mandibular advancement osteotomy	182	5 (2.8%)	Arrhythmia (4) Unstable angina (1) Hypertension (160 cases)	Heart rate and rhythm disturbances Ischaemic heart disease Blood pressure disturbances
Spiegel (2005)[34]	Uvulopalatoplasty	117	4 (3.4%)	Hypertension (3) Tachycardia (1)	Blood pressure disturbances Heart rate and rhythm disturbances

ACE=Adverse cardiac event, MI=Myocardial infarction, NR=Not reported. [a]Mackay (2020) reported two adverse cardiac events (MI and angina) that occurred within a single patient. [b]Riley (1997) reported five patients who developed an ACE (either arrhythmias or unstable angina) and also reported 160 cases of perioperative hypertension

risk. This may justify our review's lower incidence of ACEs. A study conducted by Atherton *et al*.[37] which evaluated medical emergencies in dental practice, found that, on average, there was one reported cardiac complication over a 40-year career. Although this study focused on specific procedures within maxillofacial surgery, these findings indicate that ACE may be less common among this patient population, which may support our lower incidence.

The impact of ACEs on maxillofacial surgical outcomes was disproportionately high, with over 37% of patients requiring ICU management (Clavien–Dindo score of 4). A common ACE associated with ICU admission was IHD. It has been suggested that myocardial injuries are one of the most frequently reported cardiac complications in non-cardiac surgeries, with their incidence varying from 8% in 2014 to 17.9% in recent years.[38-40] The mere occurrence of IHD and

Table 6: Pooled incidence rates of each ACE category

ACE category	Effect size (%)	95% Confidence interval	I^2	*P*
Blood pressure disturbances	0.20	-0.16, 0.57	46.17	0.16
Heart rate and rhythm disturbances	3.85	2.23, 5.45	97.46	0.001
Heart failure and other complications	0.53	-0.04, 1.10	95.07	0.001
Ischaemic heart disease	0.21	0.13, 0.29	1.94	0.41

ACE=Adverse cardiac event

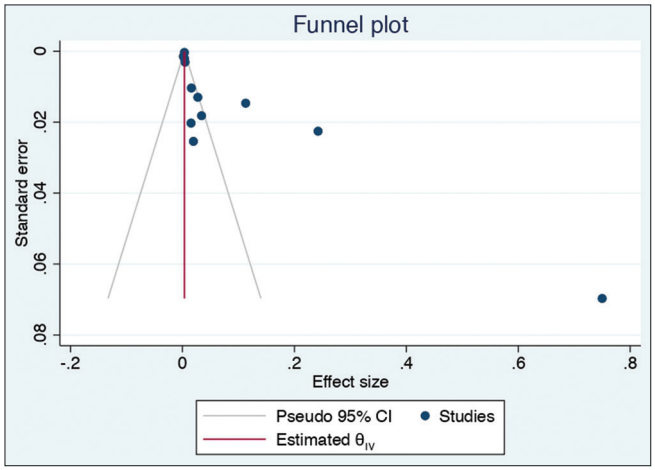

Figure 4: Funnel plot of the included studies ($n = 12$). The plot includes a pseudo 95% confidence interval to assess publication bias and study heterogeneity. This funnel plot reveals an asymmetrical distribution of data points with a concentration on the right side indicative of publication bias as introduced in the review

other ACEs is associated with a plethora of short- and long-term consequences, such as death. After adjusting for sex, age, alcohol consumption and comorbidities, mortality incidence was higher among patients with ACEs than those without.[36] In our review, death was reported in seven patients (2.4%): one patient with ventricular fibrillation, two patients with myocardial infarction and four patients with heart failure. Other studies have shown a similar mortality incidence, ranging from 0.5% to 2% by day 30.[41,42] Also, perioperative ACEs are the largest contributor to increased hospital stay and healthcare costs, with patients experiencing ACEs having double the average stay and up to five times the cost.[43] All these show that although the incidence of perioperative ACEs in maxillofacial surgeries is fairly low, its impact on surgical outcomes can be detrimental both to the patient and the healthcare system.

When considering potential precipitating factors, anaesthetic considerations must be evaluated. Anaesthetic agents influence the development of ACEs, particularly heart rate, rhythm disturbances, and blood pressure changes. In our review, only four studies provided recounts of the anaesthetic details of the surgeries[23,25,29,33] and only three studies provided specific anaesthetic agents administered.[23,25,29] Propofol and ketamine were used for sedation as infusions and for induction as boluses.[23,25,29] These medications are sedative–hypnotic agents with haemodynamic considerations.[44] Propofol is believed to inhibit the sympathetic nervous system and is associated with bradycardia and hypotension.[45,46] Contrastingly, ketamine has less clinically relevant hypotensive and bradycardic effects.[47,48] Regardless, the study authors did not consider using either agent to contribute to ACEs. However, remifentanil was suggested to have contributed to the high incidence (24.2%) of intraoperative bradycardia in one study.[29] In addition to its activity on opioid receptors, remifentanil increases the parasympathetic tone; thus, its usage carries the risk of severe vagal-mediated cardiovascular depression.[49-51] Lastly, all three studies used midazolam at either premedication or an induction dose. Midazolam has shown more excellent cardiorespiratory stability than thiopental and diazepam, favouring its suitability as both a bolus and long-term infusion.[52]

The occurrence of particular ACEs, such as the heart rate rhythm and blood pressure disturbances, may be associated with TCR. This reflex is particularly relevant for maxillofacial surgeries because these procedures are performed at the areas of innervation by the trigeminal nerve (CN V).[53] Stimulation of the sensory branches of this CN may cause heart rate abnormalities (bradycardia, asystole), changes to blood pressure (hypotension), apnoea and gastric hypermobility.[53] In our review, heart rate and rhythm disturbances, specifically bradycardia, were frequently reported. However, only two studies in our review suggested a potential relation between intraoperative bradycardia and this unique brainstem reflex.[29,30] TCR-related bradycardia did not precipitate detrimental complications in both studies. Most cases were resolved spontaneously once the stimuli were halted, and only a minority of patients required intravenous medication such as atropine. These findings concur with other studies, which also surmised that most TCR-induced bradycardia events are self-limiting

Table 7: Management of adverse cardiac events and Clavien–Dindo classification

First author (year)	Adverse cardiac event	Management	Clavien–Dindo classification
Braidy (2011)[23]	Blood pressure disturbances	Antihypertensive medications (labetalol 10 mg)	2
	Heart rate and rhythm disturbances	Rate control medications (labetalol 30 mg)	
Buitelaar (2006)[24]	Heart rate and rhythm disturbances	Death[a]	5
	Ischaemic heart disease		
	Heart failure and complications		
Christensen (2019)[25]	Blood pressure disturbances	Resolved spontaneously	1
	Ischaemic heart disease		
Cramer (2016)[26]	Ischaemic heart disease	Required intensive care	4
	Heart failure and complications		
Dean (2010)[27]	Ischaemic heart disease	Required intensive care	4
Gates (2021)[28]	Ischaemic heart disease	Required intensive care	4
	Heart failure and complications		
Ivosevic (2017)[29]	Heart rate and rhythm disturbances	Resolved spontaneously	1
Joshi (2017)[30]	Heart rate and rhythm disturbances	Resolves spontaneously	2
		Atropine (for two patients)	
Lalabekyan (2021)[31]	Ischaemic heart disease	Death[b]	5
Mackay (2020)[32]	Ischaemic heart disease	Coronary artery stent	3
Riley (1997)[33]	Heart rate and rhythm disturbances	Antiarrhythmic medications	3
	Ischaemic heart disease	Coronary bypass surgery	
	Blood pressure disturbances		
Spiegel (2005)[34]	Blood pressure disturbances	Antihypertensive medications	2
	Heart rate and rhythm disturbances	Antiarrhythmic medications	

[a]Death occurred in six of the 53 patients (11.3%) who developed an adverse cardiac event: ventricular fibrillation (*n*=1), myocardial infarction (*n*=1), heart failure (*n*=4). Deaths occurred on the day of surgery, post-op day 2, 15, 20 and 21. [b]Death occurred in one of the three patients (33.3%) who developed a myocardial infarction on post-op day 4

once the stimuli are removed.[54] However, in some cases, a TCR response may lead to asystole, apnoea and death.[55] Although less common, these negative outcomes should not be taken lightly. Currently, most research surrounding TCR in maxillofacial surgeries is in the form of case reports and series. However, there are still several unanswered questions regarding TCR-induced intraoperative cardiac events. Future research should address these timely and pertinent areas of concern, such as incidence, presentation and perioperative management.

Lastly, practitioners must consider preventative approaches for perioperative ACEs in maxillofacial surgeries. Firstly, patient profiles, including their comorbidities, play a predisposing role to ACEs in non-cardiac surgeries. In our review, the most commonly captured comorbidities were heart conditions [e.g. coronary artery disease (CAD), arrhythmias, congestive heart failure (CHF)]. Notably, CAD and CHF are independent risk factors for a major ACE in non-cardiac surgeries.[41] This review also captured patients with renal insufficiency, diabetes and cerebrovascular disease, which are predictors of cardiac complications according to the Revised Cardiac Risk Index.[41] As the demographic ages and the burden of patient comorbidities rise, the practice of conducting a thorough preoperative evaluation for elective maxillofacial surgeries should be standardised across sites, which is a critical component in minimising the risk of ACEs. In addition, considering the high incidence of IHD that this review revealed, which eventually requires ICU management, preoperative monitoring may be beneficial. Although not routinely indicated, patients at high cardiac risk, determined through a preoperative evaluation, may benefit from laboratory testing to determine baseline troponin levels.[56] This helps to stratify the risk further and inform subsequent decisions.

Future research in maxillofacial surgeries should focus on several areas. Firstly, large-scale prospective studies examining postoperative cardiac complications should be conducted with an explicit follow-up period for assessing them; future reviews of this topic can provide an incidence rate in person-years format. In addition, future research should strive to provide details about the operation's anaesthetic approach, including information surrounding the technique(s), types and dosage of medications, duration of anaesthetic exposure, ventilation management, etc., It is well known that the anaesthetic aspects are contributory towards precipitating intraoperative complications.

Ultimately, this information can be used to understand better the anaesthetic considerations, benefits, and risks of particular approaches and refine guidelines surrounding anaesthesia in maxillofacial surgeries. Lastly, future prospective studies are required to better understand ACEs' long-term effects following maxillofacial surgery.[57]

Our study had limitations. Firstly, the review's reliance on a relatively small number of studies (12 studies) may have limited the breadth of its analysis. Secondly, publication bias may be evidenced by the asymmetry of the funnel plot and Egger's test *P* value <0.01 [Figure 4]. Thirdly, despite this review's attempt at standardisation, the varying definitions of ACEs across studies may still introduce discrepancies in reporting and categorisation. This could lead to the underreporting or overreporting of such events. Fourthly, due to the lack of reporting in follow-up periods across the included studies, we were unable to provide an incidence rate in a person-year format. Fifthly, geographic bias may be a concern since the studies were primarily conducted in Western countries and may not fully represent global populations. Lastly, the review did not adjust for all potentially confounding variables, such as using specific anaesthetic agents that may influence ACEs.

CONCLUSION

Our analysis revealed a 2.58% pooled incidence of perioperative ACEs and found that these ACEs can often negatively affect surgical outcomes (i.e. necessitating ICU admission). In addition, this review conducted separate analyses to evaluate the incidence rates of specific ACE categories that may interest researchers and clinicians in this field. This review maps out the current evidence on this topic and can spark future data-driven research. This hypothesis-generating study reveals areas of interest, such as contributory factors and long-term implications, for future researchers.

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Conflicts of interest

There are no conflicts of interest.

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SUPPLEMENTARY MATERIAL

Search development details

Embase Classic + Embase < 1947 to 2023 05 May>

1. maxillofacial disorder/or maxillofacial implant/or maxillofacial injury/or maxillofacial surgery/ 18919
2. exp face surgery/ 55664
3. exp mandible/su or exp orthognathic surgery/or exp jaw/su 20376
4. exp oral surgery/ 61585
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10. exp heart arrest/ 129597
11. exp heart muscle ischemia/ 102640
12. exp heart injury/ 56540
13. major adverse cardiac event/ 15144
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25. 24 not (exp juvenile/not exp adult/) 3291