Treatment Delay Impact on Open Reduction Internal Fixation of Mandibular Fractures: A Systematic Review

Nicholas Stone, MD*
Alex Corneman, MD*
Anthony R. Sandre, MSc, BSc†
Forough Farrokhyar, PhD, MPhil‡§
Achilleas Thoma, MD, MSc, FRCSC*‡§
Michael J. Cooper, MD, FRCSC*

Background: The impact of mandible fracture treatment delay has been contested in the literature for decades, with conventional wisdom favoring earlier surgical treatment to prevent postoperative complications, primarily infection. Through a systematic review of all available evidence, this study aims to determine whether delay to open reduction and internal fixation of traumatic mandibular fractures influences outcomes.
Methods: MEDLINE, EMBASE, CINAHL, and Web of Science were systematically searched for English language literature pertaining to the above research question and screened in duplicate. Methodological quality scoring was performed using MINORS criteria. Qualitative and quantitative findings from relevant studies are presented.
Results: Twenty eligible studies including 2,671 patients had open reduction internal fixation, with or without adjunct mandibulomaxillary fixation. All studies were observational cohort or case-control studies of low methodological quality with a mean MINORS score of 6.5 of 16 (40.6%) for noncomparative studies and 11.2 of 24 (46.7%) for comparative studies. Only 5 of 20 (25%) studies recommended earlier treatment. Due to insufficient reporting of data and study heterogeneity, the impact of treatment delay on complications could not be quantitatively analyzed.
Conclusions: There is substantial heterogeneity and no consensus on the definition of "early" versus "delayed" surgical treatment for patients with traumatic mandibular fractures. The majority of included studies do not make a recommendation for earlier treatment. Future, well-designed prospective studies are essential to determine if there is an optimal surgical treatment delay of mandibular fractures that mitigates the risk of infectious and noninfectious complications. *(Plast Reconstr Surg Glob Open 2018;6:e1829; doi: 10.1097/GOX.0000000000001829; Published online 18 June 2018.)*

INTRODUCTION

Although closed reduction of mandible fractures via mandibulomaxillary fixation (MMF) has therapeutic value, open reduction internal fixation (ORIF) has become the standard of care for achieving anatomic reduction for a wide variety of mandibular fractures, including condylar head fractures.[1] However, mandible ORIF is considered to have a higher risk of postoperative infectious complications, as compared with MMF,[2–5] given the introduction of hardware in a grossly contaminated oral cavity. Intuitively, earlier ORIF should reduce the open fracture contamination exposure, though delayed ORIF allows for soft-tissue edema to subside and wound closure under reduced tension, which may theoretically decrease the risk of subsequent wound dehiscence and hardware exposure.

Early expert opinion suggested that ORIF for mandibular fractures should be performed within 6 hours of injury to reduce complication rates.[6] This time threshold was later extended to 24 hours,[7] and by the 1990s to within 48–72 hours.[8] To date, there remains no consensus on the optimal ORIF treatment delay or whether delayed

treatment increases complication rates. At our center, this poses a scheduling challenge for booking mandible ORIF cases as a "Priority 2" (to be completed within 24 hours), or a "Priority 3" (to be completed within 72 hours).

Previous reviews have addressed, at least in part, the topic of mandible fracture ORIF treatment delay.[9–11] However, earlier reviews analyzed heterogeneous populations of patients with various facial fractures,[9–11] included patients treated exclusively with closed surgical techniques,[9–11] and were either outdated,[9] or not truly systematic in nature.[10,11] This study is the first systematic review to focus specifically on patients with mandible fractures receiving ORIF and includes several studies not analyzed in the aforementioned reviews.

The primary research question of this systematic review is: in patients with traumatic mandible fractures, does "early" compared with "delayed" ORIF impact postoperative complications, primarily infection?

METHODS

Search Strategy and Study Screening

The search strategy was designed based on our research question that was formulated a priori using a "Population, Intervention, Comparison, Outcome, Timing" (PICOT)[12] format (Table 1). The inclusion/exclusion criteria were also determined a priori (Table 2).

The online databases Medline, Embase, CINAHL, and Web of Science were searched from inception until December 22, 2016. All database searches utilized wildcard truncation, synonyms, and MeSH terms for the following search terms: "mandible," "fracture," "complications," "time factors," and "surgery." The Cochrane Central Register of Controlled Trials[13] and clinicaltrials.gov[14] were searched for any relevant published or unpublished studies. References of relevant studies and previously published reviews were also searched. This systematic review was registered in PROSPERO.[15]

Titles, abstracts, and full text studies were screened in duplicate by 2 reviewers (N.S., A.C.). Discussion took place to address any disagreements about study inclusion or exclusion, and if needed, the senior author (M.J.C.) resolved any uncertainties.

Data Abstraction

Data were extracted into a Microsoft Excel spreadsheet (2011 release; Microsoft, Redmond, WA) and included study characteristics, patient demographics, time

Table 1. PICOT Research Question

Population
Primarily adult patients with traumatic mandibular fractures
Intervention
"Delayed" ORIF ± closed reduction adjunct (ie, postoperative MMF)
Comparison
"Early" ORIF ± closed reduction adjunct (ie, postoperative MMF)
Outcome
Primary: infectious complications
Wound infection, abscess, hardware infection, osteomyelitis
Secondary: noninfectious complications
Wound dehiscence, delayed union, hardware failure, malocclusion, malunion, nonunion
Timing
No explicit restriction for follow-up time specified

Table 2. Inclusion and Exclusion Criteria

Inclusion criteria
English language full-text studies
Human patients with focus on adult population
ORIF of traumatic mandible fracture(s)
Reporting of treatment delay related data (ie, time from injury to ORIF surgical treatment)
Reporting of postoperative complications
Exclusion criteria
Non-English language studies
Abstracts, case reports, or review articles
Focus on pediatric population
Closed reduction only treatment of mandible fracture(s)
Pathologic mandible fractures secondary to nontraumatic etiology (eg, oral cancer, diabetes, bisphosphonate-related osteonecrosis, osteoporosis)
Facial fractures independent of mandible fractures

factors, fracture location, mechanism of injury, and postoperative complications. Studies that grouped patients as cases (presence of postoperative complication) and controls (absence of postoperative complications) and reported treatment delay data (ie, time from injury to mandible ORIF) in each group were classified as case-control studies,[16] whereas studies that grouped the patients by treatment delay and reported postoperative complication data in each group were classified as cohort studies.

ORIF-specific patient data were extracted wherever possible if stratification allowed to maximize data inclusion.[8] Studies that did not stratify for patients receiving MMF without ORIF were excluded from this systematic review to maintain population homogeneity.[4,17–24] Mandible fracture location and complication data were recorded based on number of patients (n) with a fracture in a given region of the mandible, or if not reported, then the number of fractures (N) reported for a given mandibular region.

Data Analysis

Due to study heterogeneity and inadequate reporting of data, quantitative synthesis of the data into a meta-analysis was not feasible. Instead, descriptive statistics such as weighted means and proportions were calculated for the baseline characteristics data if reported by an acceptable number of studies. Data reported in terms of number of fractures were not used in our quantitative analysis to avoid overrepresentation of outcomes such as complications, which were not necessarily independent for each mandible fracture (eg, a patient with a trifocal mandibular fracture reporting malocclusion is recorded as 1 case of malocclusion rather than 3).

Assessing Methodological Quality

The validated criteria from Methodological Index for Non-Randomized Studies (MINORS)[25] were used for assessing the quality of all included studies in duplicate (N.S. and A.S.). A 50% score was set as an arbitrary methodological quality threshold. A 12-week average follow-up period was agreed upon a priori to sufficiently allow for manifestation of most relevant postoperative complications. The raw scores were recorded and were converted into calculated percentages.

RESULTS

Literature Search, Eligibility Assessment, and Article Selection

After initially retrieving 11,233 studies, 2,670 (23.8%) duplicates were removed. The remaining 8,563 studies were searched systematically yielding 19 full-text, primary research studies.[8,16,26–42] One additional study was sourced from the subsequent reference search.[43] A total of 20 articles were included in the study and are depicted in a flow diagram (Fig. 1) using a modified "Preferred Reporting Items for Systematic Reviews and Meta-Analyses" (PRISMA)[44] template.

Methodological Quality Assessment of Included Studies

The 20 included studies were assigned a MINORS score ranging from 4 to 8 out of 16 for noncomparative studies, and ranging from 6 to 15 out of 24 for comparative studies (Tables 3, 4). The average MINORS score for case–control studies was 10.9 of 24 (45.4%), and all were comparative. The average MINORS score for cohort studies was 6.5 of 16 (40.6%) for noncomparative studies, and 12.0 of 24 (50.0%) for comparative studies. The average MINORS score for all studies included in this systematic review was 6.5 of 16 (40.6%) for noncomparative studies and 11.2 of 24 (46.7%) for comparative studies. Only 9 of
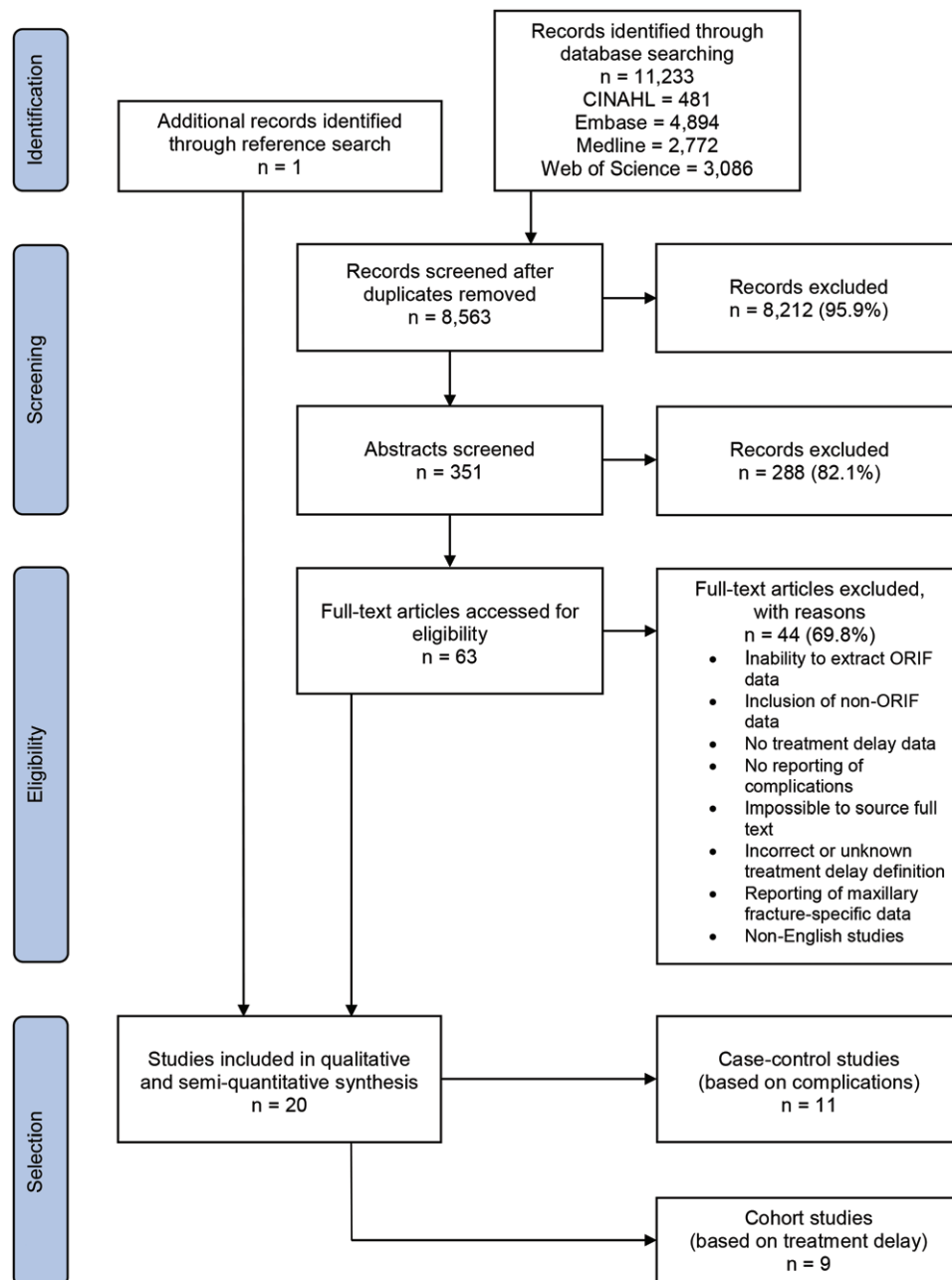

Fig. 1. Adapted PRISMA flow diagram depicting systematic review of literature relating to impact of treatment delay on outcomes in traumatic mandible fracture ORIF.

Table 3. Methodological Quality Scoring of Included Case–control Studies Using MINORS Criteria[25]

MINORS Criteria	Odom and Snyder-Warwick[26]	Gutta et al.[27]	Luz et al.[28]	Barker et al.[29]	Mahajan et al.[30]	Ellis and Walker[16]	Anderson and Alpert[31]	Iizuka and Lindqvist[32]	Smith[33]	Frost et al.[43]	Wagner et al.[34]
1. Clearly stated aim?	2	2	2	2	2	2	0	2	2	2	1
2. Inclusion of consecutive patients?	1	1	2	2	1	2	1	1	1	1	2
3. Prospective data collection?	0	0	0	0	0	2	0	1	0	0	1
4. Endpoints appropriate to aim of study?	1	2	2	2	2	1	1	1	1	1	1
5. Unbiased assessment of study endpoint?	0	0	0	0	0	0	0	0	0	0	0
6. Follow-up period appropriate to aim of study?	0	2	0	0	0	2	0	1	0	0	0
7. Loss to follow-up less than 5%?	1	0	1	2	1	2	1	0	1	1	1
8. Prospective calculation of study size?	0	0	0	0	0	0	0	0	0	0	0
9. Adequate control group?	1	1	2	2	2	0	1	2	1	1	1
10. Contemporary groups?	2	1	2	2	2	0	2	2	2	2	2
11. Baseline equivalence of groups?	2	1	0	1	0	1	0	0	1	1	1
12. Adequate statistical analysis?	1	1	1	2	2	0	0	0	0	1	0
Total score	11/24	11/24	12/24	15/24	12/24	14/24	6/24	10/24	9/24	10/24	10/24

Note: Each criterion receives a maximum score of 2, for a maximum total score of 24 for comparative studies, and 16 for noncomparative studies.

20 included studies had a calculated MINORS score greater than or equal to 50%, of which only 2 studies made a recommendation for earlier ORIF treatment.

A low MINORS score was primarily assigned due to a lack of: prospective data collection, assessor blinding, and sample size calculations (Tables 3, 4). Additional factors contributing to low scoring included a lack of adequate control groups, and several studies having greater than 5% loss to follow-up and inadequate follow-up periods.

Baseline Characteristics of Included Studies

There were a total of 2,671 patients from the 20 included studies published between 1979 and 2016 (Table 5), and only 1 study was prospective in nature.[16] All studies were observational, with more case–control studies (11/20) than cohort studies (9/20). Five of 20 studies made an overall recommendation for earlier treatment, whereas 14 studies did not make a recommendation for earlier treatment. Among these 14 studies, only 1 found a "loose trend toward better outcomes with delayed fixation" but overall did not suggest an association between timing of surgical repair and postoperative complications.[29] One study did not have a clear recommendation for or against earlier treatment.[39]

With respect to patient demographics (Table 6), 77.84% of patients were male (16/20 studies reporting), and the average age of patients was 31.3 years old (14/20 studies reporting). The mean time delay from injury to ORIF surgery was approximately 116 hours or 4.8 days (8/20 studies reporting). The follow-up time averaged 13.0 weeks (7/20 studies reporting) and ranged from 0.7 to 100 weeks (11/20 studies reporting). Table 7 demonstrates that the most commonly fractured anatomic region of the mandible was the angle, with 679 patients affected (6/20 studies reporting), followed by the mandibular body, with 190 patients affected (5/20 studies reporting). Table 8 demonstrates that assault was the most common mechanism causing mandibular fractures, with 870 patients affected (10/20 studies reporting), followed by 532 cases of blunt trauma (9/20 studies reporting), and 373 cases of road traffic accidents (13/20 studies reporting).

Four hundred fifty-five patients (18.5%) had at least 1 postoperative complication following ORIF, based on 19 of 20 studies reporting the total number of patients with complications (Table 9). Two hundred thirteen patients (8.2%) had infectious complications of any type (19/20 studies reporting). Infection was the most commonly reported complication, followed by 128 patients (7.1%) with malocclusion (11/20 studies reporting), and 52 patients (3.5%) with wound dehiscence (9/20 studies reporting).

Attempted Meta-analysis

Treatment delay time thresholds were too variable to pool cohort study data, with only 2 studies sharing time intervals among cohort groups (Fig. 2). There was inadequate reporting of mean treatment delay times to pool data for 7 of 11 case–control studies. Four of the 20 included studies reported sufficient treatment delay data to facilitate depiction in a Forest plot (Fig. 3). The data from 2 studies suggested that treatment delay was longer for pa-

Table 4. Methodological Quality Scoring of Included Cohort Studies Using MINORS Criteria[25]

MINORS Criteria	Spinelli et al.[35]	Zrounba et al.[36]	Gazal[37]	Lucca et al.[38]	Okoturo et al.[39]	Peled et al.[40]	Tuovinen et al.[41]	Nakamura et al.[42]	Maloney et al.[8]
Clearly stated aim?	2	2	2	2	1	2	1	2	2
Inclusion of consecutive patients?	1	1	1	1	1	1	1	1	1
Prospective data collection?	0	0	0	0	1	0	0	0	0
Endpoints appropriate to aim of study?	2	2	0	2	2	2	2	2	0
Unbiased assessment of study endpoint?	0	0	0	0	0	0	0	0	0
Follow-up period appropriate to aim of study?	2	2	0	2	1	2	0	2	0
Loss to follow-up less than 5%?	1	2	1	1	1	1	2	1	1
Prospective calculation of study size?	0	0	0	0	0	0	0	0	0
Adequate control group?	—	1	—	2	1	1	—	—	2
Contemporary groups?	—	2	—	2	2	2	—	—	2
Baseline equivalence of groups?	—	0	—	2	1	1	—	—	1
Adequate statistical analysis?	—	1	—	1	0	0	—	—	0
Total score	8/16	13/24	4/16	15/24	11/24	12/24	6/16	8/16	9/24

Note: Each criterion receives a maximum score of 2, for a maximum total score of 24 for comparative studies, and 16 for noncomparative studies.

tients with complications,[28,30] whereas 2 studies suggested a longer treatment delay for patients without complications.[27,29] The heterogeneity score was 83%, and therefore it was unreliable to pool mean treatment time by postoperative complications.

DISCUSSION

There is insufficient data to reliably determine the importance of treatment delay as an independent predictor of postoperative complications following ORIF of traumatic mandible fracture(s). Only 5 of the 20 studies included in this systematic review concluded that prolonged treatment delay increased the risk of postoperative complications for traumatic mandible fractures. There was significant variation in the time thresholds proposed delineating "early" versus "delayed" ORIF, ranging from 6 hours to 7 days (Fig. 2). Significant time threshold heterogeneity for cohort studies, incomplete data reporting of mean treatment delay times for case–control studies, and overall insufficient stratification of reported data prevented synthesis of the collected data into a formal meta-analysis. The optimal treatment delay for minimizing complications in patients requiring mandible fracture ORIF remains unknown.

Alternative Risk Factors for Postoperative Complications

Alternative risk factors, other than treatment delay, have been posited as contributors to the development of postoperative complications in patients with mandible fractures (Table 10). It has been suggested that these factors may be confounders resulting in prolonged treatment delay, such as noncompliance and comorbid substance use.[19,20]

With respect to patient factors increasing complication rates, Malanchuk and Kopchak[22] demonstrated that age was a significant predictor of infection for toothbearing mandible fractures treated with open or closed reduction, with patients less than 20 years old and greater than 60 years old having infection rates of 9.4% and 55%, respectively. Periodontal disease has been linked to delayed healing of mandibular body fractures.[45] Luz et al.[28] found that 75% of patients with complications following ORIF for mandible fractures were partially edentulous,

whereas 76.2% of patients without complications were fully dentate. One of the most significant contributors for developing complications in patients with traumatic mandible fractures is substance use, including alcohol abuse.[4,19–21,23,32,45] Domingo et al.[5] found that as many as 53.6% of drug users with mandible fractures developed surgical-site infection and suggested this may be due to their relatively poor nutrition, wound healing, and compliance with postoperative oral care. Smoking has also been reported to increase post-ORIF complication rates 4-fold and infection rates 6-fold, as compared with nonsmokers receiving ORIF.[5,26,27]

With regard to mandible fracture factors influencing postoperative complications, higher risk anatomic regions include the mandibular angle[22,34] and the body; Luz et al.[28] reported that 43.8% of body fractures had complications requiring reoperation. Patients with comminuted[21,22,28] and multifocal[26] mandible fractures were found to be at higher risk of developing complications, including infection. Czerwinski et al.[21] reported that the rate of comminution in patients with complications was 32% compared with 22% in patients without complications. Compared with closed fractures, open fractures have been reported to have as high as a 14-fold increased complication rate (14% versus 1%),[5] and another study found that 80% of patients with postoperative complications had open mandibular fractures.[28] Similarly, Anderson and Alpert[31] reported that 100% of patients with complications (predominantly infectious) had teeth in the line of their mandible fracture, which are considered open fractures by definition,[8] and theoretically create a conduit for bacterial seeding. In keeping with this hypothesis, Wagner et al.[34] reported that 69% of patients (9 of 13) receiving mandible fracture treatment involving tooth extraction had post-ORIF complications.

Lastly, there is evidence to suggest that ORIF surgical technique is a factor in predicting increased complication rates. An included study[31] reported a 46% infection rate (6/13 mandible fractures) associated with improper ORIF technique. Odom and Snyder-Warrick[26] reported that ORIF utilizing intraoral incision was associated with a 16.8% complication rate, compared with 0% with extraoral incision, and 27% with combined intraoral and extraoral incisions. However, these data may have been confounded

Table 5. Summary of Key Information for Included Case-control and Cohort Studies

Author	Year	Country	Study Design	Sample Size (n)	Treatment Intervention	Recommendation for Early Treatment?	MINORS Score Raw	Percent
Case-control studies								
Odom and Snyder-Warwick[26]	2016	United States	Retrospective	342	ORIF ± MMF	No	11/24	46
Gutta et al.[27]	2014	United States	Retrospective	363	ORIF ± MMF	No	11/24	46
Luz et al.[28]	2013	Brazil	Retrospective	62	ORIF	Yes	12/24	50
Barker et al.[29]	2011	United States	Retrospective	83	ORIF ± MMF*	No	15/24	63
Mahajan et al.[30]	2009	India	Retrospective	52	ORIF + MMF	Yes	12/24	50
Ellis and Walker[16]	1996	United States	Prospective	81	ORIF	No	14/24	58
Anderson and Alpert[31]	1992	United States	Retrospective	52	ORIF	Yes	6/24	25
Iizuka and Lindqvist[32]	1992	Finland	Retrospective*	214	ORIF + MMF	No	10/24	42
Smith[33]	1991	United Kingdom	Retrospective	40	ORIF + MMF	No	9/24	38
Frost et al.[43]	1983	United Kingdom	Retrospective	75	ORIF	No	10/24	42
Wagner et al.[34]	1979	United States	Retrospective*	82	ORIF + MMF	No	10/24	42
Total (case-control studies)	—	—	10 Retrospective; 1 prospective	1,446	4 ORIF; 3 ORIF ± MMF; 4 ORIF + MMF	Yes (3); no (8)	10.9/24	45
Cohort studies								
Spinelli et al.[35]	2016	Italy	Retrospective	389	ORIF	No	8/16	50
Zroumba et al.[36]	2015	Switzerland	Retrospective	47	ORIF	No	13/24	54
Gazal[37]	2015	Saudi Arabia	Retrospective	91	ORIF	Yes	4/16	25
Lucca et al.[38]	2010	United States	Retrospective	92	*ORIF ± MMF	No	15/24	63
Okoturo et al.[39]	2008	Nigeria	Retrospective*	28	ORIF ± MMF	Unknown	11/24	46
Peled et al.[40]	1997	Israel	Retrospective	143	ORIF ± MMF	No	12/24	50
Tuovinen et al.[41]	1994	Denmark	Retrospective	279	ORIF + MMF	No	6/16	38
Nakamura et al.[42]	1994	Japan	Retrospective	110	ORIF + MMF	No	8/16	50
Maloney et al.[8]†	1991	United States	Retrospective	46	ORIF + MMF	Yes	9/24	38
Total (cohort studies)	—	—	9 Retrospective	1,225	3 ORIF; 3 ORIF ± MMF; 3 ORIF + MMF	Yes (2); no (6); unknown (1)	6.5/16, 12/24	46
Total (all studies)	—	—	19 Retrospective; 1 prospective	2,671	7 ORIF; 6 ORIF ± MMF; 7 ORIF + MMF	Yes (5); no (14); unknown (1)	6.5/16 11.2/24	45

n, number of patients with associated parameter. —, not applicable.

*Denotes uncertainty.

†Denotes that data from a subset of patients receiving ORIF were able to be extracted from articles where not every patient in the total sample size received ORIF treatment.

Table 6. Patient Demographics and Time-related Data

Author	Patient Demographics			Mean Time from Injury to Surgery (h)	Follow-up Time (wk)		Substance Use (n)		
	Sample size (n)	Male Sex (n)	Mean Age (y)		Mean	Range	Alcohol	Tobacco	Illicit Drugs
Case–control studies									
Odom and Snyder-Warwick[26]	342	294	29.8	184.8	—	—	—	174	—
Gutta et al.[27]	363	319	35.5	—	13.6	4-*	—	—	—
Luz et al.[28]	62	55	28.0	—	—	—	—	—	—
Barker et al.[29]	83	65	28.9	160.8	—	—	—	—	—
Mahajan et al.[30]	52	—	30.61	275.52	—	—	—	—	—
Ellis and Walker[16]	81	68	27.2	74.4	19.4	6–64	—	—	—
Anderson and Alpert[31]	52	—	—	—	—	—	—	—	—
Iizuka and Lindqvist[32]	214	175	33.9	76.8	7.1	3–16	72	—	—
Smith[33]	40	32	—	—	—	—	6	—	—
Frost et al.[43]	75	54	40	—	—	—	—	—	—
Wagner et al.[34]	82	—	33	—	—	—	9	—	1
Total (case–control studies)	1,446	83.71†	32.47	146.81	12.2	3–64	87	174	1
Cohort studies									
Spinelli et al.[35]	389	258	28.7	60	—	24–100	98	—	82
Zrounba et al.[36]	47	24	35	—	—	12-*	3	17	—
Gazal[37]	91	82	—	—	4	4	—	—	—
Lucca et al.[38]	92	72	28.74	55.68	11.6	0.7–12.4	28	32	11
Okoturo et al.[39]	28	23	29	2,328	8.9	6–24	—	—	—
Peled et al.[40]	143	86	—	—	24	24	—	—	—
Tuovinen et al.[41]	279	227	—	—	—	4–52	—	—	—
Nakamura et al.[42]	110	92	27.1	—	—	20–32.8	—	—	—
Maloney et al.[8]‡	46	—	—	—	—	—	—	—	—
Total (cohort studies)	1,225	73.28†	28.91	68.72	14.4	0.7–100	129	49	93
Total (all studies)	2,671	77.84†	31.30	115.78	13.0	0.7–100	216	223	94

n, number of patients with associated parameter; —, not reported.

*Denotes uncertainty.

†Refers to male sex percentage in population.

‡Denotes that data from a subset of patients receiving ORIF were able to be extracted from articles where not every patient in the total sample size received ORIF treatment.

Table 7. Anatomic Distribution of Mandible Fractures

Author	Fracture Location (n)						
	Angle	Body	Condylar	Ramus	Subcondylar	Symphyseal	Parasymphyseal
Case–control studies							
Odom and Snyder-Warwick[26]	52	18	—	2	3	7	18
Gutta et al.[27]	205(N)	177(N)	114(N)	4(N)	—	80(N)	—
Luz et al.[28]	22	30	23	—	—	28	—
Barker et al.[29]	—	—	—	—	—	—	—
Mahajan et al.[30]	—	—	—	—	—	—	—
Ellis and Walker[16]	81	24	1	—	—	11	—
Anderson and Alpert[31]	14	28	—	5	—	—	—
Iizuka and Lindqvist[32]	121	90	—	—	60	20	—
Smith[33]	15(N)	6(N)	—	—	—	19(N)	—
Frost et al.[43]	—	—	—	—	—	—	—
Wagner et al.[34]	49(N)	26(N)	—	1	—	6(N)	18(N)
Cohort studies							
Spinelli et al.[35]	389	—	—	—	—	—	—
Zrounba et al.[36]	—	—	1	—	—	—	—
Gazal[37]	—	—	1	—	—	—	—
Lucca et al.[38]	36(N)	15(N)	17(N)	—	34(N)	—	47(N)
Okoturo et al.[39]	14(N)	12(N)	—	0	—	3(N)	10(N)
Peled et al.[40]	90(N)	56(N)	—	—	0	—	70(N)
Tuovinen et al.[41]	128(N)	130(N)	—	—	95(N)	94(N)	—
Nakamura et al.[42]	42(N)	31(N)	—	—	8(N)	62(N)	—
Maloney et al.[8]	—	—	—	—	—	—	—
Total (all studies)	679/579(N)	190/338(N)	25/131(N)	8/4(N)	63/137(N)	66/264(N)	18/127(N)

n, number of patients with associated parameter; N, number of fractures with associated parameter; —, not reported.

by the fact that more complex and comminuted mandible fractures tend to require a combined approach.[28]

Strengths

To date, this is the first systematic review on mandible fracture treatment delay that focuses specifically on ORIF intervention timing. Ensuring the best possible methodological quality was of high importance, and this systematic review was designed in adherence with PRISMA guidelines.[44] The search strategy was constructed in collaboration with our health sciences librarian using a PICOT question formulated a priori and was also registered a priori in the

Table 8. Mechanism of Injury Contributing to Traumatic Mandible Fractures

Author	Mechanism of Injury (n)						
	Assault	Blunt Trauma	Fall	Gunshot Wound	Road Traffic Accident	Sport	Work Accident
Case–control studies							
Odom and Snyder-Warwick[26]	212	—	34	10	62	14	—
Gutta et al.[27]	270	—	29	—	22	24	6
Luz et al.[28]	17	—	8	9	18	3	1
Barker et al.[29]	37	9	13	3	21	—	—
Mahajan et al.[30]	—	—	—	—	—	—	—
Ellis and Walker[16]	73	—	2	—	5	1	—
Anderson and Alpert[31]	—	52	—	—	—	—	—
Iizuka and Lindqvist[32]	128	8	29	2	37	—	—
Smith[33]	18	—	7	—	13	2	—
Frost et al.[43]	38	—	25	—	11	—	1
Wagner et al.[34]	—	82	—	—	—	—	—
Total (case–control studies)	793	151	147	21	189	44	8
Cohort studies							
Spinelli et al.[35]	75	141	—	—	81	49	43
Zrounba et al.[36]	—	11	22	—	4	7	3
Gazal[37]	—	76	10	—	6	—	—
Lucca et al.[38]	—	—	—	—	—	—	—
Okoturo et al.[39]	2	14	1	—	11	—	—
Peled et al.[40]	—	—	—	0	—	—	—
Tuovinen et al.[41]	—	139	28	—	82	19	3
Nakamura et al.[42]	—	—	—	—	—	—	—
Maloney et al.[8]	—	—	—	—	—	—	—
Total (cohort studies)	77	381	61	0	184	75	49
Total (all studies)	870	532	208	21	373	119	57

n, number of patients with associated parameter; —, not reported.

Table 9. Postoperative Complications following ORIF of Traumatic Mandibular Fractures

Author	Complications of Interest (n)										
	Delayed Union	Hardware Failure	Malocclusion	Malunion	Nonunion	Wound Dehiscence	Infection (All Cause)	Abscess	Hardware Infection	Osteomyelitis	Total
Case–control studies											
Odom and Snyder-Warwick[26]	—	—	—	—	—	—	32	—	—	—	60
Gutta et al.[27]	—	15	29	—	21	11	56	—	31	—	96
Luz et al.[28]	—	—	—	1	10	—	9	—	7	2	20
Barker et al.[29]	—	—	—	4	0	—	2	—	—	—	4
Mahajan et al.[30]	—	—	—	—	—	—	7	—	—	—	7
Ellis and Walker[16]	—	—	—	—	—	—	6	—	—	—	13
Anderson and Alpert[31]	—	1	0	—	1	—	12	—	—	—	12
Iizuka and Lindqvist[32]	—	—	29	—	—	—	13	—	—	—	—
Smith[33]	1	—	3	—	—	1	1	—	—	—	6
Frost et al.[43]	—	—	—	—	5(N)	—	9(N)	—	—	—	16
Wagner et al.[34]	3	—	—	0	0	—	9	—	—	—	13
Total (case–control studies)	4	16	61	5	32	12	147	0	38	2	247
Cohort studies											
Spinelli et al.[35]	—	—	21	—	5	17	32	—	—	—	53
Zrounba et al.[36]	—	2	—	—	2	3	2	—	—	—	6
Gazal[37]	—	—	8	—	—	—	5	—	—	—	50
Lucca et al.[38]	—	—	11	3	—	3	6	—	—	—	19
Okoturo et al.[39]	0	3	7	0	—	4	4	—	—	—	13
Peled et al.[40]	—	—	3	—	—	6	4	—	—	0	16
Tuovinen et al.[41]	—	1	13	—	0	5	10	—	—	—	32
Nakamura et al.[42]	2	4	4	—	—	2	1	1	—	—	17
Maloney et al.[8]*	—	—	—	—	—	—	2	—	—	—	2
Total (cohort studies)	2	10	67	3	7	40	66	1	0	0	208
Total (all studies)	6	26	128	8	39	52	213	1	38	2	455

n, number of patients with associated parameter; N, number of fractures with associated parameter; —, not reported.
*Denotes that data from a subset of patients receiving ORIF were able to be extracted from articles where not every patient in the total sample size received ORIF treatment.

PROSPERO database. The literature search was conducted in duplicate and the included studies were also scored in duplicate using MINORS, a validated tool for assessing the methodological quality of nonrandomized studies.

Limitations

Incomplete data reporting and insufficient data stratification were frequently encountered, as the majority of included studies were retrospective in nature. Six of 20 included
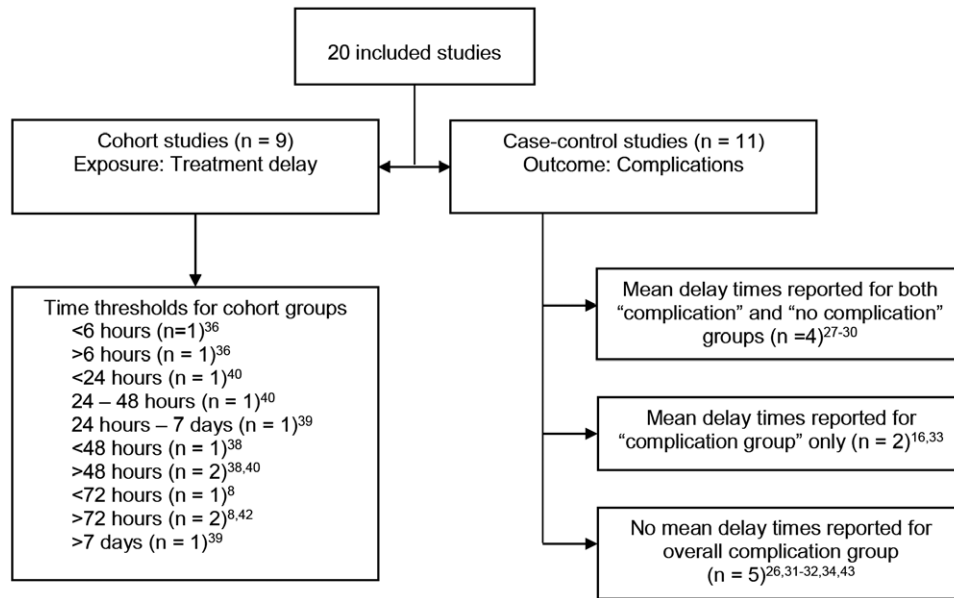
Fig. 2. Time-relevant group classification for included cohort and case–control studies detailing barriers to representing data in meta-analysis using a Forest plot. Treatment delay thresholds for cohort studies are highly variable prohibiting data pooling, while case–control studies had inadequate reporting of mean time delay data.
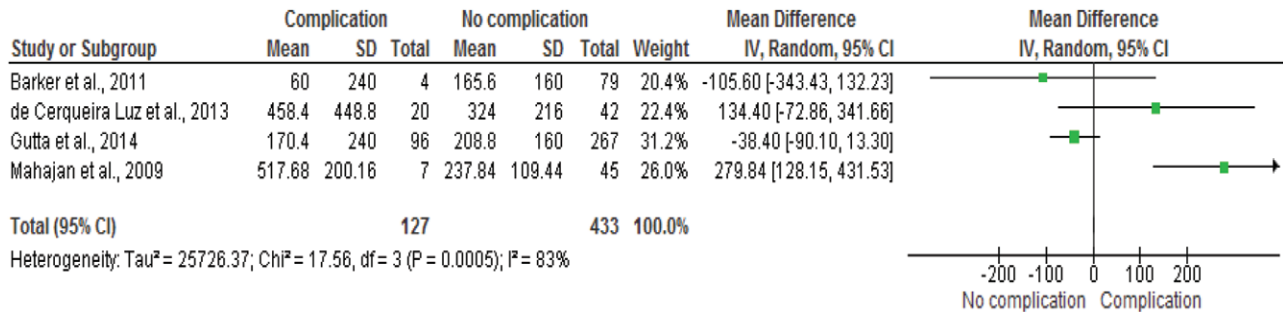

Fig. 3. Forest plot for included case–control studies with sufficient reporting of mean time delay from injury to surgery (hours) demonstrating duration of treatment delay for "complication" and "no complication" groups. Treatment delay was longer on average by 69.32 hours for the pooled groups with "complications."

studies did not report mean patient age making exclusion of irrelevant studies more difficult.[8,31,33,37,40,41] Reported follow-up times were regularly shorter than 12 weeks, and 9 of 20 included studies did not report any follow-up data (Table 6). Inadequate follow-up periods were, however, penalized as part of the MINORS scoring criteria (Tables 3, 4).

There was variation among the types of mandible fracture included across studies with Spinelli et al.[35] focusing on angle fractures only, Barker et al.[29] excluding condylar and alveolar fractures, and 5 of 20 included studies not reporting mandible fracture location.[8,29,30,36,43] It is therefore difficult to compare complication rates between such studies, given that mandible fracture location is considered an important factor influencing the development of complications.[16]

ORIF hardware has also changed over the decades, with the earlier studies in the 1970s to 1980s utilizing interosseous wiring in as many as 93.8–96.0% of cases,[17,34] whereas recent studies have tended toward mini-plate use

exclusively.[35,36] Early adopters of mini-plate hardware may have encountered more complications related to operator learning before the popularization and refinement of this modern ORIF technique.[31]

The definition of treatment delay in the literature was highly variable. Unfortunately, some studies needed to be excluded during the full-text review, as they did not report time from injury to ORIF treatment, but rather used intervals such as injury to admission[2] or diagnosis to treatment,[3] or did not specify a time interval at all.[46]

Among the 20 included studies, there was still heterogeneity with respect to whether MMF was used as an adjunct to ORIF (Table 5). The utilization of MMF in addition to ORIF was deemed acceptable for inclusion, as MMF did not contribute to the development of mutually exclusive reported complications during review of the included studies.

There was heterogeneous reporting of parameters such as fracture location and complication data (Ta-

Table 10. Factors Implicated to be Associated with Postoperative Complications following Surgical Treatment of Mandible Fractures

Patient factors
Advanced age[22,28]
Poor dental status[28,45]
Noncompliance[8,30,45]
Substance/alcohol abuse[4,5,19–21,23,28,32,45]
Tobacco use[5,26,27]
Fracture factors
Angle/body fractures[22,28,34]
Multifocal/comminuted fractures[21,22,26,28]
Open/tooth-bearing fractures[5,8,28,31]
Fractures requiring tooth extraction[34]
Surgical factors
Improper ORIF technique[31]
Intraoral incision approach[26]

Table 11. Recommended Outcome Set for Future Studies Investigating Surgical Treatment Delay for Traumatic Mandible Fractures

Infection (all cause)
Hardware infection
Osteomyelitis
Hardware failure
Malocclusion
Malunion
Nonunion
Wound dehiscence

bles 7, 9), either in terms of number of patients affected (n),[16,26,28,31,32,35] or number of fracture cases (N).[27,33,34,38–42] This prevented pooling of data as it could not be assumed that each fracture case was attributed to an individual patient, such as in patients with multifocal fractures. A paucity of data reporting and stratification was also problematic for reporting substance abuse data, with only 1 study individually stratifying by number of patients using tobacco, alcohol, and illicit drugs.[38] No useful data could be extracted from studies like Luz et al.[28] that reported all forms of substance abuse (ie, smoking, alcohol, and illicit drug use) in a single category, and many studies did not report substance use data at all (Table 6). Therefore, sample sizes were too small to determine if complications were correlated with any particular type of substance abuse.

Formal statistical analysis in the form of *P* values or confidence intervals was lacking among included studies to substantiate recommendations supporting shorter treatment delay.[8,31,37] In general, there was a lack of stratified time delay data for cohort study subgroups and case–control subgroups, thereby preventing meaningful statistical calculations that could determine quantitatively if in fact treatment delay was associated with an increased risk of complications. Even in the best-case scenario (Fig. 3), small sample sizes, large confidence intervals, and a heterogeneity score > 50% led our statistician to recommend against pooling of data in a formal meta-analysis.

Future Directions

A well-designed prospective cohort study is the next logical step to answer the question of whether treatment delay is an independent factor impacting postoperative mandible fracture complications and accurately estimate an optimal time threshold for treatment delay. A priori sample size calculations will be necessary to ensure adequate study power for patients and operative characteristics adjustments.[47] A prospective design will ensure complete and consistent data collection and reporting for the primary and secondary outcomes, but also ensure appropriate stratification for other factors such as fracture location, fracture etiology, substance abuse, and especially treatment delay data. Based on the most commonly reported complications in this systematic review, we propose that all future studies include the following outcomes: infection (all cause), osteomyelitis,

hardware infection, malocclusion, malunion, nonunion, wound dehiscence, and hardware failure (Table 11). Lastly, confounding factors such as substance abuse (ie, tobacco, alcohol, and illicit drugs), noncompliance, fracture complexity, and comorbid injury severity must be collected and controlled for to ensure that treatment delay is the only independent variable in the study design.

CONCLUSIONS

There is no consensus on whether ORIF treatment delay is an independent risk factor for the development of postoperative complications in patients with traumatic mandible fractures. There is no consistently utilized time threshold distinguishing "early" versus "delayed" treatment, and 14 of 20 included studies did not conclude that treatment delay was a predictor of postoperative complications. Future well-designed prospective studies of higher methodological quality are essential to determine if there exists an optimal treatment delay threshold that mitigates complication risks.

Michael James Cooper, MD, FRCSC
Division of Plastic Surgery
McMaster University
237 Barton St. East
Hamilton, Ontario, L8L 2X2
E-mail: Michael.cooper@medportal.ca

REFERENCES

1. Zhang B, Yang M, Zhou Q, et al. Delayed open reduction and single screw internal fixation as a treatment option in cases of failed non-surgical treatment of bilateral condylar head fractures with fragmentation. *J Craniomaxillofac Surg*. 2016;44:1655–1661.
2. Stone IE, Dodson TB, Bays RA. Risk factors for infection following operative treatment of mandibular fractures: a multivariate analysis. *Plast Reconstr Surg*. 1993;91:64–68.
3. Terris DJ, Lalakea ML, Tuffo KM, et al. Mandible fracture repair: specific indications for newer techniques. *Otolaryngol Head Neck Surg*. 1994;111:751–757.
4. Furr AM, Schweinfurth JM, May WL. Factors associated with long-term complications after repair of mandibular fractures. *Laryngoscope*. 2006;116:427–430.
5. Domingo F, Dale E, Gao C, et al. A single-center retrospective review of postoperative infectious complications in the surgical management of mandibular fractures: postoperative antibiotics add no benefit. *J Trauma Acute Care Surg*. 2016;81:1109–1114.
6. Champy M, Loddé JP, Schmitt R, et al. Mandibular osteosynthesis by miniature screwed plates via a buccal approach. *J Maxillofac Surg*. 1978;6:14–21.
7. Cawood JI. Small plate osteosynthesis of mandibular fractures. *Br J Oral Maxillofac Surg*. 1985;23:77–91.

8. Maloney PL, Welch TB, Doku HC. Early immobilization of mandibular fractures: a retrospective study. *J Oral Maxillofac Surg.* 1991;49:698–702; discussion 702.

9. Hermund NU, Hillerup S, Kofod T, et al. Effect of early or delayed treatment upon healing of mandibular fractures: a systematic literature review. *Dent Traumatol.* 2008;24:22–26.

10. Barker DA, Park SS. Is fixation of mandible fractures urgent? *Laryngoscope.* 2011;121:906–907.

11. Hurrell MJ, Batstone MD. The effect of treatment timing on the management of facial fractures: a systematic review. *Int J Oral Maxillofac Surg.* 2014;43:944–950.

12. Thoma A, McKnight L, McKay P, et al. Forming the research question. *Clin Plast Surg.* 2008;35:189–193.

13. The Cochrane Central Register of Controlled Trials (CENTRAL). Available at http://www.cochranelibrary.com/about/central-landing-page.html. Accessed December 22, 2016.

14. ClinicalTrials.gov: A service of the U.S. National Institutes of Health. Available at http://clinicaltrials.gov. Accessed December 22, 2016.

15. PROSPERO: international prospective register of systematic reviews. Available at http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42017059641. Accessed December 19, 2017.

16. Ellis E 3rd, Walker LR. Treatment of mandibular angle fractures using one noncompression miniplate. *J Oral Maxillofac Surg.* 1996;54:864–871; discussion 871.

17. James RB, Fredrickson C, Kent JN. Prospective study of mandibular fractures. *J Oral Surg.* 1981;39:275–281.

18. Moulton-Barrett R, Rubinstein AJ, Salzhauer MA, et al. Complications of mandibular fractures. *Ann Plast Surg.* 1998;41:258–263.

19. Maloney PL, Lincoln RE, Coyne CP. A protocol for the management of compound mandibular fractures based on the time from injury to treatment. *J Oral Maxillofac Surg.* 2001;59:879–884; discussion 885.

20. Biller JA, Pletcher SD, Goldberg AN, et al. Complications and the time to repair of mandible fractures. *Laryngoscope.* 2005;115:769–772.

21. Czerwinski M, Parker WL, Correa JA, et al. Effect of treatment delay on mandibular fracture infection rate. *Plast Reconstr Surg.* 2008;122:881–885.

22. Malanchuk VO, Kopchak AV. Risk factors for development of infection in patients with mandibular fractures located in the tooth-bearing area. *J Craniomaxillofac Surg.* 2007;35:57–62.

23. Webb LS, Makhijani S, Khanna M, et al. A comparison of outcomes between immediate and delayed repair of mandibular fractures. *Can J Plast Surg.* 2009;17:124–126.

24. Lee UK, Rojhani A, Herford AS, et al. Immediate versus delayed treatment of mandibular fractures: a stratified analysis of complications. *J Oral Maxillofac Surg.* 2016;74:1186–1196.

25. Slim K, Nini E, Forestier D, et al. Methodological index for non-randomized studies (minors): development and validation of a new instrument. *ANZ J Surg.* 2003;73:712–716.

26. Odom EB, Snyder-Warwick AK. Mandible fracture complications and infection: the influence of demographics and modifiable factors. *Plast Reconstr Surg.* 2016;138:282e–289e.

27. Gutta R, Tracy K, Johnson C, et al. Outcomes of mandible fracture treatment at an academic tertiary hospital: a 5-year analysis. *J Oral Maxillofac Surg.* 2014;72:550–558.

28. Luz JG, Moraes RB, D'Ávila RP, et al. Factors contributing to the surgical retreatment of mandibular fractures. *Braz Oral Res.* 2013;27:258–265.

29. Barker DA, Oo KK, Allak A, et al. Timing for repair of mandible fractures. *Laryngoscope.* 2011;121:1160–1163.

30. Mahajan SV, Datarkar AN, Borle RM. Time lapse from the occurrence of trauma to the definitive management of mandibular fractures: a retrospective study. *J Maxillofac Oral Surg.* 2009;8:320–323.

31. Anderson T, Alpert B. Experience with rigid fixation of mandibular fractures and immediate function. *J Oral Maxillofac Surg.* 1992;50:555–560; discussion 560.

32. Iizuka T, Lindqvist C. Rigid internal fixation of mandibular fractures. An analysis of 270 fractures treated using the AO/ASIF method. *Int J Oral Maxillofac Surg.* 1992;21:65–69.

33. Smith WP. Delayed miniplate osteosynthesis for mandibular fractures. *Br J Oral Maxillofac Surg.* 1991;29:73–76.

34. Wagner WF, Neal DC, Alpert B. Morbidity associated with extraoral open reduction of mandibular fractures. *J Oral Surg.* 1979;37:97–100.

35. Spinelli G, Lazzeri D, Arcuri F, et al. Management of mandibular angle fractures by two conventional 2.0-mm miniplates: a retrospective study of 389 patients. *Craniomaxillofac Trauma Reconstr.* 2016;9:206–210.

36. Zrounba H, Hoarau R, Zweifel D, et al. Are open mandibular fractures still an emergency? *Rev Stomatol Chir Maxillofac Chir Orale.* 2015;116:285–288.

37. Gazal G. Evaluation of the effectiveness of early or delayed treatment upon healing of mandibular fractures: a retrospective study. *Eur J Dent.* 2015;9:87–91.

38. Lucca M, Shastri K, McKenzie W, et al. Comparison of treatment outcomes associated with early versus late treatment of mandible fractures: a retrospective chart review and analysis. *J Oral Maxillofac Surg.* 2010;68:2484–2488.

39. Okoturo EM, Arotiba GT, Akinwande JA, et al. Miniplate osteosynthesis of mandibular fractures at the Lagos University Teaching Hospital. *Nig Q J Hosp Med.* 2008;18:45–49.

40. Peled M, Ardekian L, Abu-el-Naaj I, et al. Complications of miniplate osteosynthesis in the treatment of mandibular fractures. *J Craniomaxillofac Trauma.* 1997;3:14–17.

41. Tuovinen V, Nørholt SE, Sindet-Pedersen S, et al. A retrospective analysis of 279 patients with isolated mandibular fractures treated with titanium miniplates. *J Oral Maxillofac Surg.* 1994;52:931–935; discussion 935.

42. Nakamura S, Takenoshita Y, Oka M. Complications of miniplate osteosynthesis for mandibular fractures. *J Oral Maxillofac Surg.* 1994;52:233–238; discussion 238.

43. Frost DE, El-Attar A, Moos KF. Evaluation of metacarpal bone plates in the mandibular fracture. *Br J Oral Surg.* 1983;21:214–221.

44. Moher D, Liberati A, Tetzlaff J, et al.; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med.* 2009;6:e1000097.

45. Adell R, Eriksson B, Nylén O, et al. Delayed healing of fractures of the mandibular body. *Int J Oral Maxillofac Surg.* 1987;16:15–24.

46. Chole RA, Yee J. Antibiotic prophylaxis for facial fractures. A prospective, randomized clinical trial. *Arch Otolaryngol Head Neck Surg.* 1987;113:1055–1057.

47. Caddedu M, Farrokhyar F, Thoma A, et al.; Evidence-Based Surgery Working Group. Users' guide to the surgical literature: how to assess power and sample size. Laparoscopic vs open appendectomy. *Can J Surg.* 2008;51:476–482.