Titanium Internal Fixator Removal in Maxillofacial Surgery: Is It Necessary? A Systematic Review and Meta-Analysis

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Abstract: Titanium plates and screws are essential devices in maxillofacial surgery since late 1980s, but despite their wide use there is no consensus in titanium internal fixators removal after bone healing. A systematic literature review and meta-analysis were conducted on seventeen retrospective studies. Effect size and 95% confidence intervals were calculated for plate removal (per plate and per patient) and for removal causes (infection, pain, screws complications, exposition, palpability). Odds ratio, 95% confidence intervals, and χ^2 test were measured for sex, smoking, and implant site. Heterogeneity was evaluated with Cochran and Inconstancy test. Obtained data were used to design Forest and Funnel plots. The aim of the study is to identify and clarify reasons and risk factors for plates and screws removal. Infection is the most frequent reason; the habit of tobacco usage and implant site (mandibula) are the main risk factors. The administration of antibiotic prophylaxis is essential, and patients must quit smoking before and after surgery. In conclusion there is no scientific evidence supporting the removal of internal devices as mandatory step of the postoperative procedure.

Key Words: device removal, internal fixators removal, maxillofacial surgery, titanium plate and screws

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Titanium miniplates are worldwide used by maxillofacial surgeons in orthognathic and trauma surgery to improve stability in the fracture or osteotomy site by tight approximation and larger contact surface leading to osteosynthesis.[1] Nowadays the Cranio Maxillo Facial surgeon approach refers to Champy et al[2] technique described in 1978, who added modification to Michelet et al[3] method described in 1973. First plates were manufactured in vitallium (alloy formed by stainless steel and cobalt chrome),[4] whereas currently titanium is the main element, used since late 1980s, starting from the treatment of mid-face fractures and of mandibular ones.[5,6] The main advantages of titanium plates are modulus of elasticity closer to the cortical bone, capability of osseointegration, high tensile strength, nonmagnetic, no heat and electricity conduction, light weigh.[7,8] Titanium histocompatibility and high resistance to corrosion are widely demonstrated in vitro and in vivo, but doubts have been raised concerning the long-term behavior of permanent titanium implants, both local and systemic side effects.[9] Haug [10] reported no association between tumor formation, allergic reactions or toxicity related to pure titanium. Otherwise Katou et al[7] supported the relation between titanium and chronic inflammation followed by fibrous encapsulation. Increased titanium levels in lymph nodes are demonstrated due to local transport of the finest particles deposited mainly in the nearest lymph nodes and only later, in the more distant cervical lymph nodes; however no foreign body reaction or toxicity were observed.[11]

Despite their wide use, there is no consensus in titanium plates and screws removal. The Strasbourg Osteosynthesis Research Group (SORG) made the following recommendation in 1991: "A plate which is intended to assist the healing of bone becomes a non-functional implant once this role is completed. It may then be regarded as a foreign body. While there is no clear evidence to date that a plate causes actual harm, our knowledge remains incomplete. It is therefore not possible to state with certainty that an otherwise symptomless plate, left in situ, is harmless. The removal of a non-functioning plate is desirable provided that the procedure does not cause undue risk to the patient."[12] Many experts are in favor of internal devices removal,[2–4,13,14] but just as many advocate the removing surgery only for clinically evidence due to infection, pain or fracture.[10,15,16] From a literature review, due to these different points of view, plate removal rate varies from 2% in Posnik et al[17] to 55% in Borstlap et al.[18] Nowadays the scientific community is split in 2: on one side surgeons claim that removing the devices is a necessary step in the procedure because they lost their primary function once osteogenesis takes place, on the other side the removal is considered a nonindispensable step because of the lack of risk for the patient related to any sort of release of titanium particles from the plate or any alteration of the sensibility. Primary aim of this research is to acknowledge how many researchers have taken interest in the matter, how different CMF units deal with the problem and to evidence the gap between different expertise. The investigation is finalized to detect reasons and risk factors for titanium plates removal used in orthognathic and trauma surgeries and perform a systematic literature review and meta-analysis. This research was inspired by the systematic literature review and meta-analysis conducted by Gomez-Barrachina et al[19,20] in 2020.

MATERIALS AND METHODS

This literature systematic review followed the PRISMA guidelines (Preferred Reporting Items for Systematic Reviews and Meta-Analyses).[21]

PICO Question

To formulate a proper research, PICO method[22] was adopted. The Population detected was "patients who underwent maxillofacial surgery," the Intervention was "titanium plate and screws removal" and the Outcome "cause of removal, risk factor and benefits."

Study Selection Criteria

The inclusion criteria are: retrospective studies published between 2001 and 2021 which evaluated patients who underwent maxillofacial surgery (either trauma or orthognathic surgery) by using titanium plates and screws. The retrospective studies have more reliability ascribable to the rapid data collection from database, the immediate availability of patients to be included in the study and the application of inclusion criteria that could have been influenced and modified by different interpretation in a prospective study. No limit was set to the language or to the size of the sample. Exclusion criteria were papers that presented only the abstract. The time limit was set considering the beginning of the wide diffusion of titanium plates in the late 1990s.

Search Strategy and Screening of Articles

The research was conducted in PubMed by following these steps. Three keywords were identified: "Device removal," "Internal fixators," and "Maxillofacial surgery." Synonymous for the previous keywords were sought and added to the research: "Bone plate," "removal technique," and "removing." Subsequently MeSH terms were included: "Device Removal" [Mesh], "Internal Fixators" [Mesh], and "Orthognathic Surgical Procedures" [Mesh]. Boolean operators AND/OR were inserted. Eventually the final query was the following: ("Internal Fixators" [MeSH Terms] OR "bone plate* "[Text Word] AND ("Device Removal" [MeSH Terms] OR "removal technique* "[Text Word] OR "removing" [Text Word] AND "Orthognathic Surgical Procedures" [MeSH Terms].

Data Extraction

As shown in Supplemental Table 1, Supplemental Digital Content 1, http://links.lww.com/SCS/E527, the following variables were extracted from each article: author(s), year of publication, journal, typology of study, sample size, source of information (eg, hospital record and database, questionnaire proposed to patients), demographic information (age, sex), smoking, health conditions, surgery performed (trauma, Le Fort I, bilateral split sagittal osteotomies, etc.), drugs administrated, plates and screws used, risk factor identified, period between primary surgery and removal, percentage of removal (both in overall both related to patients variables).

Quality Evaluation

Adjust Newcastle-Ottawa Quality Assessment Scale[23] for case-control studies (2020) was applied to assess the quality of the cohort studies included in the systematic review. NOS is a "star-system" that evaluate each study in three categories: selection, comparability, and outcome. The highest score reachable is 9, score 7 to 9 indicates "high-quality", 4 to 6 "high risk of bias," and 0 to 3 "very high risk of bias."

Variables and Synthesis of the Results

Combined effect size (CES), 95% confidence intervals (95% CI), and SE were estimated for titanium plates and screws removal (per patient and per plate) and for the removing causes (infection, pain, screws complication, exposition, palpability). Odds ratio (OR) and 95% CI were calculated for the possible risk factor for the plates and screws removal: sex, smoking, and implant site. OR >1 indicates association, OR <1 indicates no association. OR is a ratio and therefore its sample distribution has a strong right skew. Consequently, the variance is estimated through the logarithmic transformation, according to Woolf's method. χ^2 test was applied to risk factors. The level of significance α was set at 0.05 for the 95% CI. SE, which indicates the variability and reliability of the proportion, denotes if the results are applicable to the general population. This explains why Forest plots for risk factors have logarithmic axes.

Statistical Analysis

95% CI were calculated for device removal and their reasons to compare each study size to the general population. Heterogeneity was considered using Cochran Test (Q test) and Inconsistency Test (I^2) . A P-value <0.1 was marked to consider Q test statistically significant. The setting of such low P-value is due to little power Cochrane Test to detect heterogeneity if the number of considered studies is limited. A percentage of 50% was settled for the same reason for I^2: a higher percentage indicated a considerable heterogeneity. The data were used to delineate the Forest Plot to compare the results and to distinguish which study had statistical significance and which not. Publication bias was estimated using Funnel Plot. The statistical analysis was performed using Microsoft Excel 16.50 and Meta-Essentials: Workbooks for meta-analysis.[24]

RESULTS

The selection processes was performed on PubMed using the inclusion previously described (PRISMA flow diagram, Fig. 1). Seventeen retrospective studies were included in our study. A 20 years period limit was analyzed from the least recent paper by Islamoglu et al[25] published in 2001 to the latest by Sukegawa et al[26] released in 2018. The studies involve patients from all over the world: Belgium (570 patients), Canada (135), Finland (153), Germany (162), Japan (240), Iran (142), Ireland (535), Italy (164), Oman (465), Sweden (323), Turkey (66), UK (1112), and USA (338); therefore, sample population quite different from an ethnical standpoint. The greatest sample size was analyzed by Mosbah et al[27] with 658 patients, while the smallest sample size was analyzed by Islamoglu et al[25] with 66 patients (total mean 259). All the articles are in English. The adjust Newcastle-Ottawa Scale Quality Assessment Scale was applied to evaluate quality as shown in Supplemental Table 2, Supplemental Digital Content 1, http://links.lww.com/SCS/E527[17,28,29]: got a total score of 7/10, indicating a good study quality[26,30–35]; got a score of 6/10, which means a sufficient quality[1,27,36]; got a score of 5/10, less than enough quality[25,37]; got a score of 4/10, an unsatisfactory score; eventually[15,38] got a score of 3/10, an insufficient quality.

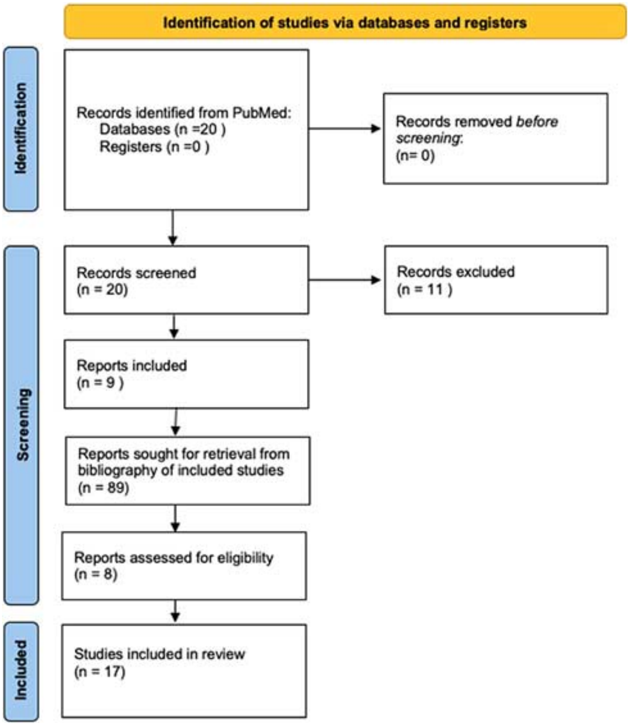

FIGURE 1. PRISMA flow diagram.

Quality Synthesis

A total number of 4405 patients was analyzed (mean 259, range: 66–658 among studies), 1182 female (mean 107, range: 14–363), and 1419 male (mean 129, range: 21–207). Four articles did not give information about patients sex.[27,30,37,38] Only 2 articles had a women-man ratio 1:1 or so are.[1,17] The mean age of included patients was 25.4 (range: 3–71). Eleven articles made explicit what kind of surgery was performed in the selected patients.[1,17,26–29,31,33–35,37] Smoker patients were included in 6 studies.[1,28,29,32,33,35] Four retrospective studies included in their inclusion criteria only trauma surgery,[25,30,36,38] 8 only orthognathic surgery,[17,26,28,29,31–33,35] 4 both operations.[1,15,27,34] Plate removal rate per patient was reported in all the studies, but plate removal per plate was calculated only in 12 articles.[1,15,25,26,28,31–36,38] The studies reported a wide variety of reasons for internal devices removal (rates referred to the total number of patients who underwent the implant removal): infection (303/764, 40%), irritation (66/764, 9%), removal from pediatric patients (58/764, 7%), patient request (54/764, 7%), pain (41/764, 5%), dehiscence (36/764, 4,7%), exposed plate (22/764, 3%), reconstruction surgery (18/764, 2%), screws complications (17/764, 2%), nonspecified reasons (15/764, 2%), palpability (15/764, 2%), temperature sensibility (6/764, 0.8%), dental implant (5/764, 0.65%), dental problems (5/764, 0.6%), foreign body reaction (4/764, 0.5%), detached plate (3/764, 0.4%), esthetics (3/764 0.4%), plate failure (3/764, 0.4%), sinusitis (3/764, 0.4%), prosthetic rehabilitation (3/764, 0.4%), swelling (1/764, 0.1%), plate breakage (1/764, 0.1%), and fobia (1/764, 0.1%). The data of Islamoglu and colleagues[25,31,34,38] were excluded from this study because they reported the rate removal referring to the plates and not to the patient or because they did not specify the complications that led to the secondary surgery. Follow up goes from 0.1 to 10.8 years. Time observation is between 1991 and 2018.

Quantitative Synthesis

Plate Removal

Random effect model was applied (Fig. 2A). A total of 765/4405 patients removed the intraoral devices. CES for plate removal per patient is 0.18 (95% CI: 0.13–0.23, ES: 0.02). Cochran and Inconstancy test results are $Q=286.74$, $P=0$, and $I^2=94.42\%$. Adjusting, CES = 0.14 (95% CI: 0.09–0.19, ES: 0.03), $Q=339.37$, $P=0$, and $I^2=94.11\%$. A total of 1364/8570 plates were removed. CES for plate removal per plate is 0.16 (95% CI: 0.09–0.23, ES: 0.03). Cochran and Inconstancy test results are $Q=895{,}75$, $P=0$, and $I^2=98.72\%$. Adjusting, CES = 0.13 (95% CI: 0.06–0.20, ES: 0.03), $Q=997.88$, $P=0$, and $I^2=98.70\%$.

Reasons for Plate Removing

Each study was carefully analyzed to identify reasons for plate removal. Random effect model was applied. 95% CI, Forest Plot, Funnel Plot, Cochran test and Inconsistency Test were calculated for each reason located as shown in Supplemental Table 3, Supplemental Digital Content 1, http://links.lww.com/SCS/E527. Twelve studies were used to evaluate infection in 2 studies the data were not adequate mathematically and have been excluded,[35,36] CES is 0.48 (95% CI: 0.32–0.64; ES: 0.07), $Q=194.37$, $P=0$, and $I^2=95.37\%$. Adjusting, CES = 0.48 (95% CI: 0.32–0.64, ES: 0.07), $Q=196.38$, $P=0$, and $I^2=95.42\%$. Seven articles provided details about pain as reason for plate removal: CES is 0.11 (95% CI: 0.06–0.16, ES: 0.02), $Q=9.01$, $P=0.173$, and $I^2=33.44\%$. Adjusting, 0.07 (95% CI: 0.02–0.13, ES: 0.01), $Q=23.74$, $P=0.005$, and $I^2=6209\%$.

Four articles supplied details about exposed plates removal: CES is 0.10 (95% CI: −0.08 to 0.27, ES: 0.02), $Q=12.72$, $P=0.005$, and $I^2=74.42\%$. Adjusting, 0.10 (95% CI: −0.08 to 0.27, ES: 0.05), $Q=12.72$, $P=0.005$, and $I^2=74.42\%$.

Screw related problems were presented in 5 studies: CES is 0.11 (95% CI: 0.01–0.2, ES: 0.04), $Q=9.98$, $P=0{,}041$, and $I^2=59.93\%$. Adjusting, CES = 0.09 (95% CI: 0.01–0.16, ES: 0.03), $Q=11.34$, $P=0.078$, and $I^2=47.11\%$.

Palpability was described in 5 studies: CES is 0.08 (95% CI: 0.01–0.16, ES: 0.03), $Q=4.75$, $P=0.314$, and $I^2=15.81\%$. Adjusting, CES = 0.07 (95% CI: −0.02 to 0.16, ES: 0.04), $Q=9.60$, $P=0.142$, and $I^2=37.51\%$.

Risk Factors

Statistical analysis was conduct for the following risk factors: sex, smoking, and implant site (Fig. 3A). Ten articles (2595 patients) gave data to evaluate odd ratio relating the risk to undergo plate removal associated to sex. CES is 1.16 (95% CI: 0.80–1.69); $Q=18.33$, $P=0.032$, and $I^2=50.89\%$. Adjusting, lnOR = 0.15 (95% CI: −0.23 to 0.52), ES(lnOR) = 0.17, $Q=18.33$, $P=0.032$, and $I^2=50.89\%$. Forest plot is represented in Figure 3B; Funnel plot in Figure 3C. Information about the habit of tobacco usage (718 patients) was extrapolated from 4 articles: CES is 2.04 (95% CI: 1.19–3.49), $Q=1.65$, $P=0.647$, and $I^2=0\%$. Adjusting, lnOR = 0.71 (95% CI: 0.18–1.25, ES (lnOR) = 0.17, $Q=1.65$, $P=0.647$, and $I^2=0\%$. Forest plot is represented in Figure 3D; Funnel plot in Figure 3E. Seven articles (3626 patients) were used to evaluate implant site as risk factor. CES is 2.84 (95% CI: 1.57–5.15), $Q=18.32$, $P=0.005$, and $I^2=67.25\%$. Adjusting, lnOR = 1.05 (95% CI: 0.45–1.64), ES(lnOR) = 0.24, $Q=18.32$, $P=0.005$, and $I^2=67.25\%$. Forest plot is represented in Figure 3F; Funnel plot in Figure 3G.

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	Removal per patient				Removal per plate			
Study name	Effect size	95% CI LL	95% CI UL	*ES*	*Effect size*	*95% CI LL*	*95% CI UP*	*ES*
Widar	0,15	0,11	0,19	0,02	//	//	//	//
Little	0,10	0,06	0,14	0,02	0,03	0,02	0,04	0,006
Posnick	0,02	0,00	0,04	0,01	//	//	//	//
Falter	0,28	0,12	0,44	0,08	0,19	0,19	0,20	0,007
Sukegawa	0,30	0,24	0,36	0,03	0,33	0,33	0,36	0,017
Rauso	0,32	0,24	0,40	0,04	0,16	0,16	0,19	0,014
Kämmerer	0,28	0,20	0,36	0,04	0,31	0,31	0,39	0,04
Kuhlefelt	0,19	0,13	0,25	0,03	0,18	0,18	0,22	0,022
Haraji	0,11	0,05	0,17	0,03	//	//	//	//
Moshab	0,10	0,08	0,12	0,01	//	//	//	//
Theodossy	0,20	0,10	0,30	0,05	0,16	0,16	0,22	0,03
O'Connell	0,06	0,04	0,08	0,01	0,03	0,03	0,04	0,005
Bakathir	0,23	0,19	0,27	0,02	//	//	//	//
Bhatt	0,16	0,10	0,22	0,03	0,17	0,17	0,21	0,021
Nagase	0,33	0,25	0,41	0,04	0,27	0,27	0,30	0,015
Islamogou	0,27	0,15	0,39	0,06	0,07	0,07	0,10	0,015
Murthy	0,08	0,02	0,14	0,03	0,04	0,04	0,07	0,015
CES= 0,18; Adj. CES=0,14; 95% CI 0,13 – 0,23, Adj. 95% CI 0,09 – 0,19; ES=0,02, Adj. ES=0,03; Q=286,74, Adj. Q=339,37; p=0 (both), I^2=96,42%, Adj. I^2=97,11%					CES= 0,16; Adj. CES=0,13; 95% CI 0,09 – 0,23, Adj. 95% CI 0,06 – 0,20; ES=0,03 (both); Q=895,75, Adj. Q=997,88; p=0 (both), I^2=98,72%, Adj. I^2=98,70%			

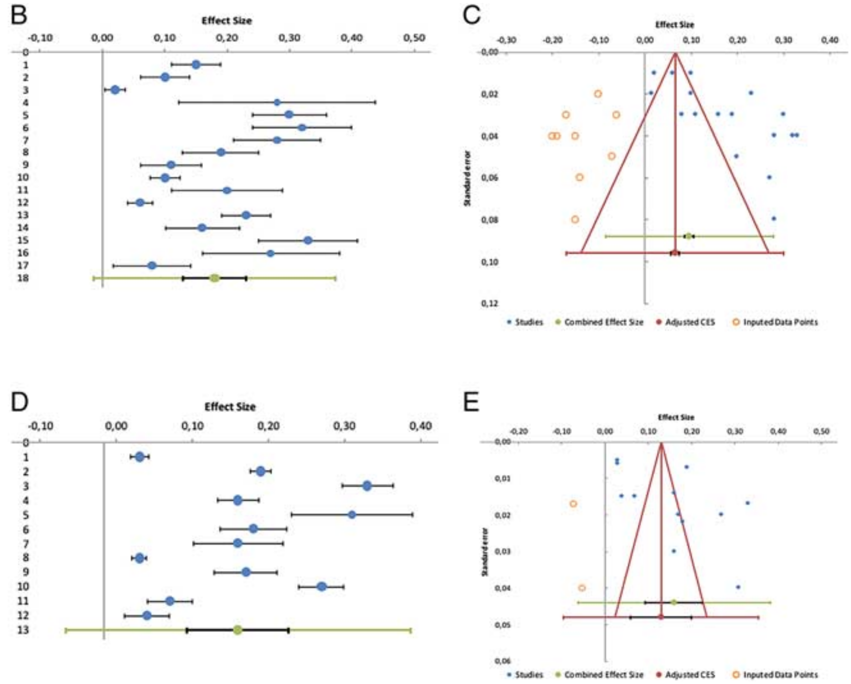

FIGURE 2. Plate removal. A, Effect size,95% confidence intervals and standard error for plate removal per patient and per plate; combined effect size, 95% confidence interval (95% CI), ES, *Q*, *P*, I^2. B, Forest plot for plate removal per patient. C, Funnel plot for plate removal per patient. D, Forest for plate removal per plate. E, Funnel plot for plate removal per plate. UL is upper limit, CES indicates is combined effect size; I^2 is inconstancy test; LL, lower limit; *Q* is Cochran test.

DISCUSSION

The aim of the study is to identify and clarify reasons and risk factors for plates and screws removal. Due to the absence of clear guidelines, the decision is up to the individual surgeon and it has implications in terms of surgery costs, surgeons' employment, operating rooms, recovery, administration of drugs, and complications. Before data extraction, NOS scale was applied as shown in Supplemental Table 2, Supplemental Digital Content 1, http://links.lww.com/SCS/E527. As it is noticeable, only 3 studies could be considered of high quality, whilst the others have an significant risk of bias that could distort the analysis and results of meta-analysis.

Figure 2A shows the results referred to plate removal among the studies per patient and per plate. A total of 4405 patients were included and 764 underwent plate and screw removal. The removal incidence varies among the studies, from 2% in Posnick et al[17] to 33% in Nagase et al.[38] Total number of implanted plates was 8579 and 1363 plates were removed. Little et al[28] and O'Connell et al[34] have the lowest incidence (3%), Sukegawa et al[26] the greatest (33%). Different calculations were taken for the internal devices removal per patient and per plate, due to many cases in which it was decided to remove all the plates inserted in primary surgery and not only the one or the ones which had determined the symptoms. This suggests that data obtained from the two measurements are different and that effect size for plate removal per plate is overestimated. The conclusion outlined from these results is that the plates removal, both for patient and for plate, has a low incidence, respectively, 14% and 13%. Although different criteria have been applied, there is no scientific evidence indicating that plates and screws removal is an inevitable step in the treatment of the patients who undergo maxillofacial surgery.

Surgery in a field exposed to mechanical forces is not without complications such as infection and pain. As shown in Supplemental Table 3, Supplemental Digital Content 1, http://links.lww.com/SCS/E527, 10 articles give specific data about infection as main reason for titanium plates removal.[1,26] The heterogeneity among the results lies in the fact that the event infection is not defined precisely. For instance, Widar et al[29] report that patients with symptomatology were treated with antibiotics and osteosynthesis devices removal, without performing a bacterial sampling . In addition, they state the impossibility to diversify between inflammation and infection. Some authors consider infection and wound dehiscence as a single occurrence,[27,30] some define infection as "the one due to wound dehiscence's and exposure of the plate in the oral cavity"[37] and others define infection as inflammation.[1] Falter et al[31] and Sukegawa et al[26] say that an "infectious reaction" was considered to be present whenever wound dehiscence over the plates, granulation tissue at the plate site or an intraoral fistula with pus at the plate site was observed, although no cultures were gained. A swelling and redness at the osteosynthesis site were considered "inflammation" needing removal; the condition was indicated as "clinical irritation." Many authors do not define what criteria were set to identify infection or inflammatory.[25,28,39] Interestingly, Kämmerer et al[32] refer a significant correlation between increasing defect length and complications: resection sizes were calculated by the authors in "tooth unit" (TUN) and it was observed that plates covering a defect <5 TUN had better prognosis while large defects, 11 to 16 TUN, had more dehiscence. The authors think that larger plates are harder to adapt all 3 dimensions creating larger dead space making dehiscence more likely.

The second most common reason for plate removal is pain, as shown in Supplemental Table 3, Supplemental Digital Content 1, http://links.lww.com/SCS/E527 . Bhatt et al[15] have the highest incidence (20%), Little et al[28] the lowest (5%). As for infection, pain has not a standard definition. None of the studies

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SEX	OR	ES	LL	UL	p-value	χ^2	Significance Level (1dg)
Widar	1,83	0,3	0,95	3,52	0,065	3,38	10%
Little	1,47	0,49	0,54	3,99	0,445	0,58	50%
Falter	1,82	0,19	1,21	2,73	0,003	8,57	1%
Sukegawa	0,69	0,3	0,38	1,25	0,215	1,53	25%
Rauso	0,62	0,34	0,32	1,21	0,159	1,96	25%
Kämmerer	0,83	0,36	0,40	1,74	0,622	0,24	75%
Kuhlefelt	2,59	0,46	1,02	6,55	0,038	4,29	5%
Theodossy	1,09	0,64	0,30	3,90	0,898	0,02	90%
O'Connell	0,6	0,54	0,20	1,76	0,347	0,88	50%
Islamogou	1,46	0,63	0,41	5,20	0,548	0,36	75%
CES=1,16, 95% CI 0,80 – 1,69, Q=18,33, p=0,032, I²=50,98%. Adj: logOR=0,15, ES(logOR)=0,17, 95% CI -0,23 – 0,53, Q=18,33, p=0,032, I²=50,89%.							

SMOKE	OR	ES	UL	IL	p-value	χ^2	Significance Level (1dg)
Widar	2,85	0,72	1,25	6,49	0,009	6,75	1%
Kämmerer	1,37	0,4	0,62	3,03	0,425	0,63	50%
Kuhlefelt	2,19	0,4	0,90	5,36	0,057	3,61	10%
Theodossy	2,19	0,63	0,62	7,72	0,208	1,58	25%
CES=2,04, 95% CI 1,19 – 3,49, Q=1,65, p=0,647, I²=0%. Adj: logOR=0,71, ES(logOR)=0,17, 95% CI 0,18 – 1,25, Q=1,65, p=0,647, I²=0%.							

SITE	OR	ES	UL	IL	p-value	χ^2	Significance Level (1dg)
Little	3,78	0,4	1,63	8,75	0,009	11,1	1%
Sukegawa	4,83	0,2	3,16	7,39	0	58,3	1%
Falter	1,07	0,3	0,55	2,06	0,843	0,04	90%
Rauso	3,05	0,21	1,92	4,84	0	24,1	1%
Moshab	2,18	0,3	1,21	3,91	0,007	7,09	1%
O'Connell	2,27	0,6	0,67	7,65	0,358	0,84	90%
Islamogou	14,5	1,04	1,84	114,9	0,009	11,1	1%
CES=2,84, 95% CI 1,57 – 5,15, Q=18,32, p=0,005, I²=67,25%. Adj: logOR=1,05, ES(logOR)=0,24, 95% CI -0,45 – 1,64, Q=18,32, p=0,005, I²=67,25%.							

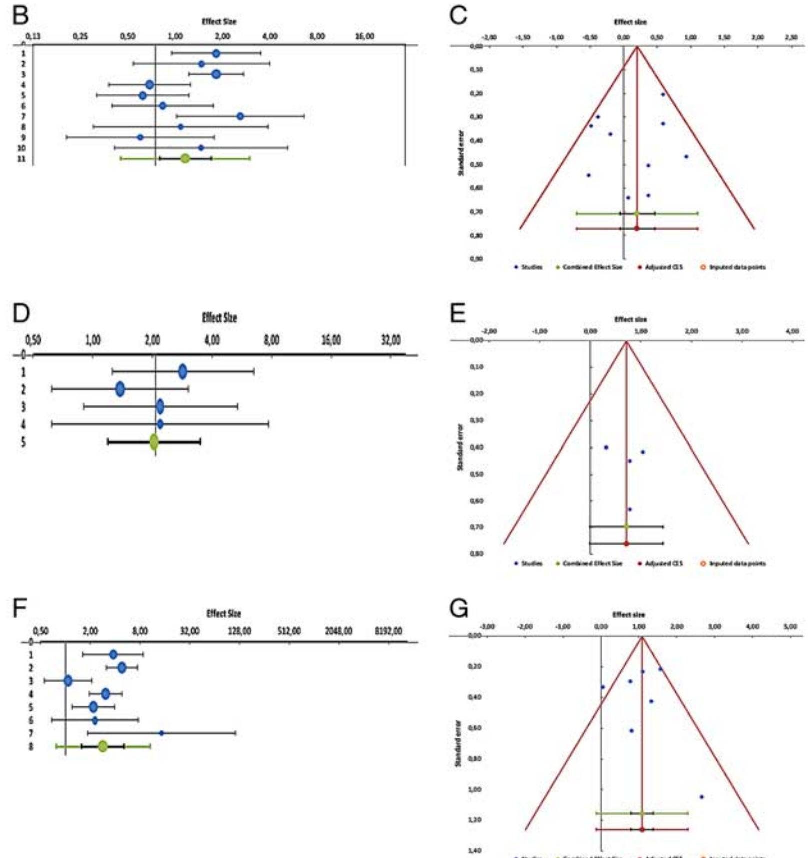

FIGURE 3. Risk factors. Table A is odds ratio (OR), SE, 95% confidence intervals, *P*-value level of significance. Combined effect size (CES), 95% confidence interval (95% CI), *Q*, *P*-value, and I^2. B, Forest plot for smoke. C, Funnel plot for smoke. D, Forest plot for sex. E. Funnel plot for smoke. F, Forest plot for osteotomy site. G, Funnel plot for osteotomy site.

define which criteria were applied to assume particular symptoms as pain. It is interesting to note that some authors consider pain associated to discomfort and thermal sensibility.[38] Alpert et al[4] were the first to considerate sensibility to temperature variance as reason for plate removal, instead for Nagase et al[38] the change in indoor/outdoor temperature is more likely to cause the event in some patient. Plate insertion site is suggested to be related to discomfort: it seems that there is a decreasing incidence of discomfort from superior to inferior along the facial skeleton. The reason might be the presence of soft tissue coverage in the area and the proximity to the frontalis muscle.[38]

Sex, smoking and implant site were evaluated as risk factors. CES for sex is OR = 1.16, that indicates a weak association. Analyzing each single study, it is noticeable that in each work the association between sex and plate removal is always irrelevant (Fig. 3A). Kuhlefelt et al[33] study is the only one that demonstrates a moderate association, with OR = 2.59, while other authors determine weak association,[25,28,29,31,35] and many established no association with OR < 1.[1,26,34] Calculating the chi-square test,[31,33] resulted to be statistically significant, respectively, at 1% and 5%. Due to statistics, sex is not a risk factor, although in some cases women seem to be likely to report discomfort than men. This consideration has not been proven scientifically. CES for smoking is OR = 2.04 and indicates a moderate association. Each study reports an OR > 2, except for one study, whose OR is equal to 1.37 (Fig. 3A).[32] Applying the χ^2 test, Widar et al[29] is the only study which is statistically significant at 1%. The rest of results have lower significance level (< 95%): although OR is > 1, meaning an association between smoking and the secondary surgery, the validity of the data is confirmed in the 50% of the cases,[32] 90%[33] and 75%.[35] The statistics make tobacco usage to be consider a risk factor, though more evidence is necessary. In addition to the well-known consequences, smoking influences the wound healing.[40] The mainstream smoke is rich of reactive oxygen species and reactive nitrogen species, which are able to cause cellular damage and/or death via oxidative stress processes.[41] Nicotine increases platelet aggregation causing the reduction of microvascular perfusion, decreases microvascular prostacyclin level and inhibits fibroblasts, red blood cells and macrophages function. Fibroblasts and mesenchymal stem cells produce fundamental cytokines for the initial inflammatory response and the formation of granulation tissue. In 2004 Wong et al[42] analyzed fibroblast behavior to a low-moderate exposition to smoke: it was discovered that moderate levels of nicotine, though not sufficient to kill cells, could affect ATP production by primary fibroblast, stimulating the production and activation of stress response protein. These survival factors increased cell life, blocking apoptosis. This could lead to an accumulation of fibroblast and a build-up connective tissue, resulting in excessive over-healing, fibrosis and scar. Smoking impacts also on bone healing[41]: it reduces blood supply to the injury site, decreases antioxidants that contrast nicotine effect on endothelial nitric oxidase synthase and raises reactive oxygen species levels. High dose of nicotine is toxic for osteoblast proliferation, but, in smaller ones, it actually stimulates the growth of these cells.[43]

This paradox may be explained because of the stress response protein that led to an excessive osteoblasts' proliferation, as previously described. Immune system is impacted by smoking effects as well: surgical site infection occurred more often in smoker patients due to inflammatory response dysregulation.[39,44–47] The plates implant site appears to be a considerable risk factor for their subsequent removal and the mandible is the more susceptible. In order to simplify the statistical analysis it is important to underline that Le Fort surgeries were considered as maxilla, while the bilateral split sagittal osteotomies were categorized as mandible. Genioplasty was not taken in account for the present study. CES is OR = 2.84 (Fig. 3A), providing a moderate association between mandible and removal. A part for Falter et al[31] and O'Connell et al,[34] each χ^2 test study is evaluated valid at 1% significance level. According to Rauso et al,[1] complications are higher in the mandible due to vigorous and traumatic forces and collection of food particles, while the maxilla is less affected by the mobility of facial skeleton. Little et al[28] suppose that the difference in maxilla and mandible plate removal incidences lies in a more consistent blood supply of the maxilla and in greater forces exposition of the mandible. O'Connell et al[34] explain that the higher incidence of plate removal from mandible is correlated to higher frequency of trauma; the authors report the greatest frequency of complications in the angle fractures compared to other mandibular fractures, probably due to biomechanical forces that occur in the angle region during chewing. In contrast, Moshab et al[27] report a greater susceptibility to removal from the parasymphyseal region. Widar et al[29] state jaw surgery to be a strong risk factor for plates removal, especially if associated with infection, in line with previous reported results. The anatomical features with flexion and movement within the mandibular body during function might be acceptable as explanation, although not scientifically proven. The authors report a lower number of postoperative infections and subsequent less plate removal in maxillary surgery, due to improved vascularization, less muscular tension and trauma during bone drilling as due to thinner cortical bone in the maxilla. The same explanation is provided by Kuhlefelt et al[33]: extensive movement and rotation of the lower jaw increase stress on miniplates, that could arise from the forceful soft tissue stretching in general and to suprahyoid and infrahyoid muscles traction. On the contrary, Theodossy et al[35] do not deem the direction of mandibular movements as risk factor. Alpha et al[48–51] show that fewer disturbance of healing occur when the fixation plates are closer to the inferior border of the mandible.[48] Better vascularization and protection from the intraoral microbiological environment due to longer distance from the mucosal incision might be determining factors for the lower border plates success . Additional plates inserted on each side of the mandible limit the space, decrease the distance to the area of incision and support the "infection theory." According to Murthy et al[36] in trauma surgery the stability is considered the best agent against infection and for the mandible the achievement of stability is possible only with rigid fixation. The authors assume that angular region is the more inclined to undergo plate removal due to large forces are developed in this area that might overcome the rigidity of the plate.[1,30]

Some authors consider that another risk factor could be the operating timing in primary surgeries. Widar et al[29] calculated a mean operating timing of 190 minutes (range: 57–460); it was not classified as risk factor, but applying a Poisson regression, the authors reveal a trend towards higher risk for plate removal in relation to operating timing if surgery lasts <100 or >200 minutes. Shorter operating time could result in inaccurate fixation, longer operating time may be related to increased number of plates installed and consequentially a prolonged exposure of the osteotomy site to the oral environment and microbiome.[29,35] The authors have different opinion about age as possible risk factor. Patients mean age is 25.4 (range: 3–71), but the sample is not representative for the general population, considering the higher incidence of trauma in young people. Little et al[28] claim older people are more at risk to undergo plates removal because osteotomies tend to have more often complications with advancing age. Bakathir et al[30] report most patients who require plate removal being under 30 years old, in contrast with Moshab et al[27] study, which reported a higher incidence of plate removal in patients above 30 years old. An increased incidence of plate removal over the age of 30 in orthognathic patients was reported due to increased periosteal stripping and the lower periosteal blood supply with advancing age.[52,53] Moreover, the changes in bone density with aging could explain the higher incidence of plate removal in patients above 30 years old.[35] Aging may determinate complications in patients due to the reduction of immune defenses, the changes in the bacterial flora in the oral cavity and for the thinning and loss of hydration of the mucosa that make the subject more prone to discomfort. Nevertheless, it might not be considered as risk factor because of the impossibility to calculate the Odd ratio due to insufficient data. As reported in the introduction, this study was inspired by Gomez-Barrachina et al[20] work. The study differs for several reasons: clinical trials, cohort and case-control studies were included, no time period limitation was set and at least 25 patients-sample size were considered. Consequentially, 6 cohort and prospective studies were considered in authors' evaluation and statistical analysis, thus distorting the results. Moreover, the authors took into consideration only orthognathic surgeries and excluded facial fractures. With no time period limit, 2 studies dated 1998 and 1999 were included, making the use of titanium plates and screws not guaranteed. Plate removal has low incidence and infection is the main reason for plate removal, both outcomes demonstrated in this study. Gòmez-Baracchina et al[20] defined as risk factors sex and smoking, and not the osteotomy site: this conclusion is in contrast with the previous results, specifically the consideration of sex and osteotomy site as risk factor. The previous statistical analysis showed that sex has a weak association with devices removal (OR: 1.16). Regarding implant site, the exclusion of facial fractures influenced the OR calculation and distorted the result in Gòmez-Barrachina et al[20] study.

CONCLUSION

Supporting evidence, no indication for plates removal is suggested. Titanium plates and screws should remain in place unless they become symptomatic. Choosing to reoperate the patient is a decision that is not scientifically supported and could led to complications. Infection is the main reason that makes surgeons decide to reoperate. There is no clear definition of infection and therefore this result is certainly over or underestimated, given that many authors have considered infection and inflammation the same. Antibiotic prophylaxis plays an important role in reducing the incidence of infection. The strongest risk factor identified is implant site: the worse outcome is expected in mandibular surgery, while the upper jaw surgery is likely to be without complications due to the better vascularization and the least deposition of food debris and saliva. Smoking is another risk factor, while sex is not. Clearly nothing can be done about the treatment on the osteotomy site as it depends on the type of the surgery, whether orthognathic or trauma. On the other side, it is essential to take care about smoking, advising the patients not to smoke at least 6-8 weeks before and after surgery to promote wound healing.

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