Immediate implant placement in non-infected sockets versus infected sockets: a systematic review and meta-analysis

Master’s Thesis

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5th Year, group 13

Imme.
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Immediate implant placement in non-infected sockets versus infected sockets: a systematic review and meta-analysis

Master’s Thesis
# EVALUATION TABLE OF THE MASTER’S THESIS
## OF THE TYPE OF SYSTEMIC REVIEW OF SCIENTIFIC LITERATURE

**Evaluation:** ........................................................................................................................................................................

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| No. | MT parts | MT evaluation aspects                                                                                                           | Compliance with MT requirements and evaluation | 
|-----|----------|---------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------|
|     |          |                                                                                                                                | Yes   | Partially | No   |
| 1   | Summary  | Is summary informative and in compliance with the thesis content and requirements?                                               | 0.3   | 0.1       | 0    |
|     | (0.5 point) |                                                                                                                               |                                                |
| 2   |          | Are keywords in compliance with the thesis essence?                                                                             | 0.2   | 0.1       | 0    |
| 3   | Introduction, aim and tasks (1 point)                                                                                           | Are the novelty, relevance and significance of the work justified in the introduction of the thesis? | 0.4   | 0.2       | 0    |
|     |          | Are the problem, hypothesis, aim and tasks formed clearly and properly?                                                          | 0.4   | 0.2       | 0    |
| 4   |          | Are the aim and tasks interrelated?                                                                                             | 0.2   | 0.1       | 0    |
| 5   |          | Is the electronic search strategy described in such a way that it could be repeated (year of search, the last search day; keywords and their combinations; number of found and selected articles according to the combinations of keywords)? | 0.4   | 0.1       | 0    |
| 6   |          | Is the protocol of systemic review present?                                                                                     | 0.6   | 0.3       | 0    |
| 7   |          | Were the eligibility criteria of articles for the selected protocol determined (e.g., year, language, publication condition, etc.) | 0.4   | 0.2       | 0    |
| 8   |          | Are all the information sources (databases with dates of coverage, contact with study authors to identify additional studies) described and is the last search day indicated? | 0.2   | 0.1       | 0    |
| 9   | Selection criteria of the studies, search methods and strategy (3.4 points)                                                   | Is the selection process of studies (screening, eligibility, included in systemic review or, if applicable, included in the meta-analysis) described? | 0.4   | 0.2       | 0    |
| 10  |          |                                                                                                                                |                                                |
| 11  |          | Is the data extraction method from the articles (types of investigations, participants, interventions, analysed factors, indexes) described? | 0.4   | 0.2       | 0    |
| 12  |          | Are all the variables (for which data were sought and any assumptions and simplifications made) listed and defined?            | 0.4   | 0.2       | 0    |
| 13  |          | Are the methods, which were used to evaluate the risk of bias of individual studies and how this                                | 0.2   | 0.1       | 0    |
|   |   | Information is to be used in data synthesis, described? |
|---|---|---|
| 14 |   | Were the principal summary measures (risk ratio, difference in means) stated? | 0.4 | 0.2 | 0 |
| 15 |   | Is the number of studies screened: included upon assessment for eligibility and excluded upon giving the reasons in each stage of exclusion presented? | 0.6 | 0.3 | 0 |
| 16 | Systemization and analysis of data (2.2 points) | Are the characteristics of studies presented in the included articles, according to which the data were extracted (e.g., study size, follow-up period, type of respondents) presented? | 0.6 | 0.3 | 0 |
| 17 |   | Are the evaluations of beneficial or harmful outcomes for each study presented? (a) simple summary data for each intervention group; b) effect estimates and confidence intervals) | 0.4 | 0.2 | 0 |
| 18 |   | Are the extracted and systemized data from studies presented in the tables according to individual tasks? | 0.6 | 0.3 | 0 |
| 19 |   | Are the main findings summarized and is their relevance indicated? | 0.4 | 0.2 | 0 |
| 20 | Discussion (1.4 points) | Are the limitations of the performed systemic review discussed? | 0.4 | 0.2 | 0 |
| 21 |   | Does author present the interpretation of the results? | 0.4 | 0.2 | 0 |
| 22 | Conclusions (0.5 points) | Do the conclusions reflect the topic, aim and tasks of the Master’s thesis? | 0.2 | 0.1 | 0 |
| 23 |   | Are the conclusions based on the analysed material? | 0.2 | 0.1 | 0 |
| 24 |   | Are the conclusions clear and laconic? | 0.1 | 0.1 | 0 |
| 25 | References (1 point) | Is the references list formed according to the requirements? | 0.4 | 0.2 | 0 |
| 26 |   | Are the links of the references to the text correct? | 0.2 | 0.1 | 0 |
| 27 |   | Are the literature sources cited correctly and precisely? | 0.2 | 0.1 | 0 |
| 28 |   | Is the scientific level of references suitable for Master’s thesis? | 0.2 | 0.1 | 0 |
| 29 |   | Do the cited sources not older than 10 years old form at least 70% of sources, and the not older than 5 years – at least 40%? | 0.2 | 0.1 | 0 |

**Additional sections, which may increase the collected number of points**

|   |   |   |
|---|---|---|
| 29 | Annexes | Do the presented annexes help to understand the analysed topic? | +0.2 | +0.1 | 0 |
| 30 | Practical recommendations | Are the practical recommendations suggested and are they related to the received results? | +0.4 | +0.2 | 0 |
| 31 |   | Were additional methods of data analysis and their results used and described (sensitivity analyses, meta-regression)? | +1 | +0.5 | 0 |
|   | Was meta-analysis applied? Are the selected statistical methods indicated? Are the results of each meta-analysis presented? |   |   |   |
|---|------------------------------------------------------------------------------------------------------------------|---|---|---|
| 32 |                                                                                                                  | +2 | +1 | 0 |

**General requirements, non-compliance with which reduce the number of points**

|   | Is the thesis volume sufficient (excluding annexes)? |   |   |   |
|---|------------------------------------------------------|---|---|---|
| 33 |                                                                 |   |   |   |

|   | Is the thesis volume increased artificially? | -2 points | -1 point |
|---|--------------------------------------------|-----------|----------|
| 34 |                                           |           |          |

|   | Does the thesis structure satisfy the requirements of Master’s thesis? | -1 point | -2 points |
|---|-----------------------------------------------------------------------|----------|-----------|
| 35 |                                                                       |           |           |

|   | Is the thesis written in correct language, scientifically, logically and laconically? | -0.5 point | -1 points |
|---|--------------------------------------------------------------------------------------|------------|-----------|
| 36 |                                                                                     |           |           |

|   | Are there any grammatical, style or computer literacy-related mistakes? | -2 points | -1 points |
|---|------------------------------------------------------------------------|-----------|----------|
| 37 |                                                                       |           |           |

|   | Is text consistent, integral, and are the volumes of its structural parts balanced? | -0.2 point | -0.5 points |
|---|--------------------------------------------------------------------------------------|------------|------------|
| 38 |                                                                                     |           |           |

|   | Amount of plagiarism in the thesis. | >20% (not evaluated) |
|---|-----------------------------------|----------------------|
| 39 |                                   |                      |

|   | Is the content (names of sections and sub-sections and enumeration of pages) in compliance with the thesis structure and aims? | -0.2 point | -0.5 points |
|---|-----------------------------------------------------------------------------------------------------------------|-----------|------------|
| 40 |                                                                                                                |           |           |

|   | Are the names of the thesis parts in compliance with the text? Are the titles of sections and sub-sections distinguished logically and correctly? | -0.2 point | -0.5 points |
|---|--------------------------------------------------------------------------------------------------------------------------|-----------|------------|
| 41 |                                                                                                                           |           |           |

|   | Are there explanations of the key terms and abbreviations (if needed)? | -0.2 point | -0.5 points |
|---|------------------------------------------------------------------------|-----------|------------|
| 42 |                                                                        |           |           |

|   | Is the quality of the thesis typography (quality of printing, visual aids, binding) good? | -0.2 point | -0.5 points |
|---|-----------------------------------------------------------------------------------------|-----------|------------|
| 43 |                                                                                         |           |           |

*In total (maximum 10 points):*

*Remark: the amount of collected points may exceed 10 points.*

Reviewer's comments:

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Reviewer's name and surname ___________________________ Reviewer's signature ___________________________
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1. Abstract

Aim
The aim of this study is to compare immediate implant placement in infected extraction sockets with non-infected extraction sockets in terms of implant survival (primary outcome) and secondary outcomes including marginal bone level changes (MBL), marginal gingival level changes (MGL), probing depth (PD), width of keratinized gingiva (WKG) and modified bleeding index (mBI).

Materials and methods
An electronic search was conducted in PubMed, ScienceDirect, ISI Web of Knowledge and Google Scholar between 1 January 2010 and 5 February 2020. All retrospective and prospective studies evaluating implant survival rate, MBL, MGL, mBI, PD and WKG were included for a qualitative and quantitative analysis.

Results
The present study included nine articles from which three were retrospective cohort studies and six were prospective cohort studies. In total, a pool of 1246 patients and 2281 sockets were analyzed in this study. A total of 933 immediate implants were placed in infected sites and 1348 in non-infected sites. Compared with the non-infected group, the infected group showed no significant differences in implant survival rates (risk ratio (RR)= 0.99; 95% confidence interval (CI)= 0.98 to 1.00; \( P= 0.08 \)). Additionally, no significant statistical differences were found in MBL (mean difference (MD)= -0.03; 95% CI= -0.10 to 0.04; \( P= 0.41 \)), MGL (MD= -0.07; 95% CI= -0.17 to 0.04; \( P= 0.23 \)), PD (MD= 0.06; 95% CI= -0.24 to 0.36; \( P= 0.70 \)), mBI (MD= -0.00; 95% CI= -0.09 to 0.09; \( P= 0.97 \)) and slight but significant changes were seen in WKG (MD= 0.25; 95% CI= -0.30 to 0.80; \( P= 0.38 \)) between the groups at the latest follow-up.

Conclusion
The conducted meta-analysis suggests that there is no significant difference in survival rates between infected sockets and non-infected sockets. All of the secondary outcome variables showed equal favorable results, except for WKG, which slightly but significantly favored the non-infected group.

Keywords: dental implant; immediate implant; extraction socket; fresh-socket; infection
2. Introduction

Currently, the treatment of choice to replace missing teeth has been implant supported dental rehabilitation due to its success rate and good long-term prognosis [1]. The first endosteal titanium implant was placed successfully by Brånemark in 1965 [2]. During the 1980s Brånemark introduced the original protocol for implant therapy and the recommendation included post-extraction healing time of 5-6 months before the implant was placed into the alveolar ridge [1,2]. The conventional protocol was established on the belief that only complete hard and soft tissue healing would guarantee a favorable osseointegration [3]. The immediate implant placement in fresh-socket was proposed by Schulte and Heimke [4] in 1976 and in the year 1989 Lazzara placed the first immediate implants after tooth extraction [2]. Due to the modern implantology and its findings of new designs and surfaces, it is now possible to modify the classical protocol that Brånemark introduced decades ago [5]. As of current, there are four different methods regarding the placement of implants into edentulous sites: a) immediate implant placement, when the implant is placed directly after the extraction; b) early implant placement, the implant is placed 1-2 months after the extraction; c) delayed implant placement, the implant is placed 3-4 months after the extraction; and d) late implant placement, when the implant is placed more than 4 months after the tooth extraction [6].

Immediate implant placement in fresh-socket is a protocol that has received a lot of attention and is now considered a common treatment step with predictable and successful results [2,7,8]. Immediate post-extraction implant placement offers advantages such as: a) reduced number of surgical interventions and shortening of the treatment procedure, ultimately leading to an increased patient satisfaction; b) bone preservation at the extraction site; c) ideal implant orientation; and d) optimal soft tissue esthetics due to the preservation of soft tissue envelope [1-6,8-11]. However, immediate implant placement does not always provide optimal clinical outcomes. Preclinical studies and human studies documented suggests that this surgical protocol may not always preserve the buccal bone crest, which may impair the esthetical outcome due to soft tissue recessions. To improve the esthetical outcome and to prevent the dimensional changes of the alveolar bone, numerous surgical protocols have been suggested: a) flapless technique; b) use of bone grafts; c) use of connective tissue grafts; d) provisional restorations; e) highlighting the importance of buccal bone plate thickness; and f) importance of alveolar bone thickness [1,12]. A recent clinical trial shows that using a bone replacement graft between the implant and the buccal bone plate notably improves the preservation of the bone after immediate implant placement [12].
A non-infected extraction socket has great benefit to the survival rate of immediate implant placement. However, in practice, teeth extractions are largely due to presence of chronic pathology that later leads to endodontic or periodontal apical lesions [13,14]. While immediate implant placement in infected sockets has been seen as a contraindication in the past, several recent studies have shown promising results for implants placed in sockets exhibiting apical pathosis [8,13,14].

The aim of this systematic review was to evaluate if immediate implant placement in infected extraction sockets can be considered as successful in comparison to non-infected sockets. The objectives of this present study are:

- Search for clinical data concerning immediate implant placement in non-infected extraction sockets and infected sockets.
- Evaluate the effectiveness of both protocols by comparing the implant survival rate, probing depth (PD), marginal bone level (MBL), marginal gingiva level (MGL), modified bleeding index (mBI) and width of keratinized gingiva (WKG).

### 3. Material and methods

#### 3.1. Protocol

The reporting of this systematic review was conducted by following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [15].

#### 3.2. Focus question

The following focus question was framed according to the problem, intervention, comparison and outcome (PICO) process (table 1): What is the success rate of immediate implant placement in patients with infected sockets versus non-infected sockets with the evaluation of survival rate, PD, MBL, MGL, mBI and WKG?

| Definition        | Description                                                                 |
|-------------------|-----------------------------------------------------------------------------|
| **Patient**       | Patients with infected sockets                                              |
| **Intervention**  | Immediate implant placement                                                 |
| **Comparison**    | A control group with non-infected sockets                                   |
| **Outcome**       | Implant success by evaluating the: a) survival rate; b) MBL; c) MGL; d) mBI; e) PD; and f) WKG. |
| **Focus question**| What is the success rate of immediate implant placement in patients with infected extraction sockets versus non-infected sockets with the evaluation of survival rate, PD, MBL, MGL, mBI and WKG? |
3.3. Information sources

An electronic search for articles in English language was performed using PubMed, ISI Web of Science, ScienceDirect and Google Scholar from 1 January 2010 to 5 February 2020.

3.4. Literature search strategy

The literature search strategy was done by following the PRISMA guidelines using PubMed, ISI Web of Science, ScienceDirect electronic databases and Google Scholar. The search was conducted using a combination of different search terms (see table 2).

Table 2. Keywords used to conduct the literature search.

| Concept          | Keywords                                                      |
|------------------|--------------------------------------------------------------|
| 1st keyword terms | "Infected socket*" OR "Periapical lesion*" OR "Endodontic lesion*" OR "Periodontal lesion*" OR "Radicular lesion*" OR "Periradicular lesion*" OR "Apical lesion*" OR "Apical pathology" OR "Periradicular pathology" OR "Radicular pathology" OR "Endodontic pathology" OR "Periapical pathology" OR "Apical pathological feature*" OR "Apical periodontitis" |
| 2nd keyword terms | "Immediate implant*" OR "Fresh-socket*" OR "Fresh extraction*" OR "Post-extraction" |

1st keyword terms and 2nd keyword terms were combined with AND.
* truncation symbol

3.5. Types of publications

The systematic review included only English clinical studies done on humans. Publications that were lacking full text, in vitro studies and studies done on animals were excluded.

3.6. Types of studies

The systematic review included all human retrospective and prospective observational studies published from 1 January 2010 to 5 February 2020.

3.7. Types of participants/population

Subjects, whose extraction sockets were classified as having infection and that were treated with immediate implant placement, were included in this systematic review.

3.8. Outcome variables

The primary outcome variable was the implant survival rates. The secondary outcome variables were the mean changes in MBL, MGL, WKG, mBI and PD.
3.9. Inclusion criteria
Studies were included if they followed the applied criteria: a) studies with a sample size of >5 patients in each group; b) minimum follow-up of 6 months; c) evaluated with one of the outcomes; and d) if the sockets were classified as having an infection.

3.10. Exclusion criteria
Studies were excluded if they met any of the following applied criteria: a) clinical studies with no control group; b) animal studies; c) non-English articles; d) studies that did not mention the socket morphology; e) no clear methodology description; or f) secondary sources.

3.11. Data extraction
The following data was extracted from the articles included in this review: a) first author and publication year; b) study design; c) total number of patients; d) total number of sockets and type of socket pathology; e) follow-up period; f) implant system; g) site of implant placement; h) number of smoking patients; i) treatment methodology including flap technique, granulation tissue removal, bone graft, loading time, mouth rinse and antibiotic prophylaxis; j) implant failure and implant survival outcomes; and k) secondary outcome measures namely PD, mBI, WKG, MGL and MBL.

3.12. Statistical analysis
The meta-analysis was conducted in Review Manager Software version 5.3 (The Cochrane Collaboration, Oxford, UK). The Higgins index ($I^2$) statistic test was used to measure the heterogeneity across the studies. Cochrane Handbook guidelines were adopted to interpret the heterogeneity with 0% - 40% representing low, 30% - 60% may represent moderate heterogeneity, and 50% - 60% may represent substantial heterogeneity and 75% - 100% representing considerable heterogeneity [16]. The level of $P$-value was set at <0.05.

The Mantel-Haenszel (M-H) method was used for implant survival rates and implant failure rates (dichotomous outcome variables) together with fixed-effects model. The effect size between the control group and the test group was expressed as risk ratios (RR) and 95% confidence intervals (CIs). If significant heterogeneity (>75%) was seen, the random-effects model was chosen.

The same process was followed for the continuous outcome variables (mBI, PD, MBL, MGL and WKG). However, they were based on inverse variance (IV) with effect size expressed as mean difference (MD) in millimeters and 95% CIs. A funnel plot was made with software (Review
Manager Version 5.3; The Cochrane Collaboration, Oxford, UK) for the primary outcome, to investigate the possibility of publication bias.

3.13. Risk of bias assessment

The risk of bias assessment was performed using the Joanna Briggs Institute Critical Appraisal Checklist for Cohort Studies [17]. Questions that were evaluated can be found in table 3.

Table 3. Joanna Briggs Institute Critical Appraisal Checklist for Cohort Studies.

| Question number | Defined question |
|-----------------|------------------|
| Q1              | Were the two groups similar and recruited from the same population? |
| Q2              | Were the exposures measured similarly to assign people to both exposed and unexposed groups? |
| Q3              | Was the exposure measured in a valid and reliable way? |
| Q4              | Were confounding factors identified? |
| Q5              | Were strategies to deal with confounding factors stated? |
| Q6              | Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)? |
| Q7              | Were the outcomes measured in a valid and reliable way? |
| Q8              | Was the follow-up time reported and sufficient to be long enough for outcomes to occur? |
| Q9              | Was follow-up complete, and if not, were the reasons to loss to follow-up described and explored? |
| Q10             | Were strategies to address incomplete follow up utilized? |
| Q11             | Was appropriate statistical analysis used? |

3.14. Ethical approval

The institutional approval was obtained from the Bioethics Center at Lithuanian University of Health Sciences to conduct the present systematic review and meta-analysis. Registration code: BEC-OF-146.

4. Results

4.1. Study selection

A total of 316 publications were screened, from which 294 articles were excluded based on the titles. In the next step the abstracts of all the 22 remaining studies were assessed for eligibility based on inclusion criteria. If an abstract provided insufficient amount of information to decide whether or not to include the article, the full version of the article was downloaded for further detailed evaluation.
Figure 1. PRISMA flow diagram demonstrating the study selection.

Records identified through database searching (PubMed, ISI Web of Science, ScienceDirect) (n = 855)

Additional records identified through other sources (n = 2)

Records after duplicates removed (n = 541)

Records excluded: Studies >10 years, Reviews, Animals studies (n = 225)

Records screened (n = 316)

Records excluded based on title (n = 294)

Abstracts assessed for eligibility (n = 22)

Records excluded based on abstract (n = 10)

Full-text articles assessed for eligibility (n = 12)

Full-text articles excluded (n = 3)

Reasons:
  a) Same patient records
  b) No control group
  c) Not enough details

Studies included in qualitative synthesis (n = 9)

Studies included in quantitative synthesis (n = 9)
Subsequently, the full-text of the articles that were potentially relevant was obtained for assessment of the eligibility. A total of 12 full articles were reviewed for inclusion and exclusion criteria in order to make the final decision. After a detailed review, nine records met all the required criteria and were included in this review [18-26]. Figure 1 shows the PRISMA flow diagram which demonstrates the number of publications identified, screened, assessed for eligibility and included in this review.

4.2. Study exclusion

Three studies were excluded after a full-text review due to: lack of control group [27], publication of the same patient records [28] and lack of control and test group details [29].

4.3. Quality assessment of the included studies

The quality assessment of all the cohort studies revealed moderate or good qualities; the scoring of each study is summarized in table 4.

Table 4. Quality assessment of all the included cohort studies using the Joanna Briggs Institute Critical Appraisal Checklist for Cohort Studies.

| JBI Critical Appraisal Checklist | Prospective design | Retrospective design |
|----------------------------------|---------------------|----------------------|
| Montoya-Salazar et al. 2014 [18] |                     |                      |
| Jung et al. 2013 [19]            |                     |                      |
| Crespi et al. 2010 [20]          |                     |                      |
| Crespi et al. 2010 [21]          |                     |                      |
| Hita-Iglesias et al. 2015 [22]   |                     |                      |
| Blus et al. 2015 [23]            |                     |                      |
| Bell et al. 2011 [24]            |                     |                      |
| Fugazzotto 2012 [25]             |                     |                      |
| Zuffetti et al. 2017 [26]        |                     |                      |

| Q1 |  ? | + | + | + | + | ? | + | + | ? |
| Q2 | + | + | + | + | + | + | + | + |
| Q3 | + | + | + | + | + | + | + | + |
| Q4 | - | + | N/A | N/A | N/A | - | + | N/A | + |
| Q5 | - | N/A | N/A | N/A | N/A | - | + | N/A | - |
| Q6 | + | + | + | + | + | + | + | + |
| Q7 | + | + | + | + | + | + | + | + |
| Q8 | + | + | + | + | + | + | + | + |
| Q9 | + | + | + | + | + | + | + | + |
| Q10 | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A |
| Q11 | + | + | + | + | + | + | + | + |

Abbreviations:
JBI = Joanna Briggs Institute
N/A = Not applicable
? = Unclear
* = Yes
- = No
4.4. Study characteristics

The characteristics of the included studies are presented in table 5. Three of the included studies were of retrospective design [24-26] and the other remaining six studies were of prospective design [18-23]. In total, a pool of 1346 patients and 2281 sockets were used in this present systematic review. A total of 933 immediate implants were placed in infected sites and 1348 in non-infected sites. Seven of the studies included smoking patients [18-21,24-26]. Only two of the studies specified the total number of smokers [19,24]. One of the studies did not mention if smoking patients were included or excluded [23]. Three of the studies mentioned the exclusion of heavy smokers (>10 cigarettes a day) [20,21,25].

Most of the studies placed the implants in the incisor, canine or premolar area [18-23], while two of the studies included the molar area as well [24, 26]. Only one study exclusively reported on the incisor replacement [25]. Six of the studies used flapless approach [20-25], while two of the studies proceeded with a flap technique [18, 19] and one study used both flap and flapless approach [26]. No grafting material was used in three of the studies reviewed [20-23].

A delayed loading protocol was followed for all implants in six of the studies [18,19,21,22,24,25]. Only one study used an immediate loading protocol [20], while the two remaining studies used different types of loading protocols [23,26]. The patients received a pre-operative antibiotic prophylaxis in seven of the studies [18,20-24,26] and five of the studies prescribed post-operative antibiotics for the patients [18-22,25-26]. A post-operative instruction on chlorhexidine rinse was made in five of the studies [18-21,26], while only one study followed a pre-operative mouth rinse protocol [26]. Details of the treatment procedures are presented in table 6.

All of the included studies reported the number of failed implants [18-26] and four of the included studies reported about MBL changes [18-21]. Changes in mBI were reported by three studies [18, 20, 21] MGL and PD were reported by two studies [18,21] and WKG changes were reported by three studies [18,19,21]. The minimum follow-up period of the secondary outcome variables (MBL, MGL, PD, mBI and WKG) was one year and the maximum follow-up period was five years. Table 7 shows detailed information about the extracted data from the different follow-up periods regarding MBL, MGL, PD, mBI and WKG.
Table 5. Characteristics of the included studies.

| Study                        | Study design | Patients, (n) |.Sockets, (n) |Smoking patients, (n) | IS pathology                              | Age, (y) | Site                                   | Follow up, (m) | Implant system                        |
|------------------------------|--------------|---------------|--------------|----------------------|-------------------------------------------|----------|---------------------------------------|----------------|--------------------------------------|
| Montoya-Salazar et al. 2014  | Prospective  | 18            | 18           | 18                   | IS Smokers included (ASA II)              | 18-50    | Incisors, canines and premolars       | 36             | MIS Ibérica, C1, Israel               |
| Jung et al. 2012             | Prospective  | 27            | 12           | 15                   | IS Periapical pathologies                 | 31-87    | Incisors, canines and premolars       | 60             | Straumann, standard plus or tapered effect, Switzerland |
| Crespi et al. 2010           | Prospective  | 37            | 197          | 78                   | IS Heavy smokers excluded (>10 cigarettes/d) | 32-71    | Incisors, canines and premolars       | 48             | Sweden-Martina, Italy                |
| Crespi et al. 2010           | Prospective  | 30            | 15           | 15                   | IS Heavy smokers excluded (>10 cigarettes/d) | 34-71    | Incisors, canines and premolars       | 24             | Sweden-Martina, Seven, Italy         |
| Hita-Iglesias et al. 2016    | Prospective  | 60            | 66           | 102                  | IS Non-smokers only                       | 18-72    | Incisors, canines and premolars       | 12             | Zimmer dental, USA                   |
| Blus et al. 2015             | Prospective  | 86            | 83           | 85                   | IS Acute and chronic infection            | 26-77    | Incisors, canines and premolars       | 12             | Leader, Italy; and Bioner, Spain      |
| Bell et al. 2011             | Retrospective| 655           | 285          | 637                  | IS Chronic periapical lesions             | Mean 58.4 (IS) Mean 60.1 (NIS) | Incisors, canines, premolars and molars | 3-93           | Straumann, tissue level or bone level SLA, Switzerland |
| Fugazzotto 2012              | Retrospective| 64            | 64           | 64                   | IS Heavy smokers excluded (>10 cigarettes/d) | 21-71    | Incisors                              | 24-117         | No data                              |
| Zuffetti et al. 2017         | Retrospective| 369           | 193          | 334                  | IS Heavy smokers included (>10 cigarettes/d) | 22.8-81.9 | Incisors, canines, premolars and molars | Mean 52.1      | Biomet 3I, USA; BioHorizons, USA; Nobel Biocare, Switzerland; Astra Tech, USA; Megagen, South Korea; and Neoss, Sweden |

Abbreviations: n= numbers; y= years; m= months; N/D= no data; IS= infected socket; NIS= non-infected socket; ASA= The American Society of Anesthesiologists physical status classification system.
Table 6. Details of the treatment procedures of the included studies.

| Study                          | Flap technique | Granulation tissue | Bone graft | Loading time | Pre-op antibiotic prophylaxis | Pre-op chlorhexidine rinse | Post-op antibiotic prophylaxis | Post-op chlorhexidine rinse |
|-------------------------------|----------------|-------------------|------------|--------------|----------------|----------------|----------------|----------------|----------------|
| Montoya-Salazar et al. 2014 [18] | Flap           | Removed           | Xenograft  | Delayed      | Yes             | No            | Yes            | Yes            |                |
| Jung et al. 2012 [19]         | Flap           | Removed           | Xenograft  | Delayed      | No              | No            | Yes            | Yes            |                |
| Crespi et al. 2010 [20]       | Flapless       | Removed           | None       | Immediate    | Yes             | No            | Yes            | Yes            |                |
| Crespi et al. 2010 [21]       | Flapless       | Removed           | None       | Delayed      | Yes             | No            | Yes            | Yes            |                |
| Hita-Iglesias et al. 2016 [22]| Flapless       | Removed           | None       | Delayed      | Yes             | No            | Yes            | No             |                |
| Blus et al. 2015 [23]         | Flapless       | Removed           | Xenograft  | Immediate, early and delayed | Yes             | No            | No             | No             |                |
| Bell et al. 2011 [24]         | Flapless       | Removed           | Autograft and/or xenograft together with PRP | Delayed      | Yes             | Yes            | No             | No             |                |
| Fugazzotto 2012 [25]          | Flapless       | Removed           | Autograft or allograft or xenograft | Delayed      | No              | No             | Yes            | No             |                |
| Zuffetti et al. 2017 [26]     | Flapless or flap | Removed           | Xenograft  | Immediate, early and delayed | Yes             | No            | Yes            | Yes            |                |

Abbreviations:
Pre-op= pre-operative;
Post-op= post-operative.
Table 7. Data of the primary and secondary outcomes of the included studies.

| Author                         | Number of implants, (n) | Failed implants, (n) | Implant survival rate, (%) | MBL, mean ± SD, (mm) | MGL, mean ± SD, (mm) | PD, mean ± SD, (mm) | mBI, mean ± SD | WKG, mean ± SD, (mm) |
|-------------------------------|-------------------------|----------------------|---------------------------|----------------------|----------------------|----------------------|----------------|---------------------|
| Montoya-Salazar et al. 2014 [18] | 18 18 36 1 0 1 | 94.4 100 | 1 y: 0.73 ± 0.22 2 y: 0.84 ± 0.15 3 y: 0.53 ± 0.13 | 1 y: 0.73 ± 0.29 2 y: 0.54 ± 0.15 3 y: 0.60 ± 0.16 | 1 y: 0.88 ± 0.75 2 y: 0.83 ± 0.85 3 y: 1.00 ± 0.59 | 1 y: 2.53 ± 0.44 2 y: 2.76 ± 0.80 3 y: 2.51 ± 0.44 | 1 y: 0.88 ± 0.75 2 y: 0.83 ± 0.85 3 y: 0.94 ± 0.63 | 1 y: 1.38 ± 0.84 2 y: 1.05 ± 0.99 3 y: 1.00 ± 1.02 |
| Jung et al. 2012 [19]         | 12 15 27 0 0 0   | 100 100 | 5 y: 1.5 ± 0.8 (mesial) 1.7 ± 0.7 (distal) | 5 y: 1.4 ± 0.5 (mesial) 1.5 ± 0.6 (distal) | N/D | N/D | N/D | 5 y: 3.3 ± 1.5 |
| Crespi et al. 2010 [20]       | 19 7 78 275 2 0 2 | 98.9 100 | 1 y: 0.77 ± 0.39 2 y: 0.82 ± 0.52 4 y: 0.79 ± 0.38 | 1 y: 0.86 ± 0.47 2 y: 0.84 ± 0.46 4 y: 0.78 ± 0.38 | N/D | N/D | 4 y: 0.78 ± 0.23 4 y: 0.75 ± 0.39 | N/D |
| Crespi et al. 2010 [21]       | 15 15 30 0 0 0   | 100 100 | 1 y: 0.83 ± 0.51 2 y: 0.86 ± 0.54 | 1 y: 0.80 ± 0.47 2 y: 0.82 ± 0.52 | 1 y: 0.16 ± 0.13 2 y: 0.20 ± 0.13 | 1 y: 1.80 ± 0.64 2 y: 1.99 ± 0.57 | 1 y: 0.69 ± 0.30 2 y: 0.72 ± 0.36 | 1 y: 3.64 ± 0.34 2 y: 3.62 ± 0.36 |
| Hita-Iglesias et al. 2016 [22] | 66 102 168 6 2 8 | 90.8 98.1 | N/D | N/D | N/D | N/D | N/D | N/D |
| Blus et al. 2015 [23]         | 83 85 168 2 1 3 | 97.6 98.8 | N/D | N/D | N/D | N/D | N/D | N/D |
| Bell et al. 2011 [24]         | 28 5 637 922 7 8 15 | 97.5 98.7 | N/D | N/D | N/D | N/D | N/D | N/D |
| Fugazzotto 2012 [25]          | 64 64 128 1 1 2 | 98.1 98.2 | N/D | N/D | N/D | N/D | N/D | N/D |
| Zuffetti et al. 2017 [26]      | 19 3 334 527 3 7 10 | 98.4 ± 0.9 97.9 ± 0.8 | N/D | N/D | N/D | N/D | N/D | N/D |

Abbreviations: 
N/D= no data; 
IS= infected socket; 
NIS= non-infected socket; 
SD= standard deviation; 
= numbers; 
= years.
4.5. Quantitative synthesis

4.5.1. Implant survival rates and failure rates (primary outcome variables)

In total 933 immediate implants were placed in infected sockets and 1348 in non-infected sockets [18-26]. The number of failed implants was 22 for the infected socket group and 19 for the non-infected socket group resulting in overall implant survival rates of 97.64% (911/933) for the infected group and 98.57% (1329/1348) for the non-infected group (table 8). Both of the groups showed similar results (RR=0.99; 95%CI= 0.98 to 1.00; P= 0.08). Additionally, there was no significant difference in the implant failure rates between the infected and non-infected groups (RR=1.80; 95%CI=0.98 to 3.31; P= 0.06) as seen in table 9.

Table 8. Implant survival rates of the included studies.

| Study or Subgroup | Infected Events | Non-Infected Events | Total Events | Total Weight | Risk Ratio M-H, Fixed, 95% CI |
|-------------------|----------------|---------------------|-------------|-------------|-----------------------------|
| Bell et al. 2011 [24] | 278 | 285 | 629 | 637 | 38.4% | 0.99 [0.97, 1.01] |
| Crespi et al. 2010 [20] | 195 | 197 | 78 | 78 | 11.1% | 0.99 [0.97, 1.02] |
| Crespi et al. 2010 [21] | 15 | 15 | 15 | 15 | 1.5% | 1.00 [0.88, 1.13] |
| Fugazzotto 2012 [25] | 63 | 64 | 63 | 64 | 6.2% | 1.00 [0.96, 1.04] |
| Hita-Iglesias et al. 2015 [22] | 60 | 66 | 100 | 102 | 7.8% | 0.93 [0.86, 1.01] |
| Jung et al. 2013 [19] | 12 | 12 | 15 | 15 | 1.4% | 1.00 [0.87, 1.15] |
| Montoya-Salazar et al. 2014 [18] | 17 | 18 | 18 | 18 | 1.8% | 0.95 [0.81, 1.10] |
| Zuffetti et al. 2017 [26] | 190 | 193 | 327 | 334 | 23.6% | 1.01 [0.98, 1.03] |
| Blus et al. 2015 [23] | 81 | 83 | 84 | 85 | 8.2% | 0.99 [0.95, 1.03] |
| Total (95% CI) | 933 | 1348 | 100.0% | 0.99 [0.98, 1.00] |

Heterogeneity: Chi² = 5.29, df = 8 (P = 0.73); I² = 0%
Test for overall effect: Z = 1.77 (P = 0.08)

Table 9. Implant failure rates of the included studies.

| Study or Subgroup | Infected Events | Non-Infected Events | Total Events | Total Weight | Risk Ratio M-H, Fixed, 95% CI |
|-------------------|----------------|---------------------|-------------|-------------|-----------------------------|
| Bell et al. 2011 [24] | 7 | 285 | 8 | 637 | 33.3% | 1.96 [0.72, 5.34] |
| Crespi et al. 2010 [20] | 2 | 197 | 0 | 78 | 4.8% | 1.99 [0.10, 41.09] |
| Crespi et al. 2010 [21] | 0 | 150 | 0 | 15 | Not estimable |
| Fugazzotto 2012 [25] | 1 | 64 | 1 | 64 | 6.7% | 1.00 [0.06, 15.64] |
| Hita-Iglesias et al. 2015 [22] | 6 | 66 | 2 | 102 | 10.6% | 4.64 [0.96, 22.29] |
| Jung et al. 2013 [19] | 0 | 12 | 0 | 15 | Not estimable |
| Montoya-Salazar et al. 2014 [18] | 1 | 18 | 0 | 18 | 3.4% | 3.00 [0.13, 69.09] |
| Zuffetti et al. 2017 [26] | 3 | 193 | 7 | 334 | 34.5% | 0.74 [0.19, 2.83] |
| Blus et al. 2015 [23] | 2 | 83 | 1 | 85 | 6.7% | 2.05 [0.19, 22.16] |
| Total (95% CI) | 933 | 1348 | 100.0% | 1.80 [0.98, 3.31] |

Heterogeneity: Chi² = 3.39, df = 6 (P = 0.76); I² = 0%
Test for overall effect: Z = 1.89 (P = 0.06)
4.5.2. Marginal bone level changes

Four of the included studies reported the marginal bone level measurements [18-21]. In total 242 implants in the infected sockets and 126 implants in non-infected sockets were included in this analysis (table 10a-c). One of the studies reported three follow-up periods of 1, 2 and 3 years [18]. Another study reported three follow-up periods but of 1, 2 and 4 years [20]. The last two studies reported 1 and 2 years [21] and 5 years [19] respectively. No significant difference was found between the different groups at follow-up times, at 1 year the MD was -0.05 (95% CI= -0.15 to 0.04; \( P=0.25 \)) at year 2 the MD was 0.12 (95%CI= -0.14 to 0.38; \( P=0.36 \)) and at year 3 or more the MD was -0.03 (95% CI= -0.10 to 0.04; \( P= 0.41 \)).

4.5.3. Marginal gingival level changes

Two of the included studies reported the marginal gingival level changes [18,21]. The total number of implants included was 33 in the infected group and 33 in the non-infected group (table 11a-b). Meta-analysis showed no significant difference between the two groups. At 1 year follow-up the MD was -0.06 (95% CI= -0.15 to 0.03; \( P= 0.17 \)) and at 2 year follow-up the MD was -0.07 (95% CI= -0.17 to 0.04; \( P= 0.23 \)).

4.5.4. Probing depth changes

Two of the included studies reported the peri-implant probing depth measurements [18,21]. In total, 33 implants were included in both infected and non-infected group (table 12a-b). No significant difference was found between the groups at follow-up, at year 1 the MD was 0.06 (95% CI= -0.15 to 0.28; \( P= 0.58 \)) and at year 2 the MD was 0.06 (95% CI= -0.24 to 0.36; \( P= 0.70 \)).

4.5.5. Modified bleeding index changes

Three of the included studies reported the modified bleeding index (table 13a-c) [18,20,21]. One of the studies reported three follow-up periods of 1 year, 2 years and 3 years [20]. Another one reported two follow-up periods of 1 and 2 years [21] and the remaining study included only a 4 year follow-up [20]. Both of the 1 year and 2 year analysis included 33 implants in both infected and non-infected group. The 3 year or more follow-up included 215 implants in the infected sockets and 96 implants in the non-infected sockets. No statistical significant difference was seen between the groups at different follow-up times, at year 1 the MD was -0.07(95%CI= -0.28 to 0.14; \( P=0.50 \)), at year 2 the MD was -0.07 (95%CI=-0.30 to 0.15; \( P= 0.52 \)) and at year 3 or more the MD was -0.00 (95%CI=-0.09 to 0.09; \( P= 0.97 \)).
Table 10a. Marginal bone level changes at the follow-up period of 1 year.

| Study or Subgroup       | Infected Mean | Infected SD | Infected Total | Mean Difference IV, Random, 95% CI | Non-Infected Mean | Non-Infected SD | Non-Infected Total | Mean Difference IV, Random, 95% CI |
|-------------------------|---------------|-------------|----------------|-----------------------------------|-------------------|-----------------|-------------------|-----------------------------------|
| Crespi et al. 2010 [20] | 0.77 0.39     | 197 0.86    | 47 79          | 0.5 (-0.21, 0.03)                | 0.80 0.39         | 197 0.86        | 47 79             | 0.25 (-0.17, 0.17)               |
| Crespi et al. 2010 [21] | 0.83 0.51     | 15 0.8      | 47 79          | 0.7 (-0.32, 0.38)                | 0.80 0.39         | 197 0.86        | 47 79             | 0.25 (-0.17, 0.17)               |
| Montoya-Salazar et al. 2014 [18] | 0.73 0.22 | 18 0.73    | 29 18          | 0.00 (-0.17, 0.17)              | 0.80 0.39         | 197 0.86        | 47 79             | 0.25 (-0.17, 0.17)               |
| Total (95% CI)           | 230           | 111         | 100.0%         | -0.05 (-0.15, 0.04)             |                   |                 |                   |                                    |

Heterogeneity: Tau² = 0.04; Chi² = 12.12; df = 2 (P = 0.0003); I² = 88%
Test for overall effect: Z = 1.14 (P = 0.25)

Table 10b. Marginal bone level changes at the follow-up period of 2 years.

| Study or Subgroup       | Infected Mean | Infected SD | Infected Total | Mean Difference IV, Random, 95% CI | Non-Infected Mean | Non-Infected SD | Non-Infected Total | Mean Difference IV, Random, 95% CI |
|-------------------------|---------------|-------------|----------------|-----------------------------------|-------------------|-----------------|-------------------|-----------------------------------|
| Crespi et al. 2010 [20] | 0.82 0.52     | 197 0.84    | 46 79          | -0.02 (-0.14, 0.10)              | 0.80 0.39         | 197 0.86        | 47 79             | 0.25 (-0.17, 0.17)               |
| Crespi et al. 2010 [21] | 0.86 0.54     | 15 0.82     | 52 15          | 0.04 (-0.34, 0.42)              | 0.80 0.39         | 197 0.86        | 47 79             | 0.25 (-0.17, 0.17)               |
| Montoya-Salazar et al. 2014 [18] | 0.84 0.15 | 18 0.54    | 15 39.7       | 0.30 (0.20, 0.40)           | 0.80 0.39         | 197 0.86        | 47 79             | 0.25 (-0.17, 0.17)               |
| Total (95% CI)           | 230           | 112         | 100.0%         | 0.12 (-0.14, 0.38)             |                   |                 |                   |                                    |

Heterogeneity: Tau² = 0.04; Chi² = 16.12; df = 2 (P = 0.0003); I² = 88%
Test for overall effect: Z = 0.91 (P = 0.36)

Table 10c. Marginal bone level changes at the follow-up period of >3 years.

| Study or Subgroup       | Infected Mean | Infected SD | Infected Total | Mean Difference IV, Random, 95% CI | Non-Infected Mean | Non-Infected SD | Non-Infected Total | Mean Difference IV, Random, 95% CI |
|-------------------------|---------------|-------------|----------------|-----------------------------------|-------------------|-----------------|-------------------|-----------------------------------|
| Crespi et al. 2010 [20] | 0.79 0.38     | 197 0.78    | 38 74          | 0.01 (-0.09, 0.11)              | 0.80 0.39         | 197 0.86        | 47 79             | 0.25 (-0.17, 0.17)               |
| Montoya-Salazar et al. 2014 [18] | 0.53 0.13 | 18 0.6     | 18 51.3        | 0.07 (-0.17, 0.03)             | 0.80 0.39         | 197 0.86        | 47 79             | 0.25 (-0.17, 0.17)               |
| Jung et al. 2013 [19]  | 1.6 0.75      | 12 1.45     | 15 1.8        | 0.15 (-0.36, 0.66)            | 0.80 0.39         | 197 0.86        | 47 79             | 0.25 (-0.17, 0.17)               |
| Total (95% CI)           | 227           | 111         | 100.0%         | -0.03 (-0.10, 0.04)            |                   |                 |                   |                                    |

Heterogeneity: Tau² = 0.00; Chi² = 1.78; df = 2 (P = 0.41); I² = 0%
Test for overall effect: Z = 0.82 (P = 0.41)

Table 11a. Marginal gingival level changes at the follow-up period of 1 year.

| Study or Subgroup       | Infected Mean | Infected SD | Infected Total | Mean Difference IV, Fixed, 95% CI | Non-Infected Mean | Non-Infected SD | Non-Infected Total | Mean Difference IV, Fixed, 95% CI |
|-------------------------|---------------|-------------|----------------|-----------------------------------|-------------------|-----------------|-------------------|-----------------------------------|
| Crespi et al. 2010 [21] | 0.16 0.13     | 15 0.21     | 13 15          | -0.05 (-0.14, 0.04)              | 0.80 0.39         | 197 0.86        | 47 79             | 0.25 (-0.17, 0.17)               |
| Montoya-Salazar et al. 2014 [18] | 0.88 0.75 | 18 1.13    | 18 6.2        | 0.25 (-0.61, 0.11)            | 0.80 0.39         | 197 0.86        | 47 79             | 0.25 (-0.17, 0.17)               |
| Total (95% CI)           | 33            | 33          | 100.0%         | -0.06 (-0.15, 0.03)            |                   |                 |                   |                                    |

Heterogeneity: Chi² = 1.10; df = 1 (P = 0.29); I² = 9%
Test for overall effect: Z = 1.36 (P = 0.17)

Table 11b. Marginal gingival level changes at the follow-up period of 2 years.

| Study or Subgroup       | Infected Mean | Infected SD | Infected Total | Mean Difference IV, Fixed, 95% CI | Non-Infected Mean | Non-Infected SD | Non-Infected Total | Mean Difference IV, Fixed, 95% CI |
|-------------------------|---------------|-------------|----------------|-----------------------------------|-------------------|-----------------|-------------------|-----------------------------------|
| Crespi et al. 2010 [21] | 0.2 0.13      | 15 0.25     | 18 15          | 0.05 (-0.16, 0.06)              | 0.80 0.39         | 197 0.86        | 47 79             | 0.25 (-0.17, 0.17)               |
| Montoya-Salazar et al. 2014 [18] | 0.83 0.85 | 18 1.11    | 18 7.2        | -0.28 (-0.68, 0.12)            | 0.80 0.39         | 197 0.86        | 47 79             | 0.25 (-0.17, 0.17)               |
| Total (95% CI)           | 33            | 33          | 100.0%         | -0.07 (-0.17, 0.04)            |                   |                 |                   |                                    |

Heterogeneity: Chi² = 1.15; df = 1 (P = 0.28); I² = 13%
Test for overall effect: Z = 1.20 (P = 0.23)
Table 12a. Probing depth changes of the included studies at the follow-up period of 1 year.

| Study or Subgroup          | Infected | Non-Infected | Mean Difference | Weight | IV, Fixed, 95% CI |
|----------------------------|----------|--------------|-----------------|--------|-------------------|
| Montoya-Salazar et al. 2014 [18] | 2.53 0.44 | 18 2.44 0.28 | 18 0.59 0.37 | 18 79.4% 0.09 [0.15, 0.33] |
| Total (95% CI)             | 33 0.96 | 100.0%       | 0.06 [-0.15, 0.28] |
| Heterogeneity: Chi² = 1, df = 1 (P = 0.60); I² = 0% |
| Test for overall effect: Z = 0.56 (P = 0.58) |

Table 12b. Probing depth changes of the included studies at the follow-up period of 2 years.

| Study or Subgroup          | Infected | Non-Infected | Mean Difference | Weight | IV, Fixed, 95% CI |
|----------------------------|----------|--------------|-----------------|--------|-------------------|
| Montoya-Salazar et al. 2014 [18] | 2.76 0.8 | 18 2.6 0.37 | 18 0.64 0.25 | 18 54.0% 0.16 [0.25, 0.57] |
| Total (95% CI)             | 33 0.96 | 100.0%       | 0.06 [-0.24, 0.36] |
| Heterogeneity: Chi² = 1, df = 1 (P = 0.47); I² = 0% |
| Test for overall effect: Z = 0.39 (P = 0.70) |

Table 13a. Modified bleeding index changes of the included studies at the follow-up period of 1 year.

| Study or Subgroup          | Infected | Non-Infected | Mean Difference | Weight | IV, Fixed, 95% CI |
|----------------------------|----------|--------------|-----------------|--------|-------------------|
| Montoya-Salazar et al. 2014 [18] | 0.88 0.75 | 18 1.38 0.84 | 18 4.37 0.28 | 18 16.3% -0.50 [-1.02, 0.02] |
| Total (95% CI)             | 33 0.96 | 100.0%       | -0.07 [0.28, 0.14] |
| Heterogeneity: Chi² = 3.09, df = 1 (P = 0.08); I² = 68% |
| Test for overall effect: Z = 0.68 (P = 0.50) |

Table 13b. Modified bleeding index changes of the included studies at the follow-up period of 2 years.

| Study or Subgroup          | Infected | Non-Infected | Mean Difference | Weight | IV, Fixed, 95% CI |
|----------------------------|----------|--------------|-----------------|--------|-------------------|
| Montoya-Salazar et al. 2014 [18] | 0.83 0.85 | 18 1.05 0.99 | 18 0.99 0.62 | 18 14.4% -0.22 [-0.82, 0.38] |
| Total (95% CI)             | 33 0.96 | 100.0%       | -0.07 [0.30, 0.15] |
| Heterogeneity: Chi² = 2.62, df = 1 (P = 0.61); I² = 0% |
| Test for overall effect: Z = 0.64 (P = 0.52) |

Table 13c. Modified bleeding index changes of the included studies at the follow-up period of ≥3 years.

| Study or Subgroup          | Infected | Non-Infected | Mean Difference | Weight | IV, Fixed, 95% CI |
|----------------------------|----------|--------------|-----------------|--------|-------------------|
| Montoya-Salazar et al. 2014 [18] | 0.94 0.63 | 18 1.02 1.02 | 18 2.7% -0.06 [-0.61, 0.49] |
| Total (95% CI)             | 215 0.96 | 100.0%       | -0.00 [0.09, 0.09] |
| Heterogeneity: Chi² = 0.04, df = 1 (P = 0.83); I² = 0% |
| Test for overall effect: Z = 0.03 (P = 0.97) |
4.5.6. Width of keratinized gingival changes

Three studies were included [18,20,21], one of the studies reported three follow-up periods of 1 year, 2 years and 3 years [18]. Another one reported two follow-up periods of 1 year and 2 years [21] and the remaining study included one follow-up period of 5 year [19] (table 14a-c). Both of the 1 year or 2 year analysis included 33 implants in both infected and non-infected groups. The 3 year or more follow-up period included 30 implants in the infected group and 33 implants in the non-infected group. There was a slight, but significant decrease of WKG which favored the non-infected group (1 year, MD= 0.22; 95% CI= -0.17 to 0.60; \( P = 0.27 \); at year 2, MD= 0.16; 95% CI= -0.22 to 0.55; \( P = 0.40 \); and at 3 years or more, MD= 0.25; 95% CI= -0.30 to 0.80; \( P = 0.38 \)).

Table 14a. Width of keratinized gingiva of the included studies at the follow-up period of 1 year.

| Study or Subgroup          | Infected | Non-Infected | Mean Difference | Mean Difference |
|----------------------------|----------|--------------|----------------|----------------|
|                            | Mean     | SD           | Total           |               |
| Montoya-Salazar et al. 2014 18 | 3.33     | 1.08         | 18              | 2.74          |
| Crespi et al. 2010 [21]     | 3.64     | 0.68         | 15              | 3.68          |
| Total (95% CI)              | 33       | 100.0%       | 33              | 0.22 [-0.17, 0.60] |
| Heterogeneity: Chi² = 2.48, df = 1 (P = 0.12); I² = 60% |
| Test for overall effect: Z = 1.11 (P = 0.27) |

Table 14b. Width of keratinized gingiva of the included studies at the follow-up period of 2 years.

| Study or Subgroup          | Infected | Non-Infected | Mean Difference | Mean Difference |
|----------------------------|----------|--------------|----------------|----------------|
|                            | Mean     | SD           | Total           |               |
| Crespi et al. 2010 [21]     | 3.62     | 0.65         | 15              | 3.67          |
| Montoya-Salazar et al. 2014 18 | 3.33     | 1.08         | 18              | 2.61          |
| Total (95% CI)              | 33       | 100.0%       | 33              | 0.16 [-0.22, 0.55] |
| Heterogeneity: Chi² = 3.12, df = 1 (P = 0.08); I² = 68% |
| Test for overall effect: Z = 0.84 (P = 0.40) |

Table 14c. Width of keratinized gingiva of the included studies at the follow-up period of ≥3 years.

| Study or Subgroup          | Infected | Non-Infected | Mean Difference | Mean Difference |
|----------------------------|----------|--------------|----------------|----------------|
|                            | Mean     | SD           | Total           |               |
| Jung et al. 2013 [19]      | 3.3      | 1.5          | 12              | 3.7           |
| Montoya-Salazar et al. 2014 18 | 3.38     | 0.6          | 18              | 2.88          |
| Total (95% CI)              | 30       | 100.0%       | 33              | 0.25 [-0.30, 0.80] |
| Heterogeneity: Chi² = 2.06, df = 1 (P = 0.15); I² = 51% |
| Test for overall effect: Z = 0.89 (P = 0.38) |
4.6. Publication bias

No obvious visual publication bias was observed in the funnel plot analyzing the implant survival rate (primary outcome variable) seen in figure 2.

Figure 2. Funnel plot analyzing the implant survival rate, SE= standard error; RR= risk ratio.

5. Discussion

5.1. Principal findings

The results of this meta-analysis suggest that there is no statistical significant difference in implant survival rates (RR=0.99; 95% CI= 0.98 to 1.00; \( P = 0.08 \)) between immediate implant placement in infected sockets and non-infected sockets. Furthermore, all of the secondary outcome variables (MGL, MBL, mBI, and PD) showed equal favorable results except for WKG that showed a slight but significant decrease in the infected group.

Implant survival depends on the MBL changes and is one of the factors to determine the success of the implant survival [30, 31]. In this present review no significant difference was found between the two groups (1 year, MD= -0.05; 95% CI= -0.15 to 0.04; \( P = 0.25 \); year 2, MD= 0.12; 95% CI= -0.14 to 0.38; \( P = 0.36 \); >3 years, MD= -0.03; 95% CI= -0.10 to 0.04; \( P = 0.41 \)). Albrektsson and Isidor [32] suggested that implant success is valid if less than 1.5 mm of bone loss is seen during the first year after functional loading and thereafter a loss of <0.2 mm annually. Thus, meaning that marginal bone loss is inevitable. Early MBL changes are a type of adaptive non-infective process that is influenced by surgical factors (surgical trauma, bone overheating, excessive implant tightening and crestal width) and prosthetic trauma (occlusial overload, type of implant design, microgap, abutment height and foreign body reaction to cement residue) [33-35]. A study done by Galindo-Moreno et al. [36] found that early high MBL changes of 0.44 mm at six months (after loading) were strongly associated with a subsequent increase of MBL changes of >2 mm at 18
months. Hence, this six month period may be used as an indicator for long term bone loss prognosis.

Most of the included studies used guided bone regeneration (GBR) as a type of treatment method. The buccal bone plate can undergo more than 50% of horizontal reduction following the placement of immediate implants; this can lead to gingival recession, impairing the esthetics. Additionally, a mean of 1 mm vertical bone loss can be seen in the presence of a thin buccal bone [36,37]. In this study no significant changes of MGL were seen between the groups (year 1, MD= -0.06; 95% CI= -0.15 to 0.03; \(P= 0.17\); year 2, MD= -0.07; 95% CI= -0.17 to 0.04; \(P= 0.23\)).

The structural characteristics of the gingiva have been considered important for the integrity of the periodontium. A movable gingival margin facilitates the introduction of biofilm into the gingival crevice, resulting in sub-gingival plaque that triggers the activation of lymphocytes and neutrophils. This biofilm penetration induces a chronic inflammatory response [38]. However, as there are anatomical and structural differences between natural dentition and implants, the same consensus might not be applicable. The significance of the keratinized mucosa on peri-implant health has been widely discussed [39]. A study done by Pranskunas et al. [40] concluded that implants with narrow WKG (<2 mm) had significantly more plaque, signs of inflammation, decreased stability of peri-implant site and increased mucosal recession than those with wider WKG (>2 mm). These finding are supported by other studies [38,39,41]. However, when adequate plaque control is followed, data suggests no correlation between WKG and peri-implant conditions [38-41]. On the other hand, Monje and Blasi [38] found a correlation between narrow keratinized mucosa and a decrease in vestibular depth – which may impair patients’ ability to implement correct oral hygiene measures. Additionally, WKG of <2 mm is associated with increased brushing discomfort and as well as inadequate esthetical outcome [40-42]. The present review and meta-analysis showed that a slight but significant amount of WKG (1 year, MD= 0.22; 95% CI= -0.17 to 0.60; \(P= 0.27\); at year 2, MD= 0.16; 95% CI= -0.22 to 0.55; \(P= 0.40\); and at 3 years or more, MD= 0.25; 95% CI= -0.30 to 0.80; \(P= 0.38\)) is lost during the immediate implant placement in infected sites. This suggests that WKG should be of concern in clinical situations were optimum plaque control is not feasible or when there is a high esthetic demand.

Additionally, PD and mBI clinical parameters were collected and compared to determine if there were any soft tissue changes indicating inflammation. The two groups showed no significant statistical differences in both of the analyses; PD (year 1, MD= 0.06; 95% CI= -0.15 to 0.28; \(P= 0.58\); and year 2, MD= 0.06; 95% CI= -0.24 to 0.36; \(P= 0.70\)) and mBI (year 1, MD= -0.07;
Immediate loading was used in some of the included studies. In the review conducted by Pigozzo et al. [43] showed that both immediate and early loading protocols in single implant crowns had high success rate. Another study done by Gallucci et al. [44] showed a survival rate of 98.4\% and a success rate of 87\% to 100\% in immediate implant placement with immediate loading.

All of the included studies removed the granulation tissue before the implant placement. In general, most studies recommend curettage of the implant site before placement or suggest antibiotics to aid the success rate of immediate implant placement [45]. During the primary stability, the outer implant threads are in close proximity with the surrounding bone, providing mechanical interlocking between the bone and implant [46,47]. However, the inner surfaces of the threads are unable to have an implant-to-bone contact and the void formed will be occupied with blood, subsequently forming into a blood clot characterized by a fibrin coagulum with thrombocytes, neutrophils, erythrocytes and macrophages/monocytes [46]. The fibrin coagulum network will progressively form into granulation tissue when penetration of vascular units and fibroblast-like cells is initiated. This initial wound healing response will start the bone apposition between the implant and the surrounding bone, indicating the build-up of the secondary stability [46,47]. On the contrary, when in presence of infection, sites showing pathology may increase the risk of microbial interference with the initial wound healing [48,49]. Even after vigorous curettage and irrigation of the infected socket, some microbial pathogenic species are able to survive in a vegetative state at the site and once the implant is placed they might reactivate and colonize the implant surface initiating retrograde peri-implantitis and bone loss [49-51]. However, recent evidence suggests that granulation tissue collected from infected sites behave similarly to granulation tissue of healing wounds. The findings imply that the cell cultures taken from these granulation tissues contain pluripotent stem cells that might aid tissue healing if the infection is controlled [49]. The study done by Crespi et al. [49] compared two infected socket groups: for one group debridement was performed, and for the second group the granulation tissue was left. The results showed equal favorable outcomes for both of the groups after a period of one year. Although the study has showed favorable results, more long-term randomized clinical trials evaluating clinical and histological results are needed as the data is very limited.

All of the included studies used either pre-operative, post-operative or both antibiotic prophylaxes as a treatment protocol. The usage of antibiotics as a preventive measurement in healthy patients for suppressing the residual infection left during debridement, post-operative infections and oral
implant failures is still disputed [52]. Questions about the type of antibiotics, the dosage and regimen to follow still remain. Romandini et al. [53] found in their review that all introduced protocols reduced early implant failures; however, post-operative prescription due to its prolonged course was associated with higher adverse events (resistance). Nonetheless, further research is needed for a definite protocol.

5.2. Previous systematic reviews

The findings of this present meta-analysis are similar to the two previous meta-analyses done on this subject. Both of those studies indicated that the placement of immediate implants into infected sockets does not significantly affect the rate of implant survival. The quantitative analyses performed by Lee et al. [54] included only three of the studies presented in this review [18,19,21]. Clinical parameters such as MBL, MGL, PD, mBI and WKG were included in the meta-analysis. However, separate analyses for different follow-up periods to decrease the heterogeneity were not made; only the latest follow-up periods were compared. The meta-analysis done by Chen et al. [55] included all of the studies presented in this review but exclusion was made on all implants that were not placed in the esthetic zone. Clinical parameters such as MBL and MGL were included; however, meta-analysis was not conducted on PD, mBI and WKG.

5.3. Limitations and future scientific recommendations

It is important to highlight that no randomized clinical trials were found concerning this subject. It may not be feasible to compare these protocols for the reason that it can be quite challenging to apply similar selection criteria as there are many cases that present with extraction site risk factors such as presence of thin or absent buccal bone, making them less preferable for one protocol. In addition, only English studies were included, a factor that can cause bias with paper selection due to exclusion of any possible primary studies in other languages.

Numerous scientific studies made on osseointegrated implants use the terms “implant survival” and “implant success” synonymously which can generate confusion. It is of importance to differentiate these two terms in order to facilitate the same quality and outcome data within all studies. “Implant survival” is defined as implant and fixed prosthesis present in the mouth regardless of biological and technical complications, while “implant success” involves both clinical (PD, mBI, and modified plaque index) and radiological aspects [56-58]. The survival rates of modern implantology are considered high and predictable. Hence, additional criteria such as the esthetics of the peri-implant soft tissues have become one of the important factors to evaluate the implant success criteria [2,7,8]. Bone characteristics and soft tissue dimensions are critical factors in achieving a satisfactory
esthetic outcome [1,12]. Therefore, a classification of the fresh-sockets including both soft and hard tissues is necessary [59]. The authors Juodzbalys et al. [60] for example, have proposed a classification system and treatment recommendations incorporating both soft and hard tissues for immediate implant placement. The extraction sockets are divided into type I (adequate), type II (compromised) and type III (deficient). In type I, immediate implant placement is indicated and the esthetic outcomes can be satisfactory. In type II, immediate implant placement together with GBR and guided tissue regeneration (GTR) can be followed to correct the compromised hard and soft tissues. In type III however, implant placement should be delayed until socket healing. Guidelines and classifications assessing the fresh-socket morphology are helpful tools for the clinician to plan and judge future clinical situations. Only few of the included studies documented clinical and radiographic parameters such as presence of keratinized mucosa, probing depth, attachment level, plaque index, bleeding index, marginal bone level, marginal gingival level and the peri-implant maintenance therapy. Furthermore, classification of the socket pathology origin was vague and varied among the studies. For future investigation, clinical studies should be conducted with proper documentation of the fresh-socket site morphology and origin of pathology as well as treatment and measurement procedures together with appropriately set inclusion criteria.

5.4. Practical recommendations

The lack of significant statistical differences between immediate implant placement in non-infected sockets and infected sockets reported in this present review might encourage the practitioners to use immediate implant placement in infected sockets more frequently. Nonetheless, the review did not include any randomized clinical trials and as a consequence might introduce biases in the conducted meta-analysis. Additionally, long-term randomized clinical trials are of pivotal importance to refine a definite clinical protocol. Hence, a proper case selection and caution when approaching this protocol is highly recommended since factors such as bone quality, bone quantity, site of implant placement, gingival biotype and surgical experience might affect the overall success rate. Socket debridement of the infected site and administration of systemic antibiotics should be utilized given that all of the included clinical studies implemented such protocols. Additionally, in the presence of compromised bone and soft tissues – GBR or GTR should be utilized for optimum success rate.
6. Conclusion

The conducted meta-analysis suggests that there is no statistical significant difference in survival rates between infected sockets and non-infected sockets. All of the secondary outcome variables showed equal favorable results, except for WKG, which slightly but significantly favored the non-infected group. However, randomized controlled clinical trials with large samples should be made in order to draw a definite conclusion about the efficacy and safety of the treatment.
7. References

1. Blanco J, Carral C, Argibay O, Liñares A. Implant placement in fresh extraction sockets. Periodontol 2000. 2019 Feb;79(1):151-167.

2. Ebenezer V, Balakrishnan K, Asir RV, Sragunar B. Immediate placement of endosseous implants into the extraction sockets. J Pharm Bioallied Sci. 2015 Apr;7(Suppl 1):S234-7.

3. Bassir SH, El Kholy K, Chen CY, Lee KH, Intini G. Outcome of early dental implant placement versus other dental implant placement protocols: A systematic review and meta-analysis. J Periodontol. 2019 May;90(5):493-506.

4. Jyothi SG, Triveni MG, Mehta DS, Nandakumar K. Evaluation of single-tooth replacement by an immediate implant covered with connective tissue graft as a biologic barrier. J Indian Soc Periodontol. 2013;17(3):354–360.

5. Mello CC, Lemos CAA, Verri FR, Dos Santos DM, Goiato MC, Pellizzer EP. Immediate implant placement into fresh extraction sockets versus delayed implants into healed sockets: A systematic review and meta-analysis. Int J Oral Maxillofac Surg. 2017 Sep;46(9):1162–1177.

6. Canellas JVDS, Medeiros PJD, Figueredo CMDS, Fischer RG, Ritto FG. Which is the best choice after tooth extraction, immediate implant placement or delayed placement with alveolar ridge preservation? A systematic review and meta-analysis. J Craniomaxillofac Surg. 2019 Nov;47(11):1793-1802.

7. Swathi KV. Immediate implant placement: A review. J. Pharm. Sci & Res. 2016;8(11): 1315-1317

8. Waasdorp JA. Er,Cr:YSGG Laser Debridement of an Infected Socket for Immediate Implant Placement: A Case Report. Clin. Adv. Periodontics. 2018 Apr; 8: 115-119.

9. Ortega-Martínez J, Pérez-Pascual T, Mareque-Bueno S, Hernández-Alfaro F, Ferrés-Padró E. Immediate implants following tooth extraction. A systematic review. Med Oral Patol Oral Cir Bucal. 2012 Mar;17(2):e251–e261.

10. Tonetti MS, Cortellini P, Graziani F, Cairo F, Lang NP, Abundo R, Conforti GP, Marquardt S, Rasperini G, Silvestri M, Wallkamm B, Wetzel A. Immediate versus delayed implant placement after anterior single tooth extraction: the timing randomized controlled clinical trial. J Clin Periodontol. 2017 Feb;44(2):215-224.

11. Liu R, Yang Z, Tan J, Chen L, Liu H, Yang J. Immediate implant placement for a single anterior maxillary tooth with a facial bone wall defect: A prospective clinical study with a one-year follow-up period. Clin Implant Dent Relat Res. 2019 Dec; 21: 1164– 1174.

12. Clementini M, Agostinelli A, Castelluzzo W, Cugnata F, Vignoletti F, De Sanctis M. The effect of immediate implant placement on alveolar ridge preservation compared to spontaneous healing after tooth extraction: Radiographic results of a randomized controlled clinical trial. J Clin Periodontol. 2019 Jul;46(7):776-786.
13. Furtado Araújo MV, Sommerville D, Dhingra A, Schincaglia GP. Immediate Placement and Restoration of an Implant in an Infected Socket in the Esthetic Zone. Clin Adv Periodontics. 2015 May;5(2): 83-89.

14. Kim JJ, Song HY, Ben Amara H, Kyung-Rim K, Koo KT. Hyaluronic Acid Improves Bone Formation in Extraction Sockets With Chronic Pathology: A Pilot Study in Dogs. J Periodontol. 2016 Jul;87(7):790-5.

15. Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Int J Surg. 2010;8(5):336-41.

16. Higgins JPT, Green S. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from www.hanbook.cochrane.org.

17. Moola S, Munn Z, Tufanaru C, Aromataris E, Sears K, Sfetcu R, Currie M, Qureshi R, Mattis P, Lisy K, Mu P-F. Chapter 7: Systematic reviews of etiology and risk. In: Aromataris E, Munn Z (Editors). Joanna Briggs Institute Reviewer's Manual. The Joanna Briggs Institute, 2017. Available from https://reviewersmanual.joannabriggs.org/

18. Montoya-Salazar V, Castillo-Oyagüe R, Torres-Sánchez C, Lynch CD, Gutiérrez-Pérez JL, Torres-Lagares D. Outcome of single immediate implants placed in post-extraction infected and non-infected sites, restored with cemented crowns: a 3-year prospective study. J Dent. 2014 Jun;42(6):645-52.

19. Jung RE, Zaugg B, Philipp AO, Truninger TC, Siegenthaler DW, Hämmerle CH. A prospective, controlled clinical trial evaluating the clinical radiological and aesthetic outcome after 5 years of immediately placed implants in sockets exhibiting periapical pathology. Clin Oral Implants Res. 2013 Aug;24(8):839-46.

20. Crespi R, Capparè P, Gherlone E. Immediate loading of dental implants placed in periodontally infected and non-infected sites: a 4-year follow-up clinical study. J Periodontol. 2010 Aug;81(8):1140-6.

21. Crespi R, Capparè P, Gherlone E. Fresh-socket implants in periapical infected sites in humans. J Periodontol. 2010 Mar;81(3):378-83.

22. Hita-Iglesias C, Sánchez-Sánchez FJ, Montero J, Galindo-Moreno P, Mesa F, Martínez-Lara I, Sánchez-Fernández E. Immediate Implants Placed in Fresh Sockets Associated with Periapical Pathology: A Split-Mouth Design and Survival Evaluation after 1-Year Follow-Up. Clin Implant Dent Relat Res. 2016 Dec;18(6):1075-1083.

23. Blus C, Szmukler-Moncler S, Khoury P, Orrù G. Immediate implants placed in infected and noninfected sites after atraumatic tooth extraction and placement with ultrasonic bone surgery. Clin Implant Dent Relat Res. 2015 Jan;17 Suppl 1:e287-97.

24. Bell CL, Diehl D, Bell BM, Bell RE. The immediate placement of dental implants into extraction sites with periapical lesions: a retrospective chart review. J Oral Maxillofac Surg. 2011 Jun;69(6):1623-7.
25. Fugazzotto PA. A retrospective analysis of implants immediately placed in sites with and without periapical pathology in sixty-four patients. J Periodontol. 2012 Feb;83(2):182-6.

26. Zuffetti F, Capelli M, Galli F, Del Fabbro M, Testori T. Post-extraction implant placement into infected versus non-infected sites: A multicenter retrospective clinical study. Clin Implant Dent Relat Res. 2017 Oct;19(5):833-840.

27. Fugazzotto P. A retrospective analysis of immediately placed implants in 418 sites exhibiting periapical pathology: results and clinical considerations. Int J Oral Maxillofac Implants. 2012 Jan-Feb;27(1):194-202.

28. Truninger TC, Philipp AO, Siegenthaler DW, Roos M, Häggerle CH, Jung RE. A prospective, controlled clinical trial evaluating the clinical and radiological outcome after 3 years of immediately placed implants in sockets exhibiting periapical pathology. Clin Oral Implants Res. 2011 Jan;22(1):20-7.

29. Hamed MS. Clinical study of osseointegration of immediate implant in dentoalveolar socket with and without periapical pathosis. Gulf Med. J. 2012;1(S1):S80-S89.

30. Nandal S, Ghalaut P, Shekhawat H. A radiological evaluation of marginal bone around dental implants: An in-vivo study. Natl J Maxillofac Surg. 2014;5(2):126–137.

31. Koutouzis T. Crestal Bone Level Alterations in Implant Therapy. Available at: [https://www.semanticscholar.org/paper/Crestal-Bone-Level-Alterations-in-Implant-Therapy-Koutouzis/56c850da0d98af3f66be46563ad41fe3f907da95.]

32. Albrektsson, T. and Isidor, F. (1994) Consensus Report of Session IV. In: Lang, N.P. and Karring, T., Eds., Proceedings of the First European Workshop on Periodontology, Quintessence Publishing, London, 365-369

33. Nandal S, Ghalaut P, Shekhawat H. A radiological evaluation of marginal bone around dental implants: An in-vivo study. Natl J Maxillofac Surg 2014 Apr;5:126-37

34. Berberi AN, Sabbagh JM, Aboushelib MN, Noujaim ZF, Salameh ZA. A 5-year comparison of marginal bone level following immediate loading of single-tooth implants placed in healed alveolar ridges and extraction sockets in the maxilla. Front Physiol. 2014 Jan;5:29.

35. Galindo-Moreno P, León-Cano A, Ortega-Oller I, Monje A, O Valle F, Catena A. Marginal bone loss as success criterion in implant dentistry: beyond 2 mm. Clin Oral Implants Res. 2015 Apr;26(4):e28-e34.

36. Javaid MA, Khurshid Z, Zafar MS, Najeeb S. Immediate Implants: Clinical Guidelines for Esthetic Outcomes. Dent J (Basel). 2016 Jun;4(2):21.

37. Basualdo J, Ivankovic M, Kuzmicic J, Fernández E. Atraumatic extraction and immediate implant placement into infected site with the “ice cream cone” technique and L-PRF: A Case Report. Rev. Clin. Periodoncia Implantol. Rehabil. Oral. 2018;11(1):43-46.
38. Monje A, Blasi G. Significance of keratinized mucosa/gingiva on peri-implant and adjacent periodontal conditions in erratic maintenance compliers. J Periodontol. 2019 May;90(5):445-453.

39. Lin GH, Chan HL, Wang HL. The significance of keratinized mucosa on implant health: a systematic review. J Periodontol. 2013 Dec;84(12):1755-67.

40. Pranskunas M, Poskevicius L, Juodzbalys G, Kubilius R, Jimbo R. Influence of Peri-Implant Soft Tissue Condition and Plaque Accumulation on Peri-Implantitis: a Systematic Review. J Oral Maxillofac Res. 2016 Sep 9;7(3):e2.

41. Chiu YW, Lee SY, Lin YC, Lai YL. Significance of the width of keratinized mucosa on peri-implant health. J Chin Med Assoc. 2015 Jul;78(7):389-94.

42. Longoni S, Tinto M, Pacifico C, Sartori M, Andreano A. Effect of Peri-implant Keratinized Tissue Width on Tissue Health and Stability: Systematic Review and Meta-analysis. Int J Oral Maxillofac Implants. 2019 Nov/Dec;34(6):1307-1317.

43. Pigozzo MN, Rebelo da Costa T, Sesma N, Laganá DC. Immediate versus early loading of single dental implants: A systematic review and meta-analysis. J Prostheth Dent. 2018 Jul;120(1):25-34.

44. Gallucci, GO, Hamilton, A, Zhou, W, Buser, D, Chen, S. Implant placement and loading protocols in partially edentulous patients: A systematic review. Clin Oral Implant Res. 2018; 29(Suppl. 16): 106–134.

45. McCracken MS, Chavali RV, Al-Naief NS, Eleazer PD. A residual granuloma in association with a dental implant. Implant Dent. 2012 Apr;21(2):87-90.

46. Villar CC, Huynh-Ba G, Mills MP, Cochran DL. Wound healing around dental implants. Endod Top. 2011 Jan;25(1):44–62.

47. Li J, Jansen JA, Walboomers XF, van den Beucken JJ. Mechanical aspects of dental implants and osseointegration: A narrative review. J Mech Behav Biomed Mater. 2020 Mar;103:103574.

48. Esfahrood ZR, Kadkhodazadeh M, Amid R, Rokn A. Is The Periapical lesion a Risk For Periimplantitis? (A review). J Dent (Tehran). 2012 Jun;9(2):162–173.

49. Crespi R, Capparé P, Crespi G, Lo Giudice G, Gastaldi G, Gherlone E. Immediate Implant Placement in Sockets with Asymptomatic Apical Periodontitis. Clin Implant Dent Relat Res. 2017 Feb;19(1):20-27.

50. Flanagan D. Enterococcus faecalis and Dental Implants. J Oral Implantol. 2017 Feb;43(1):8-11.

51. Kusek ER. Immediate implant placement into infected sites: bacterial studies of the Hydroacoustic effects of the YSGG laser. J Oral Implantol. 2011 Mar;37 Spec No:205-11.

52. Rodríguez Sánchez F, Arteagoitia I, Rodríguez Andrés C, Caiazzo A. Antibiotic prophylaxis habits in oral implant surgery among dentists in Italy: a cross-sectional survey. BMC Oral Health. 2019 Dec;19(1):265.
53. Romandini M, De Tullio I, Congedi F, Kalemaj Z, D'Ambrosio M, Laforí A, Quaranta C, Buti J, Perfetti G. Antibiotic prophylaxis at dental implant placement: Which is the best protocol? A systematic review and network meta-analysis. J Clin Periodontol. 2019 Mar;46(3):382-395.

54. Lee J, Park D, Koo KT, Seol YJ, Lee YM. Comparison of immediate implant placement in infected and non-infected extraction sockets: a systematic review and meta-analysis. Acta Odontol Scand. 2018 Jul;76(5):338-345.

55. Chen H, Zhang G, Weigl P, Gu X. Immediate placement of dental implants into infected versus noninfected sites in the esthetic zone: A systematic review and meta-analysis. J Prosthet Dent. 2018 Nov;120(5):658-667.

56. Negm SAM. Implant success versus implant survival. Dentistry. 2016:6(2):359.

57. Moraschini V, Poubel LA, Ferreira VF, Barboza Edos S. Evaluation of survival and success rates of dental implants reported in longitudinal studies with a follow-up period of at least 10 years: a systematic review. Int J Oral Maxillofac Surg. 2015 Mar;44(3):377-88.

58. Simonis P, Dufour T, Tenenbaum H. Long-term implant survival and success: a 10-16-year follow-up of non-submerged dental implants. Clin Oral Implants Res. 2010 Jul;21(7):772-7.

59. Bhokare A, Elghannam M, Somji SH, Florio S, Suzuki T. Case Selection Criteria for Predictable Immediate Implant Placement and Immediate Provisionalization. J Oral Biol. 2018; 5(1):6.

60. Juodzbalys G, Sakavicius D, Wang HL. Classification of extraction sockets based upon soft and hard tissue components. J Periodontol. 2008 Mar;79(3):413-24.