The journal of
PROSTHETIC AND IMPLANT DENTISTRY
Official Publication of Indian Prosthodontic Society
Kerala State Branch

ANALYZING THE IMPACT OF DIFFERENT IMPLANT PLACEMENT PROTOCOLS ON THE ESTHETIC STABILITY OF SINGLE IMPLANTS: A COMPREHENSIVE SYSTEMATIC REVIEW AND META-ANALYSIS.

*Priya Pungle. S, ** Naisargi Shah P, ***Sangeeta Yadav, ****Anuradha Govardhane B, *****Adhithi Prabhu

*Lecturer, **Professor and Head of department, Department of Prosthodontics and Crown and Bridge, Terna Dental College, Navi Mumbai, Maharashtra; ***Adjunct Associate Professor, University of Minnesota School of Dentistry, USA; ****Lecturer, Department of Prosthodontics and Crown and Bridge, Terna Dental College. Navi Mumbai, Maharashtra | Corresponding Author: Dr. Priya Pungle. S, Email: priyapungle77@gmail.com

https://doi.org/10.55231/jpid.2024.v07.i03.06

Abstract

Aims: To analyze impact of different implant placement timings on the esthetic stability of a single implant restoration in maxillary anterior region.

Materials and methods: The systematic review and meta-analysis adhered to the PRISMA guidelines and were registered in the PROSPERO database. In addition to systematic searches on the national library of medicine (MEDLINE PubMed), Cochrane library, Google Scholar, and EbscoHost, manual searches were also conducted to identify articles published from January 1, 2000, to December 1, 2020. The included studies comprised randomized controlled trials, as well as prospective and retrospective cohort clinical studies. The assessment of risk of bias employed the Cochrane Collaboration's tool, MINORS tool, and a quality appraisal checklist. Utilizing the Review Manager software tool, a meta-analysis was conducted, and the robustness of the meta-analytic findings was duly evaluated.

Results: Out of 313 studies screened, seven met the predetermined inclusion and exclusion criteria for incorporation into the systematic review. The meta-analysis disclosed an effect on marginal bone loss associated with different implant placement timings. However, the overall impact on esthetic stability was not statistically significant. Furthermore, there is moderate evidence suggesting a decrease in marginal bone loss following immediate implant placement, with a mean difference of -0.33mm.

Conclusions: The timing of implant placement appears to have some impact on both marginal bone loss and pink esthetic score. However, no statistically significant difference was observed when comparing various implant placement timings in terms of pink esthetic score and marginal bone loss. The evidence lacked sufficient strength to firmly support the aforementioned observations, emphasizing the need for additional well-designed randomized clinical trials to draw definitive conclusions.

Keywords: dental implants, single-tooth implants, marginal bone loss, pink esthetic score.

The journal of
PROSTHETIC AND IMPLANT DENTISTRY
Official Publication of Indian Prosthodontic Society
Kerala State Branch

Introduction

Rehabilitating the maxillary anterior region poses a formidable challenge due to the heightened visibility and aesthetic expectations of patients.[1] This complexity in dental implant restoration arises from factors like reduced buccal bone volume, bone angulation, thin biotype, and a higher incidence of soft tissue defects.[2] The esthetic outcome of implants is further influenced by variables such as the patient's smile line, tooth and root positions, biotype of the periodontium, tooth shape, bone anatomy of the implant site, and optimal implant positioning.[3] The timing of implant placement is also considered a crucial factor affecting esthetic outcomes.[4] Various classifications for the timing of implant placement after tooth extraction exist, with one of the earliest attempts in 1993 introducing terms like immediate, recent, delayed, and mature.[5] The widely accepted classification from the Third International Team for Implantology (ITI) consensus conference categorizes implant placement into types 1, 2, and 3.6 Type 1 (immediate implant placement) involves placing implants in fresh extraction sockets within 24 hours. Type 2 (early implant placement) sees implants positioned approximately 4 to 8 weeks (up to 16 weeks) after tooth extraction. In Type 3 (late/conventional implant placement), implants are placed once most dimensional changes in the alveolar ridge have occurred, typically after 16 weeks.

When rehabilitating the maxillary anterior region, esthetic outcome is of paramount importance.[7-10] The primary determinants for evaluating esthetic stability are marginal bone and soft tissues.[10] Marginal bone level, measured from the implant platform to the alveolar crest, assesses hard tissue changes. For soft tissue esthetic evaluation, the commonly used aesthetic index is the Pink Esthetic Score (PES).[10,11] PES incorporates variables such as soft tissue color, soft tissue level, mesial and distal papilla, alveolar process deficiency, soft tissue contour, and soft tissue texture—critical factors in assessing the overall health and aesthetics of the soft tissues surrounding the implant. These variables are considered in peri-implant soft tissue evaluation to ensure not only the functional success of the implant but also its aesthetic harmony with the surrounding natural teeth and tissues.

Several studies and systematic reviews have compared different implant placement timings for single and multiple implant restorations concerning esthetic stability.[12-14] The majority of these studies have included regenerative and augmentation procedures in their assessment of esthetic outcomes. However, few studies have focused on evaluating the effect of different implant placement timings on esthetic outcomes specifically in non-augmented sites. Therefore, this systematic review aims to compare the effects of different implant placement timing protocols—immediate implant placement, early implant placement, or late implant placement—for enhanced esthetic stability, considering parameters such as Pink Esthetic Score and marginal bone loss.

Material and methods

Prospero registration and search protocol

In the course of this systematic review, the final protocol was developed following an analysis of findings from the initial pilot search. The protocol adheres to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. Following the formulation of the protocol, it was registered on the PROSPERO website, and the corresponding registration number for this study is CRD42020189405.

Focus question

The focused research question was as follows:

"Do the immediate implant placement (IIP) and early implant placement (EIP) have same effect on esthetic stability of single implant restoration in maxillary anterior region as late implant

placement?"

PICO

The PICO (patient, intervention, comparison and outcome) formulated to answer the focused question was

P: Studies with single implant restoration in maxillary anterior region (premolar to premolar)

I 1: Immediate implant placement (IIP) placed within 24hrs in fresh extraction socket

I 2: Early implant placement (EIP) with soft tissue healing within 4-8weeks or partial bone healing within 12-16weeks after extraction

C: Late implant placement (LIP) in healed bone more than 16weeks after extraction.

O: Esthetic stability by means of pink aesthetic score and marginal bone loss.

Inclusion and Exclusion Criteria:

Inclusion Criteria:

In vivo studies with Randomized Controlled Trials, Prospective and Retrospective Cohort clinical studies,

Studies published in peer-reviewed journals,

Studies clearly stating different timings of implant placement, their impact on outcome of esthetics with qualitative and quantitative results,

Studies published in English language only,

Studies published from1st January2000 to 1st December 2020,

Studies with single implant restoration in maxillary anterior region with systemically healthy patients,

Studies that include a follow-up period of one year or longer following the placement of dental implants,

Studies involving immediate implant placement wherein graft placement was done in the extraction socket for closure of the jumping distance.

Exclusion Criteria:

Case series, review articles, case reviews & case surveys and case reports.

Limited details available regarding the surgical protocol and the timing post-tooth extraction.

Studies involving both hard and soft tissue augmentation, either conducted during implant placement or as part of any subsequent surgical procedure

Studies with multiple implant restoration.

Studies with implant restoration in posterior region.

Studies with implants in medically compromised patients.

Search Strategy

Systematic electronic searches encompassed multiple databases, including the National Library of Medicine (MEDLINE PubMed), Cochrane Library, Google Scholar, and EbscoHost-Dentistry. Additionally, manual searches were conducted in pertinent journals, and cross-referencing of selected studies was meticulously performed to identify additional articles meeting the eligibility criteria. To structure the search strategy, a concept table was devised based on the PICO criteria, incorporating key concepts, controlled vocabulary terms, and free text terms. The acquisition of Medical Subject Headings (MeSH Terms) involved querying key concepts within the MeSH database, a controlled vocabulary thesaurus employed by the National Library of Medicine (NLM) for indexing articles in the MEDLINE PubMed database. (Table 1)

Study Selection:

Two blinded independent reviewers, Y.S. and G.A., independently performed this step, and

in instances of disagreement, a third reviewer, S.N., was consulted. Inter-examiner agreement was assessed using the Kappa (K) test for each reviewer's searches. The data underwent statistical analysis utilizing the Statistical Package for the Social Sciences (SPSS v 26.0, IBM). Statistical significance was determined at $p < 0.05$, with an α error of 5% and a β error of 20%, ensuring an 80% power for the study. The overall K value was 0.97, and individual values for specific databases were as follows: National Library of Medicine (MEDLINE PubMed) (K = 0.901), EbscoHost-Dentistry (K = 1.000), Cochrane (K = 0.827), and Google Scholar (K = 0.949), demonstrating the agreement between reviewers' searches. Conflicts were resolved through discussion of each article until consensus was reached. Efforts were made to contact corresponding authors of included studies for the retrieval of any missing information or clarification of specific items.

Consequent search strategy:

Following the initial literature search, all articles were screened to eliminate irrelevant publications, in vitro and animal studies, case reports, case series, and review articles. Studies were screened further based on relevance of data reported in abstracts. Finally, the full texts of the selected papers were examined to confirm study eligibility, following the inclusion and exclusion criteria for included studies.

Assessment of risk of bias in individual studies

Two reviewers, namely Y.S. and G.A., independently evaluated the risk of bias. Quality assessment for included randomized controlled studies utilized the Cochrane Collaboration's tool (RevMan 5.4), evaluating seven criteria: random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), selective reporting (reporting bias), and other bias. Studies were categorized as low risk if they met all criteria, moderate risk if one criterion was missed, and high risk if two or more were missed. For five non-randomized studies, the MINORS (Methodological Items for Non-Randomized Studies) [16] scale was employed.

Statistical analysis

In terms of statistical analysis, the extracted data underwent assessment using the Cochrane Collaboration's tool, RevMan 5.4, to examine the relationship between esthetic stability and implant placement timings. The analysis applied the inverse variance method to continuous outcome variables, presenting effect sizes as mean differences or standardized mean differences, along with 95% confidence intervals (CI). Forest plots were generated for both overall and subgroup analyses to depict effect sizes. Additionally, a funnel plot was created for the primary outcome variable to evaluate potential publication bias across studies. The significance level for the analysis was pre-set at 0.05. Mean and standard deviation values for immediate, early, and late implant placement (with marginal bone loss and pink esthetic score), along with the number of specimens per group, were utilized to calculate the mean difference with a 95% CI. A random-effect model was employed when studies were not functionally equivalent for generalizing results from the meta-analysis. Heterogeneity was assessed using the I^2 index, considering values close to 0% as indicative of non-heterogeneity, close to 25% as low heterogeneity, close to 50% as moderate heterogeneity, and close to 75% as high heterogeneity between studies.

Results

Description of studies

Total of 313 articles that were obtained through the electronic searches were exported into the Mendeley Desktop software. The six articles ob-

tained through the manual search were added to the software manually. Two hundred and forty-nine (249) articles were left after the elimination of duplicates and were subsequently taken into further consideration for the data selection process. Out of these, 110 articles were excluded after screening of the title. Twenty nine (29) articles were left after abstract screening. Seven articles met the inclusion and exclusion criteria and were thus selected in this systematic review. The findings of the comprehensive electronic and manual searches are consolidated in Figure 1, following the PRISMA (preferred reporting items for systematic reviews and meta-analyses) flowchart. All included studies reported Ethics Committee approval. Participant characteristics among the selected studies are summarized in Table 2. Clinical characteristics and outcomes from the selected studies are summarized in Table 3.[17-24] Two studies out of seven were randomized controlled studies and five were non-randomized controlled trials.

This systematic review is based on seven clinical studies examining single implants with follow-up periods ranging from 12 to 96 months. Out of 497 implants, data from 453 were available for evaluation, allowing a comparison of different implant placement timings. At the conclusion of the studies, 446 patients who had undergone a total of 453 single implants (171 Immediate Implant Placement (IIP), 49 Early Implant Placement (EIP), and 187 Late Implant Placement (LIP)) were available for assessment, resulting in an overall dropout rate of 9%. Notably, one study reported selective loss of follow-up, with an 18% dropout rate, specifically 31.3% following IIP and 21.7% following LIP.[18] More than 5 % loss was observed in one study.[20] Only one patient loss with immediate placement was observed in another similar study.[21] Whereas no follow-up loss was reported in studies with early implant placement.[22-24] The organized data for analysis was categorized under distinct headers such as Study ID, author and year of publication, study type, groups, patients lost to follow-up, implant site, hard tissue augmentation, antibiotics, implant type, age, restoration, surgical protocol. The details are compiled in Table 1. Another table for clinical outcomes was entered under following headers: marginal bone level, buccal bone thickness, pink esthetic score, patient's satisfaction, vertical soft tissue level changes, pocket depth and other outcomes are noted in Table 2.

Postoperative antibiotics were administered in most of the studies. [17-18,22-24] Cooper *et al*[20] was not

Table 1:

POPULATION	(((((dental implants[MeSH Terms]) OR (Dental Implants, Single-Tooth[MeSH Terms])) OR (single tooth implants*[tiab])) OR (implant Prosthesis*[tiab])) OR (Single implant insertion*[Tiab])) OR (Single implant Prosthesis*[Tiab]) OR (maxillary anterior region)
INTERVENTION 1	((((((immediate insertions*[tiab]) OR (immediate implant insertions*[tiab])) OR (insertions*[tiab])) OR (immediately*[tiab])) OR (fresh socket*[tiab])) OR (immediate implant placement*[tiab])) OR (implant placement timings*[tiab])
INTERVENTION 2	(((early implant placement*[tiab]) OR (early implantation*[tiab])) OR (early implant*[-tiab])) OR (early placement*[tiab])
COMPARISION	((((late implant*[tiab]) OR (late implant insertion*[tiab])) OR (conventional implant placement*[tiab])) OR (Delayed implant placement*[tiab])) OR (Delayed placement*[tiab])
OUTCOME	(esthetics*[tiab]) AND (((marginal bone loss*[tiab]) OR (alveolar bone*[tiab])) OR (pink esthetic score*[tiab]))

MeSH terms, medical subject headings. Tiab, title /abstract

Table 2: A. Patient characteristics of studies on implant placement

Author	Study type	Groups: no.of patients /no.of implants	Follow up	Loss of patients with follow up / total patients	Implant site (IIP/LIP)	Augmentation	Antibiotics	Implant type	Age (years)	Immediate restoration	Surgical protocol
Raes et al [17-18]	Prospective cohort	IIP: 16/16 LIP: 23/23	At 1 year and at 8 years	8 years IIP: 11/16 LIP: 18/23	CI/CA :17 PM :12	Not mentioned	Yes	Osseo-Speed,	IIP: 45 LIP: 40	Yes	IIP:Flapless LIP: Mucoperiosteal flap
Nima pour et al [19]	Cross-sectional retrospective	IIP: 22 LIP:20	Approx. 1years- to 1.5years	No loss	CI:5 /1; LI:3/3; C:1/2; PM:13/14	Not performed	Not mentioned	Not mentioned	IIP:40.14 LIP: 43.40	No	Fullthickness flap
Cooper et al[20]	Prospective	IIP: 55/55 LIP:58/58	1years 3years , 5years	MORE THAN 5 % loss At 1year IIP:51/55 LIP:57/58	CI: 11/11; LI:13/18; CA7/2. 1st PM:18/11; 2nd PM: 16/6	Not performed	Not mentioned	Osseo-speed™,	IIP: 45 LIP: 42	Yes	Mucoperiosteal flap as per need otherwise flapless
Raes et al [21]	Retrospective	IIP :16 LIP:23 GIP: 9	1years.	IIP: 1 patient after 3 months	15-25	Yes if buccal bone gap≥ 2.5mm	Not mentioned	Osseo-speed™,	IIP:45 LIP: 40 GIP: 35	Yes	IIP:flapless LIP:fullthickness flap
Hof et al[22]	Retrospective	IIP:26; EIP:35;LIP:13 GBR:15 ;ABG:64	2years	No loss	CI:58; LI:37; CA:24; 1stPM:34	Yes (GBR and AGB)	Yes	Nobel biocare®,	37 ± 17	Yes	Flap surgery
Palattella et al[23]	RCT	IIP: 9 EIP:9	3 to 5 years	No loss	CI:14 ;LI:2 ;CA:2	No	Yes	Institut straumann Ag	35 (21 - 49)	Yes	Fullthickness flap
De bruyn et al[24]	Prospective RCT	IIP: 62/58 EIP: 70/63	2years	No loss	IIP/EIP CI:11/11; LI:13/18; CA :7/2; 1st PM:18/11; 2nd PM:6/16	No	Yes	Osseo-speedtm implants	50(35 to 80)	-	Flap surgery

specific about use of antibiotics and Pour *et al*[19] and Raes *et al*[21] failed to mention about use of antibiotics. Out of seven, six studies mentioned about type of implant used with their brand name. Astra Tech OsseoSpeed™ implants system was used in four studies.[17-18,20,21,24] Brånemark® MK-III and Nobel Replace™ Tapered, Nobel Bio care®, Goteborg, Sweden was used in one study.[22] and TE Straumann G was used in study by Palattella *et al*[23] and pour *et al*[18] did not mention about implant type. The common protocol across all studies incorporated implant placement along with immediate provisional restoration, with the final cementation performed 10 to 15 weeks post-placement.

Risk of bias in the individual studies

Both the randomized controlled trials included in this study had shown were assessed as being at unclear risk of bias because each of these trials was at unclear risk of bias in one or more domains. (Figure no. 2)[23, 24] Quality assessment of these studies revealed good overall quality, with

Table 2. Patient characteristics of studies on implant placement.

IIP:Immediate implant placement, EIP:Early implant placement,LIP:Late implant placement, PES:Pink esthetic score, ABG: autologous bone graft, GBR: guided bone regeneration,CI: central incisor, LI: Lateral incisor, CA: canine, PM: premolar

Table 2: B. Clinical characteristics and outcomes of studies on implant placement

Author	Marginal bone loss (mm) (Mean(SD))	PES Mean(SD)	Pocket depth(mm) (Mean(SD))	other outcomes
Raes et al [17-18]	-	IIP-10.3±2.11 LIP- 9.22±2.31	not mentioned	
Nima pour et al [19]	IIP- 0.62 ±0.44 LIP- 0.43±0.39	IIP: 8.54± 1.26 LIP: 8.1±1.65	Not mentioned	Modified bleeding index, IIP: 0.49 ±0.44 LIP: 0.70 ± 0.50
Cooper et al[20]	IIP: -2.06 ± 2.38 LIP : 0.10 ±1.29	at 1year :12.15 ±0.99 at 5years: 11.18 ±1.38	at 1year :3.1 at 5 year: 3.1	
Raes et al [21]	IIP: -1.05 ±1.78 LIP: -0.18±1.26	IIP:10.33± 2.29 LIP: 10.35 (1.58)	not mentioned	-
Hof et al[22]	IIP:1.5 ± 0.8 EIP:1.2 ±0.6 LIP:1.4± 0.8	IIP:10.7 ±2.4 EIP: 10.4± 2.2, LIP: 11.2 ±2.0	COMBINED MEAN 3.6 ±1.2	-
Palattella et al[23]	IIP:0.54 ±0.51 EIP:0.46 ±0.54	not mentioned	not mentioned	Papilla index: IIP:2.0(0.7),EIP:1.7(0.8), LIP: 2.5 (0.5)
De bruyn et al[24]	IIP: 0.43±0.63 EIP:0.38±0.62	-	-	ISQ(implant stability quotient) IIP: 65± 5 EIP:74 ± 3 mucosal margin:IIP : -0.8 ± 0.7: EIP: -0.6 ± 0.6 ,

Table 3: Excluded Studies

SR NO	AUTHOR	YEAR	TITLE	REASON FOR EXCLUSION
1	Schrrop et al[25]	2014	**Early, delayed, or late single implant placement: 10-year results from a randomized controlled clinical trial**	**Included maxillary both mandibular region for implant placement and mixed results for the same.**
2	Julia Garabetyan et al.[26]	2019	The relationship between dental implant papilla and dental implant mucosa around single-tooth implant in the esthetic area: A retrospective study	Most of implants (n = 44, 48.9%) were placed with simultaneous GRB + CTG
3	Zuiderveld E et al.[27]	2019	Outcome of Treatment with Single Implants in Preserved Versus Nonpreserved Alveolar Ridges: A 1-year Cohort Study	preserved alveolar ridges, compared with nonpreserved anterior posterior region alveolar ridges
4	Arora et al.[28]	2018	Immediate and Early implant placement in single-tooth gaps in the anterior maxilla: A prospective study on ridge dimensional, clinical, and aesthetic changes.	Graft placement in immediate as well as early implant placement
5	Tonneti et al.[29]	2017	Immediate vs. Delayed Implant Placement after Anterior Single Tooth Extraction: The Timing Randomized Controlled Clinical Trial	Mentioned both maxillary / mandibular anterior region
6	Barone et al.[30]	2014	The Clinical Outcomes of Immediate Versus Delayed Restoration Procedures on Immediate Implants: A Comparative Cohort Study for Single-Tooth Replacement	Mentioned both maxillary / mandibular anterior region.
7	Mastrangelo F et al.[31]	2018	Immediate post extractive implants with and without bone graft: 3-year follow-up results from a multicenter controlled randomized trial	Only immediate placement with Bone graft.
8	David J. Meister et al.[32]	2015	Esthetic, clinical and patient-centered outcomes of immediately placed implants (Type 1) and early placed implants (Type 2): preliminary 3-month results of an ongoing randomized controlled clinical trial	Insufficient data regarding site of implant placement
9	Jonker et al.[33]	2020	Esthetics and patient related outcomes of implant placed with GBR and complete native bone- prospective clinical trial	Insufficient data regarding site of implant placement
10	Sibers et al.[34]	2010	Immediate verses delayed function of dental implants- a 1to7 year follow up study of 222 implants	Included patients receiving multiple implants
11	Soydan et al.[35]	2013	Are success and survival rates of early implant placement higher than immediate implant placement?	Mixed data for maxillary and mandibular implant , single implants with bridge , overdenture mentioned

no identified high risk of bias for any criteria. According to the risk of bias assessment conducted using the RevMan v5.4 tool, six criteria were determined to have a low risk of bias. For non-randomized studies MINORS (methodological items for non-randomized studies) [16] scale was used. The individual summary of risk of bias for the 12 points was plotted in the risk of bias graph. Categorization of scores was done as follows: Scores greater than 16 were labeled as Low risk of bias, indicating plausible bias unlikely to seriously alter the results; scores between 12 and 16 were categorized as Unclear risk of bias, suggesting plausible bias that raises some doubt about the results; and scores less than 12 were considered as High risk of bias, reflecting plausible bias that seriously weakens confidence in the results. All studies showed low risk of bias with high quality of data as all studies scored above 16. The included studies which seemed to be relatively homogenous in their study design and outcome variables considered for a quantitative analysis by means of a meta-analysis. [19,20,21-24]

Primary outcome variable: Marginal Bone Loss

Pour *et al*[19], Cooper *et al*[20], Raes *et al*[21], Hof *et*

Table 4: Summary of risk of bias for NRCS's

Sr.no	MINORS TOOL SYSTEMATIC REVIEW	1	2	3	4	5
1	A clearly stated aim.	2	2	2	2	2
2	Inclusion of consecutive patients	2	1	2	2	1
3	Prospective collection of data	2	2	2	2	2
4	Endpoints appropriate to the aim of the study	2	2	2	2	2
5	Unbiased assessment of the study endpoint	1	2	0	0	2
6	Follow-up period appropriate to the aim of the study.	2	2	2	2	2
7	Loss to follow up less than 5%	1	2	1	2	2
8	Prospective Calculation of study size	0	0	2	0	2
9	An adequate control group	0	2	0	0	0
10	Contemporary groups	2	2	2	2	2
11	Baseline equivalence of groups	2	2	2	2	2
12	Statistical analysis	2	0	1	1	1
	TOTAL SCORE (OUT OF 24) :	18	21	20	19	19

Table 4. Summary of Quality assessment of selected non randomized studies using MINORS tool

Footnote: GRADING: Low risk of bias (plausible bias unlikely to seriously alter the results) >16, Unclear risk of bias (plausible bias that raises some doubt about the results:) 12-16 or High risk of bias (plausible bias that seriously weakens confidence in the results) <12.

Figure1: Flowchart

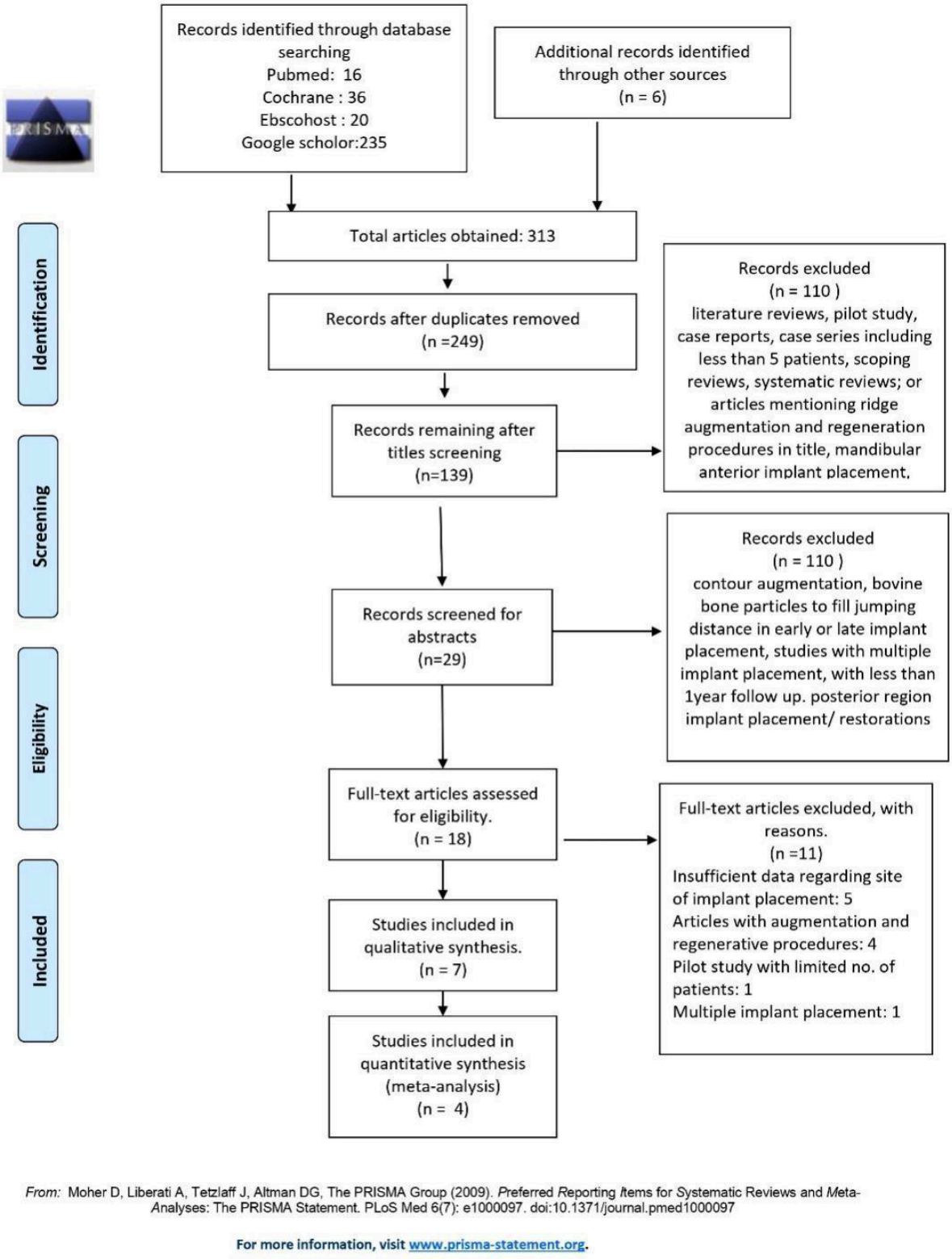

Figure 1. Flow chart for search process indicating numbers (n) of excluded studies, stages of exclusion, and reasons for exclusion.

al[22] had discussed data on marginal bone levels with IIP and LIP. Cooper *et al*.[20] showed significant bone gain in IIP and comparatively less bone gain in LIP. De Bruyn *et al* [24] and Palattella *et al* [23]showed slight difference in bone levels in IIP and EIP after implant placement.

Hof *et al*[22] after comparing all three placement timings (IIP,EIP,LIP), was found less bone loss with EIP when compared to IIP and LIP. Meta-analysis on marginal bone loss showed no significant difference comparing IIP and LIP and IIP and EIP [19,20,21-24] ([IIP Vs LIP (*P* = 0.14 , mean difference = -0.65, 95% CI [-1.51 to 0.22]] and IIP Vs EIP (*P* = 0.21, mean difference = 0.11, 95% CI [-0.06, 0.29])) (**Figure 4A and 4B**)

Primary outcome variable: Pink Esthetic Score

Four studies assessed the aesthetic outcome using the pink esthetic score (PES). [17-18,.19, 21, 22] Raes *et al*. [16-17], Raes *et al*.[21] and Hof *et al*.[22] utilized the original PES index, resulting in a score based on a total of 14 points. Pour *et al*.[19] employed a modified PES index, generating a score on a total of 10.5 points.[5] While Raes *et al*. [17-18]and Pour *et al*. reported a slightly superior aesthetic outcome for Immediate Implant Placement (IIP), whereas Raes *et al*. [17-18] and Hof *et al*.[22] described slightly higher pink esthetic scores for Late Implant Placement (LIP).However, the meta-analysis did not reveal a statistically significant difference favoring one placement timing over the other (*P* = 0.45, mean difference =0.25, 95% CI [-0.39 to 0.89]) (**Figure 5**)

Esthetic stability:

Esthetic stability was evaluated in this study in terms of Marginal Bone Loss and PES. A subgroup analysis was performed with all studies included in meta-analysis with marginal bone loss and pink esthetic score showed no significant difference for esthetic stability while comparing different implant placement timings. [17-24] (*P* = 0.29, SMD= -0.10, 95% CI (-0.54, 0.33)) (**Figure 6**)

Secondary outcome variables:

Buccal Bone Thickness:

Raes *et al*. [17-18] found that irrespective of timing of placement, buccal bone wall less than 2 mm

Figure 2: Risk of bias for RCT's

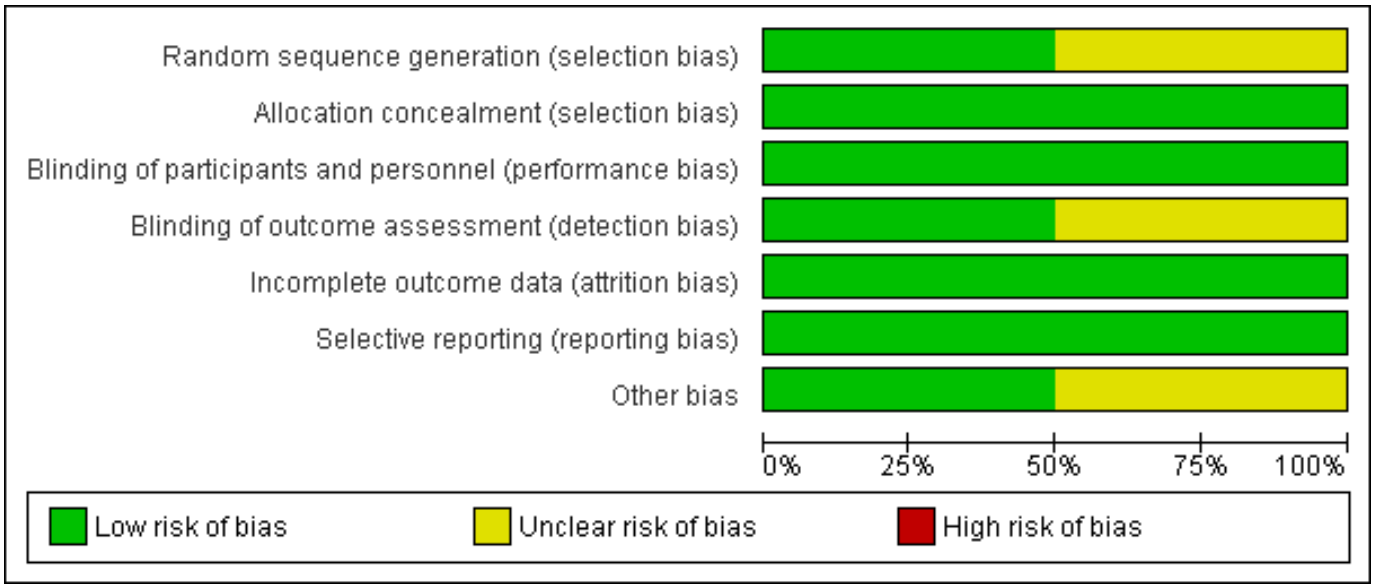

Figure 2. Graph of Quality assessment using RevMan v5.4 tool used for risk of bias assessment for randomized controlled studies

at 1-3-5 mm from the implant shoulder was observed at all implant sites with IIP and LIP with 8 years follow up. None of other studies evaluated buccal bone thickness in anterior esthetic zone.

Papillary Recession (Figure 7)

Among the studies, Raes *et al*. [17-18], Cooper *et al*.[20] and Raes *et al*.[21] were the only ones that detailed vertical changes in papilla height following Immediate Implant Placement (IIP) and Late Implant Placement (LIP) and provided separate data for the mesial and distal aspects. The overall analysis revealed statistically significant differences in papillary recession, indicating greater recession following LIP when compared to IIP (Weighted Mean Difference [WMD] 0.44 mm, 95% CI [0.23, 0.64], P = 0.002). Notably, there was low heterogeneity across studies, with an I^2 of 0% (P = 0.54)

Figure Risk of bias summary: review authors' judgments

Patients Satisfaction

Three out of seven studies evaluated patient related outcome at different timing of implant placement. Two studies performed Visual analogues scales (VAS) for general satisfaction, comfort, speech, aesthetics, functional outcome, and cleanability. High scores were given for all parameters indicative of high patient satisfaction. Following IIP, 95% patient satisfaction was found and with other placement timing satisfaction was less.

Oral health impact profile (OHIP-14) scale used by Raes *et al*. [17-18] compared patient satisfaction at one year and eight years. There was a slight but significant difference between 1 year and at least 8 years of follow-up in the late implant placement. (*P* = 0.042). Where it seems, patient satisfaction is better in case late implant placement and comparatively less satisfied in case of immediate implant with long term follow up.

Discussion

The present review exclusively analyzed the studies which placed implants at different timings without augmentation with follow up of at least 1 year in maxillary anterior esthetic zone. While evaluating esthetic stability with the help of hard and soft tissue levels by using some esthetic indices, meta-analysis suggested that immediate and late placement are equally beneficial for better success rate in clinical practice. This systematic review could not suggest the superiority of any specific placement protocol over the other for the marginal bone loss and pink esthetic score.

In recent times there are many systematic reviews related to anterior aesthetic zone to clarify what is the best time to place the implant. Graziani *et al* [14]evaluated short- and long-term favorable implant and patient related outcomes. But they failed to establish whether early implant placement has different impact on bone regeneration compared to late implant placement. [14] Bassir et

al.[12] found that early placement has better stability over immediate placement in grafted and non-grafted sites. But all these studies have assessed clinical performance only by measuring implant survival and ignores peri‐implant conditions, like of soft and hard tissues, aesthetics and patient related outcomes. These systematic reviews are inconclusive whether immediate and early implant placement have similar effect on esthetic stability as late implant placement. Existing literature lacks systematic reviews that assess esthetic stability in the maxillary anterior region, particularly concerning factors such as marginal bone loss and the Pink Esthetic Score (PES). The importance of systematic reviews in evaluating the health and esthetics of single-tooth dental implants cannot be overstated. Consequently, this systematic review aims to investigate whether Immediate Implant Placement (IIP) or Early Implant Placement (EIP) is more conducive to esthetic stability compared to Late Implant Placement (LIP) in the anterior maxillary region, with a focus on parameters like marginal bone loss and the Pink Esthetic Score (PES)

The results of the present systematic review support the hypothesis that immediate implant placement (IIP) and early implant placement (EIP) have same effect on esthetic stability of single implant restoration in maxillary anterior region as late implant placement since it has no statistical significance.

With the help of a scoping review, it was observed that there are limited studies related to different implant placement in non-augmented or without any kind of tissue regeneration procedures in anterior esthetic zone immediate, early and late with long term follow up. One of

Figure 3: Risk of bias Graph

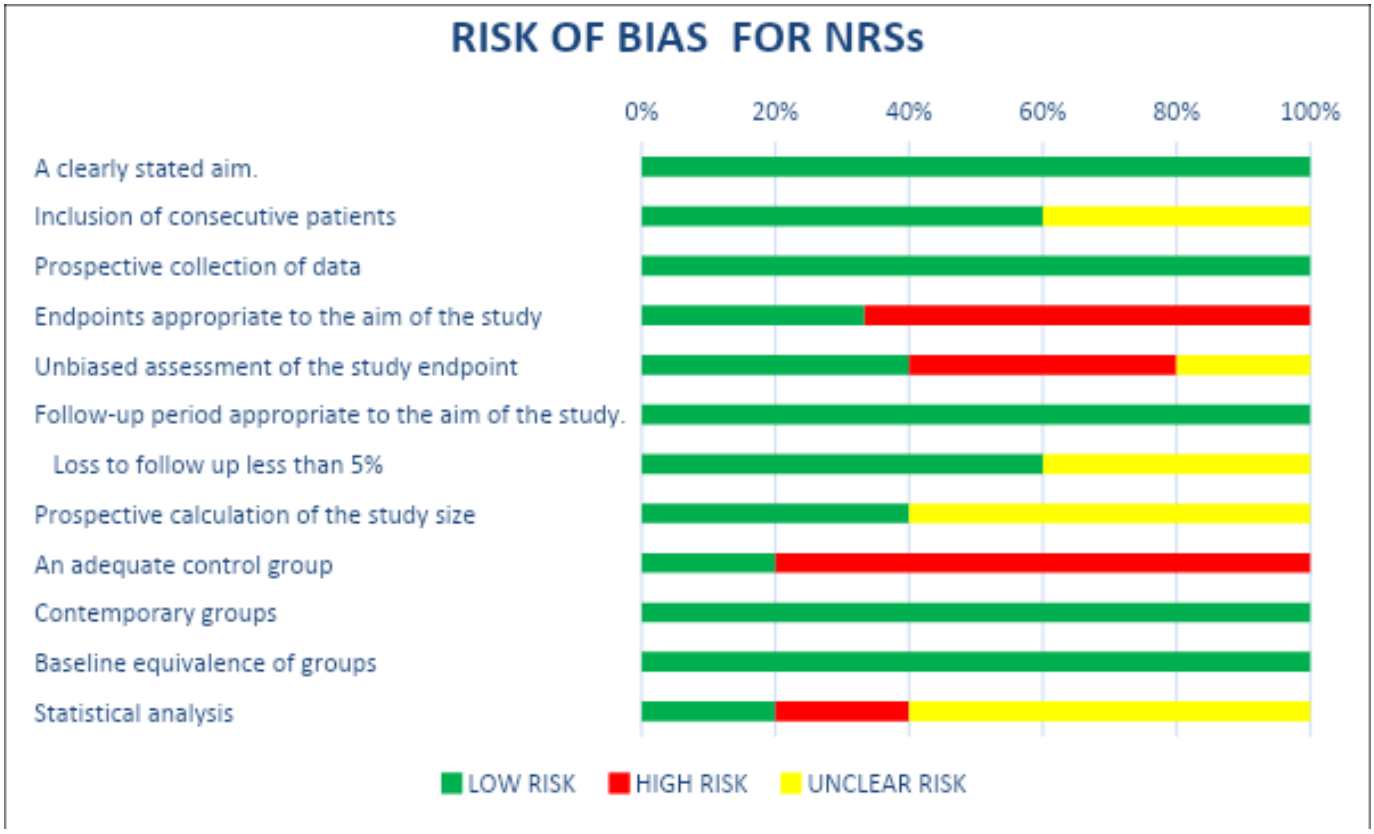

Figure 5. Graph of Quality assessment of non-randomized studies using MINORS tool.

the most important key point of this systematic review and meta-analysis was to focus on different implant placement timings in non-grafted maxillary anterior esthetic zone, as critical analysis of this long-term data can help identify and improve current treatment strategies in implant dentistry. At the same time many studies have found that there is direct-indirect effect on marginal bone loss and pink esthetic score because of some factors like thickness of the buccal bone, periodontal recession along with flap and flapless surgical procedures, timing of provisionalization, use of antibiotics, and restorations after implant placement on anterior esthetic zone.[35]

Aesthetic outcome and buccal soft tissue height of an implant-supported restoration would seem to be indeed relevant. For aesthetic predictabili-

Figure 4: A. Marginal Bone Loss with IIP and LIP

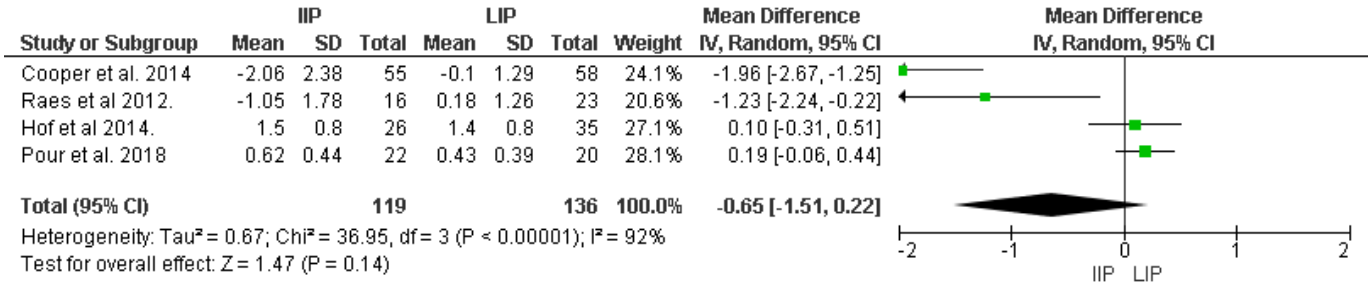

Fig. 4A. Forest plot comparing Marginal Bone Loss in immediate and late placement protocols.

B. Marginal Bone Loss with IIP and EIP

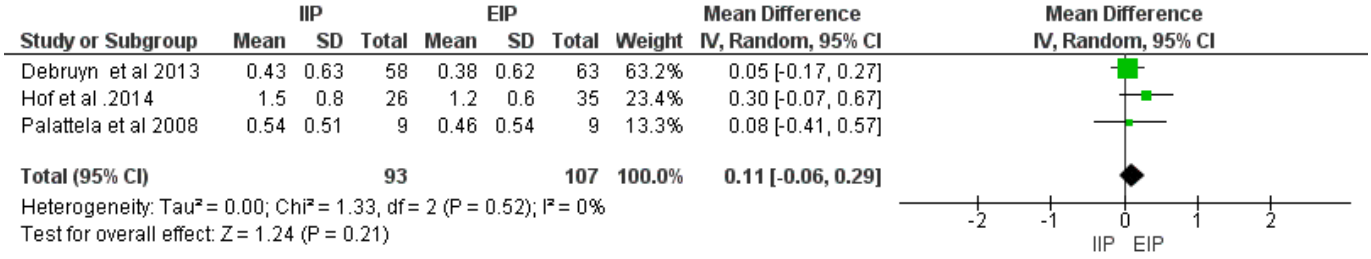

Fig. 4B. Forest plot comparing Marginal Bone Loss in immediate and early placement protocols.

Figure 5: PES (Pink Esthetic Score)

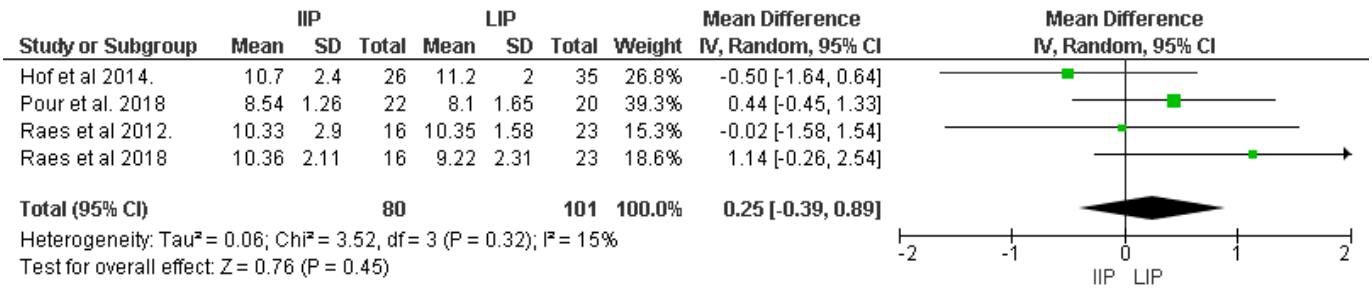

Fig 5.Forest plot comparing pink esthetic score in immediate and late placement protocols.

ty of restoration, the thickness of the buccal bone at the implant site played a fundamental role in the rehabilitation.[36,37] Hence, at the time of implant placement, this review focuses on the role of the buccal bone thickness (BBT) on facial tissue stability. In present review, only one out of seven studies, had discussed about thickness of the buccal bone. Facial bone was missing in the crestal area in 8 patients; late implant placement after long terms follow up of 8 years of function (47%).[17-18] Similarly, irrespective of timing of placement a buccal bone wall of less than 2 mm at 1-3-5 mm from the CEJ to implant was observed at all tooth sites. To assess changes in vertical soft tissue, two studies investigated implant placement combined with immediate restoration in the anterior segment of the dentition. [17-18,20] In these studies, the timing of provisionalization with the crown was established as the baseline. However, Cooper et al[20] suggested the potential for papillary re-growth following Late Implant Placement (LIP) due to the re-establishment of a contact point. Consequently, comparing Immediate Implant Placement (IIP) and LIP in terms of papillary health may yield ambiguous results. Objective comparisons of papillary and mid-facial recession can only be made between IIP and LIP when baseline registrations occur with the original tooth still in place. Historically, there were no comparative studies examining such outcomes

In the present systematic review and meta-analysis, marginal bone loss did not show a significant difference between flap and flapless procedures, regardless of what type of studies were analyzed which is in line with the results of earlier systematic reviews.[34-36] This explained that at the macroscopic scale the flapless procedure may not influence on bone remodeling. Similarly, an analysis of three long term studies with post-operative antibiotics demonstrated similar trend for marginal bone loss towards IIP site when compared with EIP[22-24] (P = 0.21, mean difference = 0.11, 95% CI [-0.06, 0.29]). These

Figure 6 : Esthetic Stability.

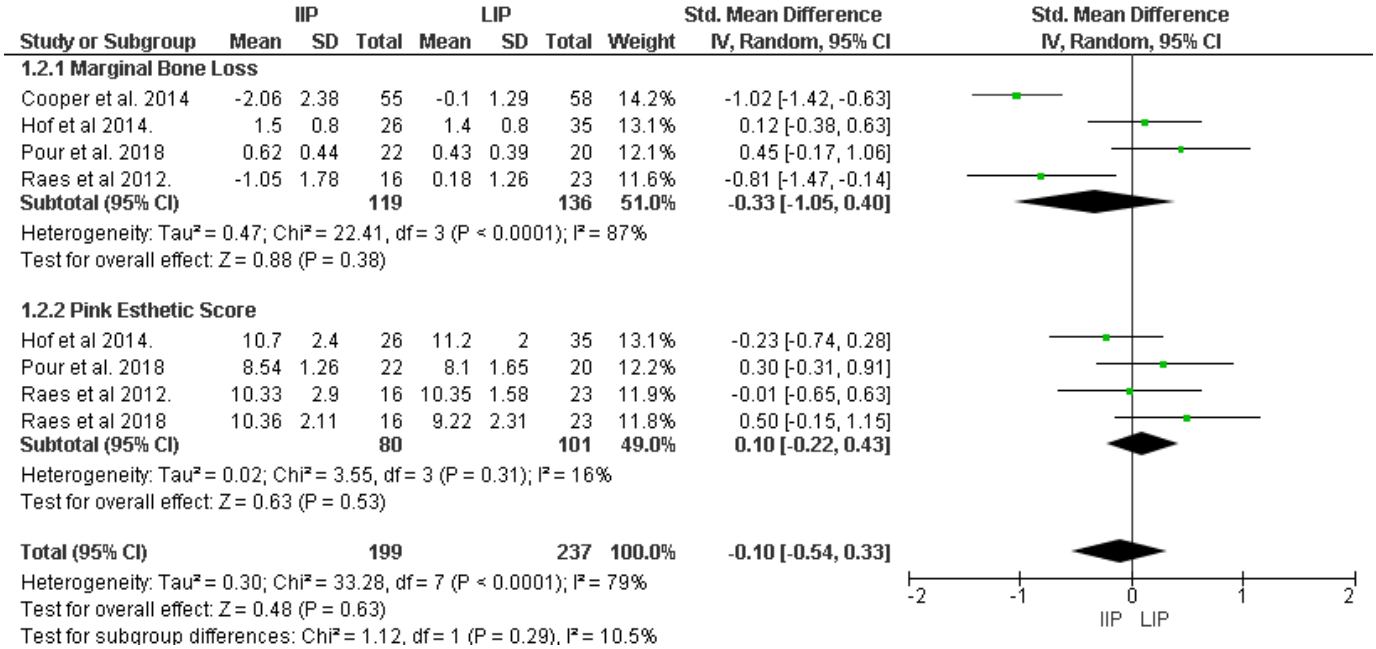

Fig 6. Forest plot comparing esthetic stability subgroup analysis in immediate and late placement protocols.

findings suggest use of antibiotics did not have any significant effect on marginal bone loss with long term clinical studies. Under subgroup analysis, the outcomes align with earlier findings, indicating that the administration of post-operative antibiotics primarily contributes to the reduction of early implant loss following Immediate Implant Placement (IIP).[39]

The consideration of jumping distance is pivotal, particularly in cases of immediate implant placement. Within this systematic review, bone augmentation was undertaken at the time of implant placement in specific sites immediately after extraction, where a greater jumping distance was observed. This approach was evident in two out of seven studies, specifically in the investigations conducted by Raes et al. and Hof et al.[17,19] They observed early bone loss in these augmented immediate placement sites whereas bone gain in non-augmented immediate placement sites. In this review, the gingival response after evaluation of anterior esthetic stability is assessed by the Pink Esthetic Score (PES) from clinical photographs on the basis of six variables scored from 0→2. According to a systematic review by Graziani *et al*,[14] it was not possible to establish whether the early placement has a different impact on bone regeneration. On further stratification of this outcome on the basis of flap and flapless surgical procedures in esthetic region, minor difference were revealed but for safety issue flapless surgery has been preferred as we have discussed earlier with respect to bone loss. The analysis was performed with a limited dataset, as Pink Esthetic Score (PES) data were available from only four studies that reported on anterior implants. The comparison specifically concentrated on Immediate Implant Placement (IIP) and Late Implant Placement (LIP), employing different scales for PES assessment.[17-18,19,21,22] (P = 0.94, mean diff =0.02; 95% CI [-0.58 to 0.62 mm]).

Limitations

While conducting this systematic review, notable limitations emerged concerning both the quan-

Figure 7: Papillary Recession:

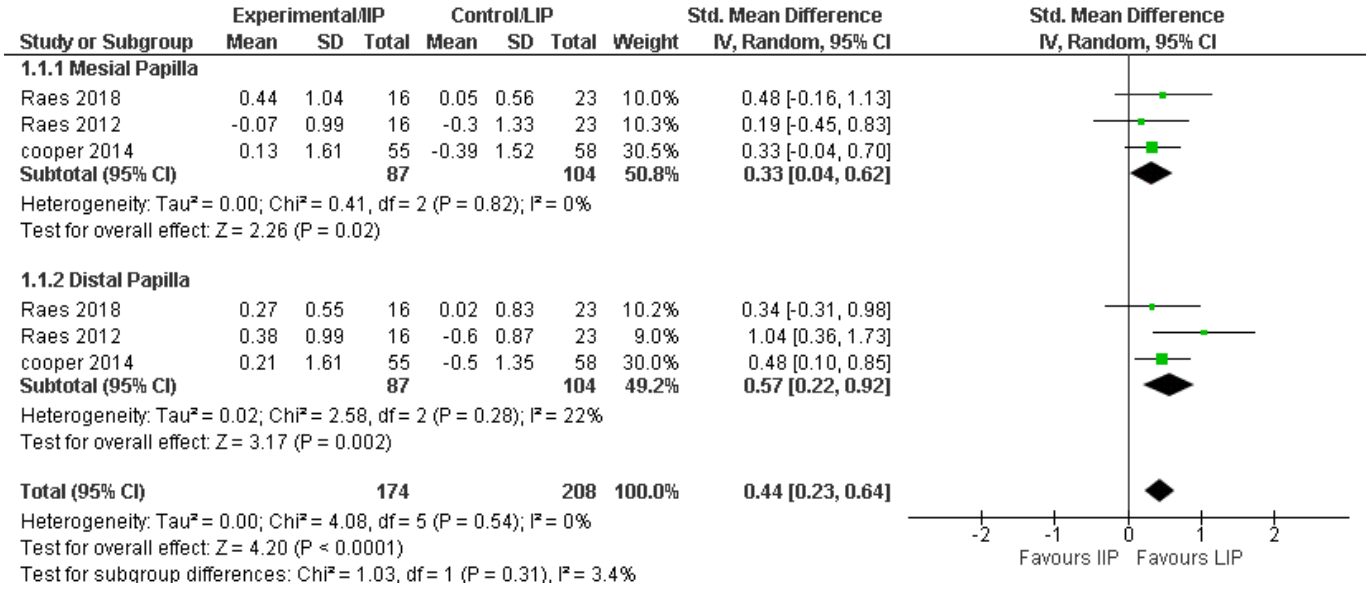

Fig 7. Forest plot comparing Papillary Recession in immediate and late placement protocols.

tity and quality of the available study material. Of the two randomized controlled trials (RCTs) incorporated, De Bruyn *et al*.[24] and Palattella *et al*.[23] showed an unclear risk of bias, while the remaining six nonrandomized studies demonstrated a low risk. The clarity of bias assessment becomes particularly crucial when making comparisons of outcome variables among Immediate Implant Placement (IIP), Early Implant Placement (EIP), and Late Implant Placement (LIP). It is pertinent to mention that only one study included in this review addressed a direct comparison of all relevant parameters.[22] In this systematic review we had only two randomized controlled trials out of seven which is very low for any strong inference for direct comparisons of different timing protocols.[23,24] As it is not feasible or ethical to perform randomized clinical studies to compare the different timings of implant placement, we have included non-randomized studies to provide evidence of the effect for interventions that are unlikely to be studied in randomized trials according to the recommendation of the Cochrane handbook.[15,41] Hence, all study designs with a control or comparison group were considered for the inclusion in this study. Thus, this systematic review could not suggest the precedence in any of implant placement timing protocol over the other for esthetic stability.

Conclusion

Based on results of this systematic review and meta-analysis, the following can be concluded:

- No significant differences were found in terms of pink esthetic score and marginal bone loss with the different implant placement timings.
- In terms of esthetic stability, LIP showed an overall better result than IIP and EIP.
- In terms of papillary recession, significant difference was found with IIP and LIP, indicating a better long term papillary health with IIP.
- More number of studies need to be carried out on graft and graftless IIP,EIP and LIP focusing on the esthetic stability in single implant restorations.
- Further studies or systematic reviews also needs to be done on effect of IIP,EIP, LIP on other parameters like implant stability, success and failure

Clinical Implication

Although no differences in soft tissue esthetic outcomes were found between immediate, early and late implant placement protocols, clinicians should expect some soft tissue esthetic alterations after tooth extraction. Hence, this systematic review will help the clinician to decide the best placement protocol considering the esthetic stability using pink esthetic score and marginal bone loss parameters in different clinical situations.

Conflict of interest statement: The author reports no conflicts of interest related to this study.

Source of funding: This study received no external funding.

References

1. Ebenezer V, Balakrishnan R, Muthumani T, Prakash D. Determination of Implant Length in Maxillary Anterior Region. Biomed Pharmacol. J 2015;8: 23-37.
2. Hämmerle CF, Tarnow D. The etiology of hard- and soft-tissue deficiencies at dental implants: A narrative review. J Clin Periodontol.2018; 45:S267–S277
3. Altay A, Sindel A, Hüseyin H, Nelli OM and Özarslan M Esthetic evaluation of implant-supported single crowns: A comparison of objective and patient-reported outcomes. Int J. Implant Dent. 2019; 5(1):2.
4. D'Addona A, Ghassemian M, Raffaelli L, Manicone F. Soft and Hard Tissue Management in Implant Therapy—Part I: Surgical Concepts. Int J Biomat.2012;1:1–8.
5. Furhauser R, Florescn D, Benesch T, Haas R, Mailath G, Watzek G. Evaluation of soft tissue around single-tooth implant crowns: The pink esthetic score. Clin Oral Implants Res. 2005; 16:639–644.
6. Proceedings of the Third ITI (International Team for

Implantology) Consensus Conference. Gstaad, Switzerland, August 2003 Int J Oral Maxillofac Implants, 19 Suppl: 7– 154 (2004).

7. Chen S, Buser D. Implants in post-extraction sites: A literature update. In: Buser D, Belser U, Wismeijer D. ITI Treatment Guide, Implants in Extraction Sockets. Berlin: Quinte.2008; 3:9–15.
8. Hämmerle H, Chen T, Wilson G.Jr. Consensus statements and recommended clinical procedures regarding the placement of implants in extraction sockets. Int J Oral Maxillofac Implants. 2004;19(3):26–28
9. Buser D, Mericske-Stern R, Bernard P, Behneke A, Behneke N, Hirt P, Belser C, Lang P. Long-term evaluation of non-submerged ITI implants. Part 1: 8-year life table analysis of a prospective multi-center study with 2359 implants. Clin. Oral Implant. Res.1997;8:161–172.
10. Belser C, Grütter L, Vailati F, Bornstein M, Weber ., Buser D. Outcome evaluation of early placed maxillary anterior single-tooth implants using objective esthetic criteria: a cross-sectional, retrospective study in 45 patients with a 2- to 4- year follow-up using pink and white esthetic scores. J Periodontal.2009;80(1):140-51.
11. Furhauser R, Florescn D, Benesch T, Haas R, Mailath G, Watzek G. Evaluation of soft tissue around single-tooth implant crowns: The pink esthetic score. Clin Oral Implants Res. 2005; 16:639–644.
12. Bassir H, Kholy K, Chen Y, Kyu L, Giuseppe I. Outcome of early dental implant placement versus other dental implant placement protocols: A systematic review and meta–analysis. J Periodontal. 2019May;90(5):493-506.
13. Cosyn J, Lat L, Seyssens L, Doornewaard R, Deschepper E, Vervaeke S.The effectiveness of immediate implant placement for single tooth replacement compared to delayed implant placement: A systematic review and meta-analysis. J Clin Periodontol.2019; 46(21):224–241.
14. Graziani F, Chappuis V, Molina A, Lazarin R, Schmid E, ChenS,et al. Effectiveness and clinical performance of early implant placement for the replacement of single teeth in anterior areas:A systematic review. J Clin Periodontol, 2019; 46(21):242–256.Res.2013; 15:819–835.
15. Higgins JP, Altman DG, Gotzsche PC, Juni P, Moher D, Oxman AD, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ 2011;343:d5928.
16. Slim K, Nini E, Forestier D, Kwiatkowski F, Panis Y, Chipponi J. Methodological index for non-randomized studies (MINORS): development and validation of a new instrument. ANZ J Surg. 2003;73(9):712-6.
17. Raes F, Cosyn J, Crommelinck E, Coessens P, De Bruyn Immediate and conventional single implant treatment in the anterior maxilla: 1-year results of a case series on hard and soft tissue response and aesthetics. J Clin Periodontol. 2011; 38(4):385–394.16.
18. Raes S, Eghbali A, Chappuis V, Raes F, De Bruyn H,Cosyn J. A long-term prospective cohort study on immediately restored single tooth implants inserted in extraction sockets and healed ridges: CBCT analyses, soft tissue alterations, aesthetic ratings, and patient-reported outcomes. Clin Implant Dent Related Res. 2018; 20(4):522–530.
19. Pour N, Ghaedi B, Sohrabi M. Soft-tissue esthetic outcomes in immediate implant placement. J Ind Periodont. May-June 2018; 22(3):314-325.
20. Cooper LF, Reside GJ, Raes F, et al. Immediate provisionalization of dental implants placed in healed alveolar ridges and extraction sockets: a 5-year prospective evaluation. Int J Oral Maxillofac Implants.2014;29(3):709–717.
21. Raes F, CosynJ, De Bruyn H. Clinical, aesthetic, and patient-related outcome of immediately loaded single implants in the anterior maxilla: A prospective study in extraction sockets, healed ridges, and grafted sites. Clin Implant Dent Rel Res. 2013;15:819–835.
22. Hof M, Bernhard P, Harald A, Philip J, Susanne V, Werner Z. Does Timing of Implant Placement Affect Implant Therapy Outcome in the Aesthetic Zone? A Clinical, Radiological, Aesthetic, and Patient-Based Evaluation. Clin Implant Dent Related Res. 2014; 6:250-275.
23. Palattella P, Ferruccio T, Cordaro L. Two-year prospective clinical comparison of immediate replacement vs. immediate restoration of single tooth in the esthetic zone. Clin. Oral Impl. Res.2008;19:1148–1153.
24. De Bruyn H, Raes F. Cooper L, Reside G, Garriga J, Tarrida L, Wiltfang M. Three years clinical outcome of immediate provisionalization of single OsseospeedTM implants in extraction sockets and healed ridges. Clin. Oral. Implants. Res.2013 ;24: 217–223.
25. Schropp L, Wenzel A, Stavropoulos A. Early, delayed, or late single implant placement: 10-year results from a randomized controlled clinical trial. Clin Oral Implants Res. 2014;25(12):1359–1365.
26. Garabetyan J, Malet J, Kerner S, DetzenL, Clotilde C, Bouchard P.The relationship between dental implant papilla and dental implant mucosa around single-tooth implant in the esthetic area: A retrospective study. Clin Oral Implants Res. 2019; 00:1–9.
27. Zuiderveld G, Henny M, Vissink A, Raghoebar G. Outcome of Treatment with single Implants in Preserved Versus Nonpreserved Alveolar Ridges: A 1-year cohort Study. Int J Oral Maxillofac Implants. Nov/Dec 2019;34(6):1457-1465.

28. Arora H, Ivanovski S. Immediate and early implant placement in single-tooth gaps in the anterior maxilla: A prospective study on ridge dimensional, clinical, and aesthetic changes. Clin Oral Implants Res.2018; 29:1143–1154.
29. Tonetti M, Cortellini P, Graziani F. Immediate versus delayed implant placement after anterior single tooth extraction: The timing randomized controlled clinical trial.J Clin Periodontol. 2017;44(2):215–224.
30. Barone A, Alfonsi F, Derchi G, Tonelli P, Toti P, Marchionni S, et al. The effect of insertion torque on the clinical outcome of single implants: A randomized clinical trial. Clin Implant Dent related res.2016;18(3):588–600.
31. Mastrangelo F, Gastaldi G, Vi nci R, Troiano G ,Tettamanti L and Gherlone E, et al. Immediate post extractive implants with and without bone graft: 3-year follow-up results from a multicenter controlled randomized trial. Implant Dent. 2018 Dec;27(6):638-645.
32. Huynh-Ba G, Meister DJ, Hoders AB, Mealey BL, Mills MP, Oates TW, McMahan CA. Esthetic, clinical and patient-centered outcomes of immediately placed implants (Type 1) and early placed implants (Type 2): preliminary 3-month results of an ongoing randomized controlled clinical trial. Clin Oral Implants Res. 2015;27(2): 241–252.
33. Jonker B, Wolvius E, Van der Tas J, Tahmaseb A, Pijpe J. Esthetics and Patient- Reported Outcomes of Implants Placed with Guided Bone Regeneration and Complete Native Bone: A Prospective Controlled Clinical Trial. The International J Oral Maxillofac Implants. 2020;35(2):406–414.
34. Siebers D, Gehrke P, Schliephake H. Delayed function of dental implants: A 1- to 7-year follow-up study of 222 implants. International Journal of Oral and Maxillofacial Implants. 2010; 25(6):1195–1202.
35. Soydan SS, Cubuk S, Oguz Y, Uckan S. Are success and survival rates of early implant placement higher than immediate implant placement? Int J Oral Maxillofac Surg. 2013;42(4): 511–515.
36. Buser D, Martin W, Belser UC. Optimizing esthetics for implant restorations in the anterior maxilla: Anatomic and surgical considerations. Int. J. Oral Maxillofac. Implants. 2004; 19:43–61.
37. Spray JR, Black CG, Morris HF, Ochi S. The influence of bone thickness on facial marginal bone response: Stage 1 placement through stage 2 uncovering. Ann. Periodntol. 2000; 5:119–128.
38. Den Hartog L, Slater JJ, Vissink A, Meijer HJ, Raghoebar GM. Treatment outcome of immediate, early and conventional single tooth implants in the aesthetic zone: A systematic review to survival, bone level, soft-tissue, aesthetics and patient satisfaction. J Clin Periodontol. 2008; 35(12):1073–1086.
39. Sclar AG. Guidelines for flapless surgery. J Oral Maxfac Surg 2007;65(71):20-32.
40. Lin G, Chan L, Bashutski D, Tae JV, Wang H. The Effect of Flapless Surgery on Implant Survival and Marginal Bone Level: A Systematic Review and Meta-Analysis. J. Periodontol. 2014;85(5): e91–e103.
41. Lang NP, Pun L, Lau KY, Li KY, & Wong MC. A systematic review on survival and success rates of implants placed immediately into fresh extraction sockets after at least 1 year. Clin Oral Implants Res. 2012; 23(5):39–66.
42. Buser D, Chappuis V, Belser UC & Chen S. Implant placement post extraction in esthetic single tooth sites: When immediate, when early, when late? Periodontology 2017;73(1): 84–102.
43. Higgins JP, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). Including non-randomized studies on intervention effects. Cochrane Handbook for Systematic Reviews of Interventions version 6.0. Cochrane 2019; section 24-1.