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Outcome of Immediate Versus Delayed Loading of Full Arch Implant-Supported Fixed Prosthesis: A Systematic Review and Meta-Analysis

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Abstract

Objective: A systematic review including meta-analysis was conducted to test the null hypothesis of no difference between immediate loading and delayed loading fixed implant-supported restoration for completely edentulous arch in terms of implant failure rates and marginal bone resorption against the alternative hypothesis of a difference.

Materials and methods: An electronic search was undertaken in January 2019. Inclusion criteria including clinical human studies, either randomized or not, studies comparing success, survival, or failure rates of immediately loaded implants with fixed restoration to delayed loaded implants on edentulous jaw, patients who were examined clinically at follow up visits for at least 12 months. The estimates of relative effect were reported in risk ratio (RR) and mean difference (MD) in millimeters.

Results:1355 studies were initially identified and 11 studies were finally included for meta-analysis. The results showed that there was no statistically significant difference between immediate loading and delayed loading (P

Conclusion: The differences in loading protocol between immediate loading and delayed loading of full arch implant-supported fixed prosthesis might not affect the failure rates of dental implants and there is no significant effect on marginal bone resorption.

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Objective: A systematic review including meta-analysis was conducted to test the null hypothesis of no difference between immediate loading and delayed loading fixed implant-supported restoration for completely edentulous arch in terms of implant failure rates and marginal bone resorption against the alternative hypothesis of a difference.

Introduction: Since Brånemark introduced the first titanium dental implant placed in a human in 1965, the concepts and techniques in implant dentistry have developed and changed with time. We have overcome the limitation by switching the concepts from the machine surface to the etched surface, from delayed placement to early placement, from multiple visits to a single visit. We have tried to serve and meet our patient expectations. Today, immediate loading of single implant shows a high success rate and predictable outcome.[1] However, immediate loading for rehabilitation of a completely edentulous arch with fixed implant-supported prosthesis is still challenging because of an increased risk of osseointegration failure due to implant micromotions during the healing phase.

Immediate loading offers several advantages over conventional loading without compromising the outcome. An immediate fixed provisional promotes a high level of patient satisfaction with respect to esthetics, phonetics, masticatory capability, physiological, and psychological comfort, enabling patients to return to their normal routine and maintain quality of life within a short period of time.[2] Other advantages to extraction with simultaneous replacement include the maintenance of vertical dimension, elimination of interim denture therapy, and potential improvement of soft tissue healing.[3] While, the conventional loading protocol dictates to achieve predictable osseointegration and minimize the risk of implant failure by submerging an implant post placement and maintaining a non-loaded implant environment for at least 2 months. This approach is believed to overcome a potential risk of immediate loading that connective tissue instead of bone could form at the bone-implant interface.[4] But the disadvantages of this classic approach are well-known to have multiple surgeries, high treatment cost, and long treatment time. During the healing period, patient can either wear an interim removable denture or remain edentulous. Many patients find these temporary prostheses uncomfortable[5] and it would be beneficial if treatment time can be shortened and esthetic can be immediately restored without compromising implant success.

Early studies of immediately loaded implants placed in edentulous jaws were well documented, with most current citations on this subject showing a range of implant survival for this procedure of greater than 95%[6-18], however, some clinicians still considered delayed loading for rehabilitation of completely edentulous arch as the gold standard of treatment since there are multiple long term follow-up studies demonstrating high survival rates. The aim of the present systematic review including meta-analysis was conducted to test the null hypothesis of no difference between immediate loading and delayed loading fixed implant-supported restoration for completely edentulous arch in term of implant failure rates and marginal bone resorption against the alternative hypothesis of a difference.

Materials and methods

Search strategies: Following the recommended methods for systematic reviews and meta-analyses (PRISMA), an electronic search without time restriction was performed in March 2019 on PubMed and Scopus databases. The aim was to answer the question developed using the PICO formula where P corresponds to adults with completely edentulous arch rehabilitated with implant-supported fixed prosthesis, I corresponds to immediate loading restoration, C corresponds to a comparison treatment of delayed loading restoration, and O corresponds to an outcome of implant failure rates and marginal bone resorption. Thus, the focused PICO question would be "Does immediate loading influence the implant failure rates compared to delayed loading in adult patients rehabilitated with implant-supported fixed prosthesis?"

The search terms were created for each PICO for searching strategy.

P	*Adult, Implant-supported, Dental restoration, Provisional restoration, Temporary restoration, "Fixed dental prosthesis", Edentulous jaw, Full arch, Dental prosthesis*
I	*Immediate load, Immediate loading, Immediately loaded, Immediate restoration, Fixed partial dental prosthesis, Fixed restoration, Provisional restoration, Temporary restoration, Permanent restoration, fixed bridge, Non-submerged, Single stage, One-stage, Immediate dental implant loading*
C	*delayed loading, delayed loaded, Submerged, Two-stage*
O	*Failure, success, survival, fracture, dislodge, complication, loose, removal*

The following terms were samples of the search strategy used on PubMed: (((((((Immediate loading OR single stage OR non-submerged)) AND (Fixed restoration OR Fixed dental prosthesis OR Fixed bridge)) AND (Maxillary jaw OR maxillary arch OR maxilla))) AND (success OR failure or complication)) AND (compare OR versus OR VS)) AND (two-stage OR submerged OR delayed load*), ((((((Full arch OR Edentulous)) AND (immediate OR immediately)) AND implant) AND fixed) AND (delayed) AND (success OR survival OR failure)

The following terms were samples of the search strategy used on Scopus: (TITLE-ABS-KEY (implant-supported) AND TITLE-ABS-KEY (full AND arch OR edentulous) AND TITLE-ABS-KEY (dental AND implant OR "Fixed dental prosthesis") AND TITLE-ABS-KEY (immediate AND load OR immediate AND loading OR immediately AND loaded) AND TITLE-ABS-KEY (delayed

AND loading OR delayed AND loaded) AND TITLE-ABS-KEY (failure OR success OR survival)), (TITLE-ABS-KEY (fixed AND dental AND prosthesis OR restoration) AND TITLE-ABS-KEY (implant) AND TITLE-ABS-KEY (immediate AND load OR immediate AND loading OR immediately AND loaded) AND TITLE-ABS-KEY (delayed AND loading OR delayed AND loaded) AND TITLE-ABS-KEY (failure OR success OR survival)), (TITLE-ABS-KEY (provisional AND restoration OR dental AND restoration OR permanent AND restoration) AND TITLE-ABS-KEY (implant) AND TITLE-ABS-KEY (immediate AND load OR immediate AND loading OR immediately AND loaded) AND TITLE-ABS-KEY (delayed AND loading OR delayed AND loaded OR submerged OR two-stage) AND TITLE-ABS-KEY (failure OR success OR survival OR complication OR loose OR dislodge)).

Inclusion and Exclusion criteria: Inclusion criteria including clinical human studies, either randomized or not, comparing implant failure rates in adult patients receiving immediate versus delayed loading restoration for rehabilitation of their completely edentulous arches either maxilla or mandible or both. For the studies published in more than one paper but with different follow-up periods, only one paper with longest follow-up period was considered, as long as the sample size remained the same. Patients have to be examined clinically with follow-up period of at least 12 months. Outcome included at least one of the following indexes: implant failure rates, implant survival rates, marginal bone resorption, or marginal bone change. In vitro study, animal study, case report, and review paper were excluded. Articles not written in English were excluded. Any articles studied on implant-supported removable prosthesis or partially edentulous arch were also excluded.

Study selection: Titles and abstracts of all records identified through electronic search were read and screened. For studies that appear to meet inclusion criteria or for which data was not clear or there was inadequate data in the title and abstract, the full-text record was obtained. Disagreements were resolved by discussion among authors.

Data extraction: One investigator extracted data from the included studies using the pre-designed data form. The recorded data included general information (first author name, year of publication, region of study, type of study), characteristics of participants (sex, age), study design (loading location, loading protocol, duration of follow up, sample size), and clinical and radiographic outcomes (CSR, failure rate, marginal bone loss).

Definition used in this systematic review:

- Immediate loading: Dental implants are connected to a dental prosthesis in occlusion with the opposing arch within 1 week subsequent to implant placement.
- Immediate restoration: Dental implants are connected to a prosthesis held out of occlusion with the opposing arch within 1 week subsequent to implant placement.
- Early loading: Dental implants are connected to a prosthesis between 1 week and 2 months after implant placement.
- Conventional loading (Delayed loading): Dental implants are allowed a healing period of more than 2 months after implant placement with no connection of a prosthesis.
- Survival: The implants and restoration being in situ with or without complications.
    - Success criteria is defined by following:
        - Absence of persisting pain or dysesthesia
        - Absence of peri-implant infection with suppuration
        - Absence of mobility
        - Absence of persisting peri-implant bone resorption greater than 1.5 mm during the first year of loading and 0.2 mm/year during the following year
- Failure: Implants having been removed.
- Complication: One or more events affecting function and/or esthetics. Such an event could be transient or repairable and not necessitating removal of implants.

- Marginal bone loss is measured from the reference point (the implant-abutment connection, implant shoulder) to the point where the bone tissue first met the implant surface at the mesial and distal sites.

Quality assessment: The quality assessment of the RCT studies was performed by using the recommended approach in the Cochrane Collaboration's tool for assessing risk of bias.[57] The classification of the risk of bias potential for each study was based on the six domains: random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants, personnel, outcome assessors (performance bias), incomplete outcome data (attrition bias), selective outcome reporting (reporting bias), and other sources of bias. A study that met all of the criteria mentioned above was classified as a low risk of bias, whereas a study that did not meet one of these criteria was classified as a moderate risk of bias. When two or more criteria were not met, the study was considered a high risk of bias. For observational studies, the Newcastle–Ottawa scale (NOS) adapted by Chambrone et al. 2015 [58] was used to evaluate the methodological quality of included articles. The subsequent topics were evaluated: (1) selection of study groups: sample size calculation, representativeness of the patients who received implants with immediate/delayed loading protocols, description of clear inclusion/exclusion criteria, detailed description of the steps following each loading protocol, training/calibration of assessors of outcomes, data collection; (2) comparability: comparability of patients on the basis of the study design or analysis and management of potential confounders; (3) outcome: evaluation of results, assessment of outcome accuracy and adequacy of follow-up of the patients; and (4) statistical analysis: appropriateness/validity of statistical analysis and unit of analysis reported in the statistical model. Also, stars (points) were given to these methodological quality criteria, as well as each study included could receive a maximum of 14 points. Studies with 11–14 stars (approximately 80% or more of the domains satisfactorily fulfilled) were arbitrarily considered as being of high quality, with 8–10 stars indicating medium quality and <8 stars suggesting low methodological quality.

Statistical analysis: Data were analyzed using the RevMan Software (version 5.3). The overall risk ratios (RR) were calculated for implant failure rates (dichotomous outcomes) and standard mean difference in millimeter for marginal bone resorption (continuous outcomes), both with a 95% confidence interval (CI). The statistical units for implant failure rates were the implant and the patient, for marginal bone resorption was the implant. The heterogeneity among the studies was evaluated using Chi-squared ad I-squared test. When statistically significant heterogeneity was found ($P < 0.1$ or $I^2 > 50\%$) a random-effect model was utilized to assess the significance of treatment effects. When no statistically significant heterogeneity was found, a fixed-effect model was applied for analysis. The I^2 statistic was used to express the total variation across studies due to heterogeneity, 25% corresponding to low heterogeneity, 50% corresponding to moderate heterogeneity, 75% corresponding to high heterogeneity. When no events were observed in both groups, the term "not estimable" was shown under the Risk Ratio column of the forest plot table and was automatically omitted from the meta-analysis. Funnel plots were drawn. Asymmetry of the funnel plot may indicate publication bias related to sample size, even though it may also represent a true relationship between sample size and effect size.

<u>Results</u>

Literature search: A search of electronic databases identified 1355 records related to question raised. 833 were removed as of duplicates. 522 were screened for inclusion based on their titles and abstracts. 375 studies were then excluded because they are obviously irrelevant to the focused question. 147 articles were screened for more detail evaluation and 131 did not fit the inclusion criteria. Full-text articles were assessed for the remaining 16 articles for eligibility to be included. 4 articles were excluded as of mixed results between single, partially edentulous, and fully edentulous jaw with inadequate data. And one was excluded due to same subject population. Finally, 11 articles[59-69] were included for qualitative and quantitative analysis in the present systematic review. Fig.1 is the summary of study selection process.

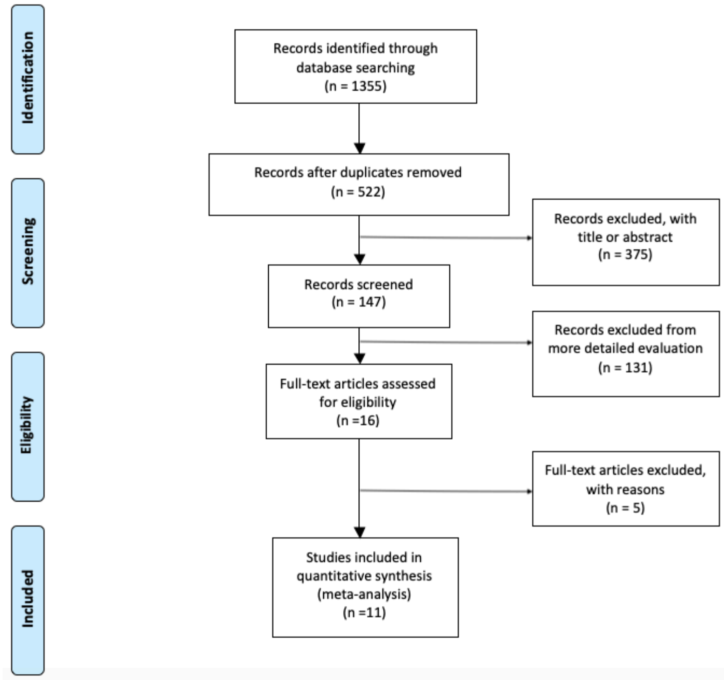

Figure1 Flow diagram of study selection process

Description of the studies: The characteristics of the included studies were shown in Table 1. The publication year ranged from 2006 to 2018. Four studies were conducted in Italy, two in Austria, two in Canada, one in Korea, one in Iran, and one in Sweden. Three randomized controlled trials, 4 retrospective studies, and 4 prospective studies were included in the review. The follow-up period ranged from 12 months to 60 months. A total of 752 patients with 4268 implants were analyzed in the meta-analysis composed of 678 patients and 2600 implants receiving immediate loading, 304 patients and 1668 implants receiving conventional loading (delayed loading). The implant location was the maxilla in 4 studies (Busenlechner el al. 2016, Busenlechner el al. 2016, Tealdo et al. 2011, Ostman et al. 2005), the mandible in 2 studies (Alfreda et al. 2014, Jokstad et al. 2014), and both maxilla and mandible in 5 studies (Degidi et al. 2006, Degidi et al. 2009, Kim et al. 2018, Najafi et al. 2016). All studies included only adult patients with overall good general health condition, no uncontrolled medical condition, and no contraindications for undergoing oral surgery. From the eleven studies, all of them[59-69] were included for meta-analysis for implant failure rates at the implant level, but only nine studies[59,62-69] were included for meta-analysis for implant failure rates at the patient level because two studies did not report number of patients as an outcome for the statistical unit. Eight studies[59-61,64,66-69] that reported on marginal bone change were used for meta-analysis for marginal bone resorption. Three studies[62-64] did not inform whether there was a statistically significant difference between two groups concerning implant failure at the implant level, and eight studies[59,62-65,67-69] at the patient level. All studies that provided information about the marginal bone resorption had reported their statistical results. For the two studies (Busenlechner el al. 2016, Busenlechner el al. 2016) that studied on mixed type of edentulous arches, only the information of completely edentulous arch was extracted and analyzed. For implant failure rates at the implant level, 2600 implants received immediate loading and 1668 implants received delayed loading, there were 67 and 35 implant failures (2.58% and 2.09%) respectively. For implant failure rates at the patient level, 251 patients received immediate loading and 174 patients received delayed loading, there were 26 and 13 failures (10.36% and 7.47%) respectively.

Article	Country	Type of study	Location	Total subjects (mean age), (M/F or total)	Total number of implants	Number of subjects in IL group (patient,implant)	Number of subjects in DL group (patient,implant)	Mean follow-up time
Alfreda et al, 2014	Canada	RCT	Mandible	42 (61.5±10.35), (18,24)	160	20, 64	22, 96	12 months
Busenlechner et al, 2016	Austria	Retrospective	Maxilla	122 (66.5±10.1), (52,70)	582	37, 179	85, 403	4.7±2.1 years
Busenlechner et al, 2016	Austria	Retrospective	Maxilla	240 (61.1±10.9), (102,138)	1215	195, 980	45, 235	3.9±2.1 years
Degidi et al, 2009	Italy	RCT	Maxilla & Mandible	38	284 (Max=74, Mand=210)	19, 130	19, 154	5 years
Degidi et al, 2006	Italy	prospective	Maxilla & Mandible	50	339 (Max=211, Mand=128)	43, 297	7, 42	2 years
Jokstad et al, 2014	Canada	RCT	Mandible	35 (62), (20,15)	140	17, 68	18, 72	5 years
Kim et al, 2018	Korea	Retrospective	Maxilla & Mandible	26 (58.9), (18,8)	370 (52 jaws)	26, 159	26, 211	55 months
Najafi et al, 2016	Iran	Prospective	Maxilla & Mandible	30 (59.3±11.7), (16,14)	156 (39 jaws)	13, 52	26, 104	32.5±13.6 months
Tealdo et al, 2011	Italy	prospective	Maxilla	49 (58.2), (24,25)	260	34, 163	15, 97	36 months
Testori et al, 2014	Italy	Retrospective	Maxilla & Mandible	80 (60.2±9.8), (38,42)	519	59, 385	21, 134	4 years
Ostman et al, 2005	Sweden	Prospective	Maxilla	40 (68.5), (22,18)	243	20, 123	20, 120	12 months

Table1 Description of the included studies

Article	Immediately after surgery (Immediate sites)	Immediately after surgery (Delayed sites)	Healing time post surgery prior to permanent prosthesis fabrication
Alfreda et al, 2014	Existing mandibular denture was converted into an interim implant-supported fixed bridge	Healing abutments were placed. Mandibular denture was hollowed out and relined with soft tissue reline material (COE-SOFT™).	3-4 months
Busenlechner et al, 2016	Screw-retained provisional acrylic partial denture avoiding distal cantilevers	Transmucosal healing and complete denture	3 months
Busenlechner et al, 2016	Screw-retained provisional acrylic partial denture avoiding distal cantilevers	Transmucosal healing and complete denture	4 months
Degidi et al, 2009	Provisional cemented or screw-retained acrylic partial dental proshesis	One-stage surgical procedure when implants showed high primary stability. Two-stage surgical procedure when primary stability was low.	6 months
Degidi et al, 2006	Provisional cemented or screw-retained acrylic partial dental proshesis	One-stage surgical procedure when implants showed high primary stability. Two-stage surgical procedure when primary stability was low.	6 months
Jokstad et al, 2014	Removable prosthesis was converted into an implant-supported FPD (relieved of the distal ends bilaterally to allow for maximum 12-mm-long cantilevers).	Implants were fitted with healing abutments. The existing removable prosthesis was relined using a soft-reline plasticized acrylic-based material (COE-SOFT™) ensuring no impingement of the healing abutments.	3-4 months
Kim et al, 2018	Fixed full-arch prosthesis was placed in the mandible	A provisional removable complete denture was placed in the maxilla	6 months
Najafi et al, 2016	30° angled multi-unit abutment for posterior implants and straight multi-unit abutment for anterior implants were connected and torqued 30 Ncm. Final impression was taken. The metal resin prosthesis was made and delivered by the third day after surgery.	Second surgery was carried out after 4 months.	4 months
Tealdo et al, 2011	Provisional fixed screw-retained prostheses were placed within 24 hours of implant placement (no cantilever).	Standard two-stage Branemark implant protocol with delayed loading.	4.5 months for IL group , 8.75 months for DL group
Testori et al, 2014	When implant number varied from 4 to 6, a hybrid prosthesis composed of a metallic bar and resin teeth was delivered. When implant number was 7 or 8, an implant-supported bridge was provided.	Implants were left to heal in a one-stage way.	6 months for IL group , 2-6 months for DL group
Ostman et al, 2005	Minimum insertion torque = 30 Ncm, ISQ > 60 for the 2 possterior fixtures and a total sum of 2000 for the 4 anterior fixtures, Provisional bridges with no cantilevers exceeding 5 mm were delivered within 12 hours.	Two-stage protocol was followed with healing period of 6 months.	3 months for IL group , 6 months for DL group

Table1 (continue) Description of the included studies

Article	Prerequisite of implant sites	Opposing arch	Implant system
Alfreda et al, 2014	Healed site at least for 3 months, No GBR or GTR had been performed at the implant sites, The bone quality and quantity allow placement of 4 implants of at least 3.75 mm in diameter and 10 mm in length between two mental foramina without the use of bone augmentation techniques, Immediately after surgery torque value ≥ 35 Ncm	Conventional complete denture (32), Removable partial denture (7), implant-supported fixed prosthesis (2)	TiUnite dental implants (NobelBiocare®)
Busenlechner et al, 2016	Healed site without prior or simutaneous application of bone augmentation procedures, 4-6 implants interantral implants were placed, Most distal implants were tilted up to 30 degrees, Implant length ranged between 8 and 16 mm, and diameter of 3.5 to 5 mm were used.	NA	NobelBiocare®
Busenlechner et al, 2016	Fresh extraction sockets without prior or simutaneous application of bone augmentation procedures, 4-6 implants interantral implants were placed, Most distal implants were tilted up to 30 degrees, Implant length ranged between 8 and 16 mm, and diameter of 3.5 to 6 mm were used.	NA	NA
Degidi et al, 2009	Sufficient residual bone volume to receive implants of at least 3.4 mm in diameter and 9.5 mm in length, insertion torque > 25 Ncm, Subjects with bone quality type D4, bruxism, smoking > 20 cigs/day were excluded.	NA	Square thread design (Maestro; Biohorizons)
Degidi et al, 2006	Sufficient residual bone volume to receive implants of at least 3.4 mm in diameter and 9.5 mm in length, insertion torque > 25 Ncm, Subjects with bone quality type D4, bruxism, smoking > 20 cigs/day were excluded.	NA	XiVE dental implants (Dentsply-Friadent)
Jokstad et al, 2014	Fully healed mandible more than 3 months with bone ridge width ≥ 7 mm and a bone height ≥ 8 mm, An augmentation procedure was allowed, but would require at least 6 months healing prior to implant surgery, sufficient bone to receive 4 implants between the two mental foramina of at least 3.75 mm in diameter and 10 mm in length, insertion torque ≥ 20 Ncm for IL group.	Dentate (1), Full denture (26), Partial removable denture (6), implant-retained prosthesis (2)	Brånemark System Mk III or Mk IV implants with a TiUnite surface (NobelBiocare®)
Kim et al, 2018	A poor prognosis for both the maxillary and mandibular teeth or complete edentulous jaws, Sufficient residual bone volume to receive implants of at least 3.4 mm in diameter for maxilla and 3.0 mm for mandible and 8-14 mm in length for both maxilla and mandible, Maximum insertion torque < 50 Ncm, Of 370 implants, 52% were immediately placed implants, The mean number of implants was 8.11 in the maxilla and 6.12 in the mandible.	A provisional removable complete denture was placed in the maxilla	Osstem Implant Co.,Ltd.,Busan, Korea and Dentium Co., Seoul, Korea
Najafi et al, 2016	Severely resorbed maxilla or mandible who required fixed prosthesis, Patients not willing to undergo bone augmentation procedures, All patients received 4 implants; two distal implants at the mental foramina or anterior sinus wall with an inclination of 45 degree relative to the occlusal plane, 2 axial implants at the most favorable implant distribution. If insertion torque ≥ 35 Ncm patient was placed in IL group, if final torque < 35 Ncm or if there was dehiscence or fenestration the required grafting patient was placed in DL group.	Natural teeth (30.7%), Implant-supported prosthesis (59%), Removable prosthesis (10.3%)	Brånemark System Mk III or Mk IV implants, Nobel Speedy Groovy, Nobel Replace Select (NobelBiocare®)
Tealdo et al, 2011	Patients with edentulous maxilla, sufficient bone volume to receive a minimum of 4 implants (4x10 mm), Patients who received bone grafting prior to implant placement were excluded. All implants achieved insertion torque values of at least 40 Ncm.	Natural dentition (15), Natural dentition with fixed implant restorations (9), Full-arch fixed implant prostheses (11), Natural dentition with RPDs (8), Mandibular implant-suppoted overdenture supported by 2 implants (6), No complete denture because they were not able to load the study prosthesis with forces comparable with the other patients.	Osteotite & Osteotite NT, Biomet 3i
Testori et al, 2014	Implant supported prosthesis relying on at least 4 implants. 375 implants were placed in the fresh extraction sockets. 144 implants were placed in healed sites. IL was not applied if intraoperatively two or more implants did not achive a tight primary stability (insertion torque > 32 Ncm).	NA	3i implant system (Biomet 3i, Garden Beach, FL, USA)
Ostman et al, 2005	Patients with edentulous maxilla, residual bone sufficient to house six implants at least 10 mm long. Sites were free of infection.	NA	Brånemark System Mk III or Mk IV implants, Nobel TiUnite, Nobel Replace Select tpaered (NobelBiocare®)

Table1 (continue) Description of the included studies

Article	Total number of failure (patient,implant)	Number of failure in IL group (patient,implant)	Number of failure in DL group (patient,implant)	CSR of IL group (pt level,implant level)	CSR of DL group (pt level,implant level)	Statistical significance of CSR between IL and DL group	Mean marginal bone resorption (IL,DL)
Alfreda et al, 2014	4 , 5	2 , 2	2 , 3	90% , 96.88%	90.9% , 96.88%	Not significant (P = 0.6581) (implant level)	0.296±0.218 , 0.037±0.141* (P=0.002)
Busenlechner et al, 2016	NA , 15	NA , 3	NA , 12	NA , 98.3%	NA , 97%	Not significant (P = 0.571)	1.1±1.3 , 1.4±1.3 Not significant (P=0.490)
Busenlechner et al, 2016	NA , 31	NA , 23	NA , 8	NA , 97.7%	NA , 96.6%	Not significant (P = 0.358)	1.5±1.7 , 0.7±1.1 Not significant (P=0.379)
Degidi et al, 2009	0 , 0	0 , 0	0 , 0	100% , 100%	100% , 100%	Not significant	IL group: 0.3 mm in 1st year, 0.6 mm from 1st -5th year. DL group: 0.3 mm in 1st year, 0.5 mm from 1st -5th year. (Not significant)
Degidi et al, 2006	3 , 4	3 , 4	0 , 0	93.02% , 98.7%	100% , 100%		IL group: 0.7 mm at 12 months, 0.9 mm at 24 months. DL group: 0.6 mm at 12 months, 1.0 mm at 24 months.
Jokstad et al, 2014	3 , 3	2 , 2	1 , 1	88.24% , 97.06%	94.44% , 98.61%	Not significant	1.3±0.7 , 1.1±0.7 Not significant
Kim et al, 2018	5 , 6	3 , 3	2 , 3	88.46% , 96.8%	92.3% , 98.6%	Not significant (P = 0.72) for implant level	NA
Najafi et al, 2016	1 , 1	0 , 0	1 , 1	100% , 100%	96.1% , 99.0%	Not significant (P > 0.05)	0.87±0.25 , 0.81±0.16 Not significant (P > 0.05)
Tealdo et al, 2011	12 , 14	8 , 10	4 , 4	76.5% , 93.9%	73.3% , 95.9%	Not significant (P = 0.42) For implant level	1.6±0.9 , 2.3±1.1* Significant (P<0.001)
Testori et al, 2014	10 , 35	7 , 19	3 , 3	88.1% , 95.1%	85.7% , 97.8%	Not significant (P = 0.18) For implant level	0.9±0.4 , 0.8±0.5 Not significant
Ostman et al, 2005	1 , 1	1 , 1	0 , 0	99.6% , 99.2%	100% , 100%	Not significant for implant level	0.78±0.90 , 0.91±1.04 Not significant

Table1 (continue) Description of the included studies

Quality assessment: Each RCT study was evaluated for risk of bias, summarized in Table2. There was one study[62] with high risk of bias and one study[59] with moderate risk of bias, and one[64] with low risk of bias according to the criteria described in the Cochrane Collaboration tool for assessing risk of bias.[57] Of the 8 included observational studies[60,61,63,65-69], two studies [60,61] received a 9-point score, five studies[63,65,66,67,69] received a 10-point score, and one study[68] received a 11-point score according to the methodological quality. Therefore, a study by Testori et al. 2014[68] was considered high quality, while the rest of the observational studies[60,61,63,65,66,67,69] were considered medium quality. (Table3)

Article	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants, personnel, and outcome assessors (performance bias)	Incomplete outcome data (Attrition bias)	Selective outcome reporting (reporting bias)
Alfreda et al, 2014	+	+	+	+	+
Degidi et al, 2009	+	?	?	+	+
Jokstad et al, 2014	+	+	+	+	+

Table2 Risk of Bias table for RCT studies

	Selection							Comparability		Outcome			Statistical analysis		
Article	Sample size calculation	Representativeness of the patients who received implants with the conventional loading protocol	Representativeness of the patients who received implants with the immediate loading protocol	Description of clear inclusion/exclusion criteria	detailed description of the steps following each loading protocol	Training/calibration of the surgeons and assessors of outcomes	Appropriate protocol of data collection	Comparability of patients on the basis of the study designs and analysis	Management of potential confounders	Evaluation of results	Assessment of accuracy outcomes	Adequacy of follow-up of the patients	Appropriateness/validity of statistical analysis	Unit of analysis reported in the statistical model	Total
Busenlechner et al, 2016		★	★	★	★			★		★	★	★	★	★	9
Busenlechner et al, 2016		★	★	★	★			★		★	★	★	★	★	9
Degidi et al, 2006		★	★	★	★		★	★		★	★	★	★	★	10
Kim et al, 2018		★	★	★	★		★	★		★	★	★	★	★	10
Najafi et al, 2016		★	★	★	★		★	★		★	★	★	★	★	10
Tealdo et al, 2011		★	★	★	★		★	★		★	★	★	★	★	10
Testori et al, 2014		★	★	★	★		★	★	★	★	★	★	★	★	11
Ostman et al, 2005		★	★	★	★		★	★		★	★	★	★	★	10

Table3 Risk of Bias table for observational studies

Meta-analyses for implant failure rates at the implant level (Figure2): Eleven studies (4268 implants) provided information about implant failure based on implants. A fixed-effects model was utilized to evaluate the implant failure rates, since statistically significant difference heterogeneity was not found (P=0.85, I^2 = 0%). The pooled estimates did not provide significant difference between immediate loading and delayed loading at the implant level (RR=1.09, 95%CI: 0.70-1.69, P=0.70).

Meta-analyses for implant failure rates at the patient level (Figure3): Nine studies (425 patients) provided information about implant failure based on patients. A fixed-effects model was utilized to evaluate the implant failure rates, since statistically significant difference heterogeneity was not found (P=0.99, I^2 = 0%). The pooled estimates did not provide significant difference between immediate loading and delayed loading at the patient level (RR=1.10, 95%CI: 0.60-2.01, P=0.75).

Meta-analyses for marginal bone resorption (Figure4): Eight studies with 3275 implants provided information regarding marginal bone loss. 2014 implants received immediate loading and 2141 implants received delayed loading. A random-effects model was utilized to evaluation, since statistically significant difference heterogeneity was found among the studies (P<0.00001, I^2 = 95%). The pooled estimates showed no significant different marginal bone resorption between immediate loading and delayed loading implants (RR=0.05, 95%CI: -0.14 to 0.24, P=0.58).

	Immediate loading		delayed loading			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
Alfreda et al, 2014	2	64	3	96	6.3%	1.00 [0.17, 5.82]
Busenlechner et al, 2016	3	179	12	403	19.4%	0.56 [0.16, 1.97]
Busenlechner et al, 2016 (2)	23	980	8	235	33.9%	0.69 [0.31, 1.52]
Degidi et al, 2006	4	297	0	42	2.3%	1.30 [0.07, 23.70]
Degidi et al, 2009	0	130	0	154		Not estimable
Jokstad et al, 2014	2	68	1	72	2.6%	2.12 [0.20, 22.82]
Kim et al, 2018	3	159	3	211	6.8%	1.33 [0.27, 6.49]
Najafi et al, 2016	0	52	1	104	2.6%	0.66 [0.03, 15.94]
Ostman et al, 2005	1	123	0	120	1.3%	2.93 [0.12, 71.16]
Tealdo et al, 2011	10	163	4	97	13.2%	1.49 [0.48, 4.61]
Testori et al, 2014	19	385	3	134	11.7%	2.20 [0.66, 7.33]
Total (95% CI)		**2600**		**1668**	**100.0%**	**1.09 [0.70, 1.69]**
Total events	67		35			

Heterogeneity: Chi^2 = 4.81, df = 9 (P = 0.85); I^2 = 0%
Test for overall effect: Z = 0.38 (P = 0.70)

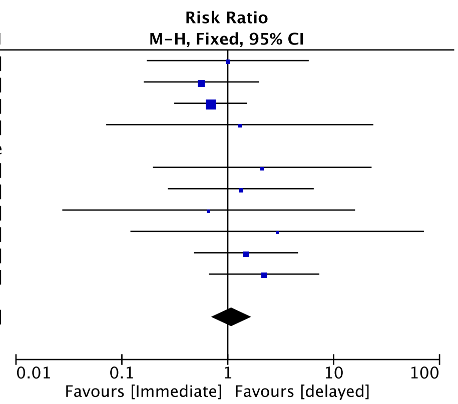

Figure2 Forest plot of relative risk ratio for failure rate at the implant level

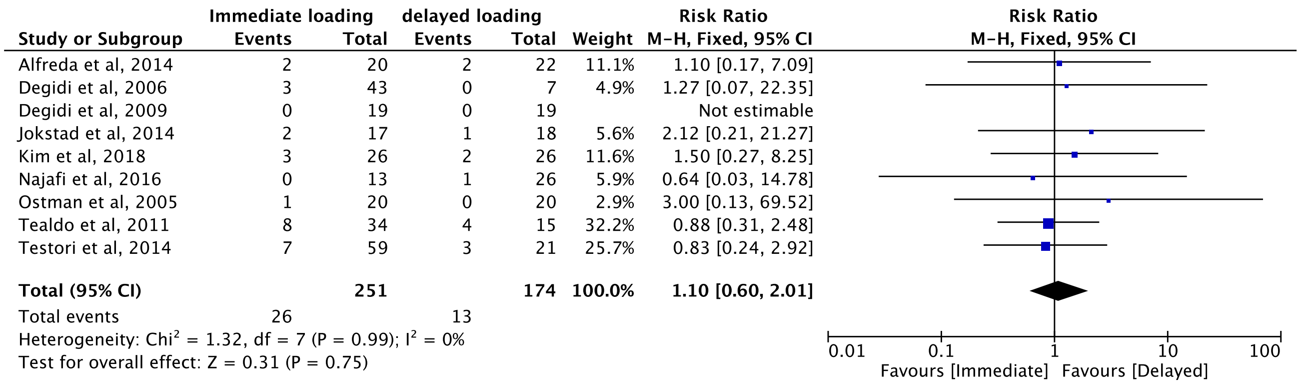

Figure3 Forest plot of relative risk ratio for failure rate at the patient level

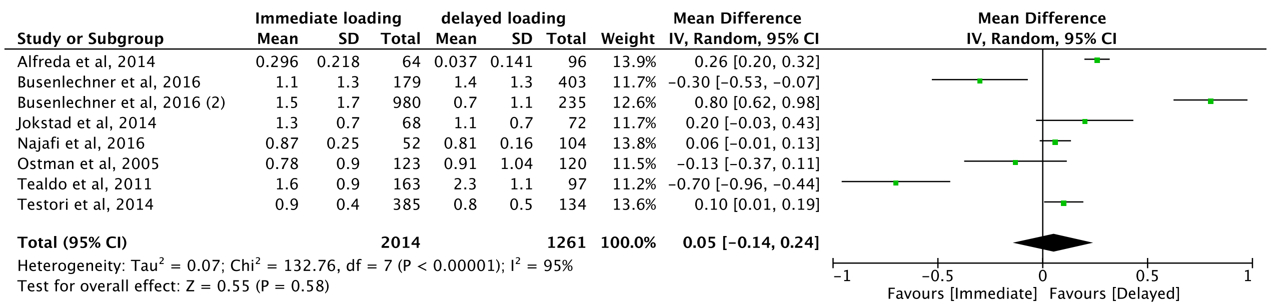

Figure4 Forest plot of the mean difference for marginal bone change

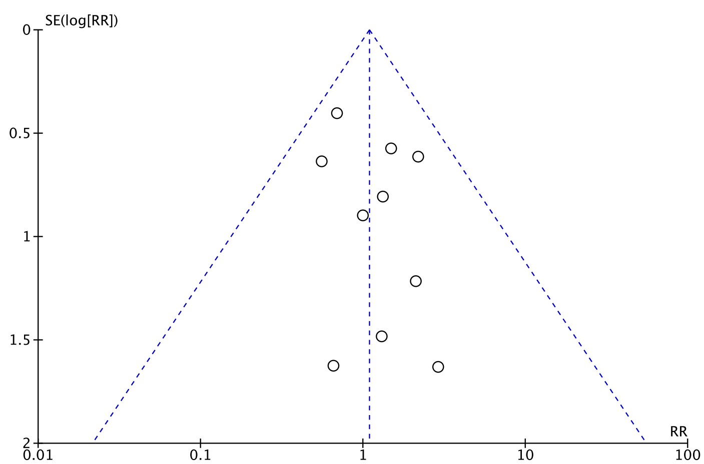

Figure5 Funnel plot for the studies reporting the outcome event of implant failure at the implant level

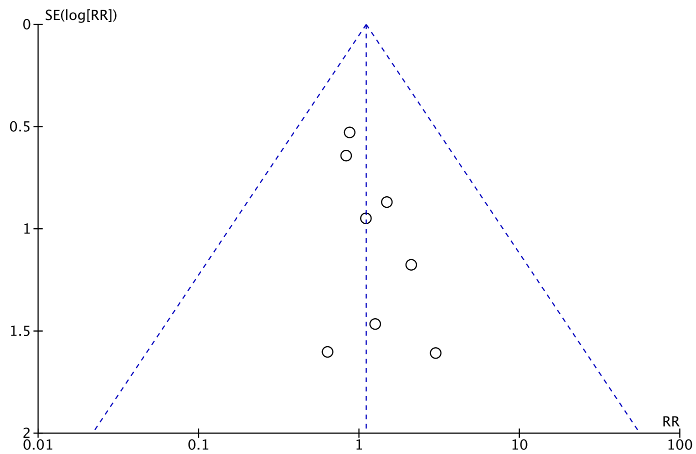

Figure6 Funnel plot for the studies reporting the outcome event of implant failure at the patient

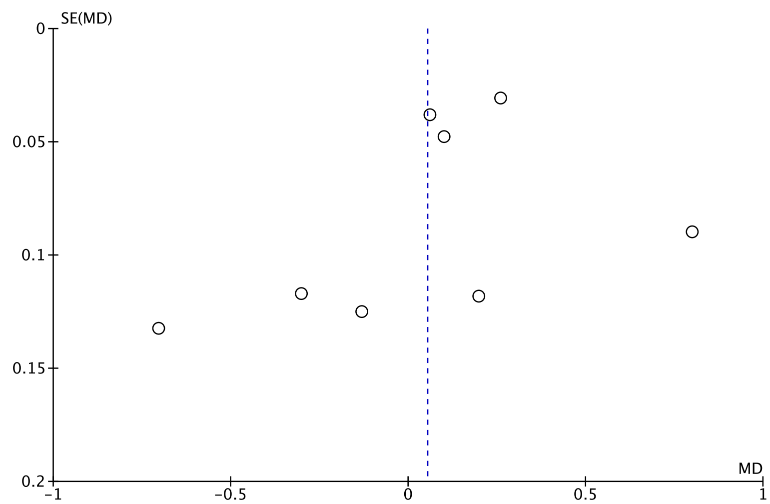

Figure7 Funnel plot for the studies reporting the mean marginal bone resorption

Discussion: Over the last several years, the new concept of immediate loading has challenged the original Brånemark surgical protocol consisted of submerging an implant post placement and maintaining a non-loaded implant environment for 4 to 6 months.[19] Several clinical studies reported high success rates of immediate loading for complete arch rehabilitation with a long term of follow-up but lacking the control group.[20-24] Therefore, the objective of this study is to systematically review with an aim to test the null hypothesis of no difference between immediate loading and delayed loading fixed implant-supported restoration for completely edentulous arch in terms of implant failure rates and marginal bone resorption against the alternative hypothesis of a difference. Three randomized controlled trials, four prospective studies, and four retrospective studies including 752 patients with 4268 implants were included in this review. All studies composed of experimental arms (immediate loading) and control arms (delayed loading). There was no significant difference heterogeneity found for implant failure rates at both the implant level and the patient level. Implant failure rates were similar for immediate loading and delayed loading after follow-up period of at least 12 months. At the implant level, there were 67 (2.58%) failures out of 2600 immediate loading implants and 35 (2.09%) failures out of 1668 delayed loading implants which determined no statistically significant difference between techniques ($P=0.70$). At the patient level, there were 26 (10.36%) failures out of 251 immediate loading implants and 13 (7.47%) failures out of 174 delayed loading implants which also determined no statistically significant difference between techniques ($P=0.75$).

Overall, there was homogeneity ($I^2 = 0\%$) of the study outcome of the failure rates at both the implant level and the patient level. All of the included studies reported no statistically significant difference between the experimental arms (immediate loading) and the control arms (delayed loading) ($P<0.05$). In certain studies, some of the implants were placed into fresh extraction sockets without prior or simultaneous application of bone augmentation procedures. When implants are placed immediately into fresh extraction sockets, only the very apical portion of implants is in bone. However, there are multiple studies showed high success rates of immediate restoration in fresh extraction sockets for full arch rehabilitation. Ciabattoni et al.[56] did a study to evaluate the clinical outcome of immediately loaded implants placed in full-arch rehabilitation immediately after extraction of hopeless teeth. One hundred and ninety-seven implants were placed in extraction sites (137 maxilla, 60 mandible) and 88 in healed sites (58 maxilla and 30 mandible). The overall cumulative implant survival rate (CISR) was 97.54%. Two implants failed in maxillary healed sites (CISR 96.55%), three in maxillary extraction sites (CISR 97.81%), and two in mandibular extraction sites (CISR 96.66%). No implant failed in healed mandibular sites (CSR 100%). All fixed prostheses maintained stability and good functionality during the follow-up, accounting for a cumulative prosthesis survival rate (CPSR) of 100%. And it is nice to note that, in all studies, a minimum of four implants were placed into each arch for supporting a fixed full arch prosthesis. This may be suggesting that immediate loading can be a treatment of choice when performing full-arch implant-supported rehabilitation with a comparable outcome of the success and failure rates compared to conventional loading protocol.

A two-stage implant placement procedure was recommended as standard, and long-term follow-up studies have demonstrated high survival rates for complete-arch fixed rehabilitations. This meta-analysis suggested a slight potential for a benefit from conventional loading compared to immediate loading, even though it was not statistically significant. The argument against immediate loading is the potential formation of connective tissue instead of bone at the bone-implant interface. It has been reported that a connective tissue capsule is formed around implants that are mobile during the healing period.[25] So if micromovement at the bone-implant interface is minimal during osseointegration, immediate loading of implants could become a successful intervention, with a reduction of the healing period.[26] It has been proven that if the micromovement was over 150 μm, it could jeopardize the osseointegration process.[28,29] The most accessible parameter to assess the primary stability is the implant insertion torque values. Insertion torque values ranging from 30 to 40 Ncm and higher have been usually determined as thresholds for immediate loading.[30,31] However, some studies assessed that immediate loading implants placed into weak bone with a final torque > 20 Ncm have an equally successful prognosis as the conventional loading implants.[32] Furthermore, if enough implants are placed, immediate loading can be performed even if not all implants achieved an adequate primary stability, but the unstable implants should be left unloaded.[33]

Moreover, there are other factors that influence the success of immediate loading such as bone quality and quantity, number of implants, implant positioning, patient selection, and clinician's surgical ability.[27] In several studies, authors introduced different techniques to optimize bone density to subsequently enhance primary stability of implants, such as subcrestal placement[34,35], underpreparation of implant sites[36], and bone condensing technique[37]. It has been reported high implant survival rates with utilization these techniques.[38]
To obtain full-arch rehabilitation with immediate loading, most studies considered 6 implants to be the lowest adequate number to achieve a predictable outcome.[27,39] Brånemark's configuration proposed using five implants for the mandible and six for the maxilla to support a complete-arch fixed prosthesis, with all implants distributed anteriorly, placed parallel to each other and splinted together by a passively fitted prosthesis.[40,41,42] Other authors reported using as many implants as possible in the maxilla (ranging from 6 to 10), and five to six implants distributed between mental foramen in the mandible, as a standard choice (Zarb & Schmitt, 1990).[43] More recently, suggestions for the use of as many as eight implants in the maxilla and six in the mandible for segmented full-arch restorations have also been proposed (Gallucci et al., 2016).[44] However, Malo et al. described a technique to achieve successful results with only 4 implants.[45] More importantly, patient selection is one critical factor that can influence the success of the immediate loading approach.[46] Most studies proposed the following criteria: good general health, adequate bone quality and quantity, absence of acute infection, and primary stability of implants. Although, several papers refer to bruxism and smoking habits as risk factors capable of jeopardizing the successful outcome of an implant-supported rehabilitation[47,48,49,50], there is still no solid consensus.[51]

Regarding marginal bone resorption, the meta-analysis showed no significant different marginal bone resorption between immediate loading and delayed loading implants (P=0.58). Marginal bone level is critical to maintain peri-implant health and esthetic outcomes. Implant location, the type of prosthesis loading concept, occlusal forces, and follow up time were the factors affecting marginal bone change.[52]

The limitation of this systematic review is that the meta-analysis included studies with variable characteristics. Some studies only studied either maxilla or mandible. Some studies included both maxilla and mandible. Many studies excluded fresh extraction sockets from their experiments, while other did not. Some did not mention whether they did it or not. Also, there were differences in study design among all the included studies (3 randomized controlled trials, 4 retrospective studies, and 4 prospective studies). Potential biases are likely to be greater for non-randomized studies compared to RCTs.[53] However, in meta-analysis for this topic, adding more information from observational studies may aid in clinical reasoning and establish a more solid foundation for causal inferences.[54]

This meta-analysis is in agreement with Papaspyridakos et al.[55] 2014 who reported that treatment with mandibular implant fixed complete dental prosthesis yields high implant and prosthetic survival rates (more than 96% after 10 years). He concluded that the loading protocol (delayed, early, and immediate) had no influence ($p > 0.05$) on the prosthetic survival rates.[55] By the time of this systematic review, none of the published systematic reviews included studies directly comparing immediate loading to delayed loading protocol in the rehabilitation of completely edentulous arches with implant-supported prostheses with both test group and control group.

In conclusion, there was no statistically significant difference between the experimental arms (immediate loading) and the control arms (delayed loading) ($P<0.05$) in terms of implant failure rates and marginal bone resorption. Future research should be focused on randomized controlled clinical trial considering that it is a higher level of evidence. However, the information from this systematic review may be useful for clinicians concerning the prognosis of fixed implant-supported prostheses in completely edentulous patients when making decision on immediate loading or delayed loading restorations.

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Literature Review

The primary goal of any prosthodontic procedure is to satisfy the patient receiving a dental treatment.[1] Patients nowadays are more educated and having more concern of their dental health. The concept of minimally invasive dentistry has become well-known. Therefore, to restore an edentulous space with traditional crown and bridge technique, where adjacent teeth needed to be sacrificed as abutment teeth, has become as of concern. Since Brånemark introduced the osseointegration system in 1977[2], implant placement has become a popular treatment option of replacing teeth. Osseointegration is defined as the direct structural and functional connection between living bone and the surface of a load-bearing artificial implant.[3] For osseointegrated dental implant, to be termed osseointegrated, it does not need to be 100 percent bone to implant contact, but it derived more from the stability of the fixation than the percentage of connection histologically. For clinical circumstances, osseointegrated implant represents that an a symptomatic rigid fixation of alloplastic material is achieved and maintained in bone during functional loading.[4]

Since Brånemark introduced the first titanium dental implant placed into a human to support a palatal obturator in 1965. The concepts and techniques in implant dentistry were developed and changed with the improved knowledge on oral implantology. The desire for fewer treatment visits, less surgical interventions, shorter healing time, and earlier esthetic restoration has driven us to overcome the early limitation from a machined surface to a rough surface, from delayed placement to early placement and immediate placement, from multiple visits to a single visit treatment in order to serve and meet our patients' expectation. Today, immediate loading of single implant shows a high success rate and predictable outcome[5], however, immediate loading for rehabilitation of completely edentulous arch with fixed implant-supported prosthesis is still challenging because of an increased risk of osseointegration failure due to implant micromotions during the healing phase.

In implant dentistry, according to the 5th ITI Consensus Conference, there are three different types of loading protocol described by Weber et al.[6] The definition of terms were as follows: *Conventional loading* of dental implants is defined as being greater than 2 months subsequent to implant placement. *Early loading* of dental implants is defined as being between 1 week and 2 months subsequent to implant placement. *Immediate loading* of dental implants is defined as being earlier than 1 week subsequent to implant placement. However, immediate and delayed loading protocols are commonly considered in completely edentulous patients.[9]

The conventional loading protocol dictates to achieve predictable proper osseointegration and minimize the risk of implant failure. Traditionally, the original Brånemark surgical protocol consisted of submerging an implant post placement and maintaining a non-loaded implant environment for 4 to 6 months.[7] This approach is believed to overcome a potential risk of immediate loading that connective tissue instead of bone could form at the bone-implant interface.[10] With this limitation, a two-stage implant placement procedure was recommended and considered as a gold standard for many clinicians. This classic approach is well-known to have multiple surgeries, high treatment cost, and long treatment time. During the healing period, patient can either wear an interim removable denture or remain edentulous. Many patients find these temporary prostheses uncomfortable[11] and it would be beneficial if treatment time can be shortened and esthetic can be immediately restored without compromising implant success. Reports from previous ITI consensus conferences in 2004 and 2009 stated that conventional and early implant loading are well-established protocols and should be considered routine.[6,8]

Nowadays, immediate loading offers several advantages over conventional loading without compromising the outcome. An immediate fixed provisional restoration promotes a high level of patient satisfaction with respect to esthetics, phonetics, masticatory capability, physiological, and psychological comfort, enabling patients to return to their normal routine and maintain quality of life within a short period of time.[11] Another advantages to extraction with simultaneous replacement include the maintenance of vertical dimension, elimination of reline procedures and interim denture therapy, and potential improvement of soft tissue healing.[12] The ability to immediately load implants placed in edentulous jaw is well documented, with most current citations on this subject showing a range of implant survival for this procedure of greater than 95%.[11,13-25] Regarding, mandibular rehabilitation, Colomina 2001 reported that immediately loaded implants placed in healed sites and restored with fixed transformed complete denture had survival rate of 96.7% after 18 months of follow-up.[26] Testori et al. 2003[27] reported higher implant survival rate of 98.9% with a longer follow up (48 months) and prosthetic survival rate of 100%. Marginal bone loss at the immediately loaded implants was within the generally accepted conventional limits for standard delayed loading protocols. He concluded that immediate loading technique can reduce treatment time but should be applied with caution with a suggestion that rehabilitation of the edentulous mandible by an immediately loaded hybrid prosthesis should be supported by 5 to 6 implants.[27] Gualini et al.[28] 2009 reported a lower implant survival rate of 91% and prosthetic survival rate of 87% after 5-year follow up. He observed very small changes in implant stability during implant loading from 1 to 5 years. Oral health conditions were good; 87% of mucosal quadrants around the implants were free from signs of inflammation. Very small marginal bone height changes were observed at the implants during the examination period, and except for four failed implant, severe complications were few. Most patients were satisfied with the functional outcome of their constructions.[28] It is with no surprise that most published data on immediate loading are for implants placed in the mandible[11,13,14,15] since it has a more desirable bone density for implant placement especially for full arch rehabilitation. However, the use of immediate loading protocols in the maxilla for single-tooth[28,29], partially edentulous[29,30], and fully edentulous applications has been shown in few studies.[13,31-35] Regarding survival rates of maxillary rehabilitation, Balshi et al. 2005[36] reported that the immediately loaded implant population (522 implants) has a survival rate of 99.0% while, surprisingly, the 30 implants placed with the conventional two-stage approach have a lower survival rate of 90.0%. And all 55 patients experienced a prosthesis survival rate of 100% for an average of 2.78 years. The sinus grafting procedures were from this study since the literature indicates a higher failure rate for implants placed in sinus-grafted receptor sites.[37] Collaert et al 2008[38] reported a convincing outcome of immediate functional loading of dental implants for full-arch maxillary restoration. One hundred and ninety-five Astra Tech TiOblast surface fixtures were installed in 25 patients (age range: 42-76 years), of whom eight were smokers, 12 had a confirmed history of periodontitis and six had poor bone quality normally deemed for delayed loading. Fixtures and abutments were inserted in a one-stage procedure and functionally loaded within 24 hours with a 10-unit provisional glass-fibre or metal-reinforced screw-retained restoration. The total survival rate was 100% with no failures occurred in implants or prostheses. Mean marginal bone loss was 0.58 mm (SD 0.58); 0.6 mm (SD 0.53); 0.63 (SD 0.61); and 0.72 (SD 0.63) after 6 and 12 months, and 2 and 3 years, respectively. The fixtures with more bone loss were all inserted in smokers. He concluded that immediate loading of a full-arch maxillary bridgework with 7-9 implants is a predictable treatment option with 100% fixture and prosthetic survival and stable bone-to-implant contact up to 3 years. The steady state in bone remodeling is indicative of a good long-term prognosis in non-smokers, yet smokers seem to be more prone to bone loss.[38] Mozzati et al. 2012[39] performed a study with 334 dental implants placed in postextraction sockets and loaded immediately on 65 patients. After two years, all prostheses were stable, and only seven implants failed during the follow-up, leading to a 100 percent prosthetic survival rate and a 97.9 percent implant survival rate. The mean (standard deviation) implant bone level measured 0.50 (0.27) millimeter at insertion, 1.90 (0.51) mm at one year and 2.06 (0.49) mm at two years. And he concluded that immediate loading of four to six implants placed in extraction sockets may be a valid way to treat the edentulous maxilla.[39] Yamada et al. [40] in 2015 placed 278 implants into 48 patients. All implants were immediately loaded 2 hours after placement with prefabricated fixed provisional prostheses. One year after immediate loading, the implant survival rate was 98.6%. Mean marginal bone level changes were -0.32 ±

0.43 mm. And scores on the Oral Health Impact Profile-54 improved significantly after prosthetic treatment. He concluded that this treatment method for edentulous maxillae is predictable, with a high implant survival rate and a clinically reasonable improvement in oral health-related quality of life.[40] However, there are a number of articles showed lower survival rates for immediate loading technique compared to conventional technique.[41,42]

The clinical success of immediate loading is highly dependent on many factors: patient selection, bone quality and quantity, implant number and design, implant primary stability, occlusal loading, and clinician's surgical ability.[43,44,45] It is in agreement that implant primary stability is undoubtedly the most important factor.[43,45] Successful implant integration is a prerequisite criterion for success of implant therapy. A secure primary stability is positively related to a secondary stability.[46] Primary stability is associated with the mechanical engagement of an implant with the surrounding bone, whereas bone regeneration and remodeling phenomena determine the secondary (biological) stability of the implant[47,48] Primary stability of an implant mostly comes from mechanical engagement with cortical bone. It is accomplished when the implant is placed in the bone in such a position that it is "well-seated."[49] Impaired primary implant stability has been shown to jeopardize the osseointegration process.[50] It has been reported that a connective tissue capsule is formed around implants with micromovements during the healing period.[10] So if micromovement at the bone-implant interface is minimal (<150 μm) during osseointegration, immediate loading of implants could become a successful intervention.[51,52,53] The success of this adaptation, however, depends on several factors, including the density and dimension of the bone surrounding the implant, the implant design, and surgical technique used.[54] Studies[55,56,57] have reported that a well-controlled micromotion positively influenced bone formation, therefore, more advanced clinical conditions, like immediate functional loading of implants seem to improve the peri-implant bone density and improve the implant integration.[54]

Bone quality is often referred to as the amount of cortical and cancellous bone in which the recipient site is drilled. A poor bone quantity and quality have been indicated as the main risk factors for implant failure as it may be associated with excessive bone resorption and impairment in the healing process compared with higher density bone.[58,59,60] Clinical studies have reported dental implants in the mandible having higher survival rates compared to those in the maxilla, especially for the posterior maxilla.[61,62] Bone quality has been considered as the basic cause of this difference. In the posterior maxilla, there is commonly thinner cortical bone combined with thicker trabecular bone compared to the mandible.[63,64] Clinically, a poor degree of bone mineralization or limited bone resistance is observed in bone with poor density, which is often referred to as "soft bone".[63,65] It has been shown that achieving optimum primary stability in soft bones is difficult and is also related to a higher implant failure rate for the implants placed in such bone.[58,66] Turkyilmaz et al.[67] reported the bone quality around the implant to be superior in the mandible compared to the maxilla. A clinical study[68] with 158 implant sites from 85 patients indicated a strong correlation between bone density and dental implant stability. Results by Miyamoto et al.[69] demonstrated that dental implant stability is positively associated with the thickness of cortical bone thickness. In contrast to the previous studies, additional studies in the posterior mandible showed high failure rates due to the poor bone quality as well as other additional factors.[70,71] Intraoperative surgical techniques, such as bone condensing, undersizing the osteotomy, have been shown to improve the bone density and increase the primary (mechanical) stability.[54] Summers in 1994[72] recommended the technique of bone condensing, where, after using the pilot drill, the cancellous bone is pushed aside with "condensers" (osteotomes), thus, increasing the density of the surrounding bone, increasing the primary implant stability. Though the use of these procedures, it has been reported high survival rates with immediate loading approach.[73]

Marginal bone loss is one of the key factors that can lead to unsuccessful treatment. Presence and maintenance of papillae is primarily related to the bone level[74,75,76], therefore bone preservation is a key factor for the esthetic outcome.[77,78] Albrektsson et al.[79] reported that primary implant stability and lack of micromovement are two of the main factors considered necessary for the achievement of predictably high success rates for osseointegrated oral implants. Primary stability of implants placed immediately after extraction strongly influences the long-term success of dental implants[80]. Bone grafting procedure plays an important role for increasing the primary stability of immediately placed implants.[82] Araújo et al.[81] evaluated the osseointegration and peri-implant tissue modeling following implant placement in fresh extraction sockets, and he found that in the absence of bone graft, the dimensions of both the buccal and the lingual bone walls around the implant were reduced. Berberi et al. in 2014[83] studied about influence of immediate loading on marginal bone loss around immediate implants. He found that one-stage immediate loading of immediately placed implants into fresh extraction sockets resulted in a significant reduction in marginal bone loss ($p < 0.002$) compared to the traditional two-stage technique. Implants that are placed immediately into fresh extraction sockets, only the very apical portion of implants is in bone. However, there are multiple studies showing high success rates of immediate restoration with immediate implants for full arch rehabilitation. Ciabattoni et al.[84] did a study to evaluate the clinical outcome of immediately loaded implants placed in full-arch rehabilitation. One hundred and ninety-seven implants were placed in extraction sites (137 maxilla, 60 mandible) and 88 in healed sites (58 maxilla and 30 mandible). The overall cumulative implant survival rate (CISR) was 97.54%. Two implants failed in maxillary healed sites (CISR 96.55%), three in maxillary extraction sites (CISR 97.81%), and two in mandibular extraction sites (CISR 96.66%). No implant failed in healed mandibular sites (CSR 100%). All fixed prostheses maintained stability and good functionality during the follow-up, accounting for a cumulative prosthesis survival rate (CPSR) of 100%. Polizzi et al.[85] conducted a study to evaluate mid-term follow-up of patients with compromised dentition treated with immediate fixed restorations on maxillary implants inserted in fresh extraction and healed sites. Ninety-two implants were placed in healed sites and sixty-eight implants were placed in extraction sites. The patients were clinically and radiographically followed for up to 5 years. There were four implants in two patients failed and were removed (overall CSR 97.33%), and two were replaced. All final prostheses were stable and in good function throughout the study. Two of the failed implants were placed in healed sites, the other two in postextraction sites. Failures of the healed site implants occurred after 2 years. The reason for failure of these two implants was progressive bone loss, and high-risk factors (smoking habit, 20 cigarettes per day) present in this patient. Extraction site implants were removed after 6 months despite the absence of inflammatory symptoms. These implants failed to osseointegrate as noticed when the provisional restoration was removed to take the impression for final prosthesis fabrication. They were successfully replaced and included in the final prosthesis. He concluded that immediate fixed restorations of maxillary implants inserted in fresh extraction and healed sites demonstrated good treatment outcomes with regard to implant survival, marginal bone changes, and soft tissue conditions. Meloni et al.[86] also presented a high success rates of immediately restored immediately placed implants in fresh extraction sockets for full arch rehabilitation. After follow-up period of at least 12 months, all the patients felt comfortable and none withdrew from the study. No implants were lost, resulting in a cumulative survival rate of 100%. Therefore, immediate loading of immediately placed implants could be a viable approach to meet patient's high expectation.

Implant surface characteristics have been shown to influence primary stability and success rates of implants. Rough implant surface has a positive effect on implant success with less marginal bone resorption compare to machined surface.[87] Tapered implants were introduced to overcome the poor bone quality and quantity limitations. The goal behind using tapered implant was to exercise a degree of compression of the surrounding bone during the insertion phase, and the decrease of their apical diameter allows to accommodate them in area with small bone volume available, like the labial concavity or between adjacent roots.[88] To obtain full-arch rehabilitation with immediate loading, most studies considered 6 implants to be the lowest adequate number to achieve a predictable outcome.[43,89] Brånemark's configuration proposed using five implants for the mandible and six for the maxilla to support a complete-arch fixed prosthesis, with all implants distributed anteriorly, placed parallel to each other and splinted together by a passively fitted prosthesis.[90,91,92] Other authors reported using as many implants as possible in the maxilla (ranging from 6 to 10), and five to six implants distributed between mental foramen in the mandible, as a standard choice (Zarb & Schmitt, 1990).[93] More recently, suggestions for the use of as many as eight implants in the maxilla and six in the mandible for segmented full-arch restorations have also been proposed (Gallucci et al. 2016).[94]

Patient selection is one critical factor that can influence the success of the immediate loading approach.[43] Most studies proposed the following criteria: good general health, adequate bone quality and quantity, absence of acute infection, and primary stability of implants. Smoking has been a well-known factor associated with a significantly higher incidence of implant failure.[95] There are evidence of a strong relationship between smoking and deleterious implant-related factors.[96] These include greater bone loss around implants, lower success rates for implants placed in grafted sites,[97,98] a higher incidence of healing complications,[99,100] reduced bone mineral density,[101] and an increased incidence of peri-implantitis.[102,103] Although a few reports have found no difference in the success of implants placed in smokers and nonsmokers,[104,105] a recent literature review[106] and at least two meta-analyses[107,108] have affirmed the trend of significantly more implant failures and biologic complications in smokers. However, Romanos et al.[109] conducted a study to evaluate the long-term success of immediately loaded implants placed in smokers and nonsmokers with edentulous jaws. Platform-switched implants were placed in the healed edentulous jaws of two groups of patients: group A patients had smoked at least 20 cigarettes a day for more than 10 years, and group B consisted of nonsmokers. All implants were loaded immediately with provisional fixed prostheses, and definitive cement-retained restorations were delivered 4 to 6 weeks later without removing the abutments. Sixty-six implants (36 in the maxilla and 30 in the mandible) were placed in eight smokers. Twelve nonsmokers received 97 implants (55 in the maxilla and 42 in the mandible). During an average loading period of 62.53 (± 44.13) months for the smokers and 98.20 (± 19.53) months for the nonsmokers, three implants failed. Two failed in group A (one because of overloading and one because of peri-implantitis) and one failed in group B (overloading), resulting in implant survival rates of 97% and 99%, respectively. It was found that implants placed in heavy smokers and loaded immediately, with no stage-two surgery and without removal of abutments during the entire observation period to avoid violating the integrity of the peri-implant soft tissue, had comparable survival and success rates as implants placed in nonsmokers.

Bruxism is a motor activity that is supposed to have the potential for causing damage to the stomatognathic structures as well as to be a risk factor for dental implants survival.[110,111,112] The caution that is urged when using implants to support dental prosthesis in bruxers is due to the common fear that bruxism can cause overloading and may affect osseointegration and/or compromise the integrity of mechanical components.[113] Although, several papers refer to bruxism and smoking habits as risk factors capable of jeopardizing the successful outcome of an implant-supported rehabilitation[114-117], there is still no solid consensus.[118]

Several studies have shown high success rates of immediately loaded implants for full arch restorations without significant differences when compared to traditional delayed loading protocol. However, when it comes to predictability, it is still a controversy among many clinicians. Thus, the aim of this systematic review is to test the null hypothesis of no difference between immediate loading and delayed loading of fixed implant-supported restoration for completely edentulous arch in term of implant failure rates and marginal bone resorption against the alternative hypothesis of a difference. By the time of this systematic review, none of the published systematic reviews included studies directly comparing immediate loading to delayed loading protocol in the rehabilitation of completely edentulous arches with implant-supported prostheses in both test group and control group.

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