

# Implant Loading Protocols for Partially Edentulous Patients with Extended Edentulous Sites— A Systematic Review and Meta-Analysis

Alexander Schrott, DMD, Dr Med Dent, MMSc<sup>1</sup>/Martine Riggi-Heiniger, MD, DMD<sup>2</sup>/  
Katsuichiro Maruo, DDS, PhD<sup>2</sup>/German O. Gallucci, DMD, Dr Med Dent, PhD<sup>3</sup>

**Purpose:** The aim of this study was to systematically review the evidence for immediate implant loading in partially edentulous patients with extended edentulous sites and evaluate potential treatment modifiers.

**Materials and Methods:** An electronic search was performed in Medline, Embase, and Central to identify studies investigating the outcome of implants subjected to immediate loading (IL) (less than 1 week), early loading (EL) (1 week to 2 months), or conventional loading (CL) (more than 2 months) with implant-supported fixed dental prostheses (IFDPs) in partially edentulous patients with extended edentulous sites, ie, at least two adjacent teeth are missing. Only human studies with at least 10 cases and a minimum follow-up time of 12 months, reporting on solid-screw-type implants with rough surfaces and a diameter of at least 3 mm, were included. Weighted means of implant survival rates and risk ratios for implant survival at 1 year using meta-analytic tools were calculated to perform the following comparisons: IL vs EL, IL vs CL, and IL in the maxilla vs mandible. Noncomparative studies reporting on IL and EL protocols were summarized through descriptive methods. **Results:** The search provided 3,872 titles, 837 abstracts, and 444 full-text articles. A total of 24 publications that comprised six comparative studies (five randomized controlled trials, one nonrandomized controlled trial) and 18 noncomparative studies were included for analysis. The comparison of weighted mean survival rates revealed no statistically significant difference between IL (97.9%) and EL (97.8%,  $P = .9405$ ), and between IL (100%) and CL (99.3%,  $P = .3280$ ). Meta-analysis showed no statistically significant difference in implant survival at 1 year between IL and EL (RR 0.90; 95% CI 0.30, 2.70;  $P = .502$ ). A meta-analysis comparing IL and CL could not be performed due to the low number of failures. No statistically significant difference was found for IL implants placed in the maxilla vs the mandible (RR 1.55; 95% CI 0.49, 4.84;  $P > .05$ ). Due to the small number of IL implants placed in the anterior, a comparison between implant survival in anterior vs posterior zones was not performed. Treatment modifiers were bone quality, primary stability, insertion torque, ISQ values, implant length, the need for substantial bone augmentation, the timing of implant placement, and the presence of parafunctional and smoking habits. **Conclusions:** IL presents similar implant survival rates as EL or CL for partially edentulous patients with extended edentulous sites in the posterior zone, as long as strict inclusion/exclusion criteria are followed. There is a lack of evidence for IL of multiple implants in the anterior zone of partially edentulous patients. Preliminary evidence suggests that IL may be equally successful in either the maxilla or mandible. Further research is needed before IL in partially edentulous patients with extended edentulous sites can be recommended in everyday practice. *INT J ORAL MAXILLOFAC IMPLANTS* 2014;29(SUPPL):239–255. doi: 10.11607/jomi.2014suppl.g4.2

**Key words:** conventional loading, dental implants, early loading, fixed dental prostheses, immediate loading, meta-analysis, partial edentulism, systematic review

The literature on dental implants demonstrates that conventional loading (CL) of implant-supported fixed dental prostheses (IFDPs) in partially edentulous

patients is associated with predictable long-term outcomes.<sup>1–6</sup> When a reduced healing time is considered, such as in early loading (EL) or immediate loading (IL)

<sup>1</sup>Clinical Instructor, Department of Oral Medicine, Infection, and Immunity, Harvard School of Dental Medicine, Boston, Massachusetts, USA.

<sup>2</sup>Research Fellow, Division of Regenerative and Implant Sciences, Harvard School of Dental Medicine, Boston, Massachusetts, USA.

<sup>3</sup>Assistant Professor, Division of Regenerative and Implant Sciences, Harvard School of Dental Medicine, Boston, Massachusetts, USA.

**Correspondence to:** Dr German O. Gallucci, Div of Regenerative and Implant Sciences, Harvard School of Dental Medicine, 188 Longwood Avenue, Boston, MA 02115, USA. Fax: +1 617-432-090. Email: german\_gallucci@hsdm.harvard.edu

©2014 by Quintessence Publishing Co Inc.

protocols, several clinical parameters such as bone volume and density, implant placement protocol, implant size, and primary stability have to be considered.<sup>7</sup>

The 2008 ITI Consensus Meeting reviewed the predictability of EL and IL protocols in partially edentulous arches and revealed different results depending on the mandibular or maxillary location of the implant-prosthetic complex.<sup>8–10</sup> In the mandible of partially edentulous patients, EL (6 to 8 weeks) was supported in the absence of modifying factors and IL appeared to be a treatment alternative in carefully selected clinical situations.<sup>9,10</sup> In the maxilla, however, EL and IL protocols were recommended only in selected patients since they appeared to be technique sensitive.<sup>8,10</sup> The recommendations from these systematic reviews were mainly based on implant survival as the primary outcome.

To determine the viability of a shortened implant healing time, a comparison among different loading protocols for partially edentulous patients seems to be of clinical relevance. However, the evaluation of the clinical relevance and practicality of early and immediate implant loading calls for a comprehensive assessment of criteria used for selecting such loading protocols and an intention-to-treat analysis (ITT) rather than the sole presentation of survival rates.

The objectives of this systematic review are to present, analyze, and summarize scientific and clinical evidence of IL protocols in partially edentulous patients with extended edentulous sites and to identify criteria associated with the selection of such loading protocols.

## MATERIALS AND METHODS

This systematic review was conducted consulting the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA),<sup>11</sup> the Standards for Developing Trustworthy Clinical Practice Guidelines published by the Institute of Medicine (IOM),<sup>12</sup> and the Cochrane Handbook for Systematic Reviews of Interventions.<sup>13</sup>

### Focus Question

The focus question was developed according to the PICO (population, intervention, comparison, outcome) format<sup>14</sup> with the population being partially edentulous patients with extended edentulous sites, intervention being IL of dental implants with IFDPs, comparison being EL and CL of dental implants with IFDPs, and outcome being implant survival.

The focus question was: In partially edentulous patients with extended edentulous sites, what is the effect of immediate implant loading with implant-supported fixed dental prostheses compared to early or conventional loading on implant survival?

Loading protocols were defined as follows<sup>10,15</sup>:

- *Conventional loading*: Dental implants are allowed a healing period greater than 2 months after implant placement with no connection to the prosthesis.
- *Early loading*: Dental implants are connected to the prosthesis between 1 week and 2 months subsequent to implant placement.
- *Immediate loading*: Dental implants are connected to the prosthesis within 1 week subsequent to implant placement.

### Search Strategy

The search strategy was developed in close collaboration with a trials search coordinator, who also serves as the Reference and Education Services Librarian at the Countway Library of Medicine of the Harvard Medical School, Boston, Massachusetts. The electronic search was performed utilizing the databases of PubMed/Medline, Embase, and the Cochrane Central Register of Controlled Trials (CENTRAL) (Table 1).

A total number of 4,496 publications were identified. This number was reduced to 3,872 publications (2,578 from PubMed, 1,294 from Embase, 0 from CENTRAL) after duplicates had been removed. All 3,872 studies were included for title screening (Fig 1). A reference manager software (EndNote X, Version 4.0.2) was utilized to search electronic databases, identify and discard duplicate publications, screen studies, and monitor reviewer agreement.

### Selection Criteria

Inclusion and exclusion criteria are summarized in Table 1. Clinical studies of all levels of the hierarchy of evidence were included as long as the investigators performed a clinical exam on all patients under investigation to collect the data. As CL in partially edentulous patients is a well-documented protocol, noncomparative studies describing the outcome of CL implants were not included. In case of multiple publications on the same study population, only the study with the longest follow-up time was included, while previous studies were consulted only to retrieve information not provided in the most recent publication.

### Screening of Studies

Screening was performed independently by two reviewers, who were calibrated during an ITI calibration meeting (AS and GG). Titles, abstracts, and full-text articles were consecutively excluded at the corresponding stages of screening (Fig 1). Accordingly, 3,872 titles, 837 abstracts, and 444 full text articles were evaluated for inclusion. For title and abstract screenings, articles which were not marked for exclusion by both reviewers,

**Table 1 Search Strategy and Selection Criteria**

**Focus Question:** In partially edentulous patients with extended edentulous sites, what is the effect of immediate implant loading with IFDPs compared to early or conventional loading on implant survival?

**Search terminology**

PubMed/Medline (NLM) No limits applied 2,579 results	(dental implantation, endosseous[MeSH] OR dental implants[MeSH] OR implantation*[all fields] OR implant[all fields] OR implants[all fields]) AND (Denture, Partial, Fixed[MeSH] OR dental prosthesis, implant-supported[MeSH] OR fixed partial denture*[all fields] OR FPD[all fields] OR FPDs[all fields] OR fixed dental prosthesis[all fields] OR fixed dental prostheses[all fields] OR bridge*[all fields] OR FDP[all fields] OR FDPs[all fields]) AND (Immediate Dental Implant Loading[MeSH] OR function[all fields] OR time[all fields] OR immediate[all fields] OR early[all fields] OR load*[all fields]) AND (English[lang] OR German[lang] OR French[lang])
Embase (Elsevier) 1974 - current 1,869 results	('tooth implantation'/exp OR implantation* OR 'implant' OR 'implants') AND ('denture'/exp OR 'tooth prosthesis'/exp OR 'fixed partial denture' OR 'fixed partial dentures' OR bridge* OR 'FPD' OR 'FPDs' OR 'fixed dental prosthesis' OR 'fixed dental prostheses' OR 'fdp' OR 'fdps') AND ('function' OR 'time' OR 'immediate' OR 'early' OR load*) AND ('survival'/exp OR 'complication'/exp OR 'treatment failure'/exp OR complication* OR success* OR failure*) AND ([english]/lim OR [french]/lim OR [german]/lim) AND [embase]/lim
Cochrane Central Register of Controlled Trials (CENTRAL) No limits applied 48 results	(implantation* OR implant OR implants) AND ("fixed partial denture" OR "fixed partial dentures" OR bridge* OR FPD OR FPDs OR "fixed dental prosthesis" OR "fixed dental prostheses" OR fdp OR fdps) AND ("function" OR "time" OR "immediate" OR "early" OR load*) AND (complication* OR success* OR failure*)

**Selection criteria**

Inclusion criteria	Human studies Partially edentulous patients receiving IFDPs Solid screw-type implants with a rough surface
Exclusion criteria	Animal or in vitro studies Follow-up time less than 12 months Case series with less than 10 cases Noncomparative studies reporting the outcome of conventional implant loading Non-solid-screw-type implants Implants with machined surfaces or hydroxyapatite (HA) coatings Implants with a diameter of less than 3 mm Studies mainly reporting on implants in single-unit gaps Implants supporting full-arch restorations or removable appliances Implants placed in irradiated bone or alveolar clefts Data retrieved from chart reviews or questionnaires Insufficient information provided on loading protocol or type of implant suprastructure Insufficient information provided to determine implant survival rates Results of the same study were published again later with a longer follow-up

were included in the next screening step. At the levels of full-text screening and data extraction, disagreements were resolved by discussion.

**Exclusion of Studies**

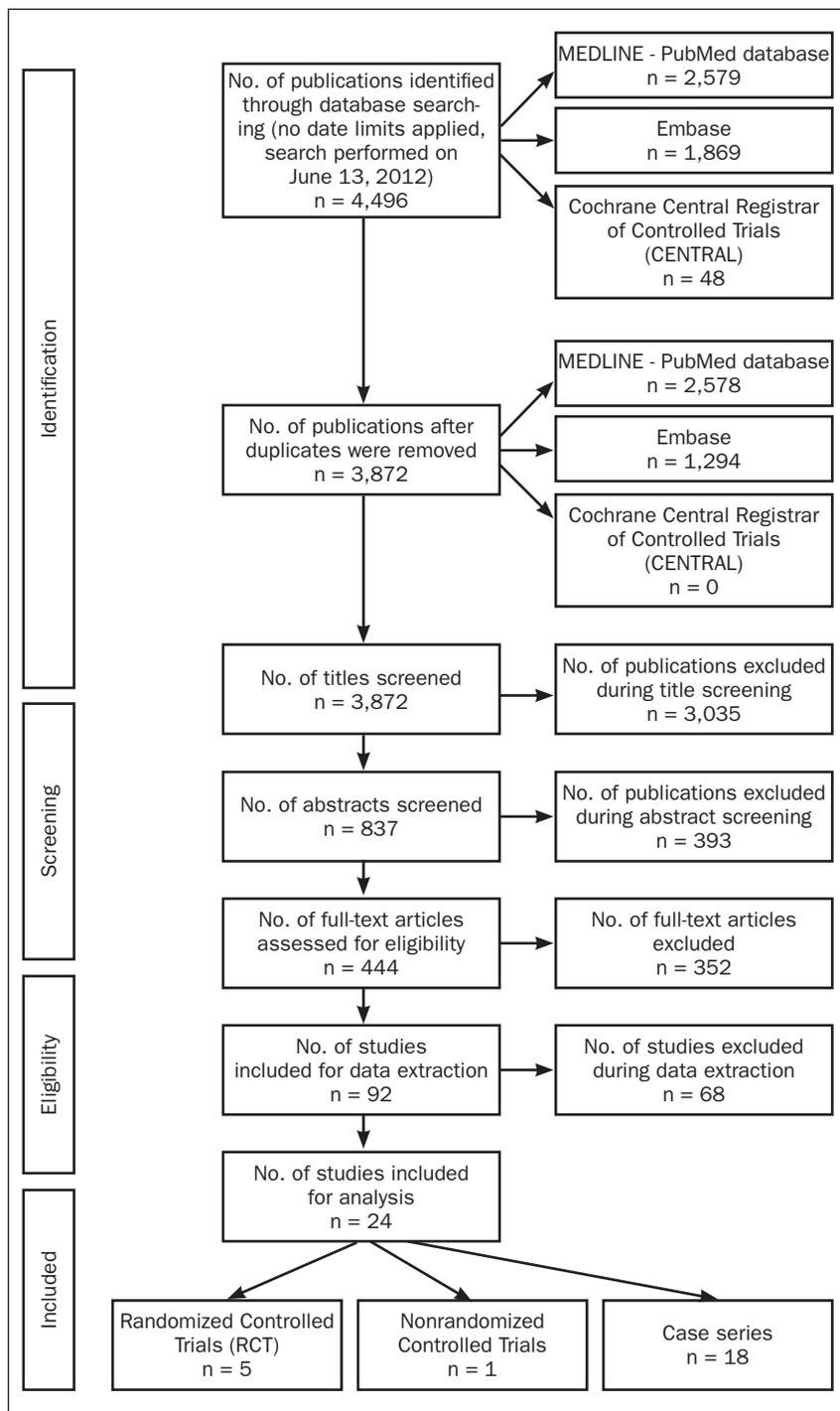
A total of 92 articles were included for data extraction. Sixty-eight articles had to be excluded from the final analysis because they did not meet the inclusion criteria (Table 2).

During full-text screening, it became evident that the majority of publications reported on implants placed in single-unit gaps and in extended edentulous sites (at least two adjacent teeth missing) without providing separate data for these two different types of restorations. To avoid the loss of valid information,

these studies were included for analysis as long as they met the remaining inclusion criteria. However, studies reporting exclusively or mainly on implants in single-unit gaps were excluded.

**Data Collection**

Data extraction was performed on the twenty-four studies included for analysis by two independent reviewers (AS and MR). Disagreement regarding data collection was resolved in personal meetings and by consulting a third senior reviewer (GG). Authors were contacted directly via email as needed for clarification or missing information. If the obtained data were still not sufficient to meet the inclusion criteria of this systematic review, the study was excluded.



**Fig 1** Search strategy and postextraction dimensional changes.

## Outcome Measures

The primary outcome measure was implant survival. Secondary outcome measures were location and time of implant failures, number and time of prosthetic failures, and treatment modifiers affecting the choice of loading protocols.

## Quality Assessment

Two independent reviewers (AS and MR) assessed the methodological quality of all included comparative studies. Randomized (RCT) and nonrandomized (NRCT) controlled trials were rated according to their risk of bias by using the Cochrane quality assessment tool for RCTs.<sup>13</sup>

**Table 2 Studies Excluded During Data Extraction**

Case series on conventional loading protocols	Astrand et al 2004, Bahat et al 2012, Balleri et al 2010, Behneke et al 2000, Bilhan et al 2010, Bornstein et al 2008, Boronat et al 2010, Carlson et al 2001, Cecchinato et al 2008, Cecchinato et al 2004, Chaushu et al 2009, Chiapasco et al 2006, Cordaro et al 2002, Cordioli et al 2001, De Bruyn et al 1992, Esposito et al 2011, Esposito et al 2011, Felice et al 2009, Felice et al 2010, Ferrigno et al 2005, Fugazzotto 2008, Halg et al 2008, Jebreen and Khraisat 2007, Johansson et al 2010, Karabuda et al 2011, Karlsson et al 1998, Khayat et al 2001, Krennmair et al 2011, Mannai 2006, Ozkan et al 2011, Pieri et al 2012, Romeo et al 2006, Romeo et al 2009, Sivoilella et al 2011, Urban and Lozada 2010, Vigolo and Zaccaria 2010, Wahlstrom et al 2010, Wennstrom et al 2004, Zinsli et al 2004
Insufficient information to separate partially and completely edentulous patients	Boronat et al 2008, Crespi et al 2007, Glauser et al 2003, Glauser et al 2005, Glauser et al 2007, Kielbassa et al 2009, Malo and Nobre 2011, Ostman et al 2010, Ostman et al 2012
Insufficient information to separate the number of maxillary and mandibular implants	Barter et al 2012, Cannizzaro et al 2011, Palmer et al 2012, Siebers et al 2010
Combined data for implants with machined and rough surfaces	Calandriello and Tomatis 2005, Degidi and Piattelli 2003, Malo et al 2007, Rocci et al 2003
Insufficient information to separate data for individual loading protocols	Bornstein et al 2007, Malo et al 2011
Insufficient information to separate data for IFDPs in partially edentulous patients	Akca and Cehreli 2008, Arisan et al 2010
Type of prosthetic restoration does not meet inclusion criteria	Bornstein et al 2010, Ostman et al 2008
Comparative study with insufficient information on the number of implants in test and control groups	Achilli et al 2007
Implants placed in cleft palate	Landes 2006
Follow-up time less than 12 months	Degidi and Piattelli 2005
Insufficient information on patient population	Smith et al 2009
Insufficient information on loading protocol	Bragger et al 2001

IFDPs = Implant-supported fixed dental prostheses.

### Statistical Analysis

Simple kappa statistics were calculated to measure reviewer agreement.<sup>13</sup> The associations between loading protocols were assessed using risk ratios (RR) for implant survival at one year. The scenarios IL vs EL, IL vs CL, and IL implants in the maxilla vs mandible were evaluated utilizing random-effects models accounting for inverse variance weighting, incorporating the estimation of heterogeneity of precisions, and effect sizes of the studies being evaluated. These meta-analyses were performed using the STATA statistical software version 11.2 with the meta-analysis command "metan."

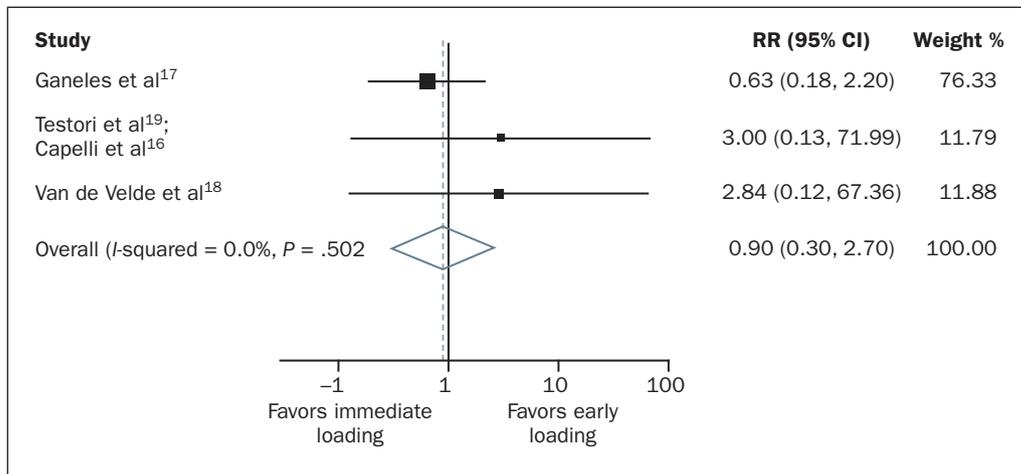
Studies without failures in both test and control groups were not taken into account and were excluded from the meta-analysis. Heterogeneity between studies was assessed using *I*-squared statistics describing the variation in RR, which is attributable to the heterogeneity of the studies.

### RESULTS

A total of 24 publications were included for final analysis, which consisted of six comparative studies (five RCTs, one NRCT) and 18 noncomparative studies (case series). Kappa statistics revealed a score of 0.74 as a measure of reviewer agreement.

#### Meta-analysis of Comparative Studies

**Immediate vs Early Loading.** Three RCTs<sup>16–18</sup> investigated the influence of IL and EL protocols on implant survival (Table 3a). IL implants were loaded within 48 hours, whereas EL implants were loaded between 28 days and 2 months after implant placement. Overall, 6 of 285 IL implants and 6 of 272 EL implants failed. The survival analysis with weighted follow-up time resulted in an overall survival rate of 97.9% for the IL group, compared to 97.8% for the EL group. The difference was not statistically significant (RR: 0.90; 95% CI: 0.30, 2.70; *P* = .9405).



**Fig 2** Forest plot for the comparison of IL and EL regarding the 1-year implant survival rates.

The heterogeneity between studies was not statistically significant (*I*-squared = 0.0%, *P* = .502) (Fig 2).

**Immediate vs Conventional Loading.** One NRCT<sup>20</sup> and two RCTs<sup>21,22</sup> compared the impact of IL or CL on implant survival (Table 3a). IL implants were loaded within 48 hours of implant placement, whereas CL implants were loaded between 3 and 3.5 months after implant placement in the mandible and 4 and 4.5 months in the maxilla. One failure out of a total of 272 implants investigated occurred in the CL group. The survival analysis with weighted follow-up time resulted in a statistically nonsignificant difference in survival rates of 100% for the IL group and 99.3% for the CL group (*P* = .3280). Meta-analysis could not be performed as there were no failures in both test and control groups of two studies. Heterogeneity between studies could not be evaluated as two out of three studies had to be excluded from the meta-analysis.

### Quality Assessment

A high risk of bias was assigned to three studies (Table 3a). In Capelli et al,<sup>16</sup> allocation was manually generated with a restricted randomization list and not all assessors were blinded. Sequence generation in Cannizzaro and Leone<sup>20</sup> was not randomized and insufficient information was provided to judge if clinical factors influenced the decision to assign patients to test or control groups. Furthermore, there was no allocation concealment and investigators were not blinded. A lack of blinding of investigators was also found in Cannizzaro et al.<sup>21</sup>

An unclear risk of bias was assessed for three studies. Ganeles et al<sup>17</sup> provided insufficient information on the method of blinding. In Van de Velde et al,<sup>18</sup> it was not clear if allocation concealment was guaranteed and if investigators were blinded besides the

radiographic evaluation. Romanos and Nentwig<sup>22</sup> reported insufficient information on sequence generation, allocation concealment, and methods of blinding.

A low risk of bias could not be assigned to any study included in this review.

### Descriptive Analysis of Noncomparative Studies

Of the 18 case series included in this review,<sup>23–40</sup> three studies reported on the same study population than previous reports,<sup>23–25</sup> resulting in a total of 15 independent publications (Table 3b). Twelve of those reported on IL and three on EL. The study population comprised between 10 and 51 patients and 20 to 111 implants, with a mean follow-up time between 12 and 96 months.

**Immediate Loading.** Combining the 12 noncomparative studies on IL included in this review, a total of 685 implants placed in 297 patients were followed for a period of 1 to 8 years. Altogether, 15 failures were reported. The survival rates ranged from 89.8% to 100%, resulting in a mean survival rate of 97.8%. Studies were conducted in academic and private practice settings.

All noncomparative studies that provided sufficient information on the implant placement protocol utilized a type 4 placement approach, ie, implants were placed in fully healed postextraction sites. Several studies did not provide information on the implant placement protocol.

Only five publications included in this systematic review reported on prostheses failures. Two publications did not experience any failures,<sup>26,27</sup> while three investigations revealed one prosthesis failure each.<sup>28–30</sup> All prosthesis failures occurred due to the loss of one of the supporting implants.

**Early Loading.** Three case series describing the outcome of EL met the inclusion criteria of this system-

atic review. Implants were loaded between 14 and 30 days after implant placement. A total of 205 implants were placed in 87 patients and followed up for 1 to 5 years. One implant failure occurred, leading to an overall mean survival rate of 99.5% for EL implants. Only one study provided information on implant placement protocol and prosthesis failure.<sup>31</sup>

### Implant and Failure Distribution

The vast majority of implants reported in the included comparative studies were placed in the posterior region of the jaw (Table 4a). Three out of six comparative studies included posterior implants only<sup>17,18,22</sup> while two studies included 94.2%<sup>16</sup> and 67.6%<sup>21</sup> of posterior implants, respectively. Cannizzaro and Leone<sup>20</sup> did not provide sufficient information on implant location and failures. Implants investigated in comparative studies were placed more frequently in the mandible than in the maxilla. The location of failure was given for 12 out of a total of 13 lost implants. All of those failures occurred in the posterior region. Five implants failed in the maxilla and seven in the mandible. Six of those failed implants were immediately loaded. All IL failures occurred in the posterior, and four out of a total of six IL implants were lost in the maxilla. All implant failures occurred within three months after implant placement.

The majority of IL implants investigated in noncomparative studies were placed in the posterior region of the jaw (80.1%) and the mandible (63.9%) (Table 4b). Twelve studies reported a total of 15 failures. Four of those failures occurred in the anterior (26.7%) and 11 occurred in the posterior (73.3%), which was in accordance with the distribution of implants placed in those regions of the jaw (19.9% vs 80.1%). The exact failure location was provided for nine implants. Six out of those implants were lost in the mandible and three failed in the maxilla. Two studies, which included six failures, did not provide sufficient information to determine which jaw the respective implants failed in.<sup>30,32</sup> All but one implant failure occurred within 6 months of placement. One failure did not occur until 12 months after implant placement.

One noncomparative study on EL reported one implant failure.<sup>31</sup> The failure occurred in the posterior region of the mandible and was not associated with the loading protocol as the implant was lost to a peri-implant infection during the healing period.

As several studies did not provide information on the exact time and location of implant drop-outs and failures, a survival analysis with weighted follow-up time comparing IL implants placed in the maxilla vs mandible could not be performed. However, the meta-analysis revealed that the difference in survival of IL implants placed in the maxilla vs mandible was not

statistically significant (RR: 1.55; 95% CI, 0.49, 4.84;  $P > .05$ ). The heterogeneity between studies was not statistically significant ( $I^2$ -squared = 0.0%,  $P = .671$ ) (Fig 3).

Due to the small number of implants placed in the anterior zone, a statistical comparison between anterior and posterior IL implants was not performed.

### Criteria for Immediate Loading

Insertion torque was a frequently applied tool to determine if an implant was suitable for IL (Table 5). It was used in 12 out of a total of 19 studies and ranged between 15 Ncm and 45 Ncm.<sup>16,20,21,25,27,30,34-39</sup> Notably, 9 of those studies required an insertion torque of at least 30 Ncm.<sup>16,20,21,25,27,36-39</sup> However, one of those studies considered an insertion torque of at least 20 Ncm sufficient if the implants were splinted together.<sup>16</sup>

Resonance frequency analysis (RFA) was utilized in six studies.<sup>26,28,29,34,35,39</sup> Minimum Implant Stability Quotient (ISQ) values required for IL ranged between 50 and 62. Three studies relied on ISQ values only to confirm adequate primary stability.<sup>26,28,29</sup> Two publications confirmed primary stability by hand only.<sup>17,18</sup>

Nine publications required a minimum implant length for IL, which ranged between 8 mm and 11 mm.<sup>18,27-29,35-39</sup> A combination of insertion torque, ISQ values, and minimum implant length as criteria for IL was applied by two investigations.<sup>35,39</sup>

Four studies explicitly excluded implants placed immediately into fresh extraction sockets,<sup>17,18,21,34</sup> while three studies included those implants.<sup>16,19,25,39</sup> Implants requiring bone augmentation procedures were excluded by nine studies.<sup>17,18,21,22,26,29,30,34,35</sup> Four publications included implants requiring minimal bone grafting to either cover bone dehiscences<sup>32</sup> or gaps present after type 1 implant placement.<sup>16,25,39</sup> Parafunctional habits were considered exclusion criteria by twelve studies.<sup>16-18,21,25-29,32,34,38</sup> Only one publication included patients with parafunctional habits.<sup>39</sup> Smokers consuming more than 10 cigarettes per day were included by eight studies,<sup>16,20-22,29,32,35,39</sup> while seven studies excluded them.<sup>17,18,26,27,30,34,38</sup>

Immediately placed provisional prostheses were either in full occlusal or light centric contact with no excursive contacts in 13 out of 19 studies.<sup>18,20-22,25,27,29,30,34-37,39</sup> The remaining six studies removed all occlusal contacts before delivering the immediate restorations.<sup>16,17,26,28,32,38</sup>

### Intention to Treat Analysis (ITT)

Table 6 summarizes how many implants were originally intended for IL and how many of those implants were ultimately not immediately loaded because they did not fulfill certain criteria established by the respective authors. Almost half of the studies analyzed in this systematic review did not provide information on ITT.

**Table 3a Comparative Studies Included for Analysis**

Study	Study type	Setting	Comparison	Patients	Mean follow-up (mo)	Patient drop-outs	Placement type	Brand
<b>Immediate vs early loading</b>								
Ganeles et al <sup>17</sup>	RCT	U, PP	IL vs EL	266	12	8	Type 4	Strauman, Standard, Standard Plus
			IL group	138	12	4		
			EL group	128	12	4		
Testori et al <sup>19</sup> ; Capelli et al <sup>16</sup>	RCT	PP	IL vs EL	52	60	1	Type 1, type 4	BIOMET 3i, Full Osseotite Tapered
			IL group	25	60	0		
			EL group	27	60	1		
Van de Velde et al <sup>18</sup>	RCT, split mouth	U	IL vs EL	13	18	1	Type 4	Straumann, Tapered Effect
			IL group	13	18	1		
			EL group	13	18	1		
Total			IL group	331				
			EL group	176				
				168				
<b>Immediate vs conventional loading</b>								
Cannizzaro and Leone <sup>20</sup>	NRCT	PP	IL vs CL	28	24	0	NR	Zimmer Dental, Spline Twist
			IL group	14	24	0		
			CL group	14	24	0		
Cannizzaro et al <sup>21</sup>	RCT	PP	IL vs CL	40	36	0	Type 4	Zimmer Dental, Tapered SwissPlus
			IL group	20	36	0		
			CL group	20	36	0		
Romanos and Nentwig <sup>22</sup>	RCT, split mouth	U	IL vs CL	12	25.3	0	NR	Dentsply, Ankylos
			IL group	12	25.3	0		
			CL group	12	25.3	0		
Total			IL group	80				
			IL group	46				
			CL group	46				

IL = immediate loading; EL = early loading; CL = conventional loading; RCT = randomized controlled trial; NRCT = nonrandomized controlled trial; PP = private practice; U = university; NR = not reported; SLA = sandblasted, large grit, acid-etched; SLActive = sandblasted, large grit, acid-etched, conditioned in nitrogen and immediately preserved in an isotonic saline solution; MTX = microtextured titanium; Implant placement: type 1 = immediate placement; type 2 = postextraction site with healed soft tissues but without significant bone healing; type 3 = postextraction site with healed soft tissues and with significant bone healing; type 4 = fully healed postextraction site. \**P* = .9405. \*\**P* = .3280.

**Table 3b Noncomparative Studies Included for Analysis**

Study	Setting	Patients	Mean follow-up (mo)	Placement type	Brand
<b>Immediate loading</b>					
Boronat-Lopez et al <sup>28</sup>	U	12	NR	NR	Impladent, Defcon TSA
Cornelini et al <sup>29</sup>	U, PP	20	12	NR	Straumann
Degidi et al <sup>34</sup>	U, PP	50	36	Type 4	Dentsply-Friadent, XiVE Plus
Luongo et al <sup>30</sup>	PP	40	12	Type 4	Straumann
Machtei et al <sup>32</sup>	U	20	12	Type 4	Biomet 3i, Osseotite
Malo and Nobre <sup>36</sup>	PP	41	12	Type 4	Nobel Biocare, NobelSpeedy Groovy
Nikellis et al <sup>37</sup>	PP	18	12–24	NR	Southern Implants
Payer et al <sup>38</sup>	U	24	60–96	Type 4	Dentsply Friadent, XiVE
Rismanchian et al <sup>26</sup>	U	10	12	Type 4	Astra Tech
Schincaglia et al <sup>24</sup> ; Fung et al <sup>35</sup>	U	10	36	Type 4	Nobel Biocare, Branemark Mk IV
Vanden Bogaerde et al <sup>25,27</sup>	PP	31	18	NR	Nobel Biocare, Branemark Mk III, IV
Vanden Bogaerde et al <sup>39</sup>	U, PP	21	18	NR	Neoss Ltd, Neoss
Total		297			
<b>Early loading</b>					
Bornstein et al <sup>23,33</sup>	U	51	60	NR	Strauman
Fischer et al <sup>40</sup>	PP, U	16	12	NR	Nobel Biocare, Nobel Replace Select
Todisco <sup>31</sup>	PP	20	12	Type 4	Zimmer Spline, Nobel Replace Select
Total		87			

PP = private practice; U = university; NR = not reported; NA = not applicable; RCT = randomized controlled trial; NRCT = non-randomized controlled trial; SLA = sandblasted, large grit, acid-etched; MTX = microtextured titanium; Implant Placement: type 1 = immediate placement; type 2 = postextraction site with healed soft tissues but without significant bone healing; type 3 = postextraction site with healed soft tissues and with significant bone healing; type 4 = fully healed postextraction site.

Surface	Implants placed	Implant failures	Implant survival rate (%)	Prosthetic failures	Prosthetic survival rate (%)	Risk of bias
SLActive	383	10	97.4	NR	NR	Unclear
	197	4	98.0	NR	NR	
	186	6	96.8	NR	NR	
Full Osseotite	104	1	99.0	1	98.1	High
	52	1	98.0	1	96.0	
	52	0	100	0	100	
SLA	70	1	98.6	0	100	Unclear
	36	1	97.2	0	100	
	34	0	100	0	100	
	557	12	97.9			
	285	6	97.9*			
	272	6	97.8*			
MTX	92	1	98.9	NR	NR	High
	46	0	100	NR	NR	
	46	1	97.8	NR	NR	
MTX	108	0	100	0	100	High
	52	0	100	0	100	
	56	0	100	0	100	
Sandblasted	72	0	100	0	100	Unclear
	36	0	100	0	100	
	36	0	100	0	100	
	272	1	99.6			
	134	0	100**			
	138	1	99.3**			

Surface	Implants placed	Implant failures	Implant survival rate (%)	Prosthetic failures	Prosthetic survival rate (%)
Avantblast	36	1	97.2	1	91.6
SLA	40	1	97.5	1	95.0
Grit-blasted, acid-etched	100	2	98.0	NR	NR
SLA	82	1	98.8	1	97.5
Osseotite	49	5	89.8	NR	NR
TiUnite	72	1	98.6	NR	NR
Sandblasted, acid-etched	46	0	100	NR	NR
Grit-blasted, etched	40	2	95.0	NR	NR
Osseospeed	20	0	100	0	100
TiUnite	20	0	100	NR	NR
TiUnite	111	1	99.1	0	100
Bimodal	69	1	98.6	NR	NR
	685	15	97.8		
SLA	104	1	99.0	NR	NR
TiUnite	37	0	100	NR	NR
MTX & TiUnite	64	0	100	0	100
	205	1	99.5		

**Table 4a Implant and Failure Distribution from Comparative Studies**

Study	Comparison	Implant distribution				Implant failures	Time from placement to failure	Failed implant position
		Anterior	Posterior	Maxilla	Mandible			
<b>Immediate vs early loading</b>								
Ganeles et al <sup>17</sup>	IL vs EL	0%	100%	32.1%	67.9%	10		
	IL	0%	100%	36.0%	64.0%	4	7, 19, 28, 56 d	2 post max, 2 post mand
	EL	0%	100%	28.0%	72.0%	6	15, 19, 28, 30, 30, 82 d	1 post max, 5 post mand
Testori et al <sup>19</sup> ; Capelli et al <sup>16</sup>	IL vs EL	5.8%	94.2%	43.3%	56.7%	1		
	IL	5.8%	94.2%	26.9%	73.1%	1	2 mo	Post max
	EL	5.8%	94.2%	59.6%	40.4%	0		
Van de Velde et al <sup>18</sup>	IL vs EL	0%	100%	100%	0%	1		
	IL	0%	100%	100%	0%	1	3 mo	Post max
	EL	0%	100%	100%	0%	0		
Total		1.1%	98.9%	42.7%	57.3%	12		
	IL	1.1%	98.9%	42.5%	57.5%	6		
	EL	1.1%	98.9%	43.0%	57.0%	6		
<b>Immediate vs conventional loading</b>								
Cannizzaro and Leone <sup>20</sup>	IL vs CL	NR	NR	38.0%	62.0%	1		
	IL	–	–	39.1%	60.9%	0		
	CL	–	–	37.0%	63.0%	1	11 d	NR
Cannizzaro et al <sup>21</sup>	IL vs CL	32.4%	67.6%	45.4%	54.6%	0		
	IL	25.0%	75.0%	48.1%	51.9%	0		
	CL	39.3%	60.7%	42.9%	57.1%	0		
Romanos and Nentwig <sup>22</sup>	IL vs CL	0%	100%	0%	100%	0		
	IL	0%	100%	0%	100%	0		
	CL	0%	100%	0%	100%	0		
Total		19.4%*	80.6%*	30.9%	69.1%	1		
	IL	14.8%*	85.2%*	32.1%	67.9%	0		
	CL	23.9%*	76.1%*	29.7%	70.3%	1		

L = immediate loading; EL = early loading; CL = conventional loading; NR = not reported; post = posterior; max = maxilla; mand = mandible.  
 \*Percentages do not account for the 92 implants from Cannizzaro and Leone.<sup>20</sup>

**Table 4b Implant and Failure Distribution from Noncomparative Studies**

Study	Implant distribution				Implant failures	Time from placement to failure	Failed implant position
	Anterior	Posterior	Maxilla	Mandible			
<b>Immediate loading</b>							
Boronat-Lopez et al <sup>28</sup>	77.8%	22.2%	69.4%	30.6%	1	NR	Ant mand
Cornelini et al <sup>29</sup>	0%	100%	0%	100%	1	2 mo	Post mand
Degidi et al <sup>34</sup>	0%	100%	0%	100%	2	5, 7 wk	2 post mand
Luongo et al <sup>30</sup>	0%	100%	12.2%	87.8%	1	5.5 mo	NR
Machtei et al <sup>32</sup>	49.0%	51.0%	67.3%	32.7%	5	During first 6 mo	2 ant, 3 post
Malo and Nobre <sup>36</sup>	30.6%	69.4%	69.4%	30.6%	1	NR	Post max
Nikellis et al <sup>37</sup>	15.2%	84.8%	23.9%	76.1%	0		NA
Payer et al <sup>38</sup>	0%	100%	0%	100%	2	NR	Post mand
Rismanchian et al <sup>26</sup>	0%	100%	40.0%	60.0%	0		NA
Schincaglia et al <sup>24</sup> ; Fung et al <sup>35</sup>	0%	100%	0%	100%	0		NA
Vanden Bogaerde et al <sup>25,27</sup>	26.1%	73.9%	62.2%	37.8%	1	12 mo	Post max
Vanden Bogaerde et al <sup>39</sup>	37.7%	62.3%	59.4%	40.6%	1	4 wk	Ant max
Total	19.9%	80.1%	36.1%	63.9%	15		
<b>Early loading</b>							
Bornstein et al <sup>23,33</sup>	0%	100%	14.4%	85.6%	1	3 wk	Post mand
Fischer et al <sup>40</sup>	37.8%	62.2%	100%	0%	0		NA
Todisco <sup>31</sup>	12.5%	87.5%	1.6%	98.4%	0		NA
Total	10.7%	89.3%	25.9%	74.1%	1		

NR = not reported; NA = not applicable; ant = anterior; post = posterior; max = maxilla; mand = mandible.

**Table 5 Criteria for Immediate Loading**

Study	Insertion torque (Ncm)	ISQ value	Implant length (mm)	Immediate implant placement	Bone augmentation	Parafuction	Smoking (> 10 cig/d)	Provisional in occlusion
<b>Comparative studies</b>								
Cannizzaro and Leone <sup>20</sup>	30*						I	Yes
Cannizzaro et al <sup>21</sup>	≥ 45			E	E	E	I	Yes
Ganeles et al <sup>17</sup>				E	E	E	E	No
Romanos and Nentwig <sup>22</sup>					E		I	Yes
Testori et al <sup>19</sup> ; Capelli et al <sup>16</sup>	≥ 30 Ncm (single implants) ≥ 20 Ncm (splinted implants)			I	I	E	I	No
Van de Velde et al <sup>18</sup>			≥ 8	E	E	E	E	Yes
<b>Noncomparative studies</b>								
Boronat-Lopez et al <sup>28</sup>		> 60	≥ 8.5			E		No
Cornellini et al <sup>29</sup>		> 62	≥ 10		E	E	I	Yes
Degidi et al <sup>34</sup>	≥ 25	≥ 60		E	E	E	E	Yes
Luongo et al <sup>30</sup>	≥ 15				E		E	Yes
Machtei et al <sup>32</sup>					I	E	I	No
Malo and Nobre <sup>36</sup>	≥ 30		≥ 10					Yes
Nikellis et al <sup>37</sup>	≥ 32		≥ 10					Yes
Payer et al <sup>38</sup>	≥ 32		≥ 11			E	E	No
Rismanchian et al <sup>26</sup>		> 60			E	E	E	No
Schincaglia et al <sup>24</sup> ; Fung et al <sup>35</sup>	≥ 20	≥ 60	≥ 8.5		E		I	Yes
Vanden Bogaerde et al <sup>27</sup>	≥ 40		≥ 8.5			E	E	Yes
Vanden Bogaerde et al <sup>25</sup>	≥ 30			I	I	E		Yes
Vanden Bogaerde et al <sup>39</sup>	≥ 30	≥ 50	≥ 9	I	I	I	I	Yes
<b>Range</b>	15–45	50–62	8–11					
<b>Frequency</b>	12/19	6/19	9/19	I: 3/19 E: 4/19	I: 4/19 E: 9/19	I: 1/19 E: 12/19	I: 8/19 E: 7/19	Yes: 13/19 No: 6/19

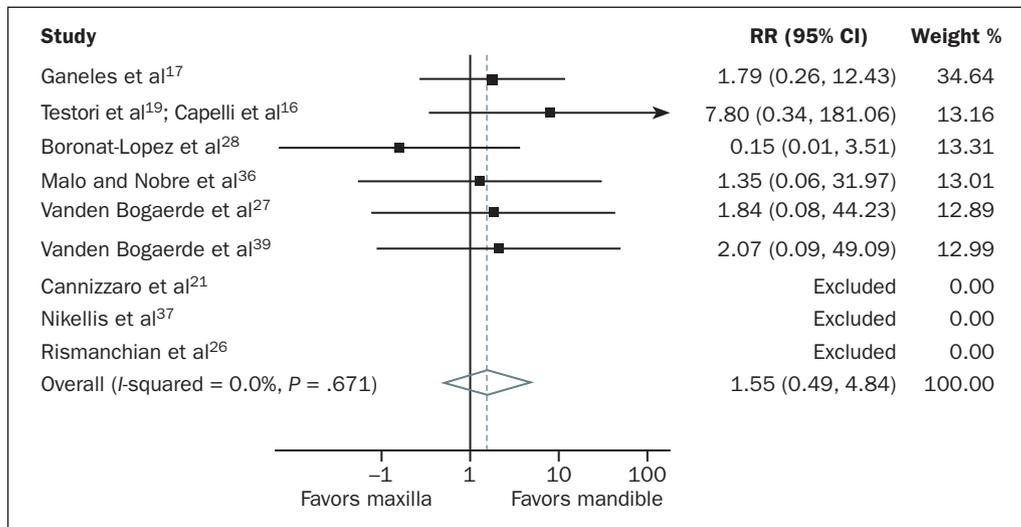
\* = torque at abutment placement; ISQ = implant stability quotient; I = included; E = excluded; Yes = full occlusal contacts or light centric/no excursive contacts; No = no occlusal contacts; Range = minimal and maximal values of the particular parameter used as loading criteria; Frequency = number of studies applying the particular parameter as a loading criteria out of a total of 19 studies.

Cannizzaro et al<sup>21</sup> excluded two patients with an unknown number of implants because of poor bone quality. As the number of implants placed in these two patients was not provided, the ITT percentage could not be calculated. One implant was not loaded until 4 months after placement because it failed to achieve the minimal insertion torque of 45 Ncm.

Ganeles et al<sup>17</sup> excluded 11 implants allocated to the IL group, because they did not achieve primary stability, were spinning after insertion, or required a sinus elevation or bone augmentation procedure. In Van de Velde et al,<sup>18</sup> one patient with an unknown number of implants had to be excluded per protocol because bone regeneration was necessary at the time of implant placement.

Boronat-Lopez et al<sup>28</sup> and Luongo et al<sup>30</sup> reported that one patient with two implants and three patients with six implants, respectively, had to be excluded due to a lack of primary stability. The implants did not reach the required RFA criterion (ISQ > 60) or an insertion torque of 15 Ncm. In Vanden Bogaerde et al,<sup>25</sup> one implant showed slight mobility and pain to pressure after six weeks of loading and hence was taken out of occlusion.

All remaining studies reporting on ITT had an intention to treat percentage of 100%, as all implants fulfilled the respective inclusion criteria and could be immediately loaded.



**Fig 3** Forest plot for the comparison of IL implants placed in the maxilla and IL implants placed in the mandible regarding the 1-year implant survival rates.

**Table 6** Intention to Treat (ITT) Analysis

Study	Implants intended for IL	Intention to treat failures	Intention to treat percentage	Reason
<b>Comparative studies</b>				
Cannizzaro et al <sup>21</sup>	52 + 2 patients (no. of implants NR)	1 + 2 patients (no. of implants NR)	NA	IT < 45 Ncm + 2 patients with BD type 4
Ganeles et al <sup>17</sup>	217	11	94.9%	5 lack of PS, 4 spinners at surgery, 2 need for GBR
Romanos and Nentwig <sup>22</sup>	36	0	100%	NA
Testori et al <sup>19</sup> ; Capelli et al <sup>16</sup>	52	0	100%	NA
Van de Velde et al <sup>18</sup>	36 + 1 patient (no. of implants NR)	1 patient (no. of implants NR)	NA	need for GBR
<b>Noncomparative studies</b>				
Boronat-Lopez et al <sup>28</sup>	43	2	95.3%	ISQ ≤ 60
Cornelini et al <sup>29</sup>	40	0	100%	NA
Luongo et al <sup>30</sup>	97	6	93.8%	IT < 15 Ncm
Nikellis et al <sup>37</sup>	46	0	100%*	NA
Payer et al <sup>38</sup>	40	0	100%	NA
Rismanchian et al <sup>26</sup>	20	0	100%	NA
Schincaglia et al <sup>24</sup> ; Fung et al <sup>35</sup>	20	0	100%	NA
Vanden Bogaerde et al <sup>27</sup>	111	0	100%	NA
Vanden Bogaerde et al <sup>25</sup>	50	1	98.0%	Pain and mobility (crown was taken out of occlusion)

IL = immediate loading; NR = not reported; NA = not applicable; BD = bone density; PS = primary stability; GBR = guided bone regeneration; IT = insertion torque in Ncm; ISQ = implant stability quotient.

\* = 5 implants were replaced by wider diameter implants at the time of surgery because they did not achieve the immediate loading criteria.

## DISCUSSION

### Quality of Included Studies and Validity of Methods

The 24 studies included in this systematic review were of different study designs and reported findings on loading protocols using a diverse range of parameters.

From the six comparative studies (five RCTs, one NRCT), three were of unclear and three of high risk of bias according to the Cochrane quality assessment tool.<sup>13</sup> Two comparative studies followed a split-mouth design,<sup>18,22</sup> but did not meet other criteria necessary to qualify for a low risk of bias. No quality assessment was performed for the 18 noncomparative studies, which

were all case series according to the purposes of this systematic review. However, the clinically relevant data were used for a descriptive analysis.

With the exception of Machtei et al,<sup>32</sup> who found a relatively low implant survival rate of 89.8%, all other included noncomparative and comparative studies homogeneously showed high survival rates for IL implants that compare well with reported survival rates of CL implants.<sup>1-6</sup>

Evaluations of prosthodontic parameters and details on prosthetic design were scarce and frequently lacking. This seems surprising since the prosthodontic phase plays a central role in the clinical implementation of loading protocols.

Initially, only IFDPs replacing two or more adjacent teeth (extended edentulous sites) in partially edentulous patients were planned for inclusion in this systematic review. During the data extraction process, however, it became evident that the vast majority of studies also included implants supporting single crowns in single-unit gaps, without providing sufficient information to separate the data for implants supporting IFDPs in extended edentulous sites. Hence, the inclusion criteria had to be modified and studies comprising mainly implants in extended edentulous sites but containing some implants in single-unit gaps were included. Studies that mainly examined implants in single-unit gaps and did not separately report data on implants in extended edentulous sites were excluded. Consequently, numerous articles with potentially useful information were not included in this systematic review.

Details on number, timing, and location of implant drop-outs were often poorly reported and only a small number of high-evidence studies were available for analysis. Furthermore, data for the comparison of IL implants placed in the maxilla vs the mandible were partly provided by noncomparative studies, with significant heterogeneity in study design and clinical protocol. Consequently, the results of the meta-analyses performed in this systematic review have to be interpreted with caution.

The insufficient reporting on implant success and the significant heterogeneity in applied success criteria allowed for implant survival only as the primary outcome measure of this systematic review, although stricter success criteria would certainly render clinically more useful information. A summary of surgical and prosthetic complications was not deemed feasible in the context of this review, due to the nonstandardized and often deficient description of complications.

### Immediate vs Early Loading

In a multicenter investigation comprising 19 clinics in private practice and universities in 10 different countries, Ganeles et al<sup>18</sup> reported on survival rates and bone level

changes of 383 implants randomly assigned to receive either IL or EL. All implants investigated were placed in completely healed sites (type 4 placement) in premolar and molar positions. After 12 months, the implant survival rates were 98% and 96.8%, respectively. The difference in survival rates was not statistically significant.

Capelli et al<sup>16</sup> compared IL and EL of 104 implants over a period of 5 years in a RCT conducted in five private practices. A total of 15 implants, 6 in the IL group and 9 in the EL group, were placed in postextraction sockets (type 1 placement). All other implants were placed in healed alveolar bone (type 4 placement). Of the 52 IL implants loaded within 48 hours and the 52 EL implants loaded at 2 months, one implant failed in the IL group. The respective survival rates of 98% and 100% were not statistically different. Testori et al<sup>19</sup> previously had reported the 1-year results of the same study population.

In a split-mouth RCT following 13 patients over a period of 18 months, Van de Velde et al<sup>18</sup> compared IL implants placed flapless and guided, with EL implants placed with a conventional surgical protocol. All implants were placed in the posterior maxilla. The authors reported survival rates of 97.2% and 100% for the IL and EL groups, respectively, and found that the difference in survival rates was statistically not significant. No prosthesis failure occurred in either group.

All three comparative studies presented similar overall results when comparing IL vs EL in partially edentulous patients (Table 3a), with the weighted means yielding no significant differences between implant survival rates for IL (97.9%) and EL (97.8%) ( $P = .9405$ ). The similarity in survival rates between IL and EL implants was confirmed by the included noncomparative studies (Table 3b). For noncomparative studies, the average survival rate was 97.8% for IL implants and 99.5% for EL implants. However, these generalized comparisons should be interpreted with caution, since they report on overall implant survival rates without correlating major treatment modifiers.

Surprisingly, a significantly lower number of noncomparative studies investigating EL implants were found compared to the number of publications on the supposedly more experimental IL protocol. One reason for this unexpected finding may be based on the exclusion of numerous articles with potentially useful information on EL implants, for the reason of not reporting separately on IFDPs in extended edentulous sites.

### Immediate vs Conventional Loading

In a NRCT conducted in a private practice setting comparing 92 implants subjected to IL and CL, Cannizzaro and Leone<sup>20</sup> reported one implant failure in the CL group, which occurred 11 days after implant placement. The survival rates were 97.8% and 100% for CL

and IL groups, respectively, after a mean follow-up time of 2 years. The authors did not provide information on prosthesis failures and the time of implant placement related to the time of extraction.

Cannizzaro et al<sup>21</sup> investigated a total of 108 implants randomly assigned to receive either IL or CL in several private practices. All implants were placed into healed alveolar ridges. No implant was lost, and survival rates after a period of 36 months were 100% for both groups. However, two implants in two patients from each group developed peri-implantitis with 3 to 4 mm of peri-implant bone loss and purulent exudate, deeming the implants not successful. No prostheses were lost during the follow-up time.

Romanos and Nentwig<sup>22</sup> compared IL and CL in a RCT with a split-mouth design conducted in a university setting. A total of 72 implants were subjected to IL or CL in either side of the posterior mandible of 12 partially edentulous patients. All implants were placed into healed alveolar bone. No implant or prostheses failure occurred over a mean follow-up time of 25.3 months.

All three comparative studies presented similarly high mean implant survival rates of 100% and 99.3%, respectively, when comparing IL and CL in partially edentulous patients with the difference being statistically not significant ( $P = .3280$ ) (Table 3a). Due to the lack of implant failures in two out of three studies, a meta-analysis could not be performed.

### Time and Distribution of Implant Failures

Failures of IL implants seem to have a tendency to occur early, as the vast majority of implant failures occurred within the first 3 months after loading. None of the included studies reported any implant failure later than 12 months of loading. Regardless, if an IL implant fails later than 12 months after loading, it can be hypothesized that the reason for failure would most likely be based on factors other than the loading protocol.

The posterior regions of the jaw may be of concern for IL implants due to the poor bone quality often found in these areas, especially in the maxilla. The finding that almost all implant failures occurred in the posterior was in accordance with the fact that the vast majority of implants reported in the included studies were placed in the posterior zone. Because of the small number of anterior implants included, it can be stated that currently there is insufficient clinical data available to support IL of anterior implants in extended edentulous sites of partially edentulous patients.

The meta-analysis performed in this systematic review comparing outcomes of IL implants in the maxilla vs the mandible showed no statistically significant differences in survival (Fig 3). However, due to the significant heterogeneity in study designs and clinical protocols of the included studies, this finding has

to be interpreted with caution. Furthermore, it has to be noted that weighted mean survival rates for IL implants according to implant location could not be calculated due to insufficient detail on time and location of implant failures and drop-outs provided by the respective studies.

### Immediate Loading Criteria

Insertion torque measurements were used to confirm primary implant stability in 12 out of 19 studies (Table 5). Required insertion torque values ranged between 15 Ncm and 45 Ncm. Implant stability quotient (ISQ) values from resonance frequency analyses (RFA) were utilized in six studies.<sup>26,28,29,34,35,39</sup> The minimum ISQ value required for IL ranged between 50 and 62. Primary stability seems to be considered of paramount importance for loading protocols with reduced healing times.

Almost all IL implants in both comparative and non-comparative studies were placed in healed sites (type 4 placement), and most of the studies excluded implants requiring substantial bone augmentation procedures.

Implant length was considered another indicator for or against IL by several studies. Based on the data assessed in this systematic review, an implant length of at least 8 to 11 mm was deemed necessary for applying an IL protocol. In cases where anatomical restrictions only allowed for implants shorter than 8 to 11 mm, a tendency towards a delayed loading approach existed. However, as several different implant brands were used in the included studies, it has to be mentioned that aspects of implant design, such as thread design to achieve sufficient primary stability, or the location of the implant-abutment interface to avoid crestal bone loss in the initial healing phase, may play a significant role when determining a minimum implant length required for IL.

Occlusion has often been presented as a treatment modifier for IL. While several occlusal scenarios such as full occlusal contacts, light centric but no excursive contacts, and no occlusal contacts have been presented in this review, it is important to bear in mind that in any case, the provisional prosthesis will be exposed to masticatory forces, pressure from the tongue, and patient habits. Therefore, immediately restored implants are unavoidably subject to a certain amount of load even if all occlusal contacts have been removed.

When parafunctional habits are present, a CL approach should be considered, as the majority of studies excluded patients with parafunction.

Strict inclusion criteria have been followed by all included studies assessing IL or EL protocols. In this context, the application of such loading protocols as a routine practice should be of no exception and any result merely based on overall survival rates may not be reproducible if the required criteria are not present.

### Intention to Treat

An ITT analysis is based on the initial treatment assignment and not on the treatment eventually received. Thus, ITT analysis is intended to avoid misleading information that can arise in interventional research.<sup>41</sup> Table 6 summarizes the number of implants originally intended for IL but not fulfilling certain criteria established by the respective authors, resulting in a change of the treatment rendered. This information is relevant to understand the predictability and practicality of IL in the treatment of partial edentulism, yet almost half of the studies analyzed in this systematic review did not provide any information on ITT. Without clear information on patient selection criteria for IL protocols, the current status of the scientific evidence should be interpreted with caution.

However, from the few studies reporting on the ITT analysis, it can be noted that IL protocols are highly technique sensitive. Common reasons leading to a change of the rendered loading protocol were lack of primary implant stability, failure to achieve the minimal insertion torque, low ISQ values, poor bone quality, and the necessity of substantial bone augmentation procedures. As the frequency of these clinical situations has been scarcely investigated, further studies containing a well-described ITT analysis are necessary to assess the practicality of IL or EL protocols and to present clear clinical recommendations.

### Clinical Significance

To develop clinically significant statements, risks and benefits of a shortened implant healing time have to be considered. Most of the included studies selected IL or EL protocols on implants that had been placed in healed edentulous sites (type 4 implant placement), which means that these patients had already been partially edentulous for at least several months. Hence, the clinical benefit of an immediate delivery of the provisional in those cases may be questioned. Moreover, an IL approach requires the fabrication of an immediate provisional, whereas this is often not necessary when applying an EL or CL approach in posterior sites. One of the clinical advantages of IL would be the delivery of a final prosthesis within the first week after implant placement. However, the inadequate reporting on prosthetic designs associated with IL, as well as the obvious technical and logistical challenges in completing definitive IFDPs in such short periods of time makes this approach a weak indication for IL in partially edentulous patients at this point in time. In addition, most of the failures of IL implants occurred within three months from implant placement. This suggests that a longer observation period with immediate provisional prostheses may be advisable before fabricating the definitive prosthesis. For cases where hopeless teeth have

to be replaced by implants, particularly in the esthetic zone, the combination of an implant placement type 1 with IL would provide clear benefits for the patient. However, a scientific validation of this approach does not exist at this time.

### Clinical Recommendations

According to the current literature presented in this systematic review, IL of dental implants placed in healed posterior extended edentulous sites of partially edentulous patients may be a predictable treatment approach if applied with extreme caution. Reasonable doubts can be raised about the clinical benefit of this treatment modality as posterior zones are of minor esthetic concern and patients with healed extraction sites have been partially edentulous for several months.

Due to insufficient documentation, IL for anterior implants in partially edentulous patients with extended edentulous sites is not supported by the literature at this time. Immediate loading of implants in extended edentulous sites immediately placed into extraction sockets, which would clearly provide the biggest clinical benefit to patients, has to be considered experimental at this point, since very limited clinical evidence exists to support such treatment. Further research is needed to investigate this tempting treatment modality.

Until further studies clarify the impact of several treatment modifiers, the following criteria should be considered when selecting a loading protocol: bone quality, primary stability, insertion torque, ISQ values, implant length, need for substantial bone augmentation, timing of implant placement, parafunction, and smoking habit.

## CONCLUSIONS

Under strict selection criteria, IL presents similar implant survival rates than EL or CL in posterior extended edentulous sites of partially edentulous patients. Insufficient evidence exists to support such treatment in the anterior zone. Despite a tendency favoring mandibular implants, differences in survival rates between the maxilla and the mandible were not statistically significant. Bone quality, primary stability, insertion torque, ISQ values, implant length, the need for substantial bone augmentation, the timing of implant placement, and the presence of parafunctional and smoking habits were common selection criteria in choosing a loading protocol. Further research is needed before IL can be recommended as a standard protocol in partially edentulous patients with extended edentulous sites. Such research should include an ITT analysis and a detailed report on prosthetic parameters.

## ACKNOWLEDGMENTS

The authors would like to thank Dr Sung-Kiang Chuang, Assistant Professor of Oral and Maxillofacial Surgery, Harvard School of Dental Medicine, Boston, Massachusetts, for the statistical analysis and Dr Paul Bain, Reference and Education Services Librarian, Countway Library of Medicine, Boston, Massachusetts, for his expertise in developing the search strategy. The authors also thank the ITI Foundation for supporting this consensus conference.

The authors wish to declare no conflicts of interests and that no external funding was received for the completion of this systematic review.

## REFERENCES

- Papaspyridakos P, Chen CJ, Singh M, Weber HP, Gallucci GO. Success criteria in implant dentistry: A systematic review. *J Dent Res* 2012;91:242–248.
- Buser D, Janner SF, Wittneben JG, Bragger U, Ramseier CA, Salvi GE. 10-year survival and success rates of 511 titanium implants with a sandblasted and acid-etched surface: A retrospective study in 303 partially edentulous patients. *Clin Implant Dent Relat Res* 2012 Dec;14:839–851.
- Astrand P, Engquist B, Anzen B, et al. A three-year follow-up report of a comparative study of ITI dental implants and Branemark System implants in the treatment of the partially edentulous maxilla. *Clin Implant Dent Relat Res* 2004;6:130–141.
- Behneke A, Behneke N, d'Hoedt B. The longitudinal clinical effectiveness of ITI solid-screw implants in partially edentulous patients: A 5-year follow-up report. *Int J Oral Maxillofac Implants* 2000;15:633–645.
- Bilhan H, Kutay O, Arat S, Cekici A, Cehreli MC. Astra Tech, Branemark, and ITI implants in the rehabilitation of partial edentulism: Two-year results. *Implant Dent* 2010;19:437–446.
- Cecchinato D, Olsson C, Lindhe J. Submerged or non-submerged healing of endosseous implants to be used in the rehabilitation of partially dentate patients. *J Clin Periodontol* 2004;31:299–308.
- Gallucci GO. Guidelines for Selecting the Appropriate Loading Protocol. In: Wismeijer D, Buser D, Belser UC (eds). *ITI Treatment Guide 4*. 1st ed. Berlin: Quintessence, 2010:57–68.
- Rocuzzo M, Aglietta M, Cordaro L. Implant loading protocols for partially edentulous maxillary posterior sites. *Int J Oral Maxillofac Implants* 2009;24(suppl):147–157.
- Cordaro L, Torsello F, Rocuzzo M. Implant loading protocols for the partially edentulous posterior mandible. *Int J Oral Maxillofac Implants* 2009;24(suppl):158–168.
- Weber HP, Morton D, Gallucci GO, Rocuzzo M, Cordaro L, Grutter L. Consensus statements and recommended clinical procedures regarding loading protocols. *Int J Oral Maxillofac Implants* 2009;24(suppl):180–183.
- Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: Explanation and elaboration. *J Clin Epidemiol* 2009;62:e1–e34.
- Academies IoMotN. Standards for Developing Trustworthy Clinical Practice Guidelines: Institute of Medicine of the National Academies; 2011.
- Higgins JPT, Green S. *Cochrane Handbook for Systematic Reviews of Interventions*: Cochrane Book Series. In: Higgins JPT, Green S (eds) *Cochrane Handbook for Systematic Reviews of Interventions*: Cochrane Book Series: The Cochrane Collaboration; 2011.
- Needleman IG. A guide to systematic reviews. *J Clin Periodontol* 2002;29(suppl 3):6–9; discussion 37–38.
- Esposito M, Grusovin MG, Willings M, Coulthard P, Worthington HV. The effectiveness of immediate, early, and conventional loading of dental implants: A Cochrane systematic review of randomized controlled clinical trials. *Int J Oral Maxillofac Implants* 2007;22:893–904.
- Capelli M, Esposito M, Zuffetti F, Galli F, Del Fabbro M, Testori T. A 5-year report from a multicentre randomised clinical trial: Immediate non-occlusal versus early loading of dental implants in partially edentulous patients. *Eur J Oral Implantol* 2010;3:209–219.
- Ganeles J, Zollner A, Jackowski J, ten Bruggenkate C, Beagle J, Guerra F. Immediate and early loading of Straumann implants with a chemically modified surface (SLActive) in the posterior mandible and maxilla: 1-year results from a prospective multicenter study. *Clin Oral Implants Res* 2008;19:1119–1128.
- Van de Velde T, Sennerby L, De Bruyn H. The clinical and radiographic outcome of implants placed in the posterior maxilla with a guided flapless approach and immediately restored with a provisional rehabilitation: A randomized clinical trial. *Clin Oral Implants Res* 2010;21:1223–1233.
- Testori T, Galli F, Capelli M, Zuffetti F, Esposito M. Immediate non-occlusal versus early loading of dental implants in partially edentulous patients: 1-year results from a multicenter, randomized controlled clinical trial. *Int J Oral Maxillofac Implants* 2007;22:815–822.
- Cannizzaro G, Leone M. Restoration of partially edentulous patients using dental implants with a microtextured surface: A prospective comparison of delayed and immediate full occlusal loading. *Int J Oral Maxillofac Implants* 2003;18:512–522.
- Cannizzaro G, Leone M, Consolo U, Ferri V, Esposito M. Immediate functional loading of implants placed with flapless surgery versus conventional implants in partially edentulous patients: A 3-year randomized controlled clinical trial. *Int J Oral Maxillofac Implants* 2008;23:867–875.
- Romanos GE, Nentwig GH. Immediate versus delayed functional loading of implants in the posterior mandible: A 2-year prospective clinical study of 12 consecutive cases. *Int J Periodontics Restorative Dent* 2006;26:459–469.
- Bornstein MM, Lussi A, Schmid B, Belser UC, Buser D. Early loading of nonsubmerged titanium implants with a sandblasted and acid-etched (SLA) surface: 3-year results of a prospective study in partially edentulous patients. *Int J Oral Maxillofac Implants* 2003;18:659–666.
- Schincaglia GP, Marzola R, Scapoli C, Scotti R. Immediate loading of dental implants supporting fixed partial dentures in the posterior mandible: A randomized controlled split-mouth study—machined versus titanium oxide implant surface. *Int J Oral Maxillofac Implants* 2007;22:35–46.
- Vanden Bogaerde L, Rangert B, Wendelhag I. Immediate/early function of Branemark System TiUnite implants in fresh extraction sockets in maxillae and posterior mandibles: An 18-month prospective clinical study. *Clin Implant Dent Relat Res* 2005;7 (suppl 1):s121–s130.
- Rismanchian M, Fazel A, Rakhshan V, Eblaghian G. One-year clinical and radiographic assessment of fluoride-enhanced implants on immediate non-functional loading in posterior maxilla and mandible: A pilot prospective clinical series study. *Clin Oral Implants Res* 2011;22:1440–1445.
- Vanden Bogaerde L, Pedretti G, Dellacasa P, Mozzati M, Rangert B, Wendelhag I. Early function of splinted implants in maxillae and posterior mandibles, using Branemark System Tiunite implants: An 18-month prospective clinical multicenter study. *Clin Implant Dent Relat Res* 2004;6:121–129.
- Boronat-Lopez A, Carrillo C, Penarrocha M, Penarrocha-Diago M. Immediately restored dental implants for partial-arch applications: A study of 12 cases. *J Oral Maxillofac Surg* 2009;67:195–199.
- Cornelini R, Cangini F, Covani U, Barone A, Buser D. Immediate loading of implants with 3-unit fixed partial dentures: A 12-month clinical study. *Int J Oral Maxillofac Implants* 2006;21:914–918.
- Luongo G, Di Raimondo R, Filippini P, Gualini F, Paoleschi C. Early loading of sandblasted, acid-etched implants in the posterior maxilla and mandible: A 1-year follow-up report from a multicenter 3-year prospective study. *Int J Oral Maxillofac Implants* 2005;20:84–91.
- Todisco M. Early loading of implants in vertically augmented bone with non-resorbable membranes and deproteinised anorganic bovine bone. An uncontrolled prospective cohort study. *Eur J Oral Implantol* 2010;3:47–58.

32. Machtei EE, Frankenthal S, Blumenfeld I, Gutmacher Z, Horwitz J. Dental implants for immediate fixed restoration of partially edentulous patients: A 1-year prospective pilot clinical trial in periodontally susceptible patients. *J Periodontol* 2007;78:1188–1194.
33. Bornstein MM, Schmid B, Belser UC, Lussi A, Buser D. Early loading of non-submerged titanium implants with a sandblasted and acid-etched surface. 5-year results of a prospective study in partially edentulous patients. *Clin Oral Implants Res* 2005;16:631–638.
34. Degidi M, Nardi D, Piattelli A. A comparison between immediate loading and immediate restoration in cases of partial posterior mandibular edentulism: A 3-year randomized clinical trial. *Clin Oral Implants Res* 2010;21:682–687.
35. Fung K, Marzola R, Scotti R, Tadinada A, Schincaglia GP. A 36-month randomized controlled split-mouth trial comparing immediately loaded titanium oxide-anodized and machined implants supporting fixed partial dentures in the posterior mandible. *Int J Oral Maxillofac Implants* 2011;26:631–638.
36. Malo P, Nobre M. Flap vs flapless surgical techniques at immediate implant function in predominantly soft bone for rehabilitation of partial edentulism: A prospective cohort study with follow-up of 1 year lap. *Eur J Oral Implantol* 2008;1:293–304.
37. Nikellis I, Levi A, Nicolopoulos C. Immediate loading of 190 endosseous dental implants: A prospective observational study of 40 patient treatments with up to 2-year data. *Int J Oral Maxillofac Implants* 2004;19:116–123.
38. Payer M, Heschl A, Wimmer G, Wegscheider W, Kirmeier R, Lorenzoni M. Immediate provisional restoration of screw-type implants in the posterior mandible: Results after 5 years of clinical function. *Clin Oral Implants Res* 2010;21:815–821.
39. Vanden Bogaerde L, Pedretti G, Sennerby L, Meredith N. Immediate/early function of Neoss implants placed in maxillas and posterior mandibles: An 18-month prospective case series study. *Clin Implant Dent Relat Res* 2010;12(suppl 1):e83–e94.
40. Fischer K, Backstrom M, Sennerby L. Immediate and early loading of oxidized tapered implants in the partially edentulous maxilla: A 1-year prospective clinical, radiographic, and resonance frequency analysis study. *Clin Implant Dent Relat Res* 2009;11:69–80.
41. Hollis S, Campbell F. What is meant by intention to treat analysis? Survey of published randomised controlled trials. *BMJ* 1999;319:670–674.