Implant Loading Protocols for Edentulous Patients with Fixed Prostheses: A Systematic Review and Meta-Analysis

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Purpose: *To report on the effect of immediate implant loading with fixed prostheses compared to early and conventional loading on implant and prosthesis survival, failure, and complications.* ***Materials and Methods:*** *An electronic and manual search was conducted to identify randomized controlled clinical trials (RCTs) as well as prospective and retrospective studies involving rough surface implants and implant fixed complete dental prostheses for edentulous patients.* ***Results:*** *The 62 studies that fulfilled the inclusion criteria featured 4 RCTs, 2 prospective case-control studies, 34 prospective cohort studies, and 22 retrospective cohort studies. These studies yielded data from 2,695 patients (2,757 edentulous arches) with 13,653 implants. Studies were grouped according to the loading protocol applied; 45 studies reported on immediate loading, 8 on early loading, and 11 on conventional loading. For the immediate loading protocol with flap surgery, the implant and prosthesis survival rates ranged from 90.1% to 100% and 93.75% to 100%, respectively (range of follow-up, 1 to 10 years). When immediate loading was combined with guided flapless implant placement, the implant survival rates ranged from 90% to 99.4%. For the early loading protocol, the implant and prosthesis survival rates ranged from 94.74% to 100% and 93.75% to 100%, respectively (range of follow-up, 1 to 10 years). For the conventional loading protocol, the implant and prosthesis survival rates ranged from 94.95% to 100% and 87.5% to 100%, respectively (range of follow-up, 2 to 15 years). No difference was identified between maxilla and mandible.* ***Conclusions:*** *When selecting cases carefully and using dental implants with a rough surface, immediate loading with fixed prostheses in edentulous patients results in similar implant and prosthesis survival and failure rates as early and conventional loading. For immediate loading, most of the studies recommended a minimal insertion torque of 30 Ncm. The estimated 1-year implant survival was above 99% with all three loading protocols. Caution is necessary when interpreting these results, as there are many confounding factors that affect treatment outcomes with each of the loading protocols.* Int J Oral Maxillofac Implants 2014;29(Suppl):256–270.
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Treatment of the edentulous jaw with dental implants represents a scientifically and clinically validated treatment modality.[1,2] Osseointegrated dental implants provide a predictable base for the restoration of function and esthetics in edentulous patients. However, the extended healing time without implant loading associated with the conventional loading protocol is a disadvantage from the patient perspective. Hence, reducing the healing period or time to loading would be of great benefit to the patient. Today, many implant surgical and prosthodontic concepts are used for the treatment of the edentulous jaw.[3] Rough implant surfaces and immediate or early loading protocols have led to faster healing times and immediate or early restoration of function and esthetics in carefully selected cases.[3] Prosthodontic protocols and materials have also significantly evolved since the mandibular hybrid prostheses with acrylic teeth on a cast gold alloy framework, especially due to the introduction of CAD/

CAM technology.[4] Choosing the most appropriate protocol for the rehabilitation of the edentulous jaw may represent a challenge and should rely on evidence-based, thorough information.

The edentulous predicament is directly related to alteration of facial esthetics and decrease in the lower facial height, as well as loss of ability to chew, taste, and smile.[2] A recent study reported that the percentage of patients with complete edentulism varies substantially among the G8 countries (Canada, France, Germany, Italy, Japan, Russia, United Kingdom, and United States of America). It ranged from 16.3% in France to 58% in Canada for patients older than 65 years of age.[5] There were no data available from Russia in the aforementioned study. In the United States of America, the percentage of edentulous patients is 10% of the total population and is expected to increase in future years as the life expectancy increases.[6,7] Although the incidence of complete edentulism in the United States has been steadily declining (approximately 6% between 1988 and 2000), the continuous growth of the population 65 years of age and older indicates that the incidence rate of complete edentulism will remain constant or even increase over the coming decades.[8] As the average life expectancy is constantly increasing, and with that the percentage of the population aged 65 and older, it becomes clear that the need for prosthodontic treatment including dental implants for completely edentulous patients will increase. Besides the continuously growing need for full-arch rehabilitations with dental implants, there is a tendency in the field of oral implantology to reduce treatment time and simplify procedures in order to increase patient acceptance and satisfaction.

Hence, the purpose of this systematic review was to investigate the effect of immediate implant loading with fixed prostheses on implant and prosthesis survival, failure, and complications in edentulous patients compared to early and conventional loading.

MATERIALS AND METHODS

This systematic review was conducted in accordance with the guidelines of Transparent Reporting of Systematic Reviews and Meta-analyses (PRISMA statement), as reported by Moher et al.[9]

Focus Question

The following focus question was developed following the PICO (population, intervention, comparison, outcome) format:

In edentulous patients, what is the effect of immediate implant loading with fixed prostheses compared to early and conventional loading on implant and prosthesis survival, failure, and complications?

Definitions of Time to Loading

The different times for loading dental implants have been somewhat confusing in the past; however, in accordance with recently published reports, the following current definitions were used for the present systematic review.[3,10]

- Immediate loading: A prosthesis is connected to the dental implants within 1 week following implant placement.
- Early loading: A prosthesis is connected to the dental implants between 1 week and 2 months following implant placement.
- Conventional loading: Dental implants are allowed to heal for a period greater than 2 months after implant placement without connection of a prosthesis.

Search Strategy

Three internet sources were used to search for eligible articles (published, early view online and accepted) in English and German that satisfied the study purpose. These included Medline-PubMed, Embase, and the Cochrane Central Register of Controlled Trials (CENTRAL). Additionally, the following journals were hand searched for potentially relevant articles: *Clinical Oral Implants Research*, *Clinical Implant Dentistry and Related Research*, *Journal of Periodontology*, *Journal of Clinical Periodontology*, *International Journal of Oral and Maxillofacial Implants*, *Journal of Prosthetic Dentistry*, *International Journal of Prosthodontics*, *Implant Dentistry*, and *Journal of Oral Implantology*. The hand search and the electronic database search extended from January 1, 1980 to August 31, 2012. The inclusion/exclusion criteria and the systematic search strategy are outlined in Table 1.

Selection Strategy and Data Collection

Titles and abstracts were initially screened by two calibrated reviewers (C-JC and PP) for potential inclusion. All titles and abstracts selected by the two reviewers were discussed individually for full-text reading inclusion. If title and abstract did not provide sufficient information regarding the inclusion criteria, the full report was obtained as well. The full-text reading of selected publications was carried out independently by the reviewers. Consensus between the reviewers was reached in every step of the review. The electronic search was supplemented by manual search of the bibliographies of all the full-text articles that were selected from the initial search and previous systematic reviews relevant to the topic. Inter-reviewer agreement between the two reviewers was always determined with the use of Cohen's kappa statistics (κ). In cases where information was not clear, the study authors were contacted by email for clarification.

Table 1 Systematic Search and Strategy

Focus question:	In edentulous patients, what is the effect of immediate implant loading compared to early or conventional loading with fixed prostheses on implant survival, failure, and complications?
Search strategy	
Population	#1 - dental implantation, endosseous[MeSH] OR dental implants[MeSH] OR implantation*[all fields] OR implant[all fields] OR implants[all fields]
Intervention or exposure	#2 - denture, complete, fixed[MeSH] OR dental prosthesis, implant-supported[MeSH] OR fixed complete denture*[all fields] OR fixed complete dental prosthesis*[all fields] OR bridge*[all fields] OR FDPs* [all fields] OR fixed rehabilitations*[all fields] OR fixed restorations*[all fields]
Comparison	#3 - 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]
Outcome	#4 - survival[MeSH] OR survival rate[MeSH] OR survival analysis[MeSH] OR intraoperative complications[MeSH] OR postoperative complications[MeSH] OR dental restoration failure[MeSH] OR prosthesis failure[MeSH] OR treatment failure[MeSH] OR complication*[all fields] OR success*[all fields] OR failure*[all fields]
Filters (language)	#5- English[lang] OR German[lang]
Search combination	#1 AND #2 AND #3 AND #4 AND #5
Database search	
Electronic	PubMed, Embase and the Cochrane Central Register of Controlled Trials (CENTRAL)
Journals	All peer reviewed dental journals available in PubMed, Embase and CENTRAL. No filters were applied for the journals
Selection criteria	
Inclusion criteria	Rough surface solid screw-type implants RCTs, observational, cross-sectional, case report (≥ 10 cases), prospective studies Retrospective studies recalling all patients under investigation Studies reporting outcomes after 12 or more months of function English and German language Human studies only
Exclusion criteria	Smooth (machined) implant surface HA implant surface Non-solid screw-type implants or implant with a diameter less than 3 mm Studies based on charts or questionnaires only, ie, no clinical examination was performed at follow-ups Insufficient information on the time of failures provided to calculate cumulative survival rate Multiple publications on the same patient cohort No author response to inquiry email for data clarification Animal studies

Quality Assessment

The assessment of study quality was performed for all the included articles. In the case of randomized controlled clinical trials (RCTs), the Cochrane Collaboration's tool for assessing risk of bias was used.[9] In the case of case-control studies and cohort studies, the methodological quality assessment of the studies was based on the Newcastle-Ottawa Quality Assessment Scale.[11] The risk of bias was assessed independently by the two reviewers who scored the methodological quality of the included studies. This assessment is referred to as the overall risk of bias.[11]

Statistical Analysis

For each study involved, event failure rates for the implants or the prostheses were calculated by dividing the total number of failure events for the implants or the prostheses by the total exposure time (follow-up time) of implants or prostheses in years. For further analysis, the failure event rate estimates were used to calculate their standard errors (standard errors were estimated by the standardized formula of failure rates divided by the square root of the number of failure cases of the implants or prostheses). With each study's estimates and standard errors obtained, the authors further determined the 95% confidence intervals (95% CI) of the summary estimates of the failure event rates. Studies without any failures in the implants or the prostheses group were excluded from the meta-analysis due to zero events. Heterogeneity between studies was assessed using *I*-squared statistics describing the variation in risk ratio (RR), which is attributable to the heterogeneity of the studies. All statistical analyses were performed using STATA (Stata

Statistical Software), and level of statistical significance (α level) was based at .05. Using the METAN command in the STATA computing environment, we assessed the heterogeneity of the study-specific failure event rates. The estimated 1-year (T = 1) survival rates were calculated via the relationship between failure event rates and the negative exponential survival function S, S(T) = exp (–T * failure event rate), by assuming constant failure event rates. The 95% CI for the survival rates were then calculated by using the 95% confidence limits of the failure event rates. The STATA software computed the I^2 statistic to assess the heterogeneity between studies and the associated *P*-value. If the heterogeneity (goodness-of-fit) *P*-value was below .05, indicating heterogeneity, meta-analysis with random effects was used to obtain a summary estimate of the event rates and the estimated 1-year survival rates. If the heterogeneity *P*-value was above .05, indicating no statistical significant heterogeneity, meta-analysis with fixed effects was used with a weighting scheme based on the study's total exposure time (follow-up time).

RESULTS

Selection of Included Studies

The initial search yielded 2,539 hits after discarding duplicate references (Fig 1). The subsequent search at the title level exhibited 826 titles (k-score = 0.80). The subsequent search at the abstract level identified 527 abstracts (k-score = 0.85). The independent abstract investigation revealed 123 articles for full-text reading (k-score = 0.90). Out of the 123 articles selected for full-text reading, 62 studies were finally selected for inclusion (one clinical trial by Fischer et al was reported in two articles as part 1 and 2, but was considered as one study).[12–74] Sixty studies were excluded.

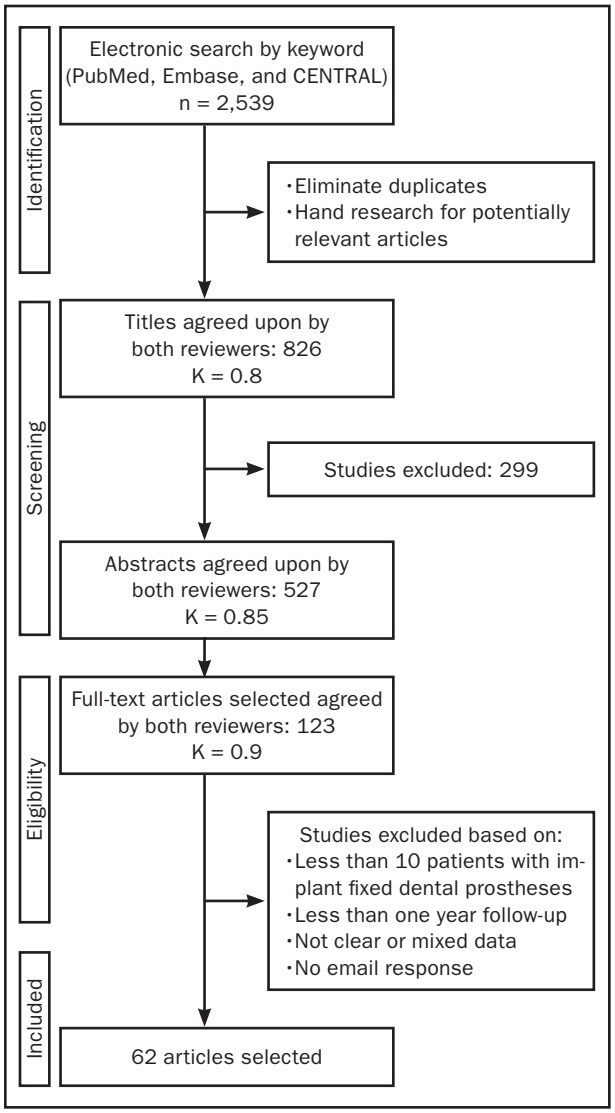

Fig 1 Search flow diagram.

Characteristics of Included Studies

The 62 included studies featured 4 RCTs, 2 prospective case-control studies, 34 prospective cohort studies, and 22 retrospective cohort studies. Thirty-one studies were conducted in universities, 28 studies in private clinics, and 3 in combination of universities and private clinics. The year of publication ranged from 2001 to 2013. The distribution of studies broken down per loading protocol is shown in Fig 2.

Implant and Prosthesis Survival and Failure with Immediate Loading. The scientific evidence on immediate loading with fixed prostheses for edentulous patients was supported by 45 studies (1 RCT, 28 prospective, and 16 retrospective).[12–55,62] These clinical studies reported data from 2,146 patients (2,206 edentulous arches) with 10,600 implants, with follow-up from 12 months to 120 months.

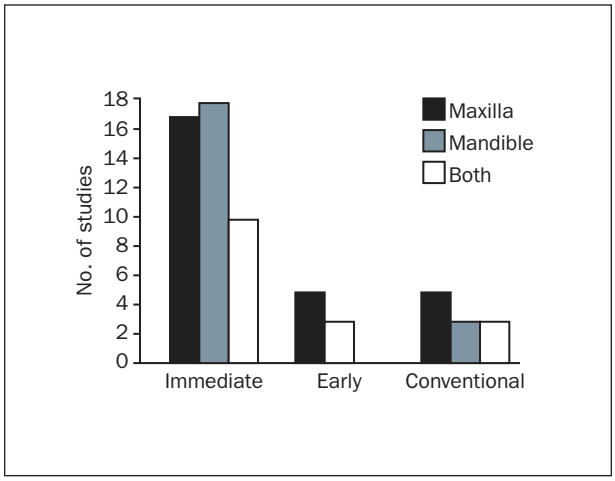

Fig 2 Distribution of studies by loading protocol for maxilla and mandible.

Table 2 Studies on Immediate Loading with Complete Dental Prostheses in the Edentulous Maxilla

Study	Study type	Brand	Patients	Implants/ patient	Prosthesis type	Follow-up time (mo)	Implants
Agliardi et al[12]	Prosp	Nobel Biocare	32	6	M-C	55.53	192
Barbier et al[14]	Prosp	Astra Tech	20	6	M-R	18	120
Crespi et al[16]	Prosp	PAD	24	4	M-R and all-acrylic	36	96
Degidi et al[17]	Prosp	Friadent	9	6 to 7	M-R	12	61
Degidi et al[18]	Prosp	Nobel Biocare	5	7 to 9	M-C	120	40
Francetti et al[19]	Prosp	Nobel Biocare	16	4	M-R	33.8	64
Ji et al[28]	Retro	Nobel Biocare and Friadent	17	4 to 8	M-R	36	115
Maló et al[21]	Retro	Nobel Biocare	242	4	M-C and M-R and all-acrylic	60	968
Mozzati et al[22]	Retro	Nobel Biocare	65	4 or 6	M-C	24	334
Pieri et al[24]	Prosp	Astra Tech	20	7 to 8	M-R	12	155
Babbush et al[25]	Retro	Nobel Biocare	109	4	M-R	12	436
Strietzel et al[31]	Retro	Alpha Bio	20	6 to 12	M-C	29	172
Tealdo[62]	Prosp	Biomet 3i	34	4 to 6	M-R	40.5	163
Agliardi et al[32]	Prosp	Nobel Biocare	61	4	M-R	26.9	244
Artzi et al[33]	Retro	DFI/ITO/SPI	32	8.6	M-C and M-R	36	302
Degidi et al[35]	Prosp	Friadent	30	7	M-R	36	210
Gillot et al[39]	Retro	Nobel Biocare	33	4 to 8	M-R	30.4	211
Meloni et al[40]	Retro	Nobel Biocare	15	6	Zirconia-ceramic and M-R	18	90
Bergkvist et al[41]	Prosp	Straumann	28	6	M-C and M-R	32	168
Johansson et al[42]	Prosp	Nobel Biocare	48	6	M-R	12	288
Pieri et al[43]	Prosp	Keystone Dental	9	5 to 8	M-R	19	66
Cannizzaro et al[37]	RCT	Zimmer	15	5 to 8	M-C and M-R	12	90
Collaert and De Bruyn[45]	Prosp	Astra Tech	25	7 to 9	M-C and M-R	36	195
Degidi et al[38]	Prosp	Friadent	20	6 to 8	M-R	12	153
Testori et al[47]	Prosp	Biomet 3i	30	6	M-C and M-R	22.1	180
Jaffin et al[51]	Retro	Straumann	29	6 to 8	M-C and M-R	24	236
Olsson et al[53]	Retro	Nobel Biocare	10	6 to 8	M-R	12	61
Total			998				5410

Retro = retrospective; Prosp = prospective; RCT = randomized controlled trial; M-R = metal-resin; M-C = metal-ceramic.
*Maximum number of stars that a study can receive is 8, based on the Newcastle-Ottawa assessment scale.

In the maxilla, the implant survival rate ranged from 90.43% to 100% based on 27 studies (range of follow-up, 1 to 10 years).[12,14,16–19,21,22,24,25,28,31,32,35,37–43,45,47,51,53,62] The number of implants placed in the maxilla was between 4 and 12 implants per patient. The prosthesis survival rate ranged from 90% to 100%, based on these 27 studies (Table 2).

In the mandible, the implant survival rate ranged from 90% to 100%, based on 28 studies (range of follow-up, 1 to 10 years).[13,15–20,23,25–34,36,43,44,46,48–50,52,54,55] The number of implants placed in the mandible was between 2 and 10 implants per patient. The prosthesis survival rate ranged from 93.75% to 100%, based on these 28 studies (Table 3).

Based on most of the 45 studies that reported on immediate loading, one of the prerequisites was an insertion torque of at least 30 Ncm (range from 10 to 80 Ncm). Only a study by Degidi et al in 2012 reported insertion torques of less than 25 Ncm. However, in all cases that some implants had insertion torques of equal or less than 20 Ncm they were always splinted with implants that had torque between 25 to 50 Ncm.[17] If resonance frequency analysis was used to assess the primary stability, an ISQ value of more than 60 was chosen as the minimum value for immediate loading.

The prosthodontic design was generally one-piece. Only the studies by Ganeles et al[55] and Jaffin et al[51] reported on a small number of segmented prostheses

Failures	Prostheses	Prosthesis failures	Implant survival rate (%)	Prosthesis survival rates (%)	Weight (%)	Overall risk of bias
2	32	0	98.96	100.00	6.04	6*
0	20	0	100.00	100.00	1.23	6*
1	24	0	98.96	100.00	1.96	6*
1	9	0	98.36	100.00	0.41	6*
0	5	0	100.00	100.00	2.72	6*
0	16	0	100.00	100.00	1.23	6*
11	17	0	90.43	100.00	2.35	6*
19	242	0	98.04	100.00	32.94	6*
7	65	0	97.90	100.00	4.55	6*
2	20	0	98.71	100.00	1.05	6*
3	109	0	99.31	100.00	2.97	5*
1	20	0	99.42	100.00	2.83	6*
10	34	0	93.87	100.00	3.74	8*
4	61	0	98.36	100.00	3.72	6*
6	32	0	93.05	100.00	6.17	5*
1	30	0	99.52	100.00	4.29	6*
4	33	0	98.10	100.00	3.64	6*
2	15	0	97.78	100.00	0.92	6*
3	28	0	98.21	100.00	3.05	6*
2	48	2	99.31	95.83	1.96	6*
2	9	0	96.97	100.00	0.71	6*
1	15	0	98.89	100.00	0.61	low
0	25	0	100.00	100.00	3.98	6*
0	20	0	100.00	100.00	1.04	6*
3	30	0	98.33	100.00	2.26	6*
16	29	0	93.22	100.00	3.21	6*
4	10	1	93.44	90.00	0.42	6*
105	998	3	98.06	99.70	100	

as well. The prosthetic materials for definitive prostheses were metal resin, metal ceramic, or full acrylic, with the latter used only for a small number of "all-on-four" rehabilitations. The materials used for provisional prostheses with immediate loading were acrylic alone, fiber-reinforced acrylic, or metal-reinforced acrylic.

Four studies implemented guided flapless surgery with the Teeth-In-An-Hour protocol (NobelGuide), which involved immediate loading with a prefabricated definitive and/or provisional prostheses, made of titanium and resin or full acrylic.[29,39,40,42] Two more studies reported on flapless surgery without stereolithographic guides.[15,37] In total, these six studies yielded data from 207 patients with 903 implants. When immediate loading was combined with guided flapless implant placement, the implant survival rates ranged from 90% to 99.4% (range of follow-up, 12 to 51 months).

Implant and Prosthesis Survival and Failure with Early Loading. The scientific evidence on early loading with fixed prostheses for edentulous patients was supported by eight studies (three RCTs, two prospective, and three retrospective).[56–59,63–67] These clinical studies reported data from 267 patients with 1,365 implants, with follow-up from 12 months to 120 months.

In the maxilla, the implant survival rate ranged from 94.7% to 100% based on five studies (range of follow-up, 1 to 3 years).[56–59,64,66] The number of implants

Table 3 Studies on Immediate Loading with Complete Dental Prostheses in the Edentulous Mandible

Study	Study type	Brand	Patients	Implants/ patient	Prosthesis type	Follow-up time (mo)	Implants
Acocella et al[13]	Retro	Astra Tech	45	5	M-R	48	225
Cannizzaro et al[15]	Prosp	Biomet 3i	80	2	M-R	12	160
Crespi et al[16]	Prosp	PDA	20	4	M-R and all-acrylic	36	80
Degidi et al[17]	Prosp	Friadent	4	6	M-R	12	21
Degidi et al[18]	Prosp	Nobel Biocare	8	5 to 6	M-C	120	44
Francetti et al[19]	Prosp	Nobel Biocare	33	4	M-R	52.8	132
Galindo and Butura[20]	Retro	Nobel Biocare	183	4	M-R	12	732
Ji et al[28]	Retro	Nobel Biocare and Frident	24	4 to 8	M-R	36	128
Mozzati et al[23]	Retro	Nobel Biocare	50	4	M-C and M-R	24	200
Weinstein et al[50]	Prosp	Nobel Biocare	20	4	M-R	30.1	80
Babbush et al[25]	Retro	Nobel Biocare	68	4	M-R	12	272
Collaert et al[26]	Prosp	Astra Tech	25	5	M-C and M-R	24	125
Hatano et al[27]	Retro	Nobel Biocare	78	3	M-R	60	234
Landázuri-Del Barrio et al[29]	Prosp	Nobel Biocare	16	4	M-R	12	64
Maló et al[30]	Retro	Nobel Biocare	91	4	M-C and M-R and all-acrylic	60	364
Strietzel et al[31]	Retro	Alpha Bio	14	6 to 10	M-C	29	111
Agliardi et al[32]	Prosp	Nobel Biocare	93	4	M-R	26.9	372
Artzi et al[33]	Retro	DFI/ITO/SPI	46	8.6	M-C and M-R	36	374
Degidi et al[34]	Prosp	Friadent	20	4	M-R	24	80
Degidi et al[36]	Prosp	Friadent	40	7	M-R	24	160
Pieri et al[43]	Prosp	Keystone Dental	15	5 to 8	M-R	19	78
Arvidson et al[44]	Prosp	Straumann	61	4 to 5	M-R	36	246
De Bruyn et al[46]	Prosp	Astra Tech	25	5	M-C and M-R	36	125
Capelli et al[48]	Prosp	Biomet 3i	23	4	M-R	29.1	92
Drago and Lazzara[49]	Prosp	Biomet 3i	27	5 to 7	M-R	12	151
Testori et al[52]	Prosp	Biomet 3i	62	5 to 6	M-R	12	325
Cooper et al[54]	Prosp	Astra Tech	10	5 to 6	M-R	12	54
Ganeles et al[55]	Retro	Straumann and Astra Tech and Frialit-2	27	5 to 8	M-C	25	161
Total			1,208				5,190

Retro = retrospective; Prosp = prospective; RCT = randomized controlled trial; M-R = metal-resin; M-C = metal-ceramic.
*Maximum number of stars that a study can receive is 8.

placed in the maxilla was between five to eight per patient. The prosthesis survival rate ranged from 93.75% to 100%, based on these five studies (Table 4).

In the mandible, the implant survival rate ranged from 98.51% to 100%, based on three studies (range of follow-up, 1 to 2 years).[63,65,67] The number of implants placed in the mandible was between four to five per patient. The prosthesis survival rates ranged from 97.78% to 100%, based on these three studies (Table 5).

The prosthodontic design was one-piece for both maxilla and mandible except for the study by Lai et al, who reported on the use of a segmented design.[64] The prosthetic materials used for the definitive prostheses were metal resin or metal ceramic.

Implant and Prosthesis Survival and Failure with Conventional Loading. The scientific evidence on conventional loading with fixed prostheses for edentulous patients was supported by 11 studies (2 RCTs, 6 prospective, and 3 retrospective), while 3 studies reported on both maxilla and mandible.[56,57,60–62,68–74] These clinical studies reported data from 282 patients (284 edentulous arches) with 1,688 implants, with follow-up from 24 months to 180 months.

Failures	Prostheses	Prosthesis failures	Implant survival rates (%)	Prosthesis survival rates (%)	Weight (%)	Overall risk of bias
2	45	1	99.11	97.78	7.10	5*
2	80	2	98.75	97.50	1.26	6*
2	20	0	97.50	100.00	1.90	6*
0	4	0	100.00	100.00	0.17	6*
0	8	0	100.00	100.00	3.47	6*
0	33	0	100.00	100.00	4.59	6*
1	183	2	99.86	98.91	5.78	5*
13	24	0	90	100.00	3.03	6*
0	50	0	100.00	100.00	3.16	6*
0	20	0	100.00	100.00	1.58	6*
0	68	0	100.00	100.00	2.15	5*
0	25	0	100.00	100.00	1.97	6*
3	78	3	98.72	96.15	9.24	5*
6	16	1	90.63	93.75	0.51	6*
5	91	0	98.63	100.00	14.37	6*
0	14	0	100.00	100.00	2.12	6*
1	93	0	99.73	100.00	6.58	6*
15	46	0	94.39	100.00	8.86	5*
0	20	0	100.00	100.00	1.26	6*
0	40	0	100.00	100.00	2.53	6*
0	15	0	100.00	100.00	0.98	6*
3	61	0	98.78	100.00	5.83	6*
0	25	0	100.00	100.00	2.96	6*
0	23	0	100.00	100.00	1.76	6*
3	27	0	98.01	100.00	1.19	6*
2	62	0	99.38	100.00	2.57	6*
0	10	0	100.00	100.00	0.43	6*
1	27	0	99.38	100.00	2.65	6*
59	1,208	9	98.86	99.25	100	

In the maxilla, the implant survival rate ranged from 94.95% to 100%, based on eight studies (range of follow-up from 2 to 15 years).[56–58,61,62,68–70,73,74] The number of implants placed in the maxilla was between four to nine implants per patient. The prosthesis survival rate ranged from 87.5% to 100%, based on these eight studies (Table 6).

In the mandible, the implant survival rate ranged from 96.47% to 100%, based on six studies (range of follow-up from 3 to 15 years).[60,68,69,71–73] The number of implants placed in the mandible was between four to six implants per patient. The prosthesis survival rate ranged from 95.56% to 100%, based on the aforementioned six studies (Table 7).

The prosthodontic design was one-piece for both maxilla and mandible. Only the study by Papaspyridakos and Lal reported on a small number of segmented prostheses as well.[69] The prosthetic materials used for the definitive prostheses were metal resin, metal ceramic or zirconia ceramic.

The estimated 1-year implant and prosthesis survival rates with 95% CI for each loading protocol are shown in Table 8. No difference was identified between maxilla and mandible.

Table 4 Studies on Early Loading with Complete Dental Prostheses in the Edentulous Maxilla

Study	Study type	Brand	Patients	Implants/ Patient	Prosthesis type	Follow-up time (mo)	Implants
Fischer and Stenberg (2012)[56] and Fischer and Stenberg (2013)[57]	RCT	Straumann	16	5 to 6	M-R	120	95
Jokstad et al[58]	RCT	Straumann	36	5 to 6	M-C	36	214
Cannizzaro et al[59]	RCT	Zimmer	15	5 to 8	M-C and M-R	12	87
Lai et al[64]	Prosp	Straumann	12	6 to 8	M-C	36	91
Nordin et al[66]	Retro	Straumann	20	6 to 7	M-R	12	122
Total			99				609

Retro = retrospective; Prosp = prospective; RCT = randomized controlled trial; M-R = metal-resin; M-C = metal-ceramic.
*Maximum number of stars that a study can receive is 8.

Table 5 Studies on Early Loading with Complete Dental Prostheses in the Edentulous Mandible

Study	Study type	Brand	Patients	Implants/ patient	Prostheses type	Follow-up time (mo)	Implants
Friberg and Jemt[63]	Retro	Nobel Biocare	67	4	M-R	12	268
Friberg and Jemt[65]	Prosp	Nobel Biocare	76	5	M-R	12	380
Collaert and De Bruyn[67]	Retro	Astra Tech	25	4 to 5	M-R	24	108
Total			168				756

Retro = retrospective; Prosp = prospective; RCT = randomized controlled trial; M-R = metal-resin; M-C = metal-ceramic.
*Maximum number of stars that a study can receive is 8.

Table 6 Studies on Conventional Loading with Complete Dental Prostheses in the Edentulous Maxilla

Study	Study type	Brand	Patients	Implants/ patient	Prostheses type	Follow-up time (mo)
Mertens et al[70]	Prosp	Astra Tech	15	6 to 8	M-C	135
Papaspyridakos and Lal[69]	Retro	Nobel Biocare	5	6 to 8	Zirconia-ceramic	3
Ravald et al[68]	Prosp	Astra Tech	10	6	M-C and M-R	162
Fischer and Stenberg (2012)[56] and Fischer and Stenberg (2013)[57]	RCT	Straumann	8	5 to 6	M-R	120
Hjalmarsson et al[61]	Retro	Astra Tech, Biomet 3i, Straumann, Nobel Biocare	53	4 to 8	M-C and M-R	60
Tealdo et al[62]	Prosp	Biomed 3i	15	6 to 9	M-R	40.5
Rasmusson et al[73]	Prosp	Astra Tech	16	4 to 6	M-R	120
Bergkvist et al[74]	Retro	Straumann	25	5 to 7	M-C and M-R	24
Total			147			

Retro = retrospective; Prosp = prospective; RCT = randomized controlled trial; M-R = metal-resin; M-C = metal-ceramic.
*Maximum number of stars that a study can receive is 8.

Table 7 Studies on Conventional Loading with Complete Dental Prostheses in the Edentulous Mandible

Study	Study type	Brand	Patients	Implants/ patient	Prostheses type	Follow-up time (mo)	Implants
Papaspyridakos and Lal[69]	Retro	Nobel Biocare	8	5 to 6	Zirconia-ceramic	36	47
Ravald et al[68]	Prosp	Astra Tech	15	5	M-C and M-R	162	85
Eliasson et al[71]	Prosp	Paragon	29	4 to 6	M-R	60	168
Gallucci et al[72]	Prosp	Straumann	45	4 to 6	M-C and M-R	60	237
Rasmusson et al[73]	Prosp	Astra Tech	20	4 to 6	M-R	120	108
Moberg et al[60]	RCT	Straumann	20	4 to 6	M-R	36	106
Total			137				751

Retro = retrospective; Prosp = prospective; RCT = randomized controlled trial; M-R = metal-resin; M-C = metal-ceramic.
*Maximum number of stars that a study can receive is 8.

Failures	Prostheses	Prosthesis failures	Implant survival rates (%)	Prosthesis survival rates (%)	Weight (%)	Overall risk of bias
5	16	1	94.74	93.75	45.81	Low
0	36	0	100.00	100.00	30.95	Low
3	15	0	96.55	100.00	4.19	Low
1	12	0	98.90	100.00	13.16	6*
1	20	0	99.18	100.00	5.89	6*
10	99	1	98.36	98.99	100	

Failures	Prostheses	Prosthesis failures	Implant survival rates (%)	Prosthesis survival rates (%)	Weight (%)	Overall risk of bias
4	67	1	98.51	98.51	31.02	6*
0	76	2	100.00	97.78	43.98	6*
0	25	0	100.00	100.00	25	6*
4	168	3	99.47	98.21	100	

Implants	Failures	Prostheses	Prosthesis failures	Implant survival rates (%)	Prosthesis survival rates (%)	Weight (%)	Overall risk of bias
94	3	15	1	96.81	93.33	17.25	6*
39	0	5	0	100.00	100.00	1.91	6*
99	5	10	1	94.95	90.00	21.80	6*
47	2	8	1	95.74	87.50	7.67	Low
324	5	53	0	98.46	100.00	26.43	8*
97	4	15	0	95.88	100.00	5.34	8*
91	3	16	0	96.70	100.00	14.84	6*
146	5	25	0	96.58	100.00	4.76	6*
937	27	147	3	97.12	97.96	100	

Failures	Prostheses	Prosthesis failures	Implant survival rates (%)	Prosthesis survival rates (%)	Weight (%)	Overall risk of bias
0	8	0	100.00	100.00	2.99	6*
3	15	0	96.47	100.00	24.36	6*
1	29	0	99.40	100.00	17.83	6*
0	45	2	100.00	95.56	25.15	6*
3	20	0	97.22	100.00	22.92	6*
3	20	0	97.17	100.00	6.75	Unclear
10	137	2	98.67	98.54	100	

Table 8 Estimated Cumulative 1-Year Survival Rate of Implants and Prostheses with Each Loading Protocol

Loading protocol	Arch	Estimated implant survival rate (%) and the 95% CI at one year	Estimated prosthesis survival rate (%) and the 95% CI at one year
Conventional	Maxilla	99.60 (99.60–99.70)	99.90 (99.80–100.0)
	Mandible	99.70 (99.50–99.90)	99.80 (99.60–99.90)
Early	Maxilla	99.30 (98.91–99.70)	99.90 (99.70–100.0)
	Mandible	98.51 (97.04–100.0)	99.50 (99.00–100.0)
Immediate	Maxilla	99.20 (99.10–99.40)	99.10 (98.22–100.0)
	Mandible	99.30 (99.20–99.50)	99.70 (99.50–99.90)

CI: Confidence intervals.

DISCUSSION

There is a tendency in the medical and dental field to reduce the treatment time and simplify treatment procedures in order to increase patient acceptance and satisfaction while maintaining long-term predictability of treatment outcomes.[75] The objective of this systematic review was to investigate the effect of immediate implant loading with fixed prostheses on implant survival, failure, and complications in edentulous patients compared to early and conventional loading in order to provide evidence-based clinical guidelines. Sixty-two studies, including 2,695 patients (2,757 edentulous arches) with 13,653 implants, were included in the present systematic review. Forty-five studies reported on immediate loading protocols, 8 on early, and 11 on conventional loading protocols.

For the edentulous maxilla, the focus question was answered in regards to survival and failure. Immediate loading with fixed prostheses in the maxilla yielded implant survival rates that ranged from 90.43% to 100%, based on 27 studies (range of follow-up, 1 to 10 years). The estimated cumulative 1-year implant survival rate was 99.2% (95% CI, 99.10 to 99.40) for immediate loading. With early loading in the maxilla, the implant survival rates ranged from 94.7% to 100%, based on 5 studies (range of follow-up, 1 to 3 years). The estimated cumulative 1-year implant survival rate was 99.3% (95% CI, 98.91 to 99.70) for early loading. When conventionally loading the implants in the maxilla, the implant survival rates ranged from 94.95% to 100%, based on eight studies (range of follow-up, 2 to 15 years). The estimated cumulative 1-year implant survival rate was 99.6% (95% CI, 99.60 to 99.70) for conventional loading. Thus, no difference was identified between immediate loading and early or conventional loading and their effect on implant survival in the edentulous maxilla.

For the edentulous mandible, the focus question was answered in regards to survival and failure. Immediate loading with fixed prostheses in the mandible yielded implant survival rates that ranged from 90% to 100%, based on 28 studies (range of follow-up, 1 to 10 years). The estimated cumulative 1-year implant survival rate was 99.3% (95% CI, 99.20 to 99.50) for immediate loading. Early loading in the mandible yielded implant survival rates that ranged from 98.51% to 100%, based on three studies (range of follow-up from 1 to 2 years). The estimated cumulative 1-year implant survival rate was 98.51% (95% CI, 97.04 to 100.00) for early loading. Finally, with conventional loading in the mandible, the implant survival rates ranged from 96.47% to 100%, based on six studies (range of follow-up from 3 to 15 years). The estimated cumulative 1-year implant survival rate was 99.7% (95% CI, 99.50 to 99.90) for conventional loading. Hence, no difference was identified between immediate loading and early or conventional loading and their effect on implant survival in the edentulous mandible.

Only three studies were identified to directly compare outcomes with different loading protocols within the same study. All three studies involved edentulous maxillary arches. One RCT by Cannizzaro et al compared immediate with early loading, and found implant survival rates of 98.89% in the immediate and 96.55% in the early loading group.[59] One case-control comparative study by Tealdo et al compared immediate with conventional loading. The authors found implant survival rates of 93.87% for the immediate and 95.88% for the conventional loading group.[62] One RCT by Fischer et al compared conventional with early loading with implant survival rates of 95.74% for conventional and 94.74% for early loading.[56,57]

The clinical implications of the aforementioned findings are obvious. With careful patient selection and appropriate training, the experienced clinician

can shorten treatment for the edentulous jaw by implementing immediate loading with fixed prostheses. Immediate loading can shorten treatment time, provide immediate restoration of function and esthetics, and mitigate the psychological impact of complete edentulism.[3] Taking into consideration that the majority of completely edentulous patients belong to older age groups, the shortening of treatment time would appear to be an additional advantage in clinical treatment and for patient acceptance.[56,57]

Various prerequisites for applying immediate loading have been reported in the literature. Primary stability has been advocated as one of the most important factors for successful osseointegration. Based on the 45 studies on immediate loading included in this review, one of the prerequisites reported by the majority of authors was the observation of an insertion torque of at least 30 Ncm. If resonance frequency analysis was used to assess the primary stability, an ISQ value of at least 60 was observed for immediate loading. The use of surface-modified implants has also played an important role in the favorable findings of the present report. Experimental studies have shown a stronger and more rapid bone tissue response to surface-modified implants.

The number of implants per patient varied between the research groups and loading protocols. For the edentulous maxilla it ranged from 4 to 12 implants per arch, and for the edentulous mandible from 2 to 10. One longitudinal retrospective study by Hatano et al reported on an "all-on-three" protocol for the mandible.[27] It was obvious that every implant loss would lead to prosthesis loss. The medium to high risk of bias of that study precluded any solid conclusion or recommendations on this protocol. A short-term prospective study by Cannizzaro et al reported on an "all-on-two" protocol for shortened dental arch rehabilitation in the mandible.[15] The decision was made to include this study in the meta-analysis, since it satisfied the inclusion criteria. However, the short-term follow-up of 1 year and the insufficient evidence coupled with the medium risk of bias of that study also precluded any clinical recommendation for this protocol. Immediate loading of two implants with a fixed prosthesis cannot be recommended since any implant loss will always lead to prosthesis loss as well. A number of prospective and retrospective studies on the "all-on-four" protocol documented favorable outcomes for both maxilla and mandible.[12,16,19–23,29,30] More long-term studies are necessary to assess the predictability of this protocol, since loss of one implant usually requires the refabrication of the prosthesis.

The prosthodontic design most frequently applied in the included studies was that of a one-piece prosthesis. Only a few studies reported on a small number of segmented restorations. For complete arch implant rehabilitation, the segmented design offers easier fabrication and prosthetic maintenance.[75] A recent systematic review showed that technical complications after placement of the definitive prosthesis may not affect the implants negatively but will result in an increased number of repairs and maintenance events.[2] The 10-year cumulative rate reported in this review for prostheses free of complications of 8.6% (95% CI, 7.1 to 10.3) highlights the advantage of segmenting implant fixed dental prostheses if possible. No correlation was identified between loading protocol and encountered complications between maxilla or mandible. It seems that once osseointegration has been achieved, there are many factors other than the loading protocol that may be related to biologic and technical complications.

The findings of the present systematic review are in agreement with the existing knowledge regarding immediate loading of the edentulous maxilla with full-arch fixed dental prostheses. The conclusions of the 2008 ITI Consensus Conference stated that for the edentulous maxilla, both immediate, 6 to 8 weeks post-implant placement, and conventional loading protocols with fixed prostheses were supported by the literature.[1,3] The present study corroborates these statements and is supported by 45 clinical studies (1 RCT, 28 prospective and 16 retrospective).[12–55,62]

As far as the edentulous mandible, the findings of the present review are also in agreement with those of the 2008 ITI Consensus Conference, which concluded that both immediate or early loading (early being 6 to 8 weeks after implant placement, since the definition was different in 2008 than at present) with fixed prostheses were equally as predictable as conventional loading.[1,3] No evidence had been found, however, regarding differences in early loading between the second to the sixth week post-implant placement. In the context of evidence from eight studies included in the present review, early loading (between 1 to 8 weeks post-implant placement) yields similar implant survival rates compared with immediate and conventional loading.

Caution is necessary when interpreting these findings, as there are many confounding factors that affect treatment outcomes with every loading protocol. Most importantly, the favorable outcomes reported in the dental implant literature are the results of treatments performed by clinicians with extended education, training, experience, and skill.

The advances in contemporary oral implantology coupled with patients' high esthetic expectations underscore the necessity for more factors to be included in the assessment of implant prostheses besides implant and prostheses survival.[76] Additionally, patient preference for a specific treatment option relies on the longitudinal efficacy of the option coupled with the associated cost and maintenance. However, in

spite of the obvious consequences in the success of dental implant therapy, patient-centered outcomes are frequently not addressed.[77] Most of the included articles did not present data on patient-centered outcomes. Restoration of function, esthetics, and patient satisfaction is the goal when treating the edentulous patient with dental implants, and thus new studies should report on these important parameters of implant treatment. In this context, well-defined success criteria should be established and used for assessing and reporting implant, prosthodontic, and patient-centered outcomes as well as biologic and technical complications.

CONCLUSIONS

With careful patient selection and using implants with rough surfaces, immediate loading with fixed prostheses in edentulous patients has the same effect on implant survival, failure, and complications as with early and conventional loading in maxillary and mandibular arches. For immediate loading, a minimal insertion torque of 30 Ncm is recommended. The estimated 1-year implant survival was above 99% with all three loading protocols. Caution is necessary when interpreting these results, as there are many confounding factors that affect treatment outcomes with every loading protocol. More comparative studies directly comparing different loading protocols are necessary. Longitudinal clinical studies should ideally report on complications in order to provide clinicians with reliable and thorough information for evidence-based treatment planning.

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