Loading Protocols for Implant-Supported Overdentures in the Edentulous Jaw: A Systematic Review and Meta-Analysis

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Purpose: *High survival rates have frequently been reported for immediately loaded implants. The aim of this systematic review was to compare immediately loaded with early and conventional loaded implants for overdenture treatment with regard to their 1-year survival rates.* ***Materials and Methods:*** *Systematic database (Medline, Embase, CENTRAL) and hand searches were performed to identify prospective studies reporting on loading protocols for two-piece implants with micro-rough surfaces and diameters > 3 mm. Studies were grouped according to loading protocol, jaw, number of implants per jaw, and splinting. Meta-analyses of comparative reports were performed based on the calculated risk difference (RD). Descriptive analyses included the remainder prospective studies. Two investigators extracted the data independently. Kappa statistics served to evaluate the inter-investigator agreement.* ***Results:*** *Of the 3,142 identified articles, 58 were included for data extraction. They comprised 11 studies comparing loading protocols as well as a further 47 prospective reports. Comparative studies were only available for mandibular overdentures. The meta-analysis revealed a statistical tendency to support conventional over immediate loading (RD: –0.03, 95% confidence interval: –0.06, 0.00). The descriptive analysis of studies with lower evidence demonstrated partially contradictory findings. There, reported survival rates for immediately loaded implants lay between 81.6% and 100%, but depended on the number of implants placed. Most investigators preferred verifying an initial high insertion torque (≥ 35 Ncm) or ISQ value (≥ 60) before considering an implant for an immediate or early loading protocol.* ***Conclusions:*** *Although all three loading protocols provide high survival rates, early and conventional loading protocols are still better documented than immediate loading and seem to result in fewer implant failures during the first year. Only a few prospective case series are available to document immediate loading of implants supporting an overdenture in the edentulous maxilla.* Int J Oral Maxillofac Implants 2014;29(Suppl):271–286. doi: 10.11607/jomi.2014suppl.g4.4

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Edentulism still has a high prevalence in the elderly population and is generally considered a common clinical entity. The treatment modalities for the completely edentulous jaw frequently incorporate conventional removable dentures.[1,2] However, these show functional shortcomings and are often associated with psychosocial limitations.[3,4]

The advent of osseointegrated implants has greatly enhanced the treatment outcomes in edentulous patients and has been advocated as a predictable and successful therapeutic concept for many decades.[5–7] Implant-supported overdentures, especially in the edentulous lower jaw, help restore oral function and may improve psychosocial well-being and oral health-related quality of life.[8] Rehabilitations with implant-supported overdentures are documented as reliable and cost-effective.[9,10] Mandibular overdentures with

two implants, retained by either splinted or unsplinted attachments are considered a globally accepted treatment option.[11–15] Single, implant–retained overdentures may also demonstrate adequate success in the completely edentulous mandible, yet long-term data are still missing.[16–19]

In the early days of implantology, Brånemark and collaborators empirically advocated an unloaded healing period of 3 months for the mandible and 6 months for the maxilla following implant placement to facilitate an uneventful osseointegration, avoid soft tissue encapsulation, and improve implant survival rates.[20,21] Successful osseointegration has been linked to sound primary stability at the time of surgery and the prevention of subsequent micromovements of the implant during the healing phase.[22] However, researchers have demonstrated that osseointegration can be achieved with early or immediate loading protocols if micromotion is contained within the suggested limits.[23] Most patients perceive the period between tooth loss and definitive rehabilitation as traumatic and uncomfortable because provisional prostheses mostly provide compromised function and esthetics.[24] Substantial benefits may be derived by shortening the provisional prosthetic period as well as reducing treatment duration.[24,25]

The immediate loading of implants in the edentulous mandible is not a new idea.[26,27] Developments such as improved implant design contributed towards increased primary implant stability,[28,29] and implants with osseoinductive surfaces promised faster osseointegration[30]; hence the concept of immediate and early loading gained popularity. Since then, high survival rates for immediately loaded splinted and unsplinted implants have frequently been reported.[24] The splinting of immediately loaded implants was advocated in order to avoid peak forces on the bone-implant interface during the healing phase and thus improve implant survival rates.[31] However, the literature is not conclusive as survival rates may not only depend on the loading protocol, but also on the number of implants, the attachment system, or the implant surface.[18,32–36]

The purpose of this systematic review and meta-analysis is to test the hypothesis that immediate loading protocols for implant-supported overdentures show 1-year survival rates similar to early or conventional loading protocols.

MATERIALS AND METHODS

This systematic review was conducted in accordance with the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) guidelines.[37]

The PICO (population, intervention, comparison, outcome) focus question formulated for this review was: "In edentulous jaws with implant-supported overdentures, what is the effect of immediate implant loading versus early or conventional loading on the 1-year implant survival?"

Search Strategy and Selection of Studies

The electronic databases CENTRAL, Embase, and PubMed were searched for relevant scientific reports published in English, German, and French between January 1980 and November 30, 2012 (Table 1).

Reference lists from review articles were screened for eligible studies to complete the hand search. Requests were posted on online forums such as the ITI-net, the IADR LinkedIn group, and ResearchGate. Finally, personal contacts were used to identify relevant unpublished studies.

Two investigators (MS and MS) performed the electronic queries based on a search design devised by an expert on database searches (FRH). Since the available research on this topic is limited, it was decided to include randomized clinical trials (RCTs), prospective case series, and prospective cohort and case control studies. Publications reporting on the same patient pool were identified and in such instance, only the most recent publication was considered.

Data Extraction

Two investigators (MS and MS) independently screened the titles and abstracts of the identified studies. Eligibility for inclusion of studies was confirmed by mutual agreement; in case of disagreement the senior investigator (FM) was consulted. Full-text analysis and data extraction was performed after agreement on the final list. The following information was extracted: name of author(s) and year of publication, study design, follow-up period in months, number of implants placed, number of implants failed, jaw, time point of failure, number of drop-outs, reported cumulative survival rates (CSR%), time of loading, overdenture attachment type, and number of implants supporting the overdenture. The two investigators performed data extraction independently and were reciprocally blinded. If relevant data could not be extracted from the full-text manuscript, the corresponding author was contacted. Those studies were only included if the relevant information was provided.

Quality Assessment

The methodological quality of case control and cohort studies was assessed with the Newcastle-Ottawa scale (NOS).[38] The Cochrane collaboration's tool for assessing the risk of bias was employed for the assessment of RCTs.[39]

Table 1 Systematic Search Strategy

Focus question:	In edentulous jaws with implant-supported overdentures, what is the effect of immediate implant loading versus early or conventional loading on the 1-year implant survival?
Search strategy	
Population	# 1 – (Removable dental prostheses* [all fields]) OR (Overdentures [all fields]) OR (Implant supported Overdentures [all fields]) OR (Implant assisted Overdentures [all fields]) OR (Overdentures [MeSH] OR Jaw, Edentulous [MeSH]) OR (Mouth, Edentulous [MeSH])
Intervention or exposure	#2 – (dental implantation, endosseous [MeSH]) OR (dental implants [MeSH]) OR (implantation* [all fields]) OR (implant [all fields]) OR (implants [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]) OR (French [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	Dental implants placed in completely edentulous human jaws Implant-supported overdenture prostheses Must specify the study design, number of patients, number of implants placed and failed, time of loading and number of dropouts Implant type: two-piece, rough-surfaced solid screws Patients must have been clinically examined during recall
Exclusion criteria	Retrospective studies Studies with observation periods of less than 12 months post loading Implants were placed in irradiated bone, or augmented bone Reports with sample size of less than 10 cases Implant diameter less than 3 mm

Outcome Measures

The primary outcome measure in this review was the effect of the loading protocol on the 1-year implant survival. Implant survival or success was defined as the absence of mobility, pain, recurring peri-implant infection and continued radiolucency around the implant.[40] The secondary outcome measure was the time point of implant failure. Furthermore, the clinical criteria for choosing either immediate or early loading of implants were extracted from the manuscripts.

The definitions of loading protocols used in this review are in agreement with the latest Cochrane review from Esposito and coworkers.[24,41] Thus, immediate loading was defined as functional loading within 7 days following implant placement. Functional loading between 7 days and 8 weeks was specified as early loading; implant loading after 8 weeks following placement was considered as conventional loading.

For the purpose of this review a worst-case scenario was employed. Hence, implants in participants lost to follow-up were considered as failures. The failures were scored on the implant level.

Statistical Analysis

The agreement of data extraction between the two investigators was assessed by kappa (κ) statistics.

A meta-analysis was performed for the prospective comparative studies (RCTs and cohort studies for mandibular overdentures) using the STATA command "metan."[42] Therefore, risk differences (RD) and the corresponding 95% confidence intervals (95% CI) for the implant survival at 1 year were calculated for the sets of studies comparing:

- Set 1: Immediate and early loading
- Set 2: Immediate and conventional loading
- Set 3: Early and conventional loading

A weighted average across these studies was provided according to a fixed-effect model; study weight corresponded to 1/study variance.[43] Heterogeneity between studies was assessed with the I^2 statistic. It describes the percentage of variation across studies that is due to heterogeneity, rather than chance.[42] A specialist bio-statistician and physician (FRH) performed

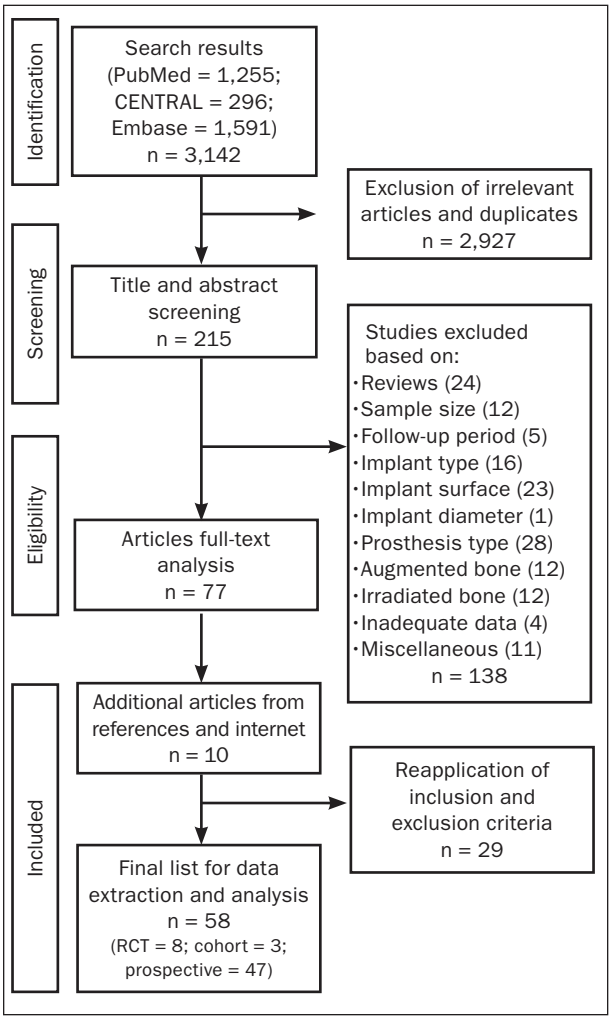

Fig 1 The search flow diagram for the systematic literature search and selection process.

Table 2 Studies Comparing Loading Protocols for Implant-Supported Overdentures in Completely Edentulous Mandibles

Study	Year	Study type	Loading protocols compared	Loading time (d)
Romeo et al[31]	2002	RCT	Immediate	2
			Conventional	90
Assad et al[48]	2007	RCT	Immediate	4
			Conventional	120
Stephan et al[35]	2007	Prospective cohort	Immediate	1
			Conventional	90
Alfadda et al[47]	2009	Prospective cohort	Immediate	0
			Conventional	120
Enkling et al[50]	2010	RCT	Immediate	0
			Conventional	90
Elsyad et al[49]	2012	RCT	Immediate	0
			Conventional	90
Turkyilmaz et al[51]	2012	RCT	Immediate	7
			Conventional	90
Røynesdal et al[55]	2001	Prospective cohort	Early	21
			Conventional	90
Ma et al[54]	2010	RCT	Early	14
			Conventional	84
Cannizzaro et al[52]	2008	RCT	Immediate	0
			Early	42
Gadallah et al[53]	2012	RCT	Immediate	7
			Early	42

RCT = randomized controlled trial; NR = not reported.

all statistical tests, using the STATA Statistical Software release 12.1.

RESULTS

Data Selection and Identification

The electronic database searches identified a total of 3,142 articles (CENTRAL = 296, Embase = 1,591, PubMed = 1,255). The flow of information through the different phases of the systematic review process is reported according to the PRISMA guidelines in Fig 1.[37] From the electronically identified reports (n = 3,142), cross-references (n = 9) and online discussion forums (n = 1), 77 full texts were analyzed. From those, three relevant RCTs assessing immediate loading in implant-supported overdentures were excluded because one had an observation period of only 6 months,[44] while the other two reported on machined surface implants.[45,46] This process resulted in a final inclusion of 58 studies for data extraction and analysis. The final list included eight RCTs and three prospective cohort studies comparing loading protocols for implant-supported overdentures in the edentulous jaw[31,35,47–55] (Table 2). The remaining 47 prospective studies were case series, RCTs, or cohort studies not comparing loading protocols[16–19,25,33,34,36,56–94] (Tables 3 to 6).

Prospective comparative studies (RCTs, cohort studies) were available only for mandibular implant-supported overdentures (Table 2). Every attempt was made to eliminate publication bias; hence, some studies were excluded because they reported data from the same cohort at different time points. In case of doubt, the corresponding author was contacted. If double publication was confirmed, only the most recent report was included in the analysis.

Arch	Brand	Attachment type	Observation period (mo)	Patients	Implants/ patient	Implants placed	Implants failed (at 1 y)	Total survived (failed)	Reported survival rate (%)
Mandible	Straumann	Bar	24	10	4	40	0	40 (0)	100
				10	4	40	1	39 (1)	97.5
Mandible	Paragon	Bar	24	5	4	20	0	20 (0)	100
				5	4	20	0	20 (0)	100
Mandible	Nobel Biocare	Bar	24	17	3	51	0	51 (0)	100
				9	3	27	0	27 (0)	100
Mandible	Nobel Biocare	Bar	60	35	2	70	2	68 (2)	98.4
				42	2	111	3	108 (3)	98.2
Mandible	SI Cace	Bar	36	16	2	32	0	32 (0)	100
				16	2	32	0	32 (0)	100
Mandible	ImplantDirect	Ball	36	18	2	36	2	30 (6)	NR
				18	2	36	0	30 (6)	NR
Mandible	Nobel Biocare	Ball	84	13	2	26	0	26 (0)	100
				13	2	26	0	26 (0)	100
Mandible	Straumann	Ball	24	11	2	22	0	22 (0)	100
				10	2	20	0	20 (0)	100
Mandible	Straumann	Ball	120	48	2	96	0	96 (0)	100
	Southern			24	2	48	0	48 (0)	100
Mandible	Swiss Plus	Bar	12	30	2	60	0	60 (0)	100
				30	2	60	2	58 (2)	96.7
Mandible	Swiss Plus	Ball	12	6	2	12	0	12 (0)	100
				6	2	12	0	12 (0)	100

The inter-investigator agreement for the data extraction was considered very good ($0.86 < \kappa < 1.00$).

Quality Assessment

The risk of extracting biased results from the comparative studies was scored as low for four studies, and only one RCT was appraised with a high risk of bias (Tables 7a and 7b).

Meta-Analysis of High Evidence Comparative Studies

The meta-analysis of the two studies comparing immediate and early loading (set 1) failed to demonstrate a difference between treatment modalities (RD: 0.03; 95% CI: –0.03, 0.08; Fig 2).[52,53]

The forest plot for the studies comparing immediate and conventional loading (set 2) combined the results of seven studies.[31,35,47–51] The analysis showed a statistical tendency in favor of the conventional loading protocols with regard to the 1-year implant survival (RD: –0.03; 95% CI: –0.06, 0.00; Fig 3).

The two studies in set 3 (early versus conventional loading)[54,55] reported no implant failures in either treatment arm (Table 2), thus a meta-analysis was redundant.

Descriptive Analysis of Studies Not Comparing Loading Protocols

Mandibular Overdentures with Splinted Implants. Seven prospective studies,[36,56,61,65–67,85] including some RCTs not comparing loading protocols, reported survival rates between 94.4% and 100% for immediately loaded and splinted implants in a follow-up period of 12 to 96 months. Those studies evaluated a total of 924 implants of which 7 had failed or the patient had dropped out after 1 year. Lethaus et al[83] were the only authors to report on early loading of four-implant bars

Table 3 Studies on Loading Protocols for Mandibular Implant-Supported Overdentures with Splinted Attachments

Study	Year	Loading time (d)	Brand	Attachment type	Observation period (mo)	Patients
Immediate						
Gatti et al[56]	2000	0	Straumann	Bar	25–60	21
Chiapasco and Gatti[61]	2003	1	Straumann, Nobel, Ha-Ti, Frialoc	Bar	36–96	82
Stricker et al[36]	2004	1	Straumann	Bar	24–36	10
Degidi and Piattelli[65]	2005	2	XiVe	Bar	24	14
Weischer et al[66]	2005	6	Frialoc	Bar	12–29	18
Martínez-González et al[67]	2006	2	Defcon	Bar	12–24	20
Stoker and Wismeijer[85]	2011	0	Straumann	Bar	12–40	124
Total (7)	2000–2011	0–6		Splinted	12–96	289
Early						
Lethaus et al[83]	2011	42	Straumann	Bar	12–60	14
Total (1)	2011	42		Splinted	12–60	14
Conventional						
Gotfredsen and Holm[57]	2000	90	Astra	Bar	12–60	11
Heydenrijk et al[58]	2002	90	Straumann	Bar	12	20
Karabuda et al[59]	2002	90	Frialit, PittEasy	Bar	12–72	18
Meijer et al[64]	2004	90	Straumann	Bar	12–60	30
Cakarer et al[78]	2011	60	Straumann, Nobel, Frialit, Swiss-Plus, Biohorizons, Bio-Lok	Bar	12–60	9
Heschl et al[81]	2013	90	XiVe	Bar	12–60	39
Mangano et al[84]	2011	90	Leone	Bar	12–60	38
Elsyad[92]	2012	90	ImplantDirect	Bar	36	30
Guljé et al[87]	2012	90	Astra	Bar	12	12
Total (9)	2000–2012	90		Splinted	12–72	207

NR = not reported.

in a study that included 60 implants. Of those, two had failed during the first year; the authors reported a survival rate of 96.7% (12- to 60-month observation period). A further nine studies[57–59,64,78,81,84,87,92] described the results of conventional loading of bars supported by two, three, or four implants. The survival rates were reported to be 96% to 100% (12 to 72 months observation period), for a total of 599 placed implants, of which seven had failed at 1 year (Table 3).

Mandibular Overdentures with Unsplinted Implants. Nine studies[17,18,33,34,68,70,74,75,86] with observation periods of 12 to 60 months and with one to four unsplinted implants in the mandible employed immediate loading concepts. Of the 520 implants placed in total, 22 had failed or the patients had dropped out during the first year after loading. Kronstrom and coworkers[17] compared within a RCT immediate loading of a single-implant versus two-implant overdentures, with reported 1-year survival rates of 82.4% and 81.6%, respectively. Thus, immediately loaded single implants for mandibular overdentures show reduced 1-year survival rates when compared to more conservative procedures like the splinting of two or more implants.

Five studies[16,19,73,77,90] evaluated the early loading of mandibular overdentures with reported survival rates of 96.6% to 100% during a 12- to 60-month period. The total number of implants placed in this group was 424, engaging either one or two implants to support Locator- or ball-retained overdentures, and with 14 failing within a 12-month period. In one of these studies, Walton and her colleagues[19] compared one- versus two-implant overdentures and reported no implant losses for the one-implant group versus 7.9% failures in the two-implant group after 1 year.

Eleven studies[57,59,62,63,71,76,78,79,91,93,94] reported on a total of 661 placed implants, loaded conventionally and supporting one- to four-implant overdentures. Of those, 21 failed within the first year after loading. The reported survival rates ranged from 90.4% to 100% during a 12 to 120 month observation period. The studies comprised of telescopic, ball, and Locator attachments (Table 4).

Implants/ patient	Implants placed	Implants failed (at 1 y)	Total survived (failed)	Reported survival rate (%)
4	84	0	73 (11)	96
4	328	0	296 (32)	96.1
2	20	0	20 (0)	100
4	92	0	92 (0)	100
4	72	4	68 (4)	94.4
4	80	0	80 (0)	100
2	248	3	245 (3)	98.8
2 or 4	924	7	874 (50)	94.4–100
4	60	2	54	96.7
4	60	2	54 (6)	96.7
2	22	0	22 (0)	100
2	40	0	38 (2)	NR
2 or 4	44	1	43 (1)	NR
2	60	0	58 (2)	100
3 or 4	33	0	32 (1)	NR
4	156	1	128 (26)	99.4
4	136	2	134 (2)	98.6
2	60	1	40 (20)	NR
4	48	2	46 (2)	96
2 or 3 or 4	599	7	543 (56)	96–100

Maxillary Overdentures with Splinted Implants. Three studies dealt with the immediate loading of implants placed in the maxilla.[25,65,72] They employed immediate loading with bars on four or five implants. A total of 312 implants were followed over a period of 12 to 24 months; the authors reported survival rates between 97.1% and 98.7%. Of the 312 implants placed, 6 had failed at 1-year postinsertion.

Van Assche et al[89] were the only group that reported prospectively on the early loading in the maxilla. Of 72 placed implants, which supported bar–retained overdentures, one short implant of 6 mm length failed during the first year.

Conventional loading of four-, five-, or six-implant bar-retained overdentures was described in five studies.[60,78,82,84,88] Of a total of 699 placed implants, 12 failed within the first year after loading. Survival rates between 97.4% and 99.3% with observation periods of 12 to 108 months were reported (Table 5).

Maxillary Overdentures with Unsplinted Implants. Eccellente et al[80] studied the immediate loading of four implants in the maxilla using telescopic attachments. In this study, 180 implants were placed and with 4 failing within the first year after loading. The authors reported a survival rate of 97.8% over a 12- to 54-month observation period.

Weng and Richter[69] also used telescopic attachments, but for two-implant maxillary overdentures with an early loading protocol. Of the 28 implants placed none was lost during the first year. However, five implants had failed at the end of a 12- to 48-month observation period.

Two studies[62,78] report in part on the conventional loading of unsplinted implants in the edentulous maxilla with telescopic and ball attachments on two or four implants. After the first year, all 28 placed implants were still in place. However, during the remaining observation periods of 12 to 120 months, four implants had failed (Table 6).

Clinical Criteria for Applying Specific Loading Protocols. Few studies adopting conventional loading were specific in assessing abutment torque values (in most cases 15 to 35 Ncm) before loading.[31,35,63,79] Harder and colleagues[94] conventionally loaded single-implant retained overdentures after verifying the implant mobility with Periotest values of –7 to –4.

Most studies describing immediate or early loading protocols advocated a specific implant insertion torque value of ≥ 30 Ncm.[16–18,25,31,34–36,52,66,72,73,75,83,85,86,90] Lower insertion torque values between 15 to 25 Ncm have also been advocated prior to immediate or early loading in a few studies.[17,33,89] Wittwer et al[70] applied Periotest values ranging between –7 to –1 for successfully employing an immediate loading protocol in the mandible (Table 8).

Resonance frequency analysis has been used in few studies for the assessment of implant stability prior to loading.[16,18,65,72] Authors have maintained an ISQ value between 60 to 75.1 prior to immediate or early loading.[16,18,65,72]

DISCUSSION

Critique of the Method

In this review, the attempt was made to identify and critically review the highest available evidence for implant loading protocols in implant-supported overdentures for patients with edentulous jaws. Today, a meta-analysis combining the results of RCTs is regarded as the highest evidence level.[95] However, the current systematic literature search provided only eight RCTs and a further three nonrandomized comparative studies for the three possible comparisons of loading protocols.

Table 4 Studies on Loading Protocols for Mandibular Implant-Supported Overdentures with Unsplinted Attachments

Study	Year	Loading time (d)	Brand	Attachment type	Observation period (mo)	Patients
Immediate						
Ormianer et al[68]	2006	0	Zimmer	Ball	12–30	10
Marzola et al[34]	2007	0	Nobel	Ball	12	17
Wittwer et al[70]	2007	0	Ankylos	Telescope	12–24	25
Eccellente et al[74]	2010	0	Ankylos	Telescope	12–60	39
Kronstrom et al[17]	2010	0	Nobel	Ball	12	17
Kronstrom et al[17]	2010	0	Nobel	Ball	12	19
Liao et al[75]	2010	0	Nobel	Ball	12	10
Liddelow and Henry[18]	2010	0	Nobel	Ball	12–36	35
Büttel et al[33]	2012	0	Straumann	Ball	24–36	20
Grandi et al[86]	2012	0	JD Evolution	Ball	12	42
Total (9)	2006–2012	0		Unsplinted	12–60	234
Early						
Walton et al[19]	2009	42	Straumann	Ball	12	42
Walton et al[19]	2009	42	Straumann	Ball	12	44
Cehreli et al[73]	2010	42	Straumann, Nobel	Ball	60	28
Al-Nawas et al[77]	2012	42	Straumann	Locator	12	91
Alsabeeha et al[16]	2011	42	Southern, Neoss	Ball and locator	12	36
El-Sheikh et al[90]	2012	28	Straumann	Ball	12	20
Total (5)	2009–2012	28–42		Unsplinted	12–60	261
Conventional						
Gotfredsen and Holm[57]	2000	90	Astra	Ball	12–60	15
Karabuda et al[59]	2002	90	Frialit, PittEasy	Ball	12–40	18
Lambrecht et al[62]	2003	112	Straumann	Ball	120	11
Lambrecht et al[62]	2003	112	Straumann	Telescope	120	23
Cune et al[63]	2004	117	Frialoc	Ball	12	18
Cooper et al[71]	2008	90	Astra	Ball	6	59
Kleis et al[93]	2010	105	3i-Biomet	Ball, L, O-ring	12	60
Akoglu et al[76]	2011	56	Straumann, Astra, Zimmer	Ball	60	36
Cakarer et al[78]	2011	60	Straumann, Nobel, Frialit, Swiss-Plus, Biohorizons, Bio-Lok	Ball	12–60	19
de Kok et al[79]	2011	56	Astra	Ball	12	10
Harder et al[94]	2011	60	Camlog	Ball	35–52	11
El-Sheikh et al[91]	2012	70	Straumann	Locator	24	10
El-Sheikh et al[91]	2012	70	Straumann	Locator	24	10
Total (11)	2000–2012	56–117		Unsplinted	12–120	300

NR = not reported.

These studies were pooled in order to have sufficient data for performing a meta-analysis in accordance with a previous meta-analysis on the same topic.[96] When interpreting the results, it also has to be considered that little evidence is available on the loading protocols for implant-supported overdentures in the treatment of the edentulous maxilla.

Retrospective studies were excluded from this systematic review. One has to distinguish between several types of bias in retrospective reports. Firstly, patient related parameters might only be retrieved from patient records. Especially in university hospitals, record-keeping is difficult because it often involves several persons due to high staff turnover as well as the fact that implant patients are often seen by different specialists. Secondly, investigated parameters are mostly not predefined, thus relevant data may not be documented. Furthermore, handling of missing data is rarely reported and

Implants/ Patient	Implants placed	Implants failed (at 1 y)	Total survived (failed)	Reported survival rate (%)
2	20	1	19 (1)	96.4
2	34	0	34 (0)	100
4	88	5	83 (5)	97.7
4	156	2	154 (2)	98.7
1	17	3	14 (3)	82.4
2	38	7	31 (7)	81.6
2	20	4	16 (4)	94
1	23	0	23 (0)	100
2	40	0	38 (2)	100
2	84	0	84 (0)	100
1 or 2 or 4	520	22	496 (24)	81.6–100
1	42	0	42 (0)	NR
2	88	7	81 (7)	NR
2	56	0	44 (12)	100
2	182	5	177 (5)	96.6
1	36	2	34 (2)	
1	20	0	20 (0)	100
1 or 2	424	14	398 (26)	96.6–100
2	31	1	30 (1)	100
2 or 4	52	1	51 (1)	NR
2	22	0	22 (0)	100
> 2	91	0	85 (6)	NR
2	36	4	32 (4)	93.9
2	118	5	98 (20)	95.9
2	120	8	112 (8)	90.4
2	72	0	72 (0)	100
2	38	0	38 (0)	NR
2	20	0	20 (0)	100
1	11	1	10 (1)	NR
2	20	0	20 (0)	100
3	30	1	29 (1)	98
1/2/3/4	661	21	619 (42)	90.4–100

such patient records might have been entirely excluded. Thirdly, it might be unclear on which basis patients are selected for a retrospective analysis. They might be included for convenience and availability. Patients with the worst outcomes might refuse further cooperation or seek treatment elsewhere and no longer be available for follow-up.[97] Therefore retrospective studies might be subject to an inclusion bias, underestimating implant failures or other adverse events.

Interpretation of Findings

The current systematic review found some contradicting evidence between the comparative studies and those prospective studies, which did not compare different loading protocols. Whereas the meta-analysis of studies with matched intervention groups shows a tendency to favor conventional loading protocols for the overdenture treatment of the edentulous mandible, some of the remainder studies reported better survival rates for immediate loading. Although mostly not reported on, patient selection for innovative immediate loading protocols may be biased by pressure for success, leading to selection of patients with few or no risk factors such as smoking, diabetes, or poor bone quality. As there is no independent control group in these studies, the inclusion bias remains unidentified. This may result in excellent success rates, which may not be reproducible in everyday practice where patients with risk factors are encountered frequently. In contrast, the comparative high evidence studies with matched intervention groups statistically tend to favor conventional loading and also found no significant difference between early and conventional loading. This discrepancy highlights the importance of developing well-designed research protocols and carefully conducting clinical studies in order to provide a high level of evidence for conscious clinical decision-making.

To address concerns about statistical versus clinical significance the results were reported as relative risks/risk differences along with their 95% CI. They represent a "common measure of combined statistical and clinical significance because it provides a direct assessment of the treatment effect size."[98]

Whereas numerous advantages of immediate loading were mentioned in the introduction, shortcomings have also to be discussed. Astonishingly, few patient-centered benefits of immediate implant loading in overdenture treatment are documented. Most studies aim to demonstrate the equality of the procedure compared to conventional loading with regard to implant survival or peri-implant bone loss. However, patients will benefit earlier from the stabilization of their denture than with conventional loading protocols.[61] There are further clinical considerations for immediate loading protocols which are also poorly investigated, but deserve mentioning. When the superstructure is inserted on the day of surgery or shortly after, the soft tissues are still traumatized from surgery and will in some cases quickly change morphology in the weeks following the intervention.[85] Thus, relines are frequently necessary during this adaptive period with implant-supported overdentures,[52] creating additional cost and multiple clinical visits.[99] Another shortcoming of immediate loading is the necessity to take an impression when the sutures are still in place and the

Table 5 Studies on Loading Protocols for Maxillary Implant-Supported Overdentures with Splinted Attachments

Study	Year	Loading time (d)	Brand	Attachment type	Observation period (mo)	Patients
Immediate						
Degidi and Piattelli[65]	2005	2	XiVe	Bar	24	20
Cannizzaro et al[25]	2007	0	Zimmer	Bar	12	12
Pieri et al[72]	2009	2	Nobel	Bar	12	22
Total (3)	2005–2009	0–2		Splinted	12–24	54
Early						
Van Assche et al[89]	2012	42	Straumann	Bar	24	12
Total (1)	2012	42		Splinted	24	12
Conventional						
Mericske-Stern et al[60]	2002	120	Straumann	Bar	12–108	41
Cakarer et al[78]	2011	60	Straumann, Nobel, Frialit, Swiss-Plus, Biohorizons, Bio-Lok	Bar	12–60	1
Katsoulis et al[82]	2011	90	Nobel	Bar	24	28
Mangano et al[84]	2011	120	Leone	Bar	12–60	34
Slot et al[88]	2012	90	Astra	Bar	12	50
Total (5)	2002–2012	60–120		Splinted	12–108	154

NR = not reported.

Table 6 Studies on Loading Protocols for Maxillary Implant-Supported Overdentures with Unsplinted Attachments

Study	Year	Loading time (d)	Brand	Attachment type	Observation period (mo)	Patients
Immediate						
Eccellente et al[80]	2011	0	Ankylos	Telescope	12–54	45
Total (1)	2011	0		Unsplinted	12–54	45
Early						
Weng and Richter[69]	2007	42	3i-Biomet	Telescope	12–48	14
Total (1)	2007	42		Unsplinted	12–48	14
Conventional						
Lambrecht et al[62]	2003	168	Straumann	Telescope	120	1
Lambrecht et al[62]	2003	168	Straumann	Ball	120	2
Cakarer et al[78]	2011	60	Straumann, Nobel, Frialit, Swiss-Plus, Biohorizons, Bio-Lok	Ball	12–60	10
Total (2)	2003–2011	60–168		Unsplinted	12–120	13

NR = not reported.

Table 7a Results of Quality Assessment of the Comparative Studies Analyzed (Newcastle – Ottawa Scale for assessment of Cohort Studies)

Study	Year	Design	Selection (max 4*)	Comparability (max 3*)	Outcome (max 3*)
Røynesdal et al[55]	2001	Cohort	* * *	* * *	* *
Stephen et al[35]	2007	Cohort	* *	* *	* *
Alfadda et al[47]	2009	Cohort	* * *	*	* *

Implants/ patient	Implants placed	Implants failed (at 1 y)	Total survived (failed)	Reported survival rate (%)
4	161	2	159 (2)	98.7
4	48	1	47 (1)	97.9
4 or 5	103	3	100 (3)	97.1
4 or 5	312	6	306 (6)	97.1–98.7
6	72	1	61 (11)	NR
6	72	1	61 (11)	NR
4	173	6	153 (20)	98.3
4	4	0	4 (0)	NR
4 or 5 or 6	120	1	119 (1)	99.2
4	152	2	148 (4)	97.4
4 or 6	250	3	247 (3)	99.3
4 or 5 or 6	699	12	671 (28)	97.4–99.3

Implants/ patient	Implants placed	Implants failed (at 1 y)	Total survived (failed)	Reported survival rate (%)
4	180	4	176 (4)	97.8
4	180	4	176 (4)	97.8
2	28	0	28 (0)	NR
2	28	0	28 (5)	NR
4	4	0	4 (0)	100
2	4	0	4 (0)	100
2	20	0	16 (4)	NR
2 or 4	28	0	24 (4)	Up to 100

surgical site might still be vulnerable. The latter will be contaminated with impression material or, even worse, with methyl-methacrylate resin monomer in case the attachments are engaged by means of direct polymerization. Last but not least, after surgery patients may be exhausted and traumatized and may not wish to extend their clinical appointment beyond the most necessary procedures. This might be especially true for overdenture treatment, because edentulism increasingly occurs in old age when the acceptance of long and invasive treatments is largely diminished[100] and treatment sessions have to be tailored to the patient's compliance, fragility, and general health.[101]

Early loading, on the other hand, eliminates these shortcomings to a great extent without challenging the patient's compliance with several months of compromised function. The patient has recovered from surgery, the sutures are removed, the incision has healed, and the vulnerable interface between implant and peri-implant tissues is no longer at risk from contamination or trauma. However, it remains unclear if early loading avoids the unfavorable necessity of an early reline. Early loading has become more frequently used with the advent of improved implant surfaces and the results of the present review support adopting this protocol.[102] It may be an acceptable compromise, as it alleviates the disadvantages of immediate (lower implant survival rate) and conventional loading protocols (prolonged compromised function).

This review suggests only a tendency for the superiority of one loading protocol with regard to the 1-year implant failure rate, as appropriate clinical studies are too few to reach statistical significance. Nevertheless, all three proposed loading protocols present excellent survival rates which are in the range of or superior to other state-of-the-art treatment options in dentistry. Therefore, other factors like patient-centered benefits and disadvantages or the costs of prosthodontic aftercare may also be considered for clinical decision-making with regard to loading protocol for an individual patient.

Table 7b Results of Quality Assessment of the Comparative Studies Analyzed (The Cochrane Collaboration tool for the assessment of the risk of bias for Randomized Controlled Trials)

Study	Year	Design	Risk of Bias
Romeo et al[31]	2002	RCT	Unclear
Assad et al[48]	2007	RCT	Unclear
Canizzarro et al[52]	2008	RCT	Low
Enkling et al[50]	2010	RCT	Low
Ma et al[54]	2010	RCT	Low
Elsyad et al[49]	2012	RCT	Unclear
Gadallah et al[53]	2012	RCT	Low
Turkyilmaz et al[51]	2012	RCT	High

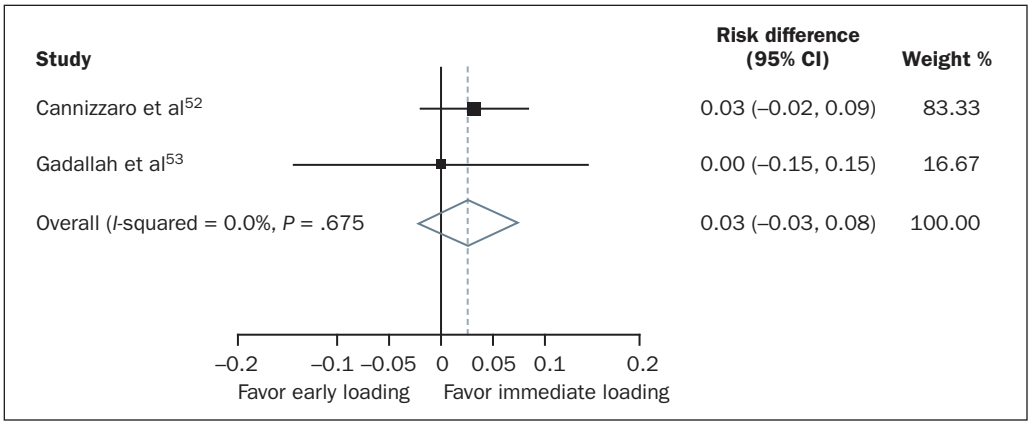

Fig 2 Forest plot for the comparison of early versus immediate loading protocols with regard to 1–year implant survival.

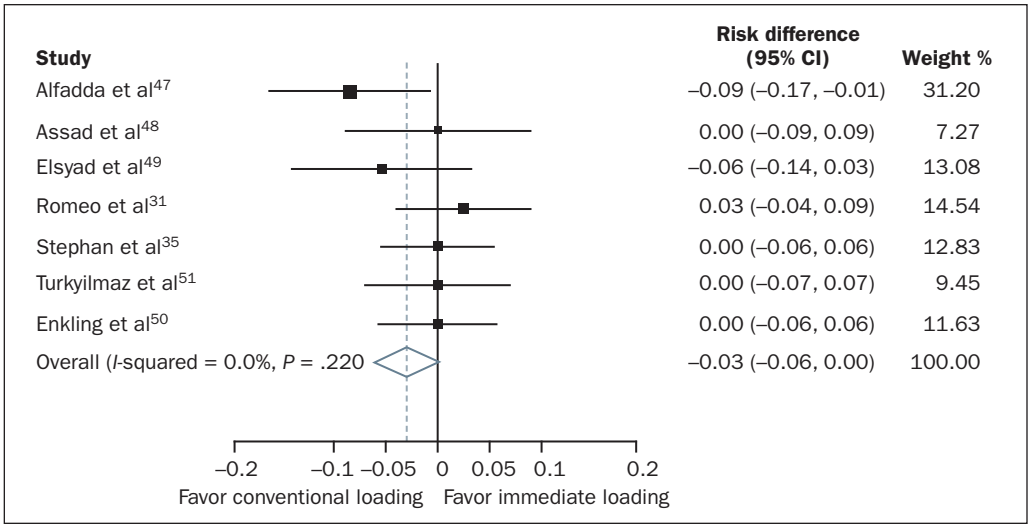

Fig 3 Forest plot for the comparison of conventional versus immediate loading protocols with regard to 1–year implant survival.

Individual Decision-Making for a Particular Loading Concept

Recommendations for the use of either immediate or early loading concepts were proposed based on clinical parameters like bone quality, primary stability of more than 35 Ncm insertion torque, or resonance frequency analysis (RFA) testing. This review was able to identify that most investigators would prefer to establish an initial high insertion torque (≥ 35 Ncm) or ISQ value (≥ 60) before engaging the implant for an immediate or early loading protocol. These items might be of special interest in immediate loading protocols to avoid overloading of the implant-bone interface early after implant placement. High primary stability is considered to be beneficial when the implant is prone to early instability due to bone remodeling.[103] The empirical evidence of the reviewed literature with regard to those parameters seems to result in high survival rates of the immediately loaded implants.

On the other hand, most studies with conventional loading protocols assessed the implant stability with either a subjective clinical assessment and/or the standard success criteria prior to abutment connection and loading. There, high primary stability seems to be less important because of the prolonged healing time and is based on the experience in implant dentistry from the last four decades.[20]

Table 8 Studies Reporting on Clinical Criteria Applied Prior to Implant Loading

Study	Year	Loading protocol	Arch	Criteria applied prior to immediate/early loading
Romeo et al[31]	2002	Immediate	Mandible	Insertion torque ≥ 35 Ncm
Stricker et al[36]	2004	Immediate	Mandible	Insertion torque ≥ 35 Ncm
Degidi and Piattelli[65]	2005	Immediate	Mandible	RFA ISQ value = 60
Degidi and Piattelli[65]	2005	Immediate	Maxilla	RFA ISQ value = 60
Weischer et al[66]	2005	Immediate	Mandible	Insertion torque ≥ 30 Ncm
Cannizzaro et al[25]	2007	Immediate	Maxilla	Insertion torque ≥ 45 Ncm
Marzola et al[34]	2007	Immediate	Mandible	Insertion torque between 20–50 Ncm
Stephan et al[35]	2007	Immediate	Mandible	Insertion torque ≥ 30 Ncm
Wittwer et al[70]	2007	Immediate	Mandible	Periotest values between –7 to –1
Cannizzaro et al[52]	2008	Immediate	Mandible	Insertion torque ≥ 48 Ncm
Pieri et al[72]	2009	Immediate	Maxilla	Insertion torque ≥ 30 Ncm; RFA ISQ value ≥ 60
Enkling et al[50]	2010	Immediate	Mandible	Insertion torque ≥ 35 Ncm
Kronstrom et al[17]	2010	Immediate	Mandible	Insertion torque values between 20–45 Ncm
Liao et al[75]	2010	Immediate	Mandible	Insertion torque ≥ 35 Ncm
Liddelow and Henry[18]	2010	Immediate	Mandible	Insertion torque ≥ 45 Ncm; RFA ISQ value ≥ 60
Stoker and Wismeijer[85]	2011	Immediate	Mandible	Insertion torque ≥ 35 Ncm
Büttel et al[33]	2012	Immediate	Mandible	Insertion torque ≥ 25 Ncm
Grandi et al[86]	2012	Immediate	Mandible	Insertion torque ≥ 40 Ncm
Cannizzaro et al[52]	2008	Early	Mandible	Insertion torque ≥ 48 Ncm
Cehreli et al[73]	2010	Early	Mandible	Abutment torque = 35 Ncm
Alsabeeha et al[16]	2011	Early	Mandible	Insertion torque ≥ 45 Ncm; RFA ISQ value 66.6–75.1
Lethaus et al[83]	2011	Early	Mandible	Abutment torque ≥ 35 Ncm
El-Sheikh et al[90]	2012	Early	Mandible	Insertion torque ≥ 35 Ncm
Van Assche et al[89]	2012	Early	Maxilla	Insertion torque ≥ 15 Ncm

RFA = resonance frequency analysis; ISQ = implant stability quotient.

CONCLUSIONS

Although all three loading protocols provide high survival rates, early and conventional loading protocols are still better documented than immediate loading and seem to result in fewer early implant failures compared to immediate loading.

Immediate loading of single implants for mandibular overdentures cannot be recommended until further evidence is available.

There are only a few prospective case-series available to document the feasibility of immediate loading of implants in the maxilla, but employing four or more implants seem to provide high survival rates.

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