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A Systematic Review of Clinical Outcomes on Patients Rehabilitated with Complete-Arch Fixed Implant-Supported Prostheses According to the Time of Loading

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Systematic review; fixed prosthesis; edentulous patients; loading protocols; dental implants.

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Abstract

Purpose: To perform a systematic review on studies assessing clinical outcomes in patients rehabilitated with complete-arch fixed implant-supported prostheses according to the time of loading.

Materials and Methods: Data obtained from patient and clinical outcomes, as implant failure, success rate, survival rate, biological complications, technical complications, mechanical complications, and marginal bone loss, were included on this review. The search was performed on databases PubMed, Scopus, and Cochrane. Cochrane Collaboration tool was used to assess the risk of bias of randomized controlled studies, and an adapted version of Newcastle–Ottawa scale was used for observational studies. All data were tabulated according to the time of loading: (1) immediate restoration/loading, (2) early loading, and (3) conventional loading.

Results: From a total of 4027 studies identified through the three databases, six of them were randomized controlled trials, five of them were prospective observational studies, and another five were retrospective observational studies. In total, 5954 implants, 1294 patients and 1305 full-arch fixed implant-supported prostheses were included in this review. There was a wide heterogeneity among clinical studies regarding the study design and treatment procedures. Thus, pooled estimates were not performed in order to avoid potential biases. The methodological assessment by the Modified Newcastle–Ottawa scale showed a moderate quality of observational studies. Regarding the RCTs studies, all of them presented at least one element of bias according to the Cochrane Collaboration tool for assessing risk of bias.

Conclusion: There is evidence of high survival-success implant rate (95-100%) for either loading protocols (immediate restoration/loading, early loading, and conventional loading). However, careful attention must be taken by clinician when interpreting the results reported in clinical studies. Future studies should be performed using standardized methodology in order to determine the true predictability regarding immediate, early, and conventional loading protocols.

In implant dentistry, different loading protocols exist. Three loading protocols have been recommended by the International Team for Implantology.[1] These protocols are defined as follows: (1) immediate restoration/loading, (2) early loading, and (3) conventional loading. In the immediate restoration/loading protocol, the dental implant has to be in occlusal function no longer than 1-week postsurgery. Early loading is when the implant is placed in occlusal function 1-week and no longer than 2-month postimplant placement. Finally, the conventional loading follows a healing period longer than 2-month postimplant placement.

Although several clinical trials have showed high success rates for immediate restoration/loading over 6 years of follow-up,[2-6] a clinical dilemma regarding the loading protocol remains. It is still unknown whether dental implants should be immediately loaded or if it is a conventional loading protocol should be followed for more consistent outcomes.[7-9] The immediate restoration/loading protocol has many advantages such as quicker achievement of occlusal function,[10,11] early restoration of esthetic appearance,[12] avoidance of a second surgery to expose the implant,[13,14] and an increase in the percentage of transverse collagen fibers.[2,15] Furthermore, with an immediate

Table 1 Search strategy

Population	#1 completely edentulous mouth OR totally edentulous mouth OR edentulous mouth OR edentulous jaw OR completely edentulous mouth
Intervention	#2 full-arch dental restoration OR full-arch dental implant supported OR full-arch dental prosthesis OR full-arch denture OR complete arch implant fixed dental prosthesis OR full-arch fixed dental prosthesis OR full-arch dental rehabilitation OR full-arch fixed dental hybrid prostheses OR hybrid implant prostheses
Comparison	Covered by Population, Intervention and Outcome search
Outcome	#3 implant failure OR survival rate OR prostheses failure OR prostheses complication OR treatment outcome OR success rate
Search combination	#1 AND #2 AND #3
Database search	PubMed, Scopus, and Cochrane

restoration/loading protocol, it is possible to avoid the use of a removable denture, which could cause functional and esthetic disturbances.[16-18]

Over the last several years, a considerable number of clinical studies and systematic reviews demonstrated that immediate and early loaded dental implants can be as effective as those treated with conventional loading protocols.[19] A recent systematic review evaluated loading protocols in edentulous patients with fixed implant-supported prostheses and reported the same effect on implant survival, failure and complications, regardless of the loading protocol when treating maxillary and mandibular arches. However, in this study, clinical studies without a control group were included.[20] Another systematic review revealed a greater risk of implant failure with immediate restoration/loading in comparison to conventional loading, although survival rates were high for both groups (98.2% in the immediate restoration/loading group and 99.6% in the conventional loading group). However, this review included partial and totally edentulous participants in the same meta-analyses.[21]

At the time of this review, none of the published systematic reviews included studies directly comparing the different loading protocols in the rehabilitation of completely edentulous arches with implant-supported prostheses. The purpose of this systematic review was to evaluate the following focused question: Does the time of loading influence the success rate and complications on complete fixed implant-supported prostheses?

Materials and methods

This review was registered at the National Institute for Health Research PROSPERO, International Prospective Register of Systematic Reviews (http://www.crd.york.ac.uk/PROSPERO) under the number: CRD42018087780. In addition, it was conducted in accordance with the guideline "Preferred reporting items for systematic reviews and meta-analysis (PRISMA)".[22]

The Population, Intervention, Comparison, Outcome, Study (PICOS) framework was used to form the following search strategy; P: completely edentulous participants rehabilitated with complete-arch implant fixed dental prostheses; I: immediate or early loading of complete-arch fixed dental prostheses; C: complete-arch implant fixed dental prostheses with conventional loading; O: implant failure rate : success rate, survival rate, biological complications, technical complications, mechanical complications, marginal bone loss, patient related outcomes; and S = randomized control trials (RCT) and observational studies. Thus, the question addressed in this review was: does the moment (time) of loading influence the success rate and complications on (of) complete-arch fixed implant-supported prostheses comparing immediate restoration/loading versus early loading versus conventional loading?

A search for relevant manuscripts was performed in the following electronic databases: PubMed (2008 to January 2018), Scopus (2006 to January 2018), and Cochrane Oral Health Group Trials Register (2005 to January 2018). The search strategy included the combination of keywords using Boolean operators (OR, AND) (Table 1). Additionally, a manual search was performed using reference lists of relevant manuscripts from high impact journals. Then, references were scanned to avoid missed data during the indexing.

The following inclusion criteria were applied in the current systematic review: (1) clinical studies RCTsr observational studies, (2) completely edentulous patients with an implant-supported prosthesis, (3) survival rate, success rate, biological complications, mechanical or technical complications, patient's-related outcomes and, marginal bone loss. In addition, only clinical studies with a control group were included. The studies that do not compare the loading protocol in the same study, in vitro, ex vivo or animal studies, and/or studies assessing single implant supported crowns, partial implant-supported prostheses and overdentures, were excluded for this systematic review.

Titles and abstracts of the studies were screened independently by two reviewers (YG and IT). After, the same reviewers conducted a full-text screening of those trials that met the inclusion criteria, as well as any article without available abstracts. Both reviewers assessed the extracted data, and if any disagreement arose, it was resolved by discussion. Data extraction and validity assessment were performed on the publications that met the inclusion criteria. Any reasons for excluding publications were recorded.

Due to the small number of publications and the heterogeneity of reported procedures, the variability of study characteristics prevented a meta-analysis. Therefore, the extracted data were tabulated into evidence tables, and the results were considered in terms of mean values.

Cochrane recommendations for systematic reviews of interventions were performed to assess the risk of bias of the

Table 2 Studies excluded

Author	Year	Reason for exclusion
Browaeys et al[25]	2013	Unclear data of the time of loading
Boedeker et al[26]	2011	Included partially and totally edentulous participants
Duda et al[27]	2016	Partially edentulous
Eliasson et al[28]	2010	Not comparing time of loading
Fisher and Stenberg[29]	2004	The same study and same outcomes with more time of follow time
Fisher and Stenberg[30]	2013	Not comparing time of loading
Grandi et al[31]	2012	Partially edentulous
Hatano et al[32]	2011	Not comparing time of loading
Meizi et al[33]	2014	Partially edentulous
Mertens and Steveling[5]	2011	Partially edentulous
Misch and Degidi[6]	2003	Not data available for each loading protocol
Shibly et al[34]	2012	Partially edentulous

included RCTs.[23] Risk of bias in the respective studies were categorized in accordance with the following criteria: low risk of bias (plausible bias unlikely to seriously alter the results) if all criteria were met; unclear risk of bias (plausible bias that raises some doubt about the results) if one or more criteria were partially met; and high risk of bias (plausible bias that seriously weakens confidence in the results) if one or more of the criteria were not met.

The Newcastle–Ottawa Scale (NOS) adapted by Chambrone et al was used to assess the risk of bias in the included prospective studies.[24] The original scale was adapted in order to specify the relevant questions for this review. Thus, the following topics were used: (1) selection of study groups: sample size calculation, representativeness of the patients who received implants with the conventional loading protocol, selection of the patients who received implants with the immediate or early loading protocol, description of clear inclusion/exclusion criteria, detailed description of the steps following each loading protocol, training/calibration of the surgeons and assessors of outcomes and appropriate protocol of data collection; (2) comparability: comparability of patients on the basis of the study design or analysis and management of potential confounders; (3) outcomes: evaluation of results, assessment of accuracy outcomes, and adequacy of follow-up of the patients; and (iv) statistical analysis: appropriateness/validity of statistical analysis and unit of analysis reported in the statistical model. Each included study could receive a maximum of 14 points. Studies with 11-14 points were arbitrarily considered as high level according to the methodological quality, with 8-10 points indicating medium-level methodological quality and with fewer than eight points indicating low methodological quality.

Results

The study selection process is summarized in Figure 1. After removing duplicates, the search strategy through the databases identified 4027 manuscripts. From these, 3999 were excluded after reviewing the title or abstract and 28 manuscripts were selected for full-text reading. After a thorough screening of the full-text manuscripts, 12 studies were excluded for not meeting the inclusion criteria (Table 2).[25-34] Furthermore, three publications reported the same outcomes in different follow-up times and the article with the longest follow-up time was included. Thus, 16 clinical studies were included for qualitative analysis. In total, 1294 patients received 5954 implants and 1305 complete-arch fixed implant-supported prostheses.

The main outcomes of included studies are listed in Tables 3 and 4, and 5. Twelve studies compared immediate and conventional loading protocols. From these, four studies were RCTs,[10,12,14,19] five were prospective studies,[4,7,18,35,36] and three were retrospective studies.[37-39] Four studies compared early loading and with conventional loading, from which two were RCTs[2,40] and two were retrospective studies.[13,41] Although data from three studies were reported in separate publications with different follow-up times and outcomes, they were not grouped under the same name.[35,36,40]

The division of studies according to the implant placement time (healed vs. fresh sockets) revealed the following results: Cannizzaro et al[19] compared immediate restoration/loading with conventional loading and showed one implant failure out of 90 implants and three implant failures out of 87 implants, respectively. All the failures were related to extraction sockets and two implants were placed in heavy smokers. Peñarrocha-Oltra et al[7] showed one implant failure out of 98 implants for the immediate group and two out of 85 implants for the conventional loading group. Concerning the immediate restoration/loading group, the failed implant was placed on a healed socket, whereas in the conventional loading group the two implants that failed were placed in extraction socket sites. Peñarrocha-Oltra et al[36] showed one implant failure in immediate restoration/loading out of 94 implants and three failures in the conventional loading out of 99 implants. For both groups, all failures consisted on extraction sockets. Tealdo et al[4] assessed the implant failure in immediate restoration/loading and conventional loading ad showed that 10 failures were in the immediate restoration/loading out of 163 implants. However, the authors did not specify whether the failures were all in extraction sockets. Conversely, the four implant failures showed in conventional loading out of 97 implants were in healed ridges. Likewise, Busenlechner et al[38] showed 23 implant failures out of 195 implants for the immediate restoration/loading group and eight

Table 3 Study characteristics of the included RCTs

Author	Participants	Implant system	Location	Follow-up	Healed socket	Time of restoration/ loading	Prostheses	Participants per group	Number of analyzed implants	Implant survival rate	Implant success rate	Implant failure	Mean marginal bone loss (mm)	SD
Alfadda Sara[10]	42	TiUnite-NobelBiocare	Mandible (fourim-plants)	1 year	Yes	Immediate (same day of surgery)	Mandibular denture was adapted to be a provisional implant-supported prostheses	22	88	Data not available	95.83%[42]	3	0.296	Lower CL: 0.078 Upper CL: 0.514
						Conventional (3-4 months)	Patient denture was relined with soft material	18	72		97.73%[42]	2	0.037	Lower CL: 0.104 Upper CL: 0.178
Cannizzaro et al[19]	30	Tapered SwissPlus-Zimmer Dental	Maxilla (five to eight implants)	1 year	Not	Immediate (same day of surgery)	Provisional metal reinforced acrylic (cemented or screw)	15	90	Data not available	Data not available	1	0.55	0.22
						Conventional (after 2 months)	Patient denture was relined with a soft material	15	87			3	0.62	0.25
Fischer et al[2]	24	SLA-Straumann	Maxilla (five to six implants)	5 years	Yes	Early (9-12 days)	Not to wear their dentures until definitive prosthesis was installed	16	94	94.7%		4	0.8	1.2
						Conventional (2.5-5.1 months)	Patient denture was relined with a soft material	8	45	95.7%	Data not available	0	0.3	
Fischer and Stenberg[40]	24	SLA-Straumann	Maxilla (five to six implants)	3 years	Yes	Early (9-12 days)	Not to wear their dentures until definitive prosthesis was installed	16	94	Data not available	100%[42]	Data not available	0.06	Min: 1.16 Max: 10.88
						Conventional (2.5-5.1 months)	Patient denture was relined with a soft material	8	45		100%[42]		0.55	Min: 2.13 Max: 7.36
Jokstad and Alkumru[14]	31	TiUnite Nobel Biocare	Mandible (four implants)	5 years	Yes	Immediate (same day of surgery)	Removable prosthesis was converted into an implant-supported prosthesis	13	52	Data not available	Data not available	0	1.3	0.7
						Conventional (3-4 months)	Patient denture was relined with COE-SOFT	18	72			1	1.1	0.7
Vercruyssen et al[12]	15	Ankylos-Denstply	Maxilla (6 implants)	not de-scribes the time of follow up	Yes	Immediate (24 hours after surgery)	Not to wear their dentures until definitive prosthesis was installed	7	42	Data not available	Data not available	0	Data not available	Data not available
						Conventional (3 months)	Not to wear their dentures until sutures had been removed	8	48			1		

Table 4 Study characteristics for the included prospective studies

Author	Patients	Implant system	Location	Follow-up	Healed socket	Time of restoration/loading	Prostheses	Patients per group	Number of analyzed implants	Implant survival rate	Implant success rate	Implant failure	Mean marginal bone loss (mm)	SD
Peñarrocha-Oltra et al[7]	36	Sweden and Martina	Mandible (four to six implants)	1 year	Not (immediate placement)	Immediate (3 days after surgery)	Provisional metal reinforced acrylic	18	98	Data not available	99.0%[43]	1	0.71mm	0.25mm
						Conventional (10-12 weeks)	Removal dentures relined	18	85		97.6%[43]	2	0.60mm	0.28mm
Peñarrocha-Oltra et al[18]	30	Sweden and Martina	Maxilla (six to eight implants)	1 year	Not (immediate placement)	Immediate (within the first week after surgery)	Provisional metal reinforced acrylic	15	94	Data not available	Data not available	Data not available	Data not available	Data not available
						Conventional (10-12 weeks)	Removal dentures relined	15	99					
Peñarrocha-Oltra et al[36]	30	Sweden & Martina	Maxilla (six to eight implants)	1 year	Not (immediate placement)	Immediate (within the first week after surgery)	Acrylic resin provisional full-arch screwed metal-reinforced prosthesis	15	94	Data not available	99%	1	0.55mm	0.26
						Conventional (10-12 weeks)	Removal dentures relined	15	99		96.8%[43]	3	0.62mm	0.23
Tealdo et al[4]	49	Biomet 3I	Maxilla (four to nine implants)	6 years	Not (immediate placement)	Immediate (within 24 hours after surgery)	Provisional fixed screw-retained prostheses	34	163	93.9%	Data not available	10	M = 1.62 D = 1.63	M = 1.12 D = 1.34
						Conventional (8 months)	Removal dentures relined	15	97	95.9%		4	M = 2.43 D = 2.48	M = 1.44 D = 1.44
Tealdo et al[35]	49	Biomet 3I	Maxilla (four to nine implants)	36 months	Not (immediate placement)	Immediate (within 24 hours after surgery)	Provisional fixed screw-retained prostheses	34	163	93.9%	Data not Available	Data not available	Data not available	Data not available
						Conventional (8 months)	Removal dentures relined	15	97	95.9%				

Table 5 Study characteristics for the included retrospectives studies

Author	Patients	Implant system	Location	Follow-up	Healed socket	Time of restoration/ loading	Prostheses	Patients per group	Number of analyzed implants	Implant survival rate (%)	Implant success rate	Implant failure	Mean marginal bone loss (mm)	SD
Busenlechner et al[37]	122	Nobel Biocare	Maxilla (four to -six implants)	8 years	Yes	Immediate (same day of surgery)	Acrylic resin provisional prostheses	37	179	98.3	Data not available	3	1.1	1.3
						Conventional (3 months)	Adaptation of the complete denture	85	403	96.7		12	1.4	1.3
Busenlechner et al[38]	240	Nobel Biocare	Maxilla (four to six implants)	8 years	Not	Immediate (same day of surgery)	Acrylic resin fibred reinforced provisional prostheses	195	980	97.6	Data not available	23	1.5	1.7
						Conventional (3 months)	Adaptation of the complete denture	45	235	96.6		8	0.7	1.1
Eliasson et al[41]	109	Nobel Biocare, Astra Tech and Straumann	Mandible (four to six implants)	5 years	Yes	Early (within the first 3 weeks)	Acrylic with metal framework prostheses	55	248	94.4	Data not available	12	0.18	Data not available
						Conventional (after 3 months)	Removal dentures relined with soft material	54	242	97.9		5	0.15	
Friberg and Jemt[13]	259	Nobel Biocare	Mandible (four to six implants)	5 years	Yes	Early (13 days after surgery)	Data not available	152	512	97.0	Data not available	13	0.2	0.51
						Early (8 days after surgery)		90	245	98.5		2	0.5	1.06
						Early (9 days after surgery)		75	200	98.6		1	0.2	0.5
						Conventional (3 months later)		68	273	99.7		1	0.2	0.42
Testori et al[39]	80	Biomet 3I	Maxilla/ mandible (four to six implants)	4 years	Not	Immediate (48 hours)	Acrylic with metal framework prostheses	59	385	95.1	Data not available	22	0.9	0.4
						Conventional (after 2 to 6 months)	Data not available	21	134	97.8		0	0.8	0.5

Table 6 Mechanical, technical, and biological complications reported on the included studies

Author	Study	Time of restoration/ loading	Mechanical complications Loose screw	Technical complications Resin/tooth fracture	Biological complications	
					Soft tissue ulcers/ adverse effects	Peri-implantitis
Cannizzaro et al[19]	RCT	Immediate (same day of surgery)	–	2	1	2
		Conventional (after 2 months)	–	2	0	1
Jokstad and Alkumru[14]	RCT	Immediate (same day of surgery)	–	6	8	
		Conventional (3-4 months)	–	3	10	
Fischer et al[2]	Prospective	Early (9-12 days)	1	18	Data not available	
		Conventional (2.5-5.1 months)	0	12		
Peñarrocha-Oltra et al[18]	Prospective	Immediate (3 days after surgery)	5	0	Data not available	
		Conventional (10-12 weeks)	0	2		
Tealdo et al[4]	Prospective	Immediate (within 24 hours after surgery)	3	4	Data not available	
		Conventional (8 months)	5	3		
Eliasson et al[41]	Retrospective	Early loading (within the first 3 weeks)	1	9	–	2
		Conventional loading (after 3 months)	0	5	–	1
Friberg et al[13]	Retrospective	Early (13 days after surgery)	1	6	13	1
		Early (8 days after surgery)	0	3	8	1
		Early (9 days after surgery)	0	5	4	2
		Conventional (3 months later)	0	1	6	1

implant failures out of 45 implants for the conventional loading group. In this regard, all failures were related to implants placed in extraction sockets. Testori et al[39] showed 19 implant failures out of 385 implants in the immediate restoration/loading group and three implant failures out of 134 implants in the conventional loading group. Regarding the 19 failed implants in the immediate restoration/loading group, 16 were in extraction sockets and three in healed ridges. All three implants that failed in the conventional loading group were placed in extraction sockets.

Table 6 shows mechanical, technical, and biological complications in edentulous patients rehabilitated with a fixed implant-supported prosthesis according to the time of loading. The most common technical complications were: resin or tooth fracture and loosening of the abutment screw. Four studies provided information concerning biological complications.[13,14,19,41] These studies showed that immediate and early loading protocols had a higher number of patients with soft tissue ulcers, hyperplasia/inflammations, and peri-implantitis.

Table 7 shows the four studies that compared the patient's satisfaction between different loading protocols.[12,18,19,41] Satisfaction regarding function, esthetics, and treatment procedures was assessed using a form, which comprised questions to be answered. Vercruyssen et al[12] and Peñarrocha-Oltra et al[18] measured the overall satisfaction using a 100- and 10-mm visual analog scale (VAS), respectively. On the other hand, Cannizzaro et al[19] and Eliasson et al[41] measured the overall satisfaction using a questionnaire with five and 16 questions, respectively.

Of the 10 observational studies included in this systematic review, three received a 12-point score,[7,18,36] two studies received an 11-point score[4,39] out of a total of 14 points (high methodological quality); two studies received a 10-point score,[37,38] one article received a 9-point score,[41] and one article received an 8-point[13] level according to the methodological quality. Regarding "selection of study groups," none of the studies reported any form of sample size calculation. Descriptions of inclusion/exclusion criteria and unit of analysis (number of

Table 7 Patient-related outcomes on the basis of included studies

Author	Study	Time of restoration/ loading	Patients per group	Patient- related outcomes
Cannizzaro et al[19]	RCT	Immediate (same day of surgery)	15	Patient satisfaction: 73%
		Conventional (after 2 months)	15	Patient satisfaction: 33%
Vercruyssen et al[12]	RCT	Immediate (24 hours after surgery)	7	Recommend procedure: VAS score: 21.3 (100 max)
		Conventional (3 months)	8	Recommend procedure: VAS score: 9.5 (100 max)
Peñarrocha-Oltra et al[18]	Prospective	Immediate (within the first week after surgery)	15	Overall satisfaction: VAS value: 9 (10 max)
		Conventional (10-12 weeks)	15	Overall satisfaction: VAS value: 9 (10 max)
Eliasson et al[41]	Retrospective	Early (within the first 3 weeks)	55	Patient satisfaction: 81%
		Conventional loading (after 3 months)	54	Patient satisfaction: 71%

patients per group) were considered properly addressed except for two studies.[13,41] Only three studies described the calibration of the surgeons and examiners of outcomes. Only three studies considered did not show adequate time of follow-up more than 1 year (Fig 2).[7,18,36]

Regarding the risk of bias assessment for the RCTs, all included studies presented a high risk in blinding of participants and personnel. Only one study clearly described the blinding process for the outcomes assessment (Fig 3).[10]

Discussion

This systematic review was conducted to answer the clinical focused question: does the time of loading influence the success rate and complications in edentulous patients rehabilitated with fixed implant-supported prostheses? The success rate outcome was assessed by only four studies.[2,10,18,36] The authors included either one of the following methods to determine the success criteria: Zarb and Albrektsson[42] or Buser et al[43] However, it is important to mention that the follow-up period of all clinical studies was 3 years[5] and 1 year.[10,18,36] Even though the studies were well-conducted, they provided only a moderate degree of evidence. Therefore, it should be noted that the extrapolation of these data must be carefully evaluated, considering that these studies could not be considered as a long-term follow-up trial.

This literature review revealed that there was a trend in failure toward the implants that were placed in extraction sockets. This might be explained by the fact that healed ridges ensure greater primary stability.[44] However, there are many factors that could influence the survival rate of the implants placed in extraction sockets such as implant surface, presence of periodontal disease, and bone quality.[45]

With respect to technical and mechanical complications, we observed that the veneer fracture was the most frequent complication. Veneer fractures may be caused by the material failure, design issues, and/or technical errors. Additionally, another common complication was the screw loosening, which might be caused by the magnitude and direction of occlusal forces and the physical properties of the components.[46,47] Besides, there was a similarity between biological complications for among loading protocols. This information suggests that soft tissue ulcers or adverse effects might have been caused by the acrylic resin used to pick up the temporary copings in the immediate loading protocol, or by the trauma caused by removable complete dentures during implants healing period in the conventional loading protocol.

There were only four studies that assessed the Patient-Centered Outcomes (PROMs) when different times of loading were used to treat completely edentulous patients with fixed implant-supported prostheses. Cannizzaro et al[19] and Eliasson et al[41] reported less patient satisfaction in the conventional loading group. This may be explained due to the fact that the patients in the immediate or early loading group had presented improved comfort, speech, improved chewing stability, and esthetics associated with denture stability in a shorter period of time. This finding agrees with previous publications.[48,49] Conversely, Vercruyssen et al[12] and Peñarrocha-Oltra et al[18] did not find statistical difference for patient satisfaction when comparing immediate restoration/loading and conventional loading. This general satisfaction may indicate that the implant therapy improved the oral status of these patients in comparison to the use of conventional denture.

In contrast to a previously published review, this systematic review included only studies that directly compared the time of loading within the same study. Papaspyridakos et al[20] reported estimated survival rates between 99.10 and 99.90% for immediate restoration/loading and conventional loading for fixed prostheses in the edentulous maxilla and mandible. Another systematic review showed that the estimated implant loss rate was low, but still significantly higher for an immediate restoration/loading protocol ($p = 0.015$) when comparing with conventional loading protocol.[50] The present systematic review may be useful for clinicians for providing information concerning the prognosis of fixed implant-supported

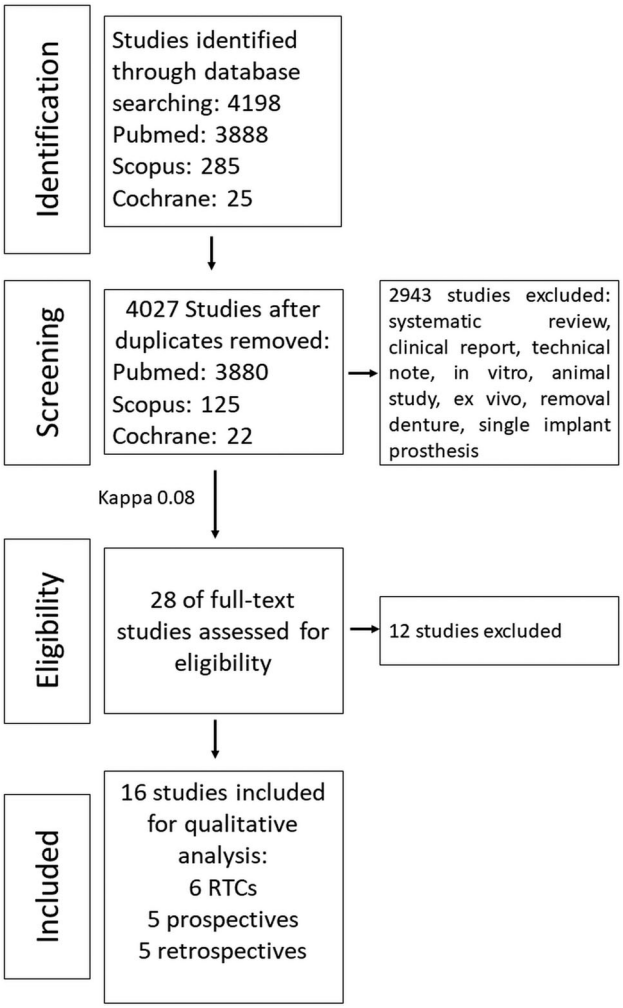

Figure 1 Flow diagram of articles found through databases.

Figure 3 Risk of bias of RCTs included.

prostheses in edentulous patients with different time loading protocols.

All six RCTs were considered to have a high risk of bias due to the lack of blinding participants and personnel. With respect to "blinding of outcome assessment," only one RCT[10] described that the patients were assessed in a blinded

		Selection of study groups							Comparability		Outcomes			Statistical analysis		
N°	Author	sample size calculation	representativeness of the patients who received implants with the conventional loading protocol		selection of the patients who received implants with the immediate or early loading protocol	description of clear of the steps following each loading protocol	training/calibration of the surgeons and assessors of outcomes	appropriate protocol of data collection	comparability of patients on the basis of the study design or analysis	management of potential confounders	evaluation of results	assessment of accuracy outcomes	adequacy of follow-up the patients	appropriateness/validity of statistical analysis	unit of analysis reported in the statistical model	TOTAL
1	Peñarrocha-Oltra D et al. 2015		*	*	*	*	*	*	*	*	*	*		*	*	12
2	Peñarrocha-Oltra D et al. 2014		*	*	*	*	*	*	*	*	*	*		*	*	12
3	Peñarrocha-Oltra D et al. 2013		*	*	*	*	*	*	*	*	*	*		*	*	12
4	Tealdo T et al. 2014		*	*	*	*		*	*	*	*	*	*	*	*	11
5	Tealdo T et al. 2011		*	*	*	*		*	*		*	*	*	*	*	11
6	Busenlechner D. et al 2016a		*	*	*	*			*		*	*	*	*	*	10
7	Busenlechner D. et al 2016b		*	*	*	*			*		*	*	*	*	*	10
8	Eliasson A et al.		*	*		*			*		*	*	*	*	*	9
9	Friberg B & Jemt T		*	*					*		*	*	*	*	*	8
10	Testori T et al.		*	*	*	*		*	*	*	*	*	*	*	*	11

Figure 2 Risk of bias of included observational studies.

fashion by a calibrated, independent investigator. Therefore, further researches should describe their methodology as clearly as possible, in order to avoid a misunderstanding concerning the research method.[24] In contrast, most of the observational studies showed a moderate level of methodological quality. The authors considered a high risk of bias when the follow-up was less than 1 year[7,18,36] due to the short period of time to evaluate survival rate, success rate, and bone loss. Moreover, regarding the appropriate protocol of data collection, only four studies described the use of a standardized technique for the radiographic evaluation of the marginal bone loss.[4,7,36,39]

The limitation of this review was the fact that the included studies showed many variable characteristics (mandible /maxilla, healed/fresh socket, and study design), which lead the authors to decide not to perform a meta-analysis. Another limitation is the inclusion of retrospective studies. However, the data presented in tables are representative and could guide future clinical studies in an effort to avoid potential bias.

Conclusions

Despite the fact that all the included studies showed a high survival-success rate (95-100%), due to the heterogeneity of the studies, there was not enough evidence to support or refute that the time of loading could influence the success rate and complications in edentulous patients rehabilitated with fixed implant-supported prostheses. Future RCTs should assess within the same study the influence of time of loading in the clinical and patient outcomes with fixed implant-supported prostheses. Future clinical trials should distinguish the outcomes from healed ridges and extraction sockets to avoid bias when interpreting the results.

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