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Surgical protocols for early implant placement in post-extraction sockets: a systematic review

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Abstract

Objectives: The aim of this systematic review was to evaluate the best timing for placing implants after tooth extraction, by comparing early vs. delayed implant placement and evaluating the hard and/or soft tissue ridge dimensional changes and the outcomes related with implant survival and prosthesis success.

Material and methods: An online search of the main databases including The National Library of Medicine (MEDLINE via Pubmed), Embase and The Cochrane Central Register of Controlled Trials was conducted up to February 2011. Randomized controlled clinical trials (RCTs), prospective cohort studies and case–control retrospective studies, with a follow-up of at least 1 month after loading of dental implants, comparing: (i) early vs. delayed implant placement, (ii) augmentation vs. no augmentation at implant placement in early placed implants and/or (iii) the comparison of various augmentation procedures at early implant placement, were conducted. A hand search of relevant journals was also performed. Screening of eligible studies, assessment of their methodological quality and data extraction were conducted in duplicate by two independent reviewers. Authors of studies were contacted for clarification or missing information.

Results: Eight studies were included, although meta-analysis could only be performed with the data from two studies comparing early vs. delayed implant. The percentage of bone height and bone width reduction favoured the early placement, with pooled mean difference between groups of 13.11% (95% CI: from 3.83 to 22.4; $P = 0.057$) and 19.85% (95% CI: from 13.85 to 25.81) respectively. Implant survival demonstrated a non-significant higher implant survival rate for the early group (RR = 1.02, 95% CI: 0.96–1.1).With regard to patient satisfaction, statistically significant differences between the groups in favour of the early group for overall satisfaction and appearance with the restoration were demonstrated at 2 years, although these differences were lost at 5 years.

Conclusions: Placement of dental implants at an early timing after tooth extraction may offer advantages in terms of soft and hard tissue preservation, when compared with a delayed protocol. Nevertheless, well-designed, high quality, randomized clinical trials, are needed, because the available evidence is today limited in terms of available studies and quality.

Teeth may be lost due to disease or trauma, or may be congenitally absent. To replace missing teeth, dental implants offer an excellent treatment option with demonstrated short- and long-term predictable outcomes. There are, however, many teeth still present in the patient's mouth with poor or hopeless prognosis that, according to the dentist opinion, need to be extracted and replaced by dental implants. The ideal timing of implant placement after dental extraction has been extensively discussed in the literature, and advantages and disadvantages have been attributed to the different protocols (Esposito et al. 1998; Chen et al. 2004; Fugazzotto 2005), although there is an increasing interest for shortening the overall treatment time and minimizing the number of surgical interventions. Late implant placement following extraction, with a healing period of 6–12 months prior to implant placement has been traditionally considered the standard of care, because a fully healed ridge will ensure implant insertion in a stable ridge dimension,

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but the bone availability for implant placement may have been hampered by the resorptive changes occurring in the ridge after tooth extraction.

To overcome these potential drawbacks, different alternative approaches have been proposed, such as immediate implant placement at the time of extraction or early implant placement following a few weeks of soft tissue healing prior to implant insertion. At a recent consensus workshop (Chen et al. 2004; Hammerle et al. 2004), three different protocols were defined: (i) immediate or type 1 when the implant are placed in the same surgical intervention as the dental extraction; (ii) type 2 or early implant placement when implants are placed in the early stages of healing (from 4 to 8 weeks); and (iii) type 3 or delayed implant placement when implants are placed when the ridge has healed (from 3 to 6 months).

In these publications, the potential advantages and disadvantages of the different protocols were discussed (Chen et al. 2004; Hammerle et al. 2004). The immediate implant placement protocol obviously results in shorter treatment time, utilizes all available existing bone in the ridge and may avoid the need for raising a flap. On the other hand, there are some potential disadvantages with immediately placed implants, such as: (i) an increased risk of infection and associated failures if the socket is infected (Rosenquist & Grenthe 1996; Takeshita et al. 1997); (ii) presence of a discrepancy between the surface of the implant and the socket wall with a need to combine with bone augmentation procedures; (iii) the need to advance the flap to cover the implants in situations aiming for a submerged implant healing (Rosenquist & Ahmed 2000); and (iv) an increased risk for compromised aesthetic outcomes (Kan et al. 2007; Chen & Buser 2009; Sanz et al. 2009).

To overcome some of these potential risks, the early implant placement protocol (type 2) has been proposed, as it may share some of the advantages of immediate placement, mainly by utilizing the socket walls before they become fully resorbed, but at the same time allowing primary healing after tooth extraction and thus achieving enough soft tissues in case of need for flap closure and reducing the risks for infection during implant placement (Zitzmann et al. 1999; Nemcovsky & Artzi 2002; Buser et al. 2008a, 2008b, 2009, 2011). Moreover, tissue augmentation procedures with the use of either bone grafts, barrier membranes and/or soft tissue grafts are usually needed mostly in the aesthetically relevant areas to compensate the ridge alterations that always occur after tooth extraction. The early implant placement protocol is particularly suitable for augmentation techniques, as the soft tissue healing after tooth extraction has occurred and there is usually enough soft tissue coverage allowing for primary healing without the need of advancing the flaps. This protocol therefore has been advocated whenever there is a need for bone augmentation, either because there are defects in one or more of the socket walls or to close the gap between the implant surface and the socket bone walls in case of wide discrepancies (Zitzmann et al. 1999; Buser et al. 2008a, 2008b, 2009, 2011). In these situations, different bone regenerative technologies have been utilized such as autologous bone grafts (Ross et al. 1989; Becker et al. 1994), bone substitutes (Block & Kent 1991; Yukna 1991) or guided bone regeneration (GBR) with resorbable and non/resorbable barriers (Rosenquist & Ahmed 2000; Buser et al. 2009).

The efficacy of these protocols in terms of enhancing the survival of the implants placed to restore the extracted teeth has been evaluated in a recent systematic review (Esposito et al. 2010), where randomized clinical trials (RCTs) comparing type 1 and 2 protocols with the standard 3 protocol were selected and analysed. Only two RCTs compared immediate vs. delayed implants and only one compared early vs. delayed implants in 46 patients. These studies failed to demonstrate differences in implant survival between the protocols, and they did not answer the question whether augmentation procedures are benefited when one particular implant placement protocol is utilized (Covani et al. 2004). One of the reasons for the lack of differences in implant survival, when the different protocols are compared is probably due to the scarcity of available clinical trials, and therefore, this evidence must be supplemented with other study designs such as prospective cohort studies and retrospective case series with the goal of not only assessing the outcome of the implants but also evaluating the potential advantages of the more rapid treatment protocols, in terms of aesthetic outcomes, patient preferences, need and efficacy for tissue augmentation approaches and the occurrence of complications.

Therefore, the objective of the present systematic review was to evaluate the scientific evidence on the efficacy of the early implant placement protocol when compared with the standard delayed implant placement protocol. The hypothesis of this investigation was that there are no differences between both protocols in terms of implant survival as well as in the soft and hard tissue changes when bone or soft tissue augmentation techniques are implemented in conjunction with the implant placement.

The primary objective of this systematic review was to obtain an overall quantitative estimate of the bone and soft tissue changes after early vs. delayed implant placement. As secondary objectives, it was aimed to compare the outcome of tissue augmentation vs. no augmentation procedures at early implant placement and to compare various augmentation procedures used in conjunction with this implant placement protocol.

Material and methods

A protocol was developed before starting the review that covered all aspects of the systematic review methodology according to the Prisma guidelines (Moher et al. 2009) including the following definitions:

- Focused question.
- Study population.
- Types of intervention.
- Types of comparisons.
- Search strategy.
- Eligibility criteria for study inclusion.
- Outcome measures.
- Screening methods and data extraction.
- Quality assessment and data synthesis.
- Assessment of heterogeneity and drawing of conclusions.

Focused question

Which are the effects of the early implant placement in post-extraction sockets when compared with delayed implant placement, in terms of hard and/or soft tissue dimensional changes and in terms of implant survival and prosthesis success?

Study population

Patients with at least one implant placed after tooth extraction.

Types of interventions and comparisons

The surgical protocol considered for this evaluation was the early implant placement (type 2) protocol. This intervention was defined at a consensus workshop as "Implant placed following tooth extraction when the complete soft tissue healing of the socket (typically 4–8 weeks after extraction) has occurred" (Hammerle et al. 2004). In the present review, studies where implant placement occurred 4–8 weeks after tooth extraction

were included, but other protocols were also considered (i.e. implants placed between 3 days and 12 weeks after tooth extraction), as these interventions could not be considered as immediate placement (tooth extraction and implant placement in the same surgical procedure) or delayed placement, when the alveolar ridge is fully healed.

As in the early surgical protocol, bone augmentation techniques are frequently carried out, we also considered the outcomes of these interventions compared with no augmentation, as well as the outcomes of comparing different augmentation approaches. The specific bone augmentation technologies assessed in this study were: autologous bone grafts, bone substitutes (allogenic, xenogenic and synthetic grafts), barrier membranes, combinations, biological factors (platelet-rich plasma, bone-morphogenetic proteins, etc.) and soft tissue augmentation procedures.

Three types of comparisons were evaluated:

- Early implants vs. delayed implants.
- Augmentation vs. no augmentation at early implants.
- Various augmentation procedures at early implants.

Selection of studies

Studies needed to be conducted in patients, older than 18 years and in good general health, where at least one tooth needed to be extracted and replaced with dental implants. A minimum sample size (10 subjects per group) was established in an attempt to minimize the publication bias.

Clinical studies were selected if the study design consisted on RCTs, prospective cohort studies and case–control retrospective case series, where the early implant placement protocol had been used and the implants had been followed up at least 1 month after placing and loading the implant-supported restoration.

Outcome measures

The primary outcome variable was the bone dimensional changes occurring between implant placement and osseo-integration, usually assessed at the time of second stage surgery or the placement of the restorations. These were assessed in terms of height, width or volume, either directly on the alveolar process (in millimetres or percentage), or indirectly, using standardized periapical radiographs or tomographic images, or by assessing the soft tissue dimensional changes assessed with a periodontal probe or with standardized clinical photographs (in millimetres or percentage).

The following *secondary outcomes* were also assessed:

- Implant survival (%) and success (%) rates.
- Peri-implant tissue health (probing pocket depth [PPD], Plaque Index [PlI], bleeding on probing [BoP]).
- Outcomes related with the aesthetic and restorative result, such as the occurrence of buccal mucosal recession or loss of interdental papilla evaluated with the (Jemt index) (Jemt 1997), or the occurrence of restorative complications.
- Occurrence of biological (peri-implant) diseases.

Search strategy

Three electronic databases (The National Library of Medicine [MEDLINE via Pubmed]; Embase and the Cochrane Central Register of Controlled Trials) were used to search for studies fulfilling the inclusion criteria, published between 1986 and February 2011.

The following search terms were used:

Population

{ (<[text words] Tooth> OR <[MeSH terms/all subheadings] "Tooth">) AND ([text words] Extraction)
OR
(<[Text words] Tooth extraction OR Extraction socket OR Alveolar socket OR dental extraction OR tooth removal OR socket OR ridge-socket OR post-extraction socket > OR <[MeSH terms/all subheadings] "Tooth Extraction" OR "Tooth socket">)}

Intervention

{ (<[text words] immediate-delayed AND implant OR "Dental Implants, Single-Tooth*" <[MeSH terms>)
OR
{ (<[text words] immediate-delayed AND implant OR "Dental Implants, Single-Tooth*" <[MeSH terms>)
OR
{ (<[text words] early implant AND implant OR "Dental Implants, Single-Tooth*" <[MeSH terms>)
AND
[text words] Socket preservation OR Ridge preservation OR bone preservation OR socket seal OR Bone filler OR autologous bone grafts OR autogenous bone OR bone substitutes OR allogenic grafts OR allografts OR xenogenic grafts OR xenografts OR synthetic grafts OR Barrier membranes OR membrane OR guided bone regeneration OR freeze dried bone allograft OR demineralized freese dried bone allograft OR DFDBA OR FDBA OR Bio-Oss OR Bio-Oss Collagen OR Alloplast OR tricalciumphosphate OR cerasorb OR Bioglass OR polymeric OR collagen sponge OR Collage OR collagen fleece OR collagen plug OR collagen plugs OR Biogide OR Ossix OR soft tissues autografts OR connective tissue grafts OR punch OR free gingival graft OR soft tissues substitutes OR allogenic soft tissues OR

[patient AND intervention]

Only studies published in the English language were included. All reference lists of the selected studies were checked for cross-references.

The following journals were hand-searched for this review from January 1999 to February 2011: *Journal of Clinical Periodontology*, *Journal of Periodontology*, *Journal of Periodontal Research*, *Clinical Oral Implants Research*, *International Journal of Oral & Maxillofacial Implants* and *Clinical Implant Dentistry and Related Research*.

Review methodology

Two reviewers (I. S. and M. G. G.) independently screened the titles and abstracts of all retrieved entries. Studies were selected when meeting the inclusion criteria, or when there was insufficient data in the title and abstract to make a clear decision. A full manuscript was obtained from the selected studies that were independently assessed by three reviewers (I. S., M. G. G., D. H.) to establish the final inclusion. Any disagreement was solved by discussion among the reviewers. The reasons for rejecting studies at this or at subsequent stages were recorded. To avoid the selection bias, the reviewers were blind to the name of the authors, institutions and journal titles. The selected studies underwent validity assessment, with special attention to duplicate publications using the same data source, to avoid a likely bigger impact of the same data in the global result.

Quality assessment

Based on the design and content of the selected studies, their quality was evaluated independently and in duplicate by two reviewers (I. S. and M. G. G.), who were blind to the name of the authors, institutions and journal titles.

Table 1 shows the different quality assessment criteria used for the selected randomized controlled trials. Following the recommendations by (Ten Heggeler et al. 2010), we utilized RCT-checklist of the CONSORT-statements (Schulz et al. 2010a, 2010b), the MOOSE-statements (Stroup et al. 2000) and the recommendations by (Needleman 1999; Esposito et al. 2001), together with the Cochrane checklist for assessing risk of bias (Higgins 2009). With these criteria, the studies were grouped into three different categories: low, unclear or high risk of bias.

Table 2 shows the different quality assessment criteria used for prospective cohort and case–control studies (Harris et al. 2001; Janket et al. 2003; Paraskevas et al. 2008) together with the Strobe statement checklist (von Elm et al. 2007a, 2007b). With these criteria, the studies were graded as (i) adequate, (ii) inadequate and (iii) not listed and grouped into three different categories: good, fair or poor quality.

Table 1. **Quality criteria for randomized clinical trials**

Validity	Quality criteria
External	Representative population group
	Eligibility criteria defined
Internal	Random allocation
	Allocation concealment
	Blinded to the patient
	Blinded to the examiner
	Blinding during statistical analyses
	Reported loss to follow-up
	Number (or %) of drop-outs
	Treatment identical except for intervention
Statistical	Sample size and power calculation
	Point estimates presented for primary outcome
	Intention to treat analyses
	Statistical test
Clinical validity	Study design
	Evaluation method
	Reason for extraction
	Calibration examiner
	Reproducibility data shown
	Validated measurement

Table 2. **Quality rating criteria for cohort studies**

	Cohort studies
Participants	Inclusion and exclusion criteria
	Homogeneity between groups
Sample size	Rationale for study size, including practical and statistical considerations
Follow-up	Period of follow-up
	Percentage lost to follow-up: <, ≥ 20%, not listed
Outcomes	Measured in a standard, valid and reliable way
Statistical methods	Description of all statistical methods including those to control for confounding
	Description of how loss to follow-up and missing data were addressed

Data extraction

Two reviewers (I. S. and M. G. G.) extracted the data independently using specially designed data extraction forms. Any disagreement was discussed, and a third reviewer (D. H.), was consulted when necessary. Authors of studies were contacted for clarification or missing information. Incomplete data were excluded until further clarification was available. When the results of a study were published more than once or results were detailed in a number of publications, the most complete data set was sought from all sources and was included only once.

Heterogeneity assessment

The statistical heterogeneity among studies was assessed using the Cochran *Q*-test (Cochran 1954) and two graphic methods (Galbraith and La'Abbé graphic, for dichotomous variables). In case of high heterogeneity values, a subgroups analysis was carried out. As a complement to the *Q*-test, the I^2 index (Higgins et al. 2003) was done to know the percentage of variation in the global estimate that was attributable to heterogeneity (I^2 = 25%: low; I^2 = 50%: moderate; I^2 = 75%: high heterogeneity).

Data synthesis

To summarize and compare studies, data on the mean change in primary (bone and soft tissue level changes) and secondary outcome variables were statistically analysed. The study-specific estimates were pooled using both the fixed effect model (Mantel–Haenzel–Peto test) and the random effect model (DerSimonian–Laird test). If a significant heterogeneity were found, the random effect model was used. For continuous variables (bone level changes, soft tissue changes), weighted mean differences and 95% confidence intervals were used to summarize the data in each study. For dichotomous variables (e.g. successful implant placement), the estimates of the effect were expressed as risk ratios (RR) or odds ratios (OR) together with their 95% confidence intervals.

Forest plots were created to illustrate the effects of the different studies and the global estimation of the meta-analysis.

STATA® 11.1 (StataCorp LP, Lakeway Drive, College Station, TX, USA) intercooled software was used to perform all analyses. Statistical significance was defined as a *P*-value < 0.05.

The publication bias was evaluated using a Funnel plot and the Egger's linear regression method. A sensitivity analysis of the meta-analysis results was also performed (Tobías 1999).

Results

The initial search resulted in 401 papers. After an initial phase of screening (96.76% of coincidences between reviewers, κ = 0.70), 29 potentially relevant papers were identified and one more was added during hand-search (Schropp et al. 2005a, 2005b). Thirty full-text papers fulfilling the inclusion criteria were finally evaluated for suitability. After a thorough evaluation of the full-text manuscripts, eight papers were finally included (96.55% of agreement between reviewers, κ = 0.93) (Fig. 1).

From this selection, five papers from the same research group reported different results and/or different follow-up of the same material (Schropp et al. 2003a, 2003b, 2004, 2005a, 2005b; Schropp & Isidor 2008). Two other papers were also produced by the same research group (Nemcovsky et al. 2000; Nemcovsky & Artzi 2002), but reporting different material. The final selection therefore consisted of four different investigations from three distinct research groups (Israel, Belgium and Denmark).

Tables 3a and b detail the design, patients, methods, outcome variables and source of funding of the selected studies. Three different study designs were used: RCT (publications by Schropp et al.), prospective cohort (Nemcovsky et al. 2000; Nemcovsky & Artzi 2002) and retrospective case–control (Cosyn & De Rouck 2009). The test groups included implants placed between 5 and 8 weeks after tooth extraction, together with the use of bone substitutes and barrier membranes (Nemcovsky et al. 2000; Cosyn & De Rouck 2009). In the studies by the Schropp group, however, the implant placement ranged between 3 and 15 days after tooth extraction in the test group, and 65–138 days in the control group. In these studies, autogenous

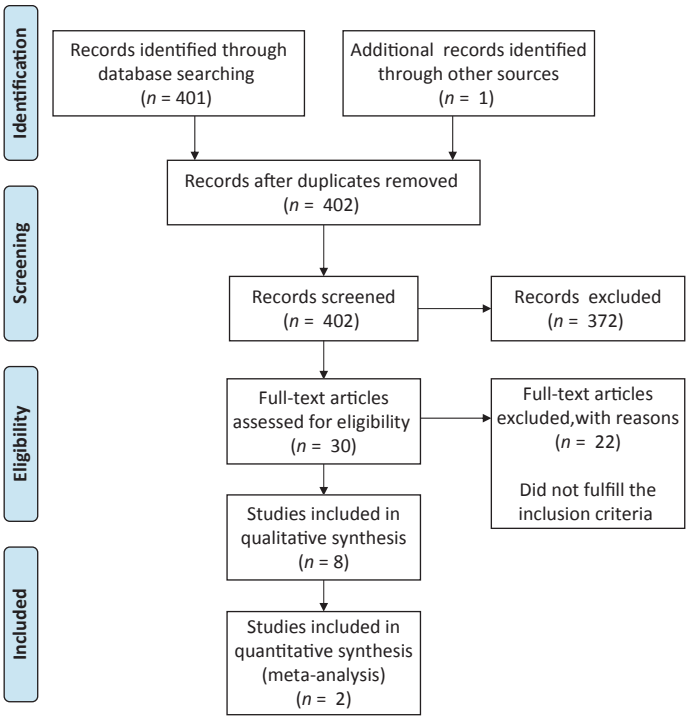

Fig. 1. Flow diagram (PRISMA format) of the screening and selection process.

bone chips were used to cover the exposed threads in the control group in the first surgery, and in both groups during the second surgery (3 months later). The control groups also differed among studies. In the first study by Nemcovsky et al. (2000), there is a lack of control group, and it is a prospective case series where one or two implants have been placed with the early placement protocol, but with a different bone augmentation technology. The second study by the same group is the real prospective cohort study, where implants placed with the early protocol are compared with a control group with a 6-month delayed implant protocol (Nemcovsky & Artzi 2002). In the series of studies from the Danish research group, the time of implant placement in the control group varied between 65 and 138 days after tooth extraction (Schropp et al. 2003a, 2003b, 2004, 2005a, 2005b; Schropp & Isidor 2008). In the study by (Cosyn & De Rouck 2009), the control group are contra-lateral non-restored teeth.

Table 4 summarizes the data on the main outcome variable, the changes in hard tissue dimensions measured between implant placement and the second stage surgery. These data were evaluated in three of the eight selected studies and expressed as changes in height, width and area, as well as in frequency distributions expressed as differences in the percentage reduction of height and area.

The bone defects present during the early placement, mostly dehiscence-type defects, were treated using a combination of bovine bone mineral and resorbable collagen mem-

Table 3a. **Methods, participants, interventions, outcomes, site and funding of the selected studies (first part)**

Study	Method	Participants	Interventions	Outcomes	Site and funding
Nemcovsky et al. (2000)	Prospective cohort study Two study groups 6–8 weeks follow-up	21 individuals (–0) male/female: NA Aged 54.9 years Selected sites: maxillary teeth Smoking habit: NA Periodontal status: NA	*Test*: immediate-delayed implants (5–7 weeks post-extraction) + Bio-Oss® + BioGide® for two implants *Control*: immediate-delayed implants (5–7 weeks post-extraction) + Bio-Oss® + BioGide®for one implant	*Hard tissue dimensions*: defect height (mm), defect width (mm), defect área (mm^2), reduction in defect área (%), reduction in defect height (%) *Implant survival Postoperative complications Periodontal probe*: 15-mm colour coded periodontal probe	University based (Tel Aviv – Israel) Not available
Nemcovsky & Artzi (2002)	Prospective cohort study Three study groups 6–8 weeks follow-up	66 individuals (–2) male/female: NA Aged NA Selected sites: 1–3 proximal maxillary teeth Smoking habit: NA Periodontal status: NA	*Test*: immediate-delayed implants (4–6 weeks post-extraction) + Bio-Oss® + BioGide® *Control*: delayed implants (6 months post-extraction) + Bio-Oss® + BioGide® *3rd group*: immediate implants (same day of extraction) + Bio-Oss® + BioGide®	*Hard tissue dimensions*: defect height (mm), defect width (mm), defect área (mm^2), reduction in defect área (%), reduction in defect height (%) *Implant survival Postoperative complications Periodontal probe*: milimetric periodontal probe	University based (Tel Aviv – Israel) Not available
Cosyn & De Rouck (2009)	Retrospective case–control study Two study groups 21 (6–68) months follow-up	27 individuals (–0) 9 male/18 female Aged NA Selected sites: 15–25 Smoking habit: NA Periodontal status: NA	*Test*: single implant placed 6 –8 weeks post-extraction + Bio-Oss® + Bio-Gide® *Control*: non-restored contralateral tooth	*Soft tissue dimensions*: keratinized mucosa width, recession, mesial and distal papila height *Clinical peri-implant outcomes*: plaque score (%), PPD, BoP *Crown dimensions*: length, width, facio-palatal *Implant success Implant survival Postoperative complication Periodontal probe*: CP 15 UNC	University based (Ghent – Belgium) Not explained

Table 3b. **Methods, participants, interventions, outcomes, site and funding of the selected studies (second part)**

Study	Method	Participants	Interventions	Outcomes	Site and funding
Schropp et al. (2003a, 2003b)	RCT Two study groups 3 months follow-up	Forty-seven individuals (−4) 21 male/26 female Aged 20–74 (mean: 48) Selected sites: 15–25/35–45 Smoking habit: NA Periodontal status: NA	*Test*: single implants placed 3–15 days (mean:10) after tooth extraction *Control*: single implants placed 99 days (65–138 days) after tooth extraction, with autogenous bone chips to cover exposed threads	*Hard tissue dimensions*: defect height (mm), defect width (mm), defect reduction (%), horizonatl gap (mm) *Implant survival Postoperative complications Periodontal probe*: NA	University based (Aarhus – Denmark) Biomet 3i
Schropp et al. (2004)	RCT Two study groups 16–18 months follow-up	46 individuals (−5) 18 male/23 female Aged 23–75 (mean: 50) Same as Schropp et al. 2003a, 2003b	*Test*: same as Schropp et al. (2003a, 2003b) *Control*: single implants 3 months after tooth extraction	*Patient satisfaction* (VAS + check boxes)	Same as Schropp et al. (2003a, 2003b)
Schropp et al. (2005a)	RCT Two study groups 16–18 months follow-up	Forty-five individuals (−6) na male/na female Aged NA Same as Schropp et al. (2003a, 2003b)	*Test*: same as Schropp et al. (2003a, 2003b) *Control*: single implants 3 months after tooth extraction	*Soft tissue dimensions*: % of complete papila (modified Jemt Index) *Crown dimensions*: % of crowns with normal height *Periodontal probe*: NA	Same as Schropp et al. (2003a, 2003b)
Schropp et al. (2005b)	RCT Two study groups 24 months follow-up	Forty-six individuals (−5) 21 male/25 female Aged NA Same as Schropp et al. (2003a, 2003b)	*Test*: same as Schropp et al. (2003a, 2003b) *Control*: same as Schropp et al. (2004)	*Hard tissue dimensions*: bone level in mm (mesial and distal) *Clinical peri-implant outcomes*: buccal, mesial, distal, lingual PPD *Implant survival Periodontal probe*: NA *Radiographic evaluation*	Same as Schropp et al. (2003a, 2003b)
Schropp & Isidor (2008)	RCT Two study groups 60 months follow-up	Forty-five individuals (−11) 21 male/24 female Aged 20–74 (mean: 48) Same as Schropp et al. (2003a, 2003b)	*Test*: same as Schropp et al. (2003a, 2003b) *Control*: single implants 3 months after tooth extraction	*Hard tissue dimensions*: bone level in mm (mesial and distal), horizonatl gap (mm) *Soft tissue dimensions*: % of complete papila *Clinical peri-implant outcomes*: buccal, mesial, distal, lingual PPD *Patient satisfaction Crown dimensions*: % of crowns with normal height *Implant survival Periodontal probe*: NA *Radiographic evaluation*	Same as Schropp et al. (2003a, 2003b)

RCT, randomized clinical trials; NA, not available.

branes (Nemcovsky et al. 2000; Nemcovsky & Artzi 2002) or autogenous bone chips harvested from the adjacent bone (Schropp et al. 2003a, 2003b). In most cases, defect reduction was greater in the early placement group than in the delayed protocol, although only differences in the reduction of defect height, width and area were statistically significant (Nemcovsky & Artzi 2002). Similar results were obtained in three studies in terms of hard tissue dimensions, favouring the early placement protocol (Nemcovsky & Artzi 2002; Schropp et al. 2003a, 2003b; Schropp & Isidor 2008).

Table 5 summarizes the data on changes in soft tissue dimensions evaluated in three studies. The changes in keratinized mucosa width, marginal recession and papilla height, were only evaluated in one study (Cosyn & De Rouck 2009). The Danish study only evaluated the papilla height using the Jemt modified index (Schropp et al. 2003a, 2003b).

The results tended to favour the delayed protocol, demonstrating greater keratinized mucosa width, less recession, greater mesial and distal papilla height (Cosyn & De Rouck 2009) and greater percentage of papilla fill (Schropp et al. 2005a, 2005b), although statistically significant differences were only reached when evaluating the distal papilla height ($P = 0.001$), and in this study, the comparison was made with a contralateral untreated control, rather than an implant-supported restoration (Cosyn & De Rouck 2009).

Table 6 summarizes the data on the changes in the peri-implant tissues reported in three studies (Schropp et al. 2003a, 2003b; Schropp & Isidor 2008; Cosyn & De Rouck 2009) evaluated through measurements of PPD, BoP and plaque scores around the selected implants.

In the Belgian study (Schropp & Isidor 2008), implant-supported restorations demonstrated worse peri-implant tissue outcomes than the contralateral unrestored teeth, demonstrating higher plaque scores and statistically significant higher BoP scores in the control group ($P = 0.001$).

The studies from the Danish group reported data on probing depths at 2 years (Schropp et al. 2003a, 2003b) and 5 years (Schropp & Isidor 2008) after the implant-supported restoration. A continuous PPD reduction was observed from baseline to 2 and 5 years, with no differences between groups. For buccal and lingual sites, the test group (early protocol) showed a trend for a greater reduction in PPD than the control group (delayed protocol), whereas at the

Table 4. **Outcome variables: changes in hard tissue dimensions, expressed as mean**

Publication	Defect height reduction				Defect width reduction				Defect area reduction				% Defect height reduction				% Defect area reduction			
	Control	Test	Diff.	*P*-value	Control	Test	Diff.	*P*-value	Control	Test	Diff.	*P*-value	Control	Test	Diff.	*P*-value	Control	Test	Diff.	*P*-value
Nemcovsky et al. (2000)	6.10	5.57	+0.53	NA	3.60	3.21	+0.39	NA	23	19.9	+3.02	0.08	NA	NA	NA	NA	97	97.05	−0.05	NA
Nemcovsky & Artzi (2002)	4.2	6	−1.8	0.031*	2.3	3.6	−1.3	0.041*	14.1	22.5	−8.4	>0.05	17.99	15.29	−13.60	0.015*	87.6	95.6	−8	NA
Schropp et al. (2003a, 2003b	1.5	3.3	−1.8	0.27	1.2	2.1	−0.9	0.27	NA	NA	NA	NA	61.6	38.2	−14	0.27	NA	NA	NA	NA

Diff., difference between the control and the test results: a positive figure means a greater value for the control group; NA, not available.
*$P < 0.05$ was considered statistically significant.

Table 5. **Outcome variables: changes in soft tissue dimensions, expressed as mean (SD)**

Publication	Keratinized mucosa width				Recession				Mesial papilla height				Distal papilla height				Jemt modified index (%)			
	Control	Test	Diff.	*P*-value	Control	Test	Diff.	*P*-value	Control	Test	Diff.	*P*-value	Control	Test	Diff.	*P*-value	Control	Test	Diff.	*P*-value
Schropp et al. (2005a)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	37	25	12	>0.05
Schropp & Isidor (2008)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	29	26	3	NA
Cosyn & De Rouck (2009)	5.5 (1.9)	5.3 (1.8)	+0.2 (1.8)	0.673	0.1 (0.9)	0.2 (0.9)	+0.3 (1.2)	0.362	3.7	3.1	+0.4 (0.9)	NA	3.5 (0.8)	2.5 (0.9)	+1 (1)	0.001*	NA	NA	NA	NA

Diff., difference between the control and the test results: a positive figure means a greater value for the control group; NA, not available.
*$P < 0.05$ was considered statistically significant.

mesial and distal sites, the changes favoured the control group.

Two studies reported data on patient satisfaction, both using a visual-analogical scale (VAS) (Schropp & Isidor 2008), although one also utilized a structured questionnaire (Schropp et al. 2004). At the 2-year evaluation, significantly higher patient satisfaction was reported in the test group, although these differences disappeared at 5 years (Table 7).

Table 8 reports the data on implant outcomes. Implant success defined after the Smith & Zarb (1989) criteria was reported in one study (Cosyn & De Rouck 2009). All implants placed were successful, although comparisons could not be done, as the control group was contralateral natural teeth. Implant survival was reported in the rest of the selected studies (Nemcovsky et al. 2000; Nemcovsky & Artzi 2002; Schropp et al. 2003a, 2003b, 2005a, 2005b; Schropp & Isidor 2008). In the control groups, the survival percentages ranged from 95% to 97.5%, in comparison with the test groups from 91% to 100%.

Four studies reported data on postoperative complications (Nemcovsky et al. 2000; Nemcovsky & Artzi 2002; Schropp et al. 2003a, 2003b; Cosyn & De Rouck 2009). The early implant placement group demonstrated less postoperative complications in one study (8% vs. 31.8%) (Nemcovsky & Artzi 2002), whereas in the Danish studies, the opposite results was reported (13% vs. 0%) (Schropp et al. 2003a, 2003b, 2004, 2005a, 2005b; Schropp & Isidor 2008). Complications were not comparable because in each study different postoperative complications were evaluated. In the Danish studies (Schropp et al. 2003a, 2003b), the most common complication in the test group was the temporary affection of the dental nerve in two cases with implants placed in the posterior mandible, whereas in the study by Nemcovsky & Artzi (2002), the most common complication was the early exposure of the healing screw. At the same time, Nemcovsky et al. (2000) reported that complications were more frequent when two contiguous implants were placed, whereas Cosyn & De Rouck (2009) described early exposure of the membrane in 4% of the cases.

Table 9 depicts data on crown dimensions. In the Danish studies, a significant difference favouring the early placement group was reported at the 1.5-year follow up (Schropp et al. 2005a, 2005b). These differences, however, decreased with time (Schropp & Isidor 2008). (Cosyn & De Rouck 2009) reported data on crown dimensions comparing

Table 6. **Outcome variables: changes in clinical peri-implant outcomes, expressed as mean (SD)**

	Plaque score (%)				% BoP				PPD all sites			
Publication	Control	Test	Diff.	*P*-value	Control	Test	Diff.	*P*-value	Control	Test	Diff.	*P*-value
Schropp et al. (2005a)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Schropp & Isidor (2008)	NA	NA	NA	NA	NA	NA		NA	NA	NA	NA	NA
Cosyn & De Rouck (2009)	18 (25)	14 (17)	+4 (19)	0.305	9 (16)	27 (21)	−18 (21)	0.001*	2.3 (0.3)	3.2 (0.6)	−0.9 (0.7)	0.001*

	PPD mesial				PPD distal				PPD buccal				PPD lingual			
Publication	Control	Test	Diff.	*P*-value	Control	Test	Diff.	*P*-value	Control	Test	Diff.	*P*-value	Control	Test	Diff.	*P*-value
Schropp et al. (2005a)	0.2	0.6	−0.4	0.24	0.2	0.3	−0.1	0.66	0.2	0.5	0.3	0.16	0.6	1.4	0.8	0.06
Schropp & Isidor (2008)	0.1	0.5	−0.4	0.48	0.1	0.5	−0.4	0.48	0.5	1.1	0.6	0.12	0.7	1.5	0.8	0.29
Cosyn & De Rouck (2009)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

PPD, probing pocket depth; BoP, bleeding on probing; Diff, difference between the control and the test results: a positive figure means a greater value for the control group; NA, not available.
*$P < 0.05$ was considered statistically significant.

implant-supported restorations with the contralateral teeth. Clinical crown length was not significantly different between implant crowns and teeth, although in terms of crown, width differences almost reached the level of significance. The buco-lingual dimension was on average, 0.4 mm smaller for implant-supported crowns, when compared with contralateral teeth, these differences being statistically significant.

Meta-analysis was carried out for the evaluation of the primary outcomes, as well as in the secondary outcome variable implant survival, by comparing the early placement protocol (IDP) and the delayed protocol (DP). With regard to the primary outcome (hard tissue changes), only two of the included studies (Nemcovsky & Artzi 2002; Schropp et al. 2003a, 2003b) showed similar comparisons and reported the same outcome variables: the reduction in defect bone height and the reduction in defect bone width. As the size of the defects of the two groups was different at baseline, the percentage of reduction, calculated as (size at baseline − size at second stage surgery)/size at baseline × 100, was used as outcome variable. Fig. 2 shows the forest plots depicting the percentage reduction in defect bone height. Both studies showed a greater percentage of reduction in defect height in the early group than in the delayed group. In the Danish study (Schropp et al. 2003a, 2003b), a non-significant mean difference of 8.4% (95% CI: from −21.91 to 38.71) was observed between groups. In the Israeli study, a significant difference of 13.6% (95% CI: from 3.85 to 23.35) was reported (Nemcovsky & Artzi 2002). The combined result (fixed effects model) was 13.11% (95% CI: from 3.83 to 22.4; $P = 0.057$), without detecting significant heterogeneity ($I^2 = 0\%$; $\tau^2 = 0$; Q-test P-value = 0.749). Even though the sample sizes in the two groups from both studies were similar, the variability of the data was different. The Israeli study reported smaller standard deviations, and hence, the relative weights of the two studies were 90.6% and 9.4% respectively (Nemcovsky & Artzi 2002; Schropp et al. 2003a, 2003b). As only two studies were available, no further analyses (such as cumulative meta-analysis, sensitivity analysis, publication bias) were performed.

Figure 3 shows the forest plots depicting the percentage reduction in defect bone width. Both studies found a greater percentage of reduction in defect width in the early group compared with the delayed group, whereas in the Danish study, the difference of 20.5% between test and control groups (95% CI: from −17.87 to 58.87) was not statistically significant (Schropp et al. 2003a, 2003b); in the Israeli study a smaller percentage reduction 19.83% (95% CI: from 13.85 to 25.81) was statistically significant (Nemcovsky & Artzi 2002). The global mean difference after combining both studies (fixed effects model) was 19.85% (95% CI: from 13.93 to 25.76; $P = 0.000$). No heterogeneity was detected ($I^2 = 0\%$; $\tau^2 = 0$; Q-test P-value = 0.973). Due to the considerable variability of the data reported by (Schropp et al. 2003a, 2003b), its relative weight to the meta-analysis was 2.37%. The study of (Nemcovsky & Artzi 2002) provided 97.63% of the global estimation.

Figure 4 shows the forest plots depicting the percentage in implant survival from the two studies reporting similar follow-up periods (Nemcovsky & Artzi 2002; Schropp et al. 2005a, 2005b). Comparisons were computed with a constant continuity correction ($k = 0.5$) for studies with zero events, as Nemcovsky reported no implant failure in the early placement group. Although the survival rates were higher in the test group, the differences between the test and control groups were not significant (RR = 1.02, 95% CI: 0.96–1.1). The Danish study (Schropp et al. 2005a, 2005b), however, showed the opposite results, with a higher survival rate for the delayed group, also non-significant (RR = 0.95, 95% CI: 0.82–1.11). No heterogeneity was present ($I^2 = 0\%$; $\tau^2 = 0$; Q-test P-value = 0.411), and thus, the fixed effects model was chosen. The pooled RR was 1.01 (95% CI: 0.95–1.08; $P = 0.698$), showing that the implant survival percentages were very similar for both protocols. The relative weights of each study differed, being 16.38% for Schropp et al. (2005a, 2005b) and 83.62% for Nemcovsky & Artzi (2002), as the number of implants in the study by Nemcovsky & Artzi (2002) ($n_{IDP} = 39$; $n_{DP} = 40$) almost doubled the number of implants used by Schropp et al. (2005a, 2005b) ($n_{IDP} = 23$; $n_{DP} = 23$), which also showed wider confidence intervals.

Tables 10 and 11 depict the quality criteria used to evaluate the quality of the selected

Table 7. **Outcome variables: patient satisfaction, as evaluated with visual analogue scale and expressed as median**

	Whole period unpleasantness				Satisfaction with restoration				Appearance				Whole period time				Overall experience			
Publication	Control	Test	Diff.	*P*-value	Control	Test	Diff.	*P*-value	Control	Test	Diff.	*P*-value	Control	Test	Diff.	*P*-value	Control	Test	Diff.	*P*-value
Schropp et al. (2004)	87	80	−7	>0.05	93	96	−3	<0.05*	93	96	−3	<0.05*	57	74	−17	<0.05*	90	96	−6	<0.05*
Schropp & Isidor (2008)	NA	NA	NA	NA	96	96.5	−0.5	0.7	93	96	−3	0.41	NA	NA	NA	NA	95	95.5	−0.5	0.52

Diff., difference between the control and the test results: a positive figure means a greater value for the control group; NA, not available.
*$P < 0.05$ was considered statistically significant.

Table 8. **Outcome variables: implant survival, success (according to Smith & Zarb 1989) and complications rate**

	% Implant success		% Implant survival		% Postopertaive complication	
Publication	Control	Test	Control	Test	Control	Test
Nemcovsky et al. (2000)	NA	NA	100	NA	0	NA
Nemcovsky & Artzi (2002)	NA	NA	100	97.5	8	31.8
Schropp et al. (2003a, 2003b)	NA	NA	91	96	13	0
Schropp et al. (2004)	NA	NA	NA	NA	NA	NA
Schropp et al. (2005a)	NA	NA	NA	NA	NA	NA
Schropp et al. (2005b)	NA	NA	91	96	NA	NA
Schropp & Isidor (2008)	NA	NA	91	95	NA	NA
Cosyn & De Rouck (2009)	100	–	NA	NA	4	NA

NA, not available.

RCTs and prospective cohort and case–control retrospective studies. The evaluation of the quality of the RCT indicates that it has a high potential of bias (Schropp et al. 2003a, 2003b; Schropp et al. 2004; Schropp et al. 2005a, 2005b; Schropp & Isidor 2008), whereas the prospective cohort study (Nemcovsky & Artzi 2002) and the case–control retrospective study (Cosyn & De Rouck 2009) were categorized as poor quality studies.

Discussion

The results from this systematic review suggest that the early implant placement protocol may offer advantages with regard to preserving the hard and soft tissues around the implants. The meta-analysis demonstrated a pooled mean difference between groups of 13.11% reduction in defect bone height, and 19.85% of reduction of defect bone width favouring the early placement group. The results from this meta-analysis, however, should be interpreted with caution, as only two studies were combined. Although no statistical heterogeneity was found when combining the studies, the Q statistic and I^2 index used have a limited power to detect true heterogeneity among studies when the meta-analysis includes a small number of studies (Cornwell 1993). The imbalance in the relative weights of each pair of combined studies is another factor that may affect the validity of this meta-analysis.

The preservation of the width and height of the bone around an implant may not be critical in our ability to place a dental implant or in the long-term success and survival of the implant-supported restorations, but it may be of great relevance when implants are placed to restore missing teeth in aesthetically relevant areas. This aesthetic challenge is based on a variety of local risk factors that are often present in the anterior maxilla. Recent studies have clearly shown that the facial bone in the anterior maxilla is usually very thin ($\leq$1 mm) (Huynh-Ba et al. 2010; Januario et al. 2011), and experimental and clinical studies have demonstrated that thin buccal bone will be quickly resorbed within 4–8 weeks following tooth extraction leading to a reduction in bone height (Schropp et al. 2003a, 2003b; Araujo & Lindhe 2005; Nevins et al. 2006). This fact clearly underlines the need of bone augmentation whenever implants are placed in critically aesthetic areas in the anterior maxilla. All these factors make this implant placement protocol very attractive, because it not only preserves the bone height and width of the ridge, when compared with the delayed protocol, as shown in this systematic review but also provides enough keratinized mucosa to allow for a successful bone augmentation procedure during the implant placement. The results of augmentation techniques depend on a tension-free primary wound closure, which would protect the biomaterials and regenerative technologies utilized. During the healing period of 4–8 weeks after tooth extraction, an additional amount of keratinized mucosa will develop in the extraction site (Schropp et al. 2003a, 2003b) that will enable the elevation of an intact flap and a tension-free closure without altering the mucogingival line, when the implants are placed with this early placement protocol, also allowing for the required bone augmentation technique in conjunction with the placement of the implant.

Within this context of improved aesthetic results, the assessment of patient-related becomes very important. In this systematic review, two studies reported data on patient satisfaction, although no data pooling was possible. Two studies assessed the same population at two different follow-up periods, at

Table 9. **Outcome variables: crown dimensions, expressed as mean (SD)**

	Crown length				Crown width				Facio-palatal dimension				% Adequate crown height			
Publication	Control	Test	Diff.	*P*-value	Control	Test	Diff.	*P*-value	Control	Test	Diff.	*P*-value	Control	Test	Diff.	*P*-value
Schropp et al. (2005a)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	5	15	−10	0.04*
Schropp & Isidor (2008)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	25	5	+20	NA
Cosyn & De Rouck (2009)	9.7 (1.5)	10 (1.7)	−0.3	0.266	7.6 (1.2)	7.8 (1.4)	−0.2	0.056	7.9 (1.1)	7.5 (0.8)	0.4	0.001*	NA	NA	NA	NA

Diff., difference between the control and the test results: a positive figure means a greater value for the control group; NA, not available.
*$P < 0.05$ was considered statistically significant.

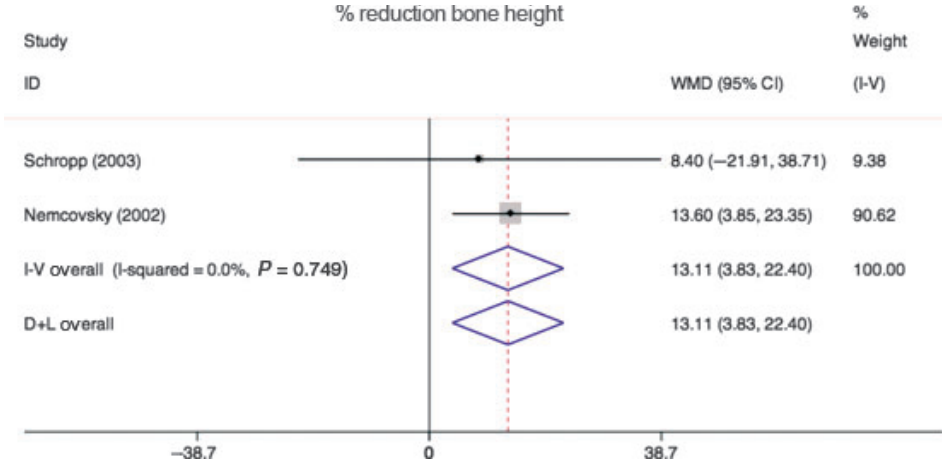

Fig. 2. Meta-analysis: changes in bone height.

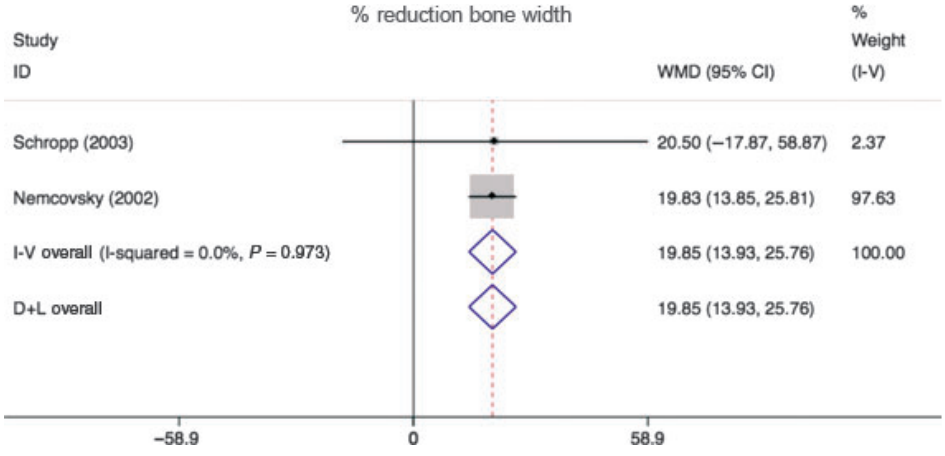

Fig. 3. Meta-analysis: changes in bone width.

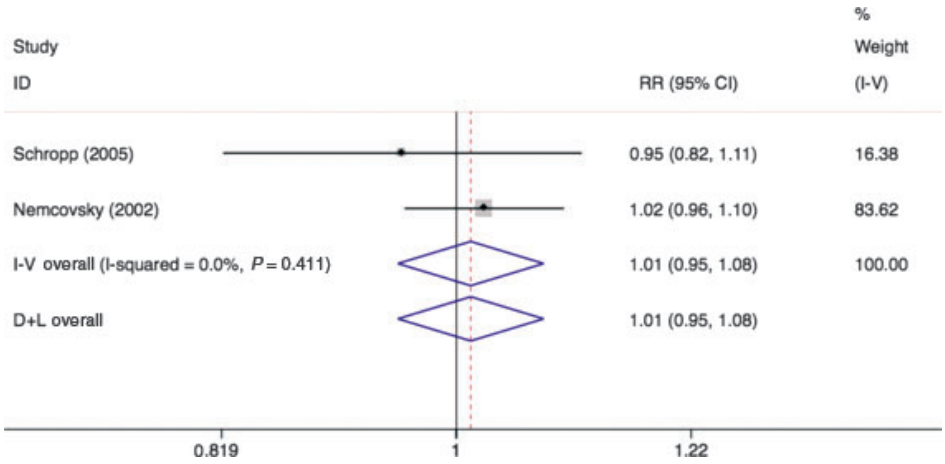

Fig. 4. Meta-analysis: implant survival.

Table 10. **Quality assessment: randomized clinical trials**

Publication	Adequate sequence generation?	Allocation concealment?	Blinding?	Incomplete outcome data addressed?	Free of selective reporting?	Free of other bias?	Risk of bias
Schropp et al. (2003a, 2003b)	No	Unclear	Unclear	Yes	Yes	No	High potential
Schropp et al. (2004)	No	Unclear	Unclear	Unclear	Yes	No	High potential
Schropp et al. (2005a)	No	Unclear	Yes (single: examiner)	No	Yes	No	High potential
Schropp et al. (2005b)	No	Unclear	Yes (single: examiner)	Yes	Yes	No	High potential
Schropp & Isidor (2008)	No	Unclear	Yes (single: examiner)	Yes	Yes	No	High potential

Table 11. **Quality assessment: observational studies**

Publication	Inclusion/ exclusion criteria	Homogeneity between groups	Rationale for study size	Lost to follow-up (%)	Statistics: description/ confounding	Addressing lost/missing data	Quality
Cosyn & De Rouck (2009)	Yes	No	Unclear	6.3	No	Not applicable	Poor
Nemcovsky & Artzi (2002)	No	No	Unclear	0	No	Unclear	Poor
Nemcovsky et al. (2000)	No	Not available	Unclear	Unclear	No	Unclear	Poor

2 and 5 years (Schropp et al. 2004; Schropp & Isidor 2008), while one other study (Cosyn & De Rouck 2009) assessed the overall patient aesthetic satisfaction, but the comparison was not with another implant placement protocol, but with the contralateral natural teeth. In both studies, patients showed a high degree of satisfaction. In the Schroop studies, at the 2-year follow-up (Schropp et al. 2004), patients were significantly more satisfied with the early placement protocol, both in terms of the appearance with the restoration and the overall experience with the treatment. These differences, however, were lost at the 5-year follow-up (Schropp & Isidor 2008).

Although the results in terms of aesthetic outcomes and stability of soft tissues are very limited in this systematic review, as these outcomes were not measured in the selected studies, several published prospective case series have reported intermediate to long-term excellent aesthetic results (Buser et al. 2008a, 2008b; Buser et al. 2009; Buser et al. 2011).

In a prospective case series replacing single-tooth in the anterior maxilla using the early placement protocol, aesthetic outcomes were reported at 1 and 3 years after placing the definitive crown using the PES aesthetic score index (Belser et al. 2009). Of 20 patients, only one (5%) patient demonstrated minor mucosal recession between 0.5 and 1 mm at the 3-year examination (Buser et al. 2009; Buser et al. 2011). The stability of the facial mucosa margin was also confirmed clinically and mesured on casts. Similarly, standardized periapical radiographs demonstrated minimal interdental bone. These results confirm similar favourable data of a previous retrospective study (Buser et al. 2008a, 2008b) in 45 patients using the same surgical approach, also showing a low risk for facial recession and minimal interdental bone loss after 2–4 years of follow up. In these studies, bone augmentation was always carried out in conjunction with the placement of the implant using the concept of GBR, with the application of a combination of an autogenous graft and a low-substitution bone filler (deproteinized bovine bone mineral), covered with a resorbable non-crosslinked porcine collagen membrane.

This concept of bone augmentation with the use of a xenogeneic bone graft and a resorbable barrier membrane, in conjunction with an early implant placement protocol, was carried out in the study that provided higher percentages in the pooled results for the main outcome variables as shown in this systematic review (Nemcovsky et al. 2002).

Even though the available scientific evidence included in this systematic review would support the use of the early implant placement protocol, the inherent limitations of the available data must be highlighted. The most important limitation is the limited number of included investigations. Even though eight studies were included in the review, five of them reported different results or different follow-up from the same investigation (Schropp et al. 2003a, 2003b, 2004, 2005a, 2005b; Schropp & Isidor 2008) and therefore, only data from four independent investigations were analysed. Another important limitation is the high heterogeneity among the studies, not only with regard to its design and methodology, but also to the definitions of the study groups and outcome variables. After strictly following the classification from the consensus workshop defining the three surgical protocols of implant installation after tooth extraction (Hammerle et al. 2004), only the Israeli studies used a period of 4–7 weeks after tooth extraction to define the early placement group (Nemcovsky et al. 2000; Nemcovsky & Artzi 2002), whereas the five Danish studies (Schropp et al. 2003a, 2003b; Schropp et al. 2004; Schropp et al. 2005a, 2005b; Schropp & Isidor 2008) placed the implants of this treatment group between 1 day and 4 weeks after tooth extraction, and the Belgium study (Cosyn & De Rouck 2009) placed it between 6 and 8 weeks. To be inclusive, we included all these healing periods after the tooth extraction as belonging to the early placement group, but it is impossible to know whether these different placing times have any influence on the reported results. Differences were even more evident among the control groups. In the Danish studies, the control group was defined as implants placed between 65 and 188 days (approximately 9–27 weeks), whereas the Israeli studies allowed 6 months (24 weeks) of healing, and the Belgium study used as controls non-restored contralateral teeth. In addition, the quality assessment of the included studies also does not allow for strong conclusions, as the only RCT demonstrated a high potential of bias, and both the prospective cohort and case–control studies were categorized as poor quality studies.

Within these limitations, the following conclusions of this systematic review can be drawn:

1. The early implant placement protocol may offer advantages in terms of soft and

hard tissues changes, when compared with the delayed implant placement protocol.

2. In light of the scarcity and quality of the available scientific evidence, well-designed, high quality, randomized clinical trials are needed to provide data allowing the establishment of clinical recommendations regarding implant placement protocols after tooth extraction.

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