Vertical Bone Augmentation for Implant Placement in the Mandible – a Systematic Review

A dissertation submitted to the University of Manchester for the degree of Master of Science in Dentistry (Oral and Maxillofacial Surgery) in the Faculty of Medical and Human Sciences

2016

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CONTENTS

Abstract.................................................................................................................................................. 4
Declaration.................................................................................................................................................. 5
Intellectual Property Statement.................................................................................................................. 6
Acknowledgements...................................................................................................................................... 7
1. Introduction: Background and Literature Review.................................................................................. 8
   1.1 Dental Implants.................................................................................................................................. 8
   1.2 Osseointegration.................................................................................................................................. 9
   1.3 Alveolar Bone Deficiency.................................................................................................................. 9
   1.4 Approaches to Vertical Alveolar Bone Deficiency in the Mandible: Bone Augmentation Procedures................................................................................................................................. 10
      1.4.1 Onlay bone grafting...................................................................................................................... 11
      1.4.2 Inlay bone grafting...................................................................................................................... 11
      1.4.3 Guided bone regeneration (GBR).............................................................................................. 11
   1.5 Bone Augmentation Materials........................................................................................................... 11
      1.5.1 Autogenous bone....................................................................................................................... 11
      1.5.2 Xenograft.................................................................................................................................... 12
      1.5.3 Allograft..................................................................................................................................... 12
      1.5.4 Alloplastic graft.......................................................................................................................... 12
   1.6 Literature Review and Rationale......................................................................................................... 12
2. Aims and Objectives............................................................................................................................... 15
3. Methods.................................................................................................................................................. 16
   3.1 Focused Question............................................................................................................................... 16
   3.2 Search Strategy................................................................................................................................... 16
   3.3 Study selection: Inclusion and exclusion criteria.............................................................................. 18
3.4 Risk of bias in studies...........................................................................21

4. Results........................................................................................................21

4.1 Study selection and characteristics......................................................21

4.2 Risk of bias in studies.............................................................................27

4.3 Results of individual studies.................................................................28

   4.3.1 Guided bone regeneration using autogenous bone.........................28

   4.3.2 Guided bone regeneration using xenograft bone substitute............29

   4.3.3 Block bone graft using autogenous bone........................................31

   4.3.4 Block bone graft using xenograft bone substitute.........................33

5. Discussion...................................................................................................38

   5.1 Summary of Evidence...........................................................................38

   5.2 Limitations............................................................................................41

6. Conclusion...................................................................................................43

   6.1 Implications for Practice and Research.............................................43

   6.2 Funding.................................................................................................43

References.....................................................................................................44

Appendix A: Search Strategy.........................................................................50

Appendix B. Reasons for Excluded Studies....................................................53

Word Count: 13,096
LIST OF TABLES AND FIGURES

Figure 1. Screening process used to identify eligible studies............................................21
Table 1. Study Characteristics............................................................................................27
Table 2. Risk of Bias in Studies..........................................................................................28
Table 3. Results of Individual Studies..................................................................................38
Table A1. Search Strategy..................................................................................................51
Table B1. Reasons for Excluded Studies. .................................................................54
ABSTRACT

PURPOSE: To examine the techniques and materials used in vertical bone augmentation for implant placement in the mandible and to evaluate vertical bone gain/loss and implant survival and success.

METHODS: A systematic review of randomized controlled trials selected from PubMed, the Cochrane Central Register of Controlled Trials (CENTRAL) and Ovid databases was performed. Outcome variables included were: vertical bone gain/loss, implant survival, and implant success. Only studies involving guided bone regeneration (GBR) and bone block grafting techniques, with autogenous or xenograft bone substitute in the mandible were considered eligible for inclusion. Only studies with a follow-up of at least 12 months after augmentation were included. Studies were analyzed for risk of bias.

RESULTS: After completing data extraction, 19 articles involving 10 RCTs were eligible for inclusion. All studies, except one, were evaluated to be at a low risk of bias. The included studies involved 262 patients and 554 implants. All studies provided measures of initial bone gain, bone resorption over time, or both. All studies provided rates of implant survival. Only 3 studies reported rates of implant success. An analysis of the results showed that both GBR and bone block grafts and both autogenous and xenograft bone can achieve sufficient levels of bone augmentation and comparable levels of resorption for implant placement and survival. Differences between the techniques and materials were minimal, but appeared to marginally favor GBR over bone block graft and autogenous bone over xenograft bone.

CONCLUSIONS: This systematic review included few trials with small sample sizes and short-term follow-up periods, with minimal differences reported in bone gain, resorption and implant survival. There is not sufficient existing evidence to determine the most effective approach to vertical augmentation in the mandible for the placement of implants. More high-quality, long-term randomized controlled trials with larger patient populations are needed.
DECLARATION

No portion of the work referred to in the dissertation has been submitted in support of an application for another degree or qualification of this or any other university or other institute of learning.
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ACKNOWLEDGEMENTS

This work is dedicated to God, my wife Jennifer and daughter Vivienne that were a strong pillar during this Master’s program, and to all my family and friends that showed me support during my studies.

The author gratefully acknowledges the following individuals from the University of Manchester: Professor Julian Yates, Dr. Jonathan Kennair. Additionally, the author gratefully acknowledges funding from the National Secretary of Higher Education, Science, Technology and Innovation of Ecuador (SENESCYT).
1. INTRODUCTION: BACKGROUND AND LITERATURE REVIEW

This research project consists of a systematic review of randomized controlled trials evaluating the vertical bone gain/loss and the incidence of implant survival and success following different bone augmentation procedures and materials in the vertically deficient mandible.

1.1 Dental Implants

Dental implants have been used successfully for several decades to improve the function and aesthetics of patients who have lost teeth, and are now widely available in dental practice. While many different materials and designs have been used in the past, the use of titanium and Schroeder’s concept of functional ankylosis (later termed osseointegration) are key points in the success of modern implant treatment. More recently and with advances in new implant and prosthetic designs these principles are “thought to have led to the well-established procedure of simple, one-step implant surgery that is preferred at present” (Porter and von Fraunhofer, 2005, p. 423). Indeed, the use of endosseous root-form implants to replace missing teeth – single teeth to fully edentulous jaws – has been practiced for over three decades (Garg, 2010). Traditionally titanium has been the preferred implant material during this time due to its mechanical properties and high biocompatibility; however, zirconia-based implants and abutments have also been introduced as a more aesthetic alternative and with similar results (Deprich et al., 2008; El Askary, 2007). While there have been many advancements in “techniques, materials, and implant design, the potential for clinical failure is a significant concern for both dentist and patient” (Porter and von Fraunhofer, 2005, p. 423).
1.2 Osseointegration

Osseointegration is the direct biological anchorage of a dental implant to bone in order to provide a base to support a fixed prosthesis (Bedrossian, 2011). As Brånemark previously reported, osseointegration leads to “permanent, functional and interactive coexistence between titanium and bone” (Bedrossian, 2011, p. 5). In order to form and remodel new bone apposition without soft tissue interference, the implant surface needs to be composed of an inert material (Bedrossian, 2011). Garg (2010) reports the three phases during the osseointegration process: 1) Osteophytic phase – where the surface of the implant is in direct contact with the bone, inducing migration of osteoblast and osteoid to the surface of the implant causing an initial reabsorption of the bone in contact with the titanium surface; 2) Osteoconductive phase – in which the bone cells take over the entire surface area of the implant; after four months the implant surface is covered by new bone; and finally, 3) Osteoadaptive phase, which is a stable phase with no gain or loss of bone beside the implant surface, however the remodeling process of the bone will continue after the implant is exposed and loaded (p. 200). When the patient has sufficient bone in the maxillary or mandibular alveolar ridge, conditions for osseointegration are optimal; in contrast, when the alveolar bone quantity and quality is deficient, osseointegration, anchorage and primary stability may be compromised, and there is an increased risk of implant failure.

1.3 Alveolar Bone Deficiency

“The design, diameter, length, and quantity of implants [used] will depend on the quality of available bone, the quantity of available bone, the location of available bone, and the type of prosthodontic application desired” (Garg, 2010, p. 97). A principal requirement for implant success and osseointegration is sufficient alveolar bone quantity and quality at the
mandibular or maxillary implant site. However, in many patients there is a reduction in bone dimension (width or height) which must be addressed so that implant placement can be undertaken and a successful outcome achieved.

In the maxilla and mandible consideration does have to be given to anatomical structures and patient differences in bony form in order to plan for successful implant placement. Anatomically in the mandible, the inferior alveolar nerve runs within the posterior part of the jaw and exits at the mental foramen. Furthermore, the profile of the bone and the presence of undercuts means that placement can be compromised if not planned adequately. Given the changes in bone morphology that can occur with age, following tooth extraction and parallel to diseases such as periodontal disease, special attention needs to be given to the planning phase of implant treatment. Therefore, if the required bone height at the implant site is not met, vertical bone augmentation procedures should be considered. Similar considerations have to be given to the maxilla but these are out with the scope of this review.

This systematic review will focus on studies of vertical ridge augmentation procedures in the mandibular implant site.

1.4 Approaches to Vertical Alveolar Bone Deficiency in the Mandible: Bone Augmentation Procedures

In the mandible in order to ensure adequate bone quantity and quality for implant osseointegration and survival, bone augmentation procedures should be considered where there is found to be a deficiency. The bone augmentation techniques addressed in this systematic review include block bone grafting and guided bone regeneration (GBR), as these are the ones most regularly used in clinical practice. Distraction osteogenesis and “sandwich or box” techniques are additional approaches used for vertical ridge augmentation; however, this systematic review will compare bone gain/loss and implant survival and success
associated with GBR and formal grafting procedures, and the different materials used.

1.4.1. Onlay bone grafting: This technique involves the harvesting of a block of bone from a donor site and placement onto the deficient area using either titanium screws or mini-plates (or a combination of). The graft can be placed on the buccal or superior alveolar cortical bone for vertical or horizontal bone augmentation. Commonly onlay bone blocks are harvested from the body or symphysis of the mandible, iliac crest or even calvarium. In addition, allograft and xenograft bone blocks are available for use in onlay grafting (Block, 2011).

1.4.2. Inlay bone grafting: This grafting technique requires a horizontal osteotomy of the deficient alveolar ridge in order to create a space between the inferior and superior aspects of the alveolar cortical bone that will receive the graft. Similar to onlay grafting, different types of bone material including block and particle bone can be used to fill the gap created by the osteotomy (Block, 2011).

1.4.3. Guided bone regeneration (GBR): This technique follows the same principles of guided tissue regeneration, maintaining a space between the host/receiving site and over lying soft tissues by a barrier membrane, which is then filled with particles of bone and will allow for new bone formation. The main function of the membrane is to “prevent gingival fibroblasts and/or epithelial cells from gaining access to the wound site and forming fibrous connective tissue” (Farzad et al., 2012, p. 3).

1.4 Bone Augmentation Materials

Several different materials can be used for these vertical bone augmentation procedures:

1.5.1. Autogenous bone: This is the patient’s own bone and can be harvested extra-orally from the iliac crest or even calvarium, or intra-orally such as mandibular ramus, symphysis, exostoses, maxillary tuberosity and cancellous bone from an implant osteotomy.
This type of bone substitute is considered ideal because it promotes rapid bone regeneration caused by its osteoinductive and osteoconductive properties (Garg, 2010).

1.5.2. Xenograft: This bone substitute is derived from animals and processed to remove any organic component; there are now many derivatives including bovine, porcine and even equine with one commonly used material being anorganic bovine bone BioOss (Wheeler, 1997). Despite a lack of osteoinductive properties, xenografts have been shown to achieve outcomes similar to autografts and allografts (El Askary, 2007).

1.5.3. Allograft: This bone substitute is derived from human cadavers and has been through decontamination and sterilization processes and stored in bone banks. It can regenerate bone by osteoinductive or osteoconductive process, can be frozen or freeze-dried bone allograft and can come in mineralized and demineralized form (Garg, 2010).

1.5.4. Alloplastic graft: This synthetic bone substitute can be considered “man-made” and includes materials such as porous hydroxyapatite, tri-calcium phosphate or bioactive glass (Wheeler, 1997). One example is Straumann BoneCeramic®, made of hydroxyapatite and beta-tricalcium phosphate (Van Assche, 2013). Alloplastic materials have also been shown to achieve outcomes similar to autografts and allografts (El Askary, 2007).

1.6 Literature Review and Rationale

Recent systematic reviews analyzing vertical bone augmentation in the mandible have generally shown favorable results regarding alveolar bone gain and implant survival and success. While there are several reviews related to bone augmentation and implants, they have rarely focused on or included randomized controlled trials (RCTs). Furthermore, few have reviewed more recent studies (post-2010), and have not focused specifically on vertical augmentation using autogenous and xenograft techniques in the mandible. However, some have reported the success of vertical ridge augmentation and below are the findings of some
recent systematic reviews related to this topic:

Rocchieta et al. (2008) performed a systematic review of 28 studies on various vertical bone augmentation techniques for implant placement in the mandible and maxilla and found “clinical and histological data supporting its potential use… [but] the generalizability of this approach is limited at this time” (p. 203). The review included mainly non-RCT studies and many animal models.

Waasdorp et al. (2010) performed a systematic review of 9 studies (no RCTs included) on the use of allogeneic block grafts for horizontal and vertical alveolar bone augmentation in the mandible and maxilla. The authors found “high rates of clinical graft incorporation (90% or greater) and implant survival (99% to 100%); however, the majority of reports involved selected defects in anterior regions with short-term follow-up” (p. 525).

Milinkovic et al. (2014) performed a systematic review of 68 studies (not limited to RCTs) on the use of varied augmentation procedures for horizontal and vertical alveolar bone deficiencies in the mandible and maxilla. In regard to vertical augmentation techniques, the authors found implant survival rates of 98.9-100% (GBR) and 96.3% (bone block grafts), without distinguishing between graft materials.

Clementini et al. (2012) performed a systematic review of 8 studies, primarily case studies, analyzing implants placed with intraoral onlay autogenous bone grafts in the mandible and maxilla and found implant success rates ranging from 72.8% to 97% after follow-up periods ranging from 6 months to 10 years.

Aloy-Prósper et al. (2015) also performed a systematic review of 6 studies analyzing implants placed with intraoral onlay autogenous bone grafts in the mandible and maxilla and found 89.5%-100% survival rates for implants in vertically augmented bone. This review was not limited to RCTs and included only 2 studies on vertical augmentation.

Lee et al. (2014) performed a systematic review of 4 RCTs of various vertical
augmentation procedures in the mandible and maxilla compared to the use of short implants. The authors found implant survival rates of 98% for vertically augmented sites and 98.7% for short implants. They did not compare mean bone gain between augmentation procedures.

Keestra et al. (2015) performed a systematic review of 51 long-term studies of various vertical augmentation procedures in the mandible and maxilla. The authors examined bone gain only and did not analyze implant survival. They found that “onlay technique, alveolar distraction, and vertical guided bone regeneration are stable for at least 4 to 5 years” (p. 3). Just one RCT was eligible for inclusion in this systematic review.

Finally, Esposito et al. (2009) performed a Cochrane systematic review of horizontal and vertical bone augmentation procedures for implant placement in the mandible and maxilla. These authors examined RCTs exclusively and found 13 eligible studies. The outcome measures included implant failure and bone gain, among others. Though the systematic review compared vertical augmentation techniques, they found “insufficient evidence to indicate which could be the preferable technique” (p. 183). In relation to bone substitutes and materials, the authors suggested that xenograft substitutes such as Bio-Oss were a better alternative to autogenous grafts.

The clinical techniques involved in vertical augmentation in the mandible for implant placement are constantly developing through improvement of materials, techniques and technology. While some systematic reviews have shown favorable results for vertical augmentation procedures for implant placement, few have focused on the results of implant survival and success and bone gain/loss from randomized controlled trials. Additionally, few of the existing reviews are updated to include RCTs from the last decade. Finally, this systematic review focuses the research question on bone gain/loss and implant survival and success related to GBR and inlay and onlay block graft procedures in the mandible using autogenous and xenograft materials.
2. AIMS AND OBJECTIVES

This study follows the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) (Liberati et al., 2009) statement guidance for systematic reviews and meta-analysis of clinical studies that assess medical interventions.

The aim of this systematic review is to analyze the effectiveness of different bone augmentation procedures and materials for the placement of dental implants in patients with mandibular alveolar bone deficiency. The objectives include comparing and analyzing the change in mandibular alveolar bone height, and the survival and success rates of dental implants, after bone block graft and guided bone regeneration (GBR), using autogenous and xenograft bone substitutes. A secondary aim of this systematic review was to evaluate the quality of the existing RCTs on this topic.

Following PICOS terms, the objective can be described:

• P (Population): adults age 16-85 with a vertical mandibular alveolar bone deficiency at implant placement.

• I (Interventions): vertical bone augmentation with block graft or GBR techniques using autograft and xenograft bone substitutes followed by implant placement.

• C (Comparison): no augmentation procedures or different augmentation procedures.

• O (Outcomes): primary outcome: vertical bone gain/loss; secondary outcome: implant survival and success

• S (Study design): randomized controlled trials (RCTs) only.
3. METHODS

3.1 Focused Question

Which vertical bone augmentation procedure is associated with the most successful gain (or minimal loss) in alveolar bone height and implant survival and success rates in the patient with a mandibular bone deficiency at the implant site?

3.2 Search Strategy

An electronic search of the PubMed, Cochrane CENTRAL, and Ovid MEDLINE databases was performed to identify potential studies for inclusion in the systematic review. The limits applied were: randomized controlled trials, studies on humans, articles in English, and studies in the last 10 years (2006-current). The electronic search was conducted several times to check for any new articles published between January 2016 and June 2016.

The following MeSH terms were used to search all databases:

- Alveolar ridge augmentation
- Alveolar bone grafting
- Alveolar bone loss
- Bone Substitutes
- Mandible
- Dental Implants
- Dental Implants, Single tooth
- Dental Implantation
- Dental Implantation, Endosseous
The following keyword terms were used:

- Osseointegration
- Mandibular
- NOT sinus
- NOT overdentures
- NOT socket preservation
- NOT ridge preservation

The complete search strategy has been replicated in Appendix A. References from previous systematic reviews, search criteria, meta-analyses, and review articles were also evaluated to be certain that no appropriate articles were missed.

In total 1,391 results were obtained from the search, of which 1,032 were duplicates, leaving 359 unique results. 1 additional follow-up study (Jung et al., 2015) was identified by checking PubMed for updates to the articles selected for inclusion. After screening the articles and applying the inclusion and exclusion criteria, 19 articles involving 10 randomized controlled trials were selected for inclusion in this systematic review.
3.3 Study selection: Inclusion and exclusion criteria

From the 360 unique studies identified in the search, 34 were selected for potential inclusion after the process of reviewing titles and abstracts.

*Inclusion criteria included:*

- Only randomized controlled trials were considered for inclusion in this systematic review.
- RCTs must have been performed on humans and published in English in the last 10 years.
- Only studies measuring the outcome of vertical bone augmentation in the mandible followed by implant placement following were included.
- The outcomes could include initial bone gain, bone resorption over time, or both.
- The studies also had to provide information on either implant survival, success or failure rates.
- If trials measured both vertical and horizontal augmentation, or both mandibular and maxillary augmentation and implant placement, they were included and information extracted.
- Augmentation procedures must have included either GBR, block graft, or both. Augmentation materials must also have included autograft material, xenograft material, or both.
- Only studies with a follow-up of at least 12 months after augmentation were included.
Exclusion criteria included:

- Studies were not randomized controlled trials
- Were performed on animals
- Were more than 10 years old
- Follow-up periods were less than 12 months
- Implants were not placed
- Implant survival or failure rates were not reported
- Bone gain/loss was not reported
- If augmentation techniques and materials did not include GBR or block graft, or autograft or xenograft.

Of the 34 studies selected for data extraction, 15 were excluded (with reasons provided in Appendix B), leaving 19 articles involving 10 randomized controlled trials that fit the criteria for inclusion in this systematic review. The screening process is detailed below in Figure 1.
Figure 1. Screening process used to identify eligible studies.
3.4 Risk of bias in studies

For each study, a quality assessment was undertaken to identify the level of bias present. The types of bias examined were selection bias (allocation concealment), performance bias and detection bias (blinding of outcome assessors), and attrition bias (addressing withdrawals). For each criterion, an evaluation of ‘adequate’, ‘inadequate’, or ‘unclear’ was assigned. If all criteria were adequate, a score of ‘low risk of bias’ was assigned. If one or more criteria were not met, a score of ‘high risk of bias’ was assigned.
4. RESULTS

4.1 Study selection and characteristics

A total of 19 articles involving 10 randomized controlled trials were ultimately selected for inclusion in this systematic review: Merli et al. (2007), Bianchi et al. (2008), Chiapasco et al. (2008), Fontana et al. (2008), Jung et al. (2009a), Felice et al. (2009a), Felice et al. (2009b), Felice et al. (2009c), Felice et al. (2009d), Merli et al. (2010), Felice et al. (2010), Esposito et al. (2011a), Esposito et al. (2011b), Ramel et al. (2012), Merli et al. (2014), Esposito et al. (2014), Felice et al. (2014), Jung et al. (2015), and Merli et al. (2015).

Furthermore, Merli et al. (2010) and Merli et al. (2014) were follow-up studies of Merli et al. (2007). Ramel et al. (2012) and Jung et al. (2015) were follow-up studies of Jung et al. (2009a). Felice et al. (2010), Esposito et al. (2011a), and Felice et al. (2014) were follow-up studies of Felice et al. (2009c). Esposito et al. (2014) was a follow-up of Felice et al. (2009d). In this systematic review, the results reported by each of the follow-up articles will be referred to by the initial publication.

All trials were published in English. Eight trials were parallel: Merli et al. (2007), Bianchi et al. (2008), Chiapasco et al. (2008), Jung et al. (2009a), Felice et al. (2009a), Felice et al. (2009b), Felice et al. (2009c), and Merli et al. (2015); and two were split-mouth: Fontana et al. (2008) and Felice et al. (2009d). In all studies, implants were placed simultaneously or following vertical bone augmentation, and both bone gain outcomes and implant survival outcomes were provided. Three studies also provided implant success rates: Bianchi et al. (2008), Chiapasco et al. (2008), and Felice et al. (2009b). Each of the included studies had a minimum of 5 participants and with a minimum age of 18 and maximum age of 85. The included studies involved 262 participants and 554 implants.
Follow up periods were as follows:

- 12 months: Fontana et al. (2008), Felice et al. (2009a), Merli et al. (2015)
- 18 months: Felice et al. (2009b)
- 24 months: Bianchi et al. (2008), Chiapasco et al. (2008)
- 36 months: Felice et al. (2009d). Esposito et al. (2011b) and Esposito et al. (2014) were follow-up studies of Felice et al. (2009d) at 12 months and 36 months, respectively.
- 60 months: Felice et al. (2009c), Jung et al. (2009a). Felice et al. (2010), Esposito et al. (2011a), and Felice et al. (2014) were follow-up studies of Felice et al. (2009c) at 12, 36, and 60 months, respectively. Ramel et al. (2012) and Jung et al. (2015) were follow-up studies of Jung et al. (2009a) at 36 and 60 months, respectively.
- 72 months: Merli et al. (2007). Merli et al. (2010) and Merli et al. (2014) were follow-ups of Merli et al. (2007) at 36 months and 72 months, respectively.

One study was performed in Switzerland: Jung et al. (2009a). Nine studies were performed in Italy: Merli et al. (2007), Bianchi et al. (2008), Chiapasco et al. (2008), Fontana et al. (2008), Felice et al. (2009a), Felice et al. (2009b), Felice et al. (2009c), Felice et al. (2009d), and Merli et al. (2015).

Six trials reported that support and materials such as implants were provided by industry free of charge: Merli et al. (2007), Felice et al. (2009a), Felice et al. (2009c), Felice et al. (2009d), and Merli et al. (2015). One trial reported that the authors had no conflict of interest, and no industry support was reported: Felice et al. (2009b). Three trials provided no information about industry donations or conflict of interest statements: Bianchi et al. (2008), Chiapasco et al. (2008), and Fontana et al. (2008).
Four studies used GBR augmentation: Fontana et al. (2008), Merli et al. (2007), Jung et al. (2009a), and Merli et al. (2015). Six studies used block bone grafts: Bianchi et al. (2008), Chiapasco et al. (2008), Felice et al. (2009a), Felice et al. (2009b), Felice et al. (2009c), and Felice et al. (2009d).

Five studies used autogenous bone augmentation materials: Bianchi et al. (2008), Chiapasco et al. (2008), Fontana et al. (2008), Felice et al. (2009b), and Merli et al. (2007). Four studies used xenograft bone augmentation materials: Felice et al. (2009c), Felice et al. (2009d), Jung et al. (2009a), and Merli et al. (2015). One study used both autogenous and xenograft bone augmentation materials: Felice et al. (2009a).

All studies included mandibular vertical augmentation procedures. Merli et al. (2007), Jung et al. (2009a), Felice et al. (2009d), and Merli et al. (2015) included both mandibular and maxillary bone augmentation. Two studies also performed horizontal mandibular bone augmentation: Jung et al. (2009a) and Merli et al. (2015).

Three studies compared multiple vertical augmentation techniques: Bianchi et al. (2008), Chiapasco et al. (2008), and Felice et al. (2009b). Bianchi et al. (2008) compared the use of autogenous inlay block bone grafting with distraction osteogenesis in the posterior mandible. Chiapasco et al. (2008) compared the use of autogenous onlay block bone grafting with distraction osteogenesis in the anterior and posterior mandible. Felice et al. (2009b) compared inlay block bone grafting with onlay bone block grafting in the posterior mandible, using autogenous bone in both groups.

Two studies compared vertical bone augmentation techniques versus the use of short implants: Felice et al. (2009c) and Felice et al. (2009d). Felice et al. (2009c) compared the use of inlay xenograft bone block grafting with short (7mm-long) implants in the posterior mandible. Felice et al. (2009d) compared the use of inlay xenograft bone block grafting with short (5mm-long) implants in the posterior mandible.
Two studies compared the use of different bone augmentation materials: Fontana et al. (2008) and Felice et al. (2009a). Fontana et al. (2008) compared the use of GBR with autogenous bone particles and an allogeneic bone matrix in the posterior mandible. Felice et al. (2009a) compared the use of inlay bone block grafting using autogenous and xenograft bone materials in the posterior mandible.

Two studies compared the use of different membranes using guided bone regeneration: Merli et al. (2007) and Jung et al. (2009a). Merli et al. (2007) used particulated autogenous bone covered by either resorbable collagen barriers supported by osteosynthesis plates or by nonresorbable titanium-reinforced e-polytetrafluoroethylene (e-PTFE) barriers. The same vertical bone augmentation technique (GBR with autogenous bone) was used with both membranes in the mandible and maxilla. Jung et al. (2009a) compared the use of a synthetic bioresorbable liquid polyethylene glycol (PEG) hydrogel membrane with a standard collagen membrane, using the same vertical augmentation procedure (GBR using xenograft substitute) in the posterior mandible and maxilla for both groups.

Finally, one study compared both bone substitute materials and membranes. Merli et al. (2015) compared the use of GBR using xenograft bone substitute and collagen porcine membranes, versus the use of GBR using an alloplastic material made of pure β-tricalcium phosphate (Ceros TCP) and porcine pericardium collagen membranes. The procedures were performed in both the mandible and maxilla.

There are no studies that compared the use of bone augmentation techniques with a control of no bone augmentation.

The characteristics for each included study are summarized in Table 1.
### Table 1. Study Characteristics.

<table>
<thead>
<tr>
<th>RCT</th>
<th>Study design (parallel vs split mouth)</th>
<th>Number of patients</th>
<th>Number of implants</th>
<th>Defect Type</th>
<th>Augmentation procedure</th>
<th>Bone substitute materials</th>
<th>Intervention</th>
<th>Follow-up Period (in months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Merli et al., 2007 (Merli et al., 2010; Merli et al., 2014)</td>
<td>Parallel</td>
<td>22</td>
<td>22</td>
<td>Mandibular and maxilla vertical</td>
<td>GBR</td>
<td>Autogenous</td>
<td>Membrane comparison</td>
<td>6 (36, 72)</td>
</tr>
<tr>
<td>Bianchi et al., 2008</td>
<td>Parallel</td>
<td>11</td>
<td>37</td>
<td>Mandibular vertical</td>
<td>Block graft</td>
<td>Autogenous</td>
<td>Augmentation technique comparison</td>
<td>24</td>
</tr>
<tr>
<td>Fontana et al., 2008</td>
<td>Split-mouth</td>
<td>5</td>
<td>25</td>
<td>Mandibular vertical</td>
<td>GBR</td>
<td>Autogenous/Allograft</td>
<td>Bone substitute comparison</td>
<td>12</td>
</tr>
<tr>
<td>Chiapasco et al., 2008</td>
<td>Parallel</td>
<td>17</td>
<td>40</td>
<td>Mandibular vertical</td>
<td>Block graft</td>
<td>Autogenous</td>
<td>Augmentation technique comparison</td>
<td>24</td>
</tr>
<tr>
<td>Jung et al., 2009a (Ramel et al., 2012; Jung et al., 2015)</td>
<td>Parallel</td>
<td>37</td>
<td>37</td>
<td>Mandibular and maxilla vertical and horizontal</td>
<td>GBR</td>
<td>Xenograft</td>
<td>Membrane comparison</td>
<td>6 (36, 60)</td>
</tr>
<tr>
<td>Felice et al., 2009a</td>
<td>Parallel</td>
<td>10</td>
<td>40</td>
<td>Mandibular vertical</td>
<td>Block graft</td>
<td>Autogenous/Xenograft</td>
<td>Bone substitute comparison</td>
<td>12</td>
</tr>
<tr>
<td>Felice et al., 2009b</td>
<td>Parallel</td>
<td>20</td>
<td>43</td>
<td>Mandibular vertical</td>
<td>Block graft</td>
<td>Autogenous</td>
<td>Augmentation technique comparison</td>
<td>18</td>
</tr>
<tr>
<td>Felice et al., 2009c (Felice et al., 2010; Esposito et al. 2011a; Felice et al., 2014)</td>
<td>Parallel</td>
<td>60</td>
<td>121</td>
<td>Mandibular vertical</td>
<td>Block graft</td>
<td>Xenograft</td>
<td>Augmentation technique comparison</td>
<td>5 (12, 36, 60)</td>
</tr>
<tr>
<td>Felice et al., 2009d (Esposito et al., 2011b; Esposito et al., 2014)</td>
<td>Split-mouth</td>
<td>30</td>
<td>128</td>
<td>Mandibular and maxilla vertical</td>
<td>Block graft</td>
<td>Xenograft</td>
<td>Augmentation technique comparison</td>
<td>4 (12, 36)</td>
</tr>
<tr>
<td>Merli et al., 2015</td>
<td>Parallel</td>
<td>50</td>
<td>61</td>
<td>Mandibular and maxilla vertical and horizontal</td>
<td>GBR</td>
<td>Xenograft/Alloplastic graft</td>
<td>Membrane and augmentation technique comparison</td>
<td>12</td>
</tr>
</tbody>
</table>
4.2 Risk of bias in studies

The results of the analysis of bias in individual studies is provided in Table 2. 9 studies presented a low risk of bias, and 1 study presented a high risk of bias (Felice et al., 2009a).

Table 2. Risk of Bias in Studies.

<table>
<thead>
<tr>
<th>RCT</th>
<th>Allocation concealment</th>
<th>Blinding of outcome assessors</th>
<th>Attrition</th>
<th>Risk of bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Merli et al., 2007 (Merli et al., 2010; Merli et al., 2014)</td>
<td>Adequate</td>
<td>Yes, when possible</td>
<td>Yes (1), explained</td>
<td>Low</td>
</tr>
<tr>
<td>Bianchi et al., 2008</td>
<td>Adequate</td>
<td>Yes, when possible*</td>
<td>None</td>
<td>Low</td>
</tr>
<tr>
<td>Fontana et al., 2008</td>
<td>Adequate</td>
<td>Yes*</td>
<td>None</td>
<td>Low</td>
</tr>
<tr>
<td>Chiapasco et al., 2008</td>
<td>Adequate</td>
<td>Yes, when possible*</td>
<td>None</td>
<td>Low</td>
</tr>
<tr>
<td>Jung et al., 2009a (Jung et al., 2015)</td>
<td>Adequate</td>
<td>Yes</td>
<td>Yes (5), explained</td>
<td>Low</td>
</tr>
<tr>
<td>Felice et al., 2009a</td>
<td>Inadequate</td>
<td>Yes, when possible</td>
<td>None</td>
<td>High</td>
</tr>
<tr>
<td>Felice et al., 2009b</td>
<td>Adequate</td>
<td>Yes, when possible*</td>
<td>None</td>
<td>Low</td>
</tr>
<tr>
<td>Felice et al., 2009c (Felice et al., 2010; Esposito et al. 2011a, Felice et al., 2014)</td>
<td>Adequate</td>
<td>Yes, when possible</td>
<td>Yes (8), explained</td>
<td>Low</td>
</tr>
<tr>
<td>Felice et al., 2009d (Esposito et al., 2011b; Esposito et al., 2014)</td>
<td>Adequate</td>
<td>Yes, when possible</td>
<td>Yes (2), explained</td>
<td>Low</td>
</tr>
<tr>
<td>Merli et al., 2015</td>
<td>Adequate</td>
<td>Yes</td>
<td>None</td>
<td>Low</td>
</tr>
</tbody>
</table>

*Blinding of outcome assessors was not explained by the authors, however, Esposito et al. (2009) contacted these authors and confirmed that outcome assessors were blinded to the treatment when possible.
4.3 Results of individual studies

4.3.1 Guided bone regeneration using autogenous bone

Two studies involved implants placed in the augmented mandible using GBR with autogenous bone particles: Merli et al. (2007) and Fontana et al. (2008).

Merli et al. (2007) augmented deficient mandibles using particulated autogenous bone covered by either resorbable collagen barriers supported by osteosynthesis plates (test group) or by non-resorbable titanium-reinforced e-polytetrafluoroethylene (e-PTFE) barriers (control group). The bone was harvested from areas near the implant site, with the surgeon free to choose the bone harvesting technique and the intraoral donor site. Bone augmentation and implant placement were done in one stage in this study. 22 implants were placed in the augmented bone; all 11 implants in the control group were placed in augmented regions of mandible, while in the test group 10 implants (91%) were placed in the mandible and 1 implant (9%) in the maxilla. After 6 years of follow-up (Merli et al., 2014), no implant failures had occurred, corresponding to a 100% survival rate. Both groups experienced a statistically significant vertical bone gain between baseline measurements and at surgical exposure: 2.2 mm in the test group ($P < .001$) and 2.5 mm in the control group ($P < .001$). There was not a significant difference in the amount of regenerated bone between the two groups. After 3 years of follow-up, patients in the test group had experienced peri-implant bone loss of 0.55 mm, while patients in the control group had experienced peri-implant bone loss of 0.53 mm (no statistically significant difference) (Merli et al., 2010). After 6 years of follow-up, patients in the test group had experienced peri-implant bone loss of 0.58 mm, while patients in the control group had experienced peri-implant bone loss of 0.49 mm (no statistically significant difference) (Merli et al., 2014).

In a split-mouth study in five female patients, Fontana et al. (2008) augmented ten edentulous sites in the posterior mandible using GBR with autogenous bone particles (control
group) and GBR with an allogeneic bone matrix (test group). In both treatments, a titanium-reinforced e-PTFE membrane was used. Patients were followed between 1-3 years after augmentation procedures. In the control group, autogenous bone was harvested from the retromolar region. Provisional micro-implants were placed at the time of augmentation, and permanent implants were placed six months later. 12 implants were placed in the sites augmented with autogenous bone. The mean crestal bone regeneration between the first and second surgeries in the group augmented with autogenous bone was 4.70 mm ± 0.48 mm. All implants were stable at abutment connection 5 months after implant placement, corresponding to a 100% survival rate.

4.3.2 Guided bone regeneration using xenograft bone substitute

Two studies involved implants placed in the augmented mandible using GBR with xenograft bone particles: Jung et al. (2009) and Merli et al. (2015).

Jung et al. (2009) augmented osseous defects in the posterior mandible and maxilla at the time of implant placement in 37 patients (37 implants total). Defects in all patients were grafted with bovine bone mineral (BioOss Spongiosa Granules) and then covered by either a synthetic bio-resorbable liquid polyethylene glycol (PEG) hydrogel membrane (test group, 19 patients) or a standard collagen membrane (control group, 18 patients). The authors did not specify how many implants were placed in the mandible or maxilla. At baseline, mean defect height was 5.95 mm ± 1.9 mm in the test group and 4.5 mm ± 1.54 mm in the control group. Six months after augmentation and implant placement, all implants were stable. At this time, vertical bone gain was measured via re-entry, and the authors found vertical bone gain of 5.63 mm ± 1.84 mm in the test group and 4.25 mm ± 1.16 mm in the control group, corresponding to vertical defect fills of 94.9% and 96.4%, respectively. This difference was not statistically significant. Patients were followed for five years, with bone level changes
measured again at 1, 3 and 5 years. At one year, the mean resorption was found to be 0.43 mm on test implants and 0.21 mm on control implants. Between the first and third year, further vertical bone resorption of 0.17mm (test group) and 0.12mm (control group) was found. None of the differences between groups were statistically significant. After 5 years, a remaining bone defect height of 2.2 ± 0.9mm was measured in the control group and 2.8 ± 1.3mm in the test group (no statistically significant differences, P = 0.399). The vertical bone gain after 5 years was 4.3 ± 1.5 mm for the control group and 4.8 ± 2.6 mm for the test group (no statistically significant differences, P = 0.493). At the 5-year follow-up, all implants were still found to be stable, corresponding to a 100% survival rate.

Merli et al. (2015) augmented deficient implant sites using GBR with a xenograft bone substitute (BioOss) and collagen porcine membranes (Bio-Gide) in one treatment group (BB group), and GBR using an alloplastic material made of pure β-tricalcium phosphate (Ceros TCP) and porcine pericardium collagen membranes (Jason) in the second treatment group (CJ group). The BB group was composed of 25 patients with 32 implants; 28 of the implants (84%) were placed in the mandible. Augmentation was undertaken at the time of implant placement. The mean vertical defect in the BB group at implant placement was 4.9 mm (1.8 mm SD). Vertical bone gain was 4.5 mm (2.0 mm SD), and mean bone loss 12 months after augmentation was 0.77 mm (0.36 mm SD). 12 months after augmentation and implant placement, all implants were found to be stable, corresponding to a 100% survival rate. There were no statistically significant differences found in implant survival rate or bone gain between the two treatment groups. A minor difference of 0.24 mm was detected for radiographic bone loss, favoring the CJ group, but the authors could not determine if this difference was clinically relevant.
### 4.3.3 Block bone graft using autogenous bone

Four studies involved implants placed in the augmented mandible using block bone graft with autogenous bone: Bianchi et al. (2008), Chiapasco et al. (2008), Felice et al. (2009a), and Felice et al. (2009b).

Bianchi et al. (2008) compared the use of autogenous inlay block bone grafting with distraction osteogenesis in the posterior mandible. The 6 patients in the block graft treatment group underwent inlay block bone grafting using iliac crest bone graft harvested from the medial surface of the anterior ilium. 3-4 months after augmentation, a total of 21 implants were placed in this group. The patients in this group were followed between 18-48 months (median 22.5 months). In the bone graft treatment group, the authors found 100% implant survival and 95.2% implant success following the criteria established by Albrektsson et al. (1986). The median vertical bone gain from the preoperative situation to the end of the surgical procedure was 5.8 mm (ranging from 5.0-6.9 mm), with a median bone resorption at implant placement of 0.9 mm (ranging from 0.5-1.2 mm), corresponding to a median value of 14.2% (mean value 14.7%, ranging from 10.0-20.6%) of bone gain obtained. The authors concluded that the patient group treated with distraction osteogenesis achieved a statistically significant greater bone height gain than the inlay group (P = .003). However, in relation to bone resorption, implant survival and implant success rates, there were no statistically significant differences between the two treatment groups, suggesting similarly predictable outcomes.

Chiapasco et al. (2008) compared the use of autogenous onlay block bone grafting with distraction osteogenesis in the anterior and posterior mandible. The 8 patients in the block graft treatment group underwent onlay block bone grafting with autogenous bone harvested from the mandibular ramus. 4-5 months after augmentation, a total of 19 implants were placed in this group. The patients in this study were followed between 24-48 months.
(mean 38 months). In the bone graft treatment group, the authors found 100% implant survival and 89.5% implant success following the criteria established by Albrektsson et al. (1986). The mean vertical bone gain from the preoperative situation to the end of the surgical procedure was 4.6 mm (ranging from 3-6 mm), with a mean bone resorption at the time of implant placement of 0.6 mm. Bone resorption was measured again at the time of abutment (3-4 months after implant placement) and at 1, 2, 3 and 4 years after prosthetic loading, corresponding to values of 0.3 mm, 0.9 mm, 1.2 mm, 1.3 mm, and 1.1 mm. The authors concluded that the patient group treated with only bone block grafts experienced significantly higher bone resorption than the distraction osteogenesis group (P = 0.01), while there were no statistically significant differences between the two treatment groups in relation to peri-implant bone resorption or implant survival or success rates.

Felice et al. (2009b) compared inlay block bone grafting with onlay bone block grafting in the posterior mandible, using autogenous bone from the iliac crest in both groups. The 20 patients were randomly assigned into onlay group (10 patients) and inlay group (10 patients). 3 to 4 months after the vertical bone augmentation, 43 implants were placed (20 in the inlay group, 23 in the onlay group), followed by loading 4 months later. Patients were followed up for a median of 18 months after loading. At the end of the follow-up period, implant survival was reported as 100% in both inlay and onlay group, and the implant success rate as 90% for the inlay group and 86.9% for the onlay group following the criteria established by Albrektsson et al. (1986). The inlay group showed 4.9 mm initial median bone gain in comparison to 6.5 mm from the onlay group after bone graft augmentation. Median resorption measured in the inlay group was 0.5 mm and in the onlay group 2.67 mm. The final bone gain after follow-up was 4.1 mm versus 4 mm. Therefore, the authors found a similar outcome with both procedures, and noted that the inlay graft technique provided a
more predictable outcome as less resorption occurred. On the other hand, they explained that this technique requires a highly skilled and experienced surgeon.

Felice et al. (2009a) compared the use of inlay bone block grafting using autogenous versus xenograft bone materials in the posterior mandible. Ten patients were included in this split-mouth study, and their posterior edentulous ridges were randomized to receive interpositional vertical augmentation with autogenous bone block graft harvested from the iliac crest or an anorganic bovine bone block (Bio-Oss). 4 months after augmentation, implants were placed (2 per augmented ridge), followed by provisional prostheses 4 months later and definitive prostheses an additional 4 months later. Patients were followed to 12 months after loading. In the autogenous bone block group, one graft failed and two implants could not be placed. However, of the implants that were placed, the authors found 100% survival after the follow-up period. 4 months after augmentation, mean 28.1% bone gain was found in the autogenous bone block group. 16 months after augmentation, 0.82 mm resorption had occurred. There were no statistically significant differences between the two treatment groups in this study.

4.3.4 Block bone graft using xenograft bone substitute

Three studies involved implants placed in the augmented mandible using block bone graft with autogenous bone substitutes: Felice et al. (2009a), Felice et al. (2009c), and Felice et al. (2009d).

Felice et al. (2009a) compared the use of inlay bone block grafting using autogenous versus xenograft bone materials in the posterior mandible. Ten patients were included in this split-mouth study, and their posterior edentulous ridges were randomized to receive interpositional vertical augmentation with autogenous bone block graft harvested from the iliac crest or an anorganic bovine bone block (Bio-Oss). 4 months after augmentation,
implants were placed (2 per augmented ridge), followed by provisional prostheses 4 months later and definitive prostheses an additional 4 months later. Patients were followed to 12 months after loading. In the xenograft bone block group, one implant failed, corresponding to a 95% survival rate after the follow-up period. 4 months after augmentation, mean 27.3% bone gain was found in the xenograft bone block group. 16 months after augmentation, 0.59 mm resorption had occurred. There were no statistically significant differences between the two treatment groups in this study.

Felice et al. (2009c) compared the use of inlay xenograft bone block grafting with short (7 mm-long) implants in the posterior mandible. 5 months after receiving augmentation with anorganic bovine bone blocks (Bio-Oss) using a sandwich technique and resorbable barriers, 61 implants were placed in the 30 patients in the augmentation group. Four months later, provisional prostheses were placed, and definitive prostheses were placed a further four months later. In 2 patients of the augmented group, the graft failed and short implants were placed instead. In addition, 3 implants had failed at 13 months after augmentation. Peri-implant bone loss (resorption) in the augmented group were measured as 0.56 mm between implant placement and loading, 1.00 mm 1 year after loading (Felice et al., 2010), 1.76 mm 3 years after loading (Esposito et al., 2011a), and 2.34 mm 5 years after loading (Felice et al., 2014). Short implants experienced statistically significantly less bone loss (0.82 mm, 95% CI 0.48; 1.16, P < 0.0001) than the long implants placed in augmented bone. At the 5-year follow-up, 3 implants had failed in the augmented group, while 5 implants failed in the short implant group (no statistically significant difference). 5 patients had dropped out of the augmented group at the 5-year follow-up, and the authors did not clarify how many implants had been placed in these patients. Implant failures were reported, rather, as having occurred in 3 of the remaining 25 patients in this group, corresponding to an implant survival rate of 88%. Notably, there was a higher complication rate in the patients in the augmented group.
(13% vs. 0% in the short implant group), as well as incidence of transient postoperative paraesthesia of the lip and chin (53% vs. 7% in the short implant group).

Felice et al. (2009d) compared the use of inlay xenograft bone block grafting with short (5 mm-long) implants in the posterior mandible. 15 patients with bilateral atrophic mandibles and 15 patients with bilateral atrophic maxillae were randomized according to a split-mouth design to receive between 1-3 5-mm short implants or at least 10-mm long implants in augmented bone. The 15 patients receiving mandibular implants had augmentation with interpositional blocks of anorganic bovine bone (BioOss). 4 months after augmentation, 30 implants were placed in the 30 patients in the mandibular augmentation group. Four months later, provisional prostheses were placed, and definitive prostheses were placed a further four months later. After 3 years of follow-up, 1 long mandibular implant failed, compared to 2 short mandibular implants (no statistically significant difference), corresponding to a 96.7% survival rate (Esposito et al., 2014). Peri-implant bone loss (resorption) in the mandibular augmented group were measured as 0.27 mm between implant placement and loading, 1.12 mm 1 year after loading (Esposito et al., 2011b), and 1.54 mm 3 years after loading (Esposito et al., 2014). In sum, long implants (in both the mandible and maxilla) in augmented bone lost on average 1.5 mm peri-implant marginal bone from implant placement to 3-year follow-up, compared to 1.2 mm in short implants. This was a statistically significant difference, but the authors thought it to have little clinical significance. Notably, 10 of the 15 patients receiving mandibular augmentation experienced transient postoperative paraesthesia. Additionally, in 5 patients of this group, the 10-mm long implants could not be placed and 7-8.5 mm implants were placed instead.
The results of the relevant arm of each study are summarized in Table 3. Please note that the results of Felice et al. (2009a) have been divided and presented under Block graft: autogenous and Block graft: xenograft.
Table 3. Results of Individual Studies.

<table>
<thead>
<tr>
<th>RCT</th>
<th>Augmentation procedure</th>
<th>Bone substitute materials</th>
<th>Implants placed</th>
<th>Vertical bone gain after augmentation</th>
<th>Resorption (follow-up period)</th>
<th>Implant survival (%)</th>
<th>Implant success (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Merli et al., 2007 (Merli et al., 2010; Merli et al., 2014)</td>
<td>GBR</td>
<td>Autogenous</td>
<td>21</td>
<td>Resorbable Barrier Group: 2.2mm; Nonresorbable Barrier Group: 2.5mm</td>
<td>Resorbable Barrier Group: 0.55mm (3 years); 0.53mm (6 years); Nonresorbable Barrier Group: 0.58mm (3 years); 0.49mm (6 years)</td>
<td>100%</td>
<td>not addressed</td>
</tr>
<tr>
<td>Fontana et al., 2008</td>
<td>GBR</td>
<td>Autogenous</td>
<td>12</td>
<td>4.70mm</td>
<td>data not provided</td>
<td>100%</td>
<td>not addressed</td>
</tr>
<tr>
<td>Jung et al., 2009a (Ramel et al., 2012, Jung et al., 2015)</td>
<td>GBR</td>
<td>Xenograft</td>
<td>37</td>
<td>Hydrogel membrane group: 5.63mm; Collagen Membrane Group: 4.25mm</td>
<td>Hydrogel membrane group: 0.43mm (1 year after implant placement); 0.66mm (3 years); Collagen Membrane Group: 0.21mm (1 year after implant placement); 0.33mm (3 years)</td>
<td>100%</td>
<td>Not addressed</td>
</tr>
<tr>
<td>Merli et al., 2015</td>
<td>GBR</td>
<td>Xenograft</td>
<td>28</td>
<td>4.5mm</td>
<td>0.77mm (1 year after augmentation)</td>
<td>100%</td>
<td>Not addressed</td>
</tr>
<tr>
<td>Bianchi et al., 2008</td>
<td>Block graft</td>
<td>Autogenous</td>
<td>21</td>
<td>5.8mm</td>
<td>0.9 mm (implant placement, 3-4 months after augmentation)</td>
<td>100%</td>
<td>95.20%</td>
</tr>
<tr>
<td>Chiapasco et al., 2008</td>
<td>Block graft</td>
<td>Autogenous</td>
<td>19</td>
<td>4.6mm</td>
<td>0.9 mm (1 year after loading), 1.2 mm (2 years), 1.3 mm (3 years), 1.1 mm (4 years)</td>
<td>100%</td>
<td>89.50%</td>
</tr>
<tr>
<td>Felice et al., 2009a</td>
<td>Block graft</td>
<td>Autogenous</td>
<td>20</td>
<td>28.10%</td>
<td>0.82mm (16 months after augmentation)</td>
<td>100%</td>
<td>Not addressed</td>
</tr>
<tr>
<td>Felice et al., 2009b</td>
<td>Block graft</td>
<td>Autogenous</td>
<td>43</td>
<td>Inlay Group: 4.90mm; Onlay Group: 6.5mm</td>
<td>Inlay Group: 0.5mm (18 months after loading); Onlay Group: 2.67mm (18 months after loading)</td>
<td>100%</td>
<td>86.9 (onlay) - 90% (inlay)</td>
</tr>
<tr>
<td>Felice et al., 2009a</td>
<td>Block graft</td>
<td>Xenograft</td>
<td>20</td>
<td>27.30%</td>
<td>0.59mm (16 months after augmentation)</td>
<td>95%</td>
<td>Not addressed</td>
</tr>
<tr>
<td>Felice et al., 2009c (Felice et al., 2010; Esposito et al., 2011a, Felice et al., 2014)</td>
<td>Block graft</td>
<td>Xenograft</td>
<td>61</td>
<td>Data not provided</td>
<td>0.56mm (at loading, 4 months after implant placement); 1.00mm (1 year after loading); 1.76mm (3 years); 2.34mm (5 years)</td>
<td>88%</td>
<td>Not addressed</td>
</tr>
<tr>
<td>Felice et al., 2009d (Esposito et al., 2011b; Esposito et al., 2014)</td>
<td>Block graft</td>
<td>Xenograft</td>
<td>30</td>
<td>Data not provided</td>
<td>0.27mm (at loading, 4 months after implant placement); 1.12mm (1 year after loading); 1.54mm (3 years)</td>
<td>96.70%</td>
<td>Not addressed</td>
</tr>
</tbody>
</table>
5. DISCUSSION

5.1 Summary of Evidence

In 33 implants placed in GBR with autogenous bone, bone gain between 2.2-4.7 mm was achieved. Bone resorption between 0.55-0.58 mm was measured after 3 years, and 0.53-0.49 mm was measured after 6 years. All 33 implants survived through follow-up (100% survival rate). No data was provided on implant success rates.

In 65 implants placed in GBR with xenograft bone, bone gain between 4.25-5.63 mm was achieved. Bone resorption between 0.43-0.77 mm was measured after 1 year, and 0.33-0.60 mm was measured after 3 years. All 65 implants survived through follow-up (100% survival rate). No data was provided on implant success rates.

In 103 implants placed in block bone grafts with autogenous bone, bone gain between 4.6-6.5 mm was achieved. One study (Felice et al., 2009a) provided bone gain as a percentage (28.1%). Bone resorption of 0.9 mm was measured in less than 1 year of follow-up, and between 0.82-2.67 mm was measured after 1-1.5 years. In one study that followed patients for 4 years (Chiapasco et al., 2008), 1.2 mm was measured after 2 years, 1.3 mm was measured after 3 years, and 1.1 mm was measured after 4 years. All 103 implants survived through follow-up (100% survival rate). Implant success rates ranged from 86.9-95.2%.

In 111 implants placed in block bone grafts with xenograft bone, data was not provided on bone gain measurements. One study (Felice et al., 2009a) provided bone gain as a percentage (27.3%). Bone resorption between 0.27-0.56 mm was measured in less than 1 year of follow-up, between 0.59-1.12 mm was measured after 1-1.5 years, and between 1.54-1.76 mm was measured after 3 years. In one study that followed patients for 5 years (Felice et al., 2009d), resorption of 2.34 mm was measured after 5 years. This was the only group in which not all implants survived through follow-up. Implant survival rates ranged between 88-96.7%. No data was provided on implant success rates.
Implants in all technique and material groups achieved sufficient initial bone gain in order to place implants with survival rates ranging between 88-100%. In fact, bone block graft with xenograft bone substitute was the only group that demonstrated implant survival rates less than 100%. Augmented mandibular sites with GBR experienced less resorption on average than bone block graft sites over several years. At 3 years’ follow-up, resorption in GBR augmented sites ranged from 0.33 mm to 0.6 mm, compared to 1.3 mm to 1.76 mm resorption in the bone block grafted sites. In addition, resorption in GBR augmented sites ranged from 0.49 mm to 0.53 mm after 6 years of follow-up, compared to resorption measured at 2.34 mm after 5 years of follow-up in bone block grafted sites. However, it is not clear if this difference is clinically significant.

When comparing resorption experienced with different bone materials used (autogenous vs. xenograft) in conjunction with guided bone regeneration, no notable differences can be observed, as both groups experienced resorption levels <1.0 mm after 1-6 years of follow-up. From these results it appears that using a xenograft bone substitute can achieve similar results to the “gold standard” of autogenous bone. In bone block grafted sites, inlay autogenous bone grafts measured resorption between 0.82 mm to 0.9 mm at 1-1.5 years’ follow-up. In a study that used autogenous onlay grafting, resorption of 2.67 mm was measured at 1.5 years’ follow-up (Felice et al., 2009b). Xenografts measured resorption between 0.59 mm to 1.12 mm at 1-1.5 years’ follow-up. After 3 years of follow-up, autogenous grafts measured on average 1.3 mm of resorption, while xenografts measured between 1.54 mm to 1.76 mm resorption. One study that followed patients for 5 years measured 2.34 mm resorption in xenografts at the last follow-up (Felice et al., 2009c). Except for the relatively rapid resorption of 2.67 mm observed with autogenous onlay grafting, it appears that similar vertical bone gain/loss results can be achieved with both xenograft and autogenous bone block grafting in the long term.
In summary, while both techniques were able to achieve sufficient bone levels to place implants with high survival rates, it appears that GBR may achieve marginally less resorption levels than bone block grafting. Additionally, GBR achieved higher implant survival rates on average than bone block grafting, though the failures were minimal. When comparing bone augmentation materials, no differences in resorption levels are observable between autogenous and xenograft bone. Again, autograft procedures achieved higher implant survival rates on average than xenograft procedures, but the failure rates were minimal.

Since it is unclear whether these small observable differences in the included trials in this systematic review are of clinical significance, it is important to consider the additional benefits to the patient and clinician of each approach. In particular, using xenograft materials such as BioOss for augmentation means there is no need to harvest autogenous bone from the patient; the procedure is less invasive and can avoid morbidity related to surgery at a second area. On the other hand, harvesting autogenous bone from certain areas can be less expensive than using xenograft material and requires technical skill.

Felice et al. (2009c) and Felice et al. (2009d) compared vertical bone augmentation in the mandible using long implants to the use of short implants and found that both interventions achieved similar results after 3 years (Esposito et al., 2014) and 5 years (Felice et al., 2014) of follow-up. Because the use of short implants is less invasive, faster and cheaper than bone augmentation, they could be an interesting alternative. However, there is not yet sufficient evidence regarding long-term survival and success of short implants in the mandible.

After performing the search strategy, data extraction, and application of inclusion and exclusion criteria, 19 studies involving 10 randomized controlled trials were considered eligible for this systematic review on vertical bone augmentation for implant placement in the
mandible. An analysis of the results of these RCTs has shown that both GBR and bone block grafts and both autogenous and xenograft bone substitutes can achieve sufficient levels of bone augmentation for implant placement and survival. Additionally, bone resorption levels were minimal with all techniques and materials. Because the differences in bone gain/loss and implant survival rates between the techniques and materials was minimal, the clinician should take into account additional advantages and disadvantages to each approach to carefully guide decision making and implementation of vertical bone augmentation in the mandible for implant placement.

5.2 Limitations

A major limitation to this systematic review lies in the small sample sizes: the 10 RCTs involved an average of 26 patients and 55 implants per study. Additionally, several studies experienced patient drop-outs: Felice et al., (2009c) (8 patients), Jung et al., (2009) (5 patients), Felice et al., (2009d) (2 patients), Merli et al., (2007) (1 patient). Although these withdrawals were explained, such attrition can introduce bias into the results of the study. These issues make it difficult to generalize the results achieved in these trials to the general population.

In addition, only 3 studies had long-term patient follow-up of 5 years or longer: Felice et al., (2009c), Jung et al., (2009), and Merli et al., (2007). Without long-term follow-up of patients, it can be difficult to have a complete understanding of the study results.

Another limitation to this systematic review is the homogeneity of trial location and authors. Nine of the ten trials were performed in Italy, and more than half of the trials (6) were performed by two principal authors: Felice and Merli.

Finally, the bone gain and resorption results were not provided in a homogeneous manner, with some authors reporting initial bone gain only or resorption levels only. Some
authors provided results in mm, while others provided a percentage. Additionally, only 3 trials provided data on implant success rates (Bianchi et al., 2008; Chiapasco et al., 2008; Felice et al., 2009b). These issues presented a challenge to performing a comparison of results among all the included studies.
6. CONCLUSIONS

6.1 Implications for Practice and Research

Overall, the conclusions of this systematic review are based on few trials with generally small sample sizes and relatively short-term follow-up periods, with minimal differences reported in bone gain, resorption and implant survival. Therefore, results should be interpreted with caution. However, based on the evidence collected from the eligible studies, results appear to marginally favor guided bone regeneration over bone block grafting for vertical augmentation in relation to bone resorption over time and implant survival rates. Additionally, while no obvious differences were discerned between autogenous and xenograft resorption over time, implant survival rates marginally favored the use of autogenous bone. However, the existing evidence is not sufficiently robust to determine the most effective approach to vertical augmentation in the mandible for the placement of implants. More high-quality, long-term randomized controlled trials with larger patient populations are needed in order to make robust conclusions for use by the clinician. It would be beneficial for researchers to provide comprehensive data including initial bone gain measurements and bone resorption over time in millimeters, rather than in percentages or for only one variable. Many studies that examine implant success rates use the criteria established by Albrektsson et al. (1986), and other authors should follow this criteria and report results in order to provide complete and standardized results.

6.2 Funding

Funding for the degree of Master of Science in Dental Specialties (Oral and Maxillofacial Surgery) for the author, including the work of this dissertation, was provided by the National Secretary of Higher Education, Science, Technology and Innovation of Ecuador (SENESCYT).
References


### Appendix A.

#### Table A1. Search Strategy.

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## Appendix B.

### Table B1. Reasons for Excluded Studies.

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