**Vascularized versus Non Vascularized Autogenous Bone Grafts For Immediate Reconstruction Of Segmental Mandibular Defects:**

 **A systematic Review**

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**Introduction**

The mandible is very important for facial aesthetics and is also responsible for mastication and speech. Resection of the mandible is often indicated in the treatment of some infections, odontogenic tumors, severe trauma and oral cancer that represent a great challenge for surgeons because of the complexity and unique anatomy of the mandible. The main target of reconstruction of discontinuity defects of the mandible is to restore cosmetics , maximize function, mastication and preserve appearance and quality of life .

Treatment of segmental mandibular defects is considered a complex process. Various techniques of reconstruction, ranging from simple bridging plates to composite free flaps have been adopted; each has its advantages and disadvantages. Till now autogenous bone grafts is considered the **Gold Standard** and the most preferred method in reconstruction of such defects.

There are various forms of the autogenous bone grafts either vascularised , non vascularised or pedicled flaps depending on the type of the defect required to be reconstructed, the most popular donor sites for the free non vascularised grafts are iliac crest (either anterior or posterior) and costochondral ( rib grafts). Mandible reconstruction was revolutionized by the introduction of microvascular surgery, and the subsequent development of vascularized bone grafts. The initial development of the vascularized iliac crest graft, later followed by the vascularized fibula, radial forearm, and scapula grafts. These types of grafts had led to the high success rate and significantly improved functional outcome seen in mandible reconstruction today.

The use of pedicled myocutaneous flaps is considered an available option for successful transfer of well-vascularized tissue into the defect. Osteomyocutaneous flaps, such as temporalis with parietal bone, sternocleidomastoid with clavicle, trapezius with scapula, pectoralis major with an associated rib, were used for mandible reconstruction with marginal success. Less resorption was found compared to nonvascularized bone grafts, but functional results were generally poor due to the less than optimal quality of the transferred bone.

The objective of the review was to identify and compare the advantages and complications of simultaneous autogenous bone grafts ( vascularised and non vascularised) for restoration of mandibular segmental defects confirmed by the literature and to influence the selection of an ideal grafting technique based on clinically relevant recommendations.

**Materials and methods :**

**Focus Question**

The focus question to be addressed was” what is the various success rates and complications of both vascularised and non vascularised bone grafts for **immediate** segmental mandibular reconstruction”

**Search strategy:**

A search in the MEDLINE (Pubmed) database was performed on 1/7/2014 using the following search query:

* #1mandible OR mandibular (Mesh Terms)
* #2 (A)- resection OR osteotomy OR discontinuity OR mandibulectomy OR mandibulotomy.
* (B)-rehabilitation OR reconstruction.
* (C)-immediate OR simultaneous.
* 4#- Success rates OR successful (Mesh Terms)

A hand search search of journals was additionally undertaken to maximize the likelihood of capturing all relevant publications **table 1**. The reporting of this review is based upon **PRISMA** guidelines.

**Study selection:**

The result of this search yielded 389 titles that were independently screened by two reviewers (M.M &A.A.E.F).

Out of the 389 titles identified via pubmed and hand search ,The two reviewers agreed to exclude 202 articles after screening titles and 187 articles were included to the second level of the search.

 After subsequent screening, out of 187 articles 8 were excluded after screening abstracts and 128 were also excluded after subsequent screening of their full texts by the same reviewers.

At each level, any disagreements were discussed until a consensus was reached . finally 51 full text articles were relevant to the inclusion and exclusion criteria of this review and also related to the answer of our PICO question formulated previously. **Fig 1**

**Excluded studies : table 2**

After full text screening the 128 articles were excluded from final analysis dueto the following reasons:

* Review articles
* Languages other than English language
* Animal studies
* Articles utilized non grafting procedures of the defects e.g Distraction osteogenesis
* Grafts other than autogenous bone

**Quality Assessment and Data Extraction:**

A Standardized descriptive table s was used to record data for each article within the inclusion and exclusion criteria. Two reviewers evaluated the descriptive tables independently and any disagreement was resolved through open discussion.

**From the included articles the following data were extracted:**

**Table 5:**

* Author
* Year
* Study design
* Number of patients
* Histopathology
* Site of the affected mandible
* Timing of grafting procedure
* Type of bone grafts
* Method of fixation
* Prosthetic rehabilitation
* Follow-up
* results

**statistical analysis:**

A preliminary analysis of the included studies showed that the majority of studies were case series studies . Moreover only 5 randomized controlled trials were identified. therefore, quantitative data analysis and subsequent meta-analysis could not be performed.

Most of such studies did not give a numerical value for their results, they evaluated outcomes such as patient facial appearance, contour , mastication and speech interms of patient satisfaction .

**Results**

 The results of this search identified 51 full articles that were included in this systematic review of immediate autogenous bone grafting procedures for mandibular segmental defects. Of these articles, 5 studies were randomized controlled trials, 12 case reports and the remaining studies were case series ( **Table** 3). Since no meta- analysis was possible the review of these studies will be **descriptive in nature**.

**Vascularized bone grafts:**

The search identified 35 articles addressing reconstruction of segmental defects using free vascularised flaps either case reports, case series or RCTs. The outcome of almost all the articles utilizing autogenous vascularised bone grafts depends on quality of life, patient satisfaction in terms of facial symmetry and function (such as swallowing and mastication) so no numerical data could be extracted from such results .some authors depend on patient questionnaire to identify patient’s opinion about the aesthetic outcome of the reconstruction procedure26.

Microvascular free flaps are popular and become the most commonly used method of mandibular reconstruction. Vascularized bone grafts are widely recognized to be the most reliable method to achieve single stage, immediate reconstruction of the mandible, and therefore they represent the gold standard against which other methods should be compared4.The focus of these results relates to the use of osseous free flaps for mandible reconstruction. Although these Vascularized bone allows for the replacement of living bone with living bone. Bone healing mainly resulting in a stable union between the flap and graft can be expected within 2–3 months in the majority of the cases in spite of preoperative or postoperative radiation therapy 52.

 Careful donor site selection will allow for the use of a single flap to reconstruct the defect in most patients. The four osteocutaneous donor sites used most commonly for mandible reconstruction are the fibula, iliac crest, radial forearm, and scapula . Each donor site differs in the quality and quantity of available bone and soft tissue, the quality of the pedicle, donor site location permitting a two-team approach, and the potential for osseintegrated dental implants .The anatomic requirements of the defect coupled with donor site factors determine flap selection .53

Several studies with a primary focus on the advantages and complications of each donor site, Since Hidalgo‘s initial report54 (1989), the free fibula osseous or osseocutenous flaps has been considered the gold standard and the flap of choice for mandibular segmental reconstruction, this type of flaps provides many advantages Over previously described methods55,56, many articles in this review reported on the advantages of the fibular flap 6,10,12,17,19,22,24 .First, it allow the surgeon to perform multiple osteotomies to shape the neomandible without divascularizing the flap dueto segmental blood supply. Also, it has a Large and reliable vascular pedicle with suffient caliber vessels .furthermore, it could be harvested by another team simultaneous to the mandibular resection57 that finally allow to decrease the overall operation time.

 Some studies discussed the success of the free fibula flap in cases of condylar reconstruction ( cases of disarticulation) ,they recommend such technique dueto the presence of fibula growth centers at its epiphesis and mid way which did not restrict growth in children.

Difficulties of segmental reconstruction using fibular flaps were mentioned briefly in the literature ;Ambulation is a major concern regarding the free vascularised fibula which is still controversial. In elderly patients , there is a delay in mobilisation that may cause some complications as gait disturbance and venous thrombosis. Peirse et al17  reported that the length and width of the fibula allow either immediate or delayed dental implant placement due to sufficient bone volume with average cross sectional 90mm2 17 .however, there is a height discrepancy between the native bone of the mandible and the graft that cause a great inter-arch space between the graft and the opposing arch causing aesthetic and functional problems. They suggested a double barrel technique to solve such problem. vertical distraction osteogenesis using a distractor device is another solution that was performed by Yi-Qun et al35 as an alternative to the double barrel procedure for treatment of such problem.

Results also showed that 9 descriptive publications4,5,11,20,26,33,42,45,48 reported on the use of iliac crest free flaps for immediate reconstruction of mandibular defects. unlike other free flaps , vascularised iliac crest flaps provides optimal bone quantity and quality and also height for implant placement .

Vayvada et al 26 recommended the used of iliac free flaps for their natural curvature that already anatomically contoured for mandibular reconstructions and it also includes sufficient soft tissue component for composite defects.The donor site scar is superior to those of other choices.Conversely, the attached soft tissue is of extensive bulkness ,higher blood loss and limited length of the harvested bone if compared with fibula is a major disadvantages of this flap.

From the limitations of this flap is the presence of short vascular pedicle, the skin island is thick and relatively un reliable and immobile and the donor site morbidity that may occur as hernia ,numbness in hip region and gait disturbance.

Scapular flaps were considered from the available donor sites that were used for immediate rehabilitation of mandibular segmental defects, 4 articles in this review describes the use of such flaps4,8,29,41.

 The scapula flap is based upon the circumflex scapula artery , Vessel length and diameter is good. Up to 14 cm of bone that is inferior in quality to the fibula and iliac crest can be harvested. An axial (parascapular flap) and/or transverse (scapular flap) skin island, and all could be based on the same pedicle. Moreover, the high reliability of soft tissue based on the subscapular system that gives a good seal of the oral mucosa without dead space .The main objection to the use of the scapular flap for mandibular reconstruction is the approximately longer operation than that of other donor sites dueto the inconvience of changing the patient’s position during the operation58,59.

In a randomized clinical trial , Head et al 4 utilized various donor sites, from them ,the radial forearm was his choice. Although up to 10 cm of bone can be obtained from the radius,the cicrculation is tenous and also osteotomies is hazardous ,furthermore ,radial donor site closure and post donor fractures are problematic.

Khosla et al16 conducted a study on the use of vascularised 7th rib musculo-osseous flap with cartilage (EVE FLAP) for immediate segmental reconstruction of a chondromyxoid fibroma affecting the mandible of a 12 years old child. after 3 years follow up,results showed that there was normal bone union, excellent range of jaw opening, although the pattern of growth of such flap is unpredictable, but they considered this method feasible for reconstruction of adolescents.

**Non vascularized bone grafts:**

The literature contains a number of studies evaluating the success and various complications associated with non vascularised bone grafts for reconstruction of mandibular defects. According to this search, 15 publications were identified evaluating the use of these type of grafts.3 randomized clinical trials1,2,3, 3 case reports7,9,13 and 9 case series18,25,28,32,36-38,40,44,50.The most popular extra oral donor sites for non vascularised bone grafts are iliac crest( either anterior or posterior) and the costochondral grafts that mainly used for reconstruction of disarticulation cases.

Autogenous bone grafts taken from the ilium is considered to be a very reliable method for the reconstruction of mandibular defects following ablation of mandibular tumors. The advantages of the non-vascularised iliac bone grafts were discussed by kim et al 44 as they claimed that this type of grafts characterized by large volume ( ranges from 50 cc to 90 cc), shorter surgery and recovery time, no necessity for microvascular surgical expertise, a 2-team approach could be performed, minimal donor site morbidity, minimal recipient site scarring. Moreover, it has the advantage of that it could be harvested in various forms such as block and particulate either cortical or cortico- cancellous. Iliac bone has been associated with large degrees of resorption . Studies have demonstrated long-term mandibular reconstruction with free iliac bone graft and implant placement.60,61Iliacgraft resorption has been attributed to its endochondral origin62 and corticocancellous morphology.

In a case report conducted by Chen et al 9 for immediate reconstruction of a hemi mandibular defect including the condyle. They recommended the use of double non vascularised costochondral grafts ,one for reconstruction of the inferior border and the other for alveolar process reconstruction.,the resulta were very promising in adolescents.

 However, in spite of significant advances in bone-grafting techniques, internal splinting, and methods of fixation, reported failure rates of greater than 50%63 and overall complication rates approaching

70%may occur using NVBGs. In addition, dental-implant success rates with NVBGs vary widely, from 60% to 90% .

**Composite pedicled flaps:**

The popularity of the pedicled flaps containing bone increased in mandibular reconstruction dueto maintainence of the blood supply to the graft that facilitates bone consolodation.64 variety of donor sites such as deltopectoral flap containing clavicle,oblique chest wall flap with rib,the posterior neck skin flap with scapula and sternomastoid muscle flap with clavicle.

According to our search ,one study recommended the composite pedicled flap for segmental mandibular reconstruction.. Barens et al 19 in a case series study postulated that pedicled ossteo- musculocutaneous flaps were considered another available option for immediate reconstruction of mandibular segmental defects other than vascularised and non-vascularised bone grafts. They conducted a study on 5 patients suffering carcinomas of mandibular body and symphysis that were treated by immediate reconstruction using sternocleidomastoid musculoclavicular graft , the results showed that this is a reliable technique where all grafts were vital and successful.

**Discussion**

Several case series compare vascularised and non vascularised bone grafts for mandibular reconstruction. Although the nonvascular bone grafts decrease the overall operation time and hospital stay, vascular flaps have shown higher incidence of bony union , faster graft consolidation , fewer operations to achieve union, and minimal donor-site morbidity.

Mandibular reconstruction can be performed immediately, at the time of the resection, or delayed. Both vascularized bone flaps (VBFs) and non vascularized bone grafts (NVBGs) are generally accepted treatment modalities for mandibular reconstruction. Success could be defined as restoration of bone continuity and complete consolidation with absence of infection both clinically and radiographically . The reconstruction was considered complete if prosthetic rehabilitation was accomplished.

Many factors were discussed in the literature affecting success rates of various autogenous bone grafts for immediate segmental mandibular reconstruction. The most common factors are the type of bone graft used whether vascularised or non vascularised, fixation methods, defect size & site, histopathology of the lesion, ,and finally radio and chemotherapy .

**Fixation Methods**

 Rigid fixation of the graft seems essential as healing is impaired by movements of the graft and infection with subsequent loss of the graft. Bony mandibular discontinuity defect can be restored using an alloplastic stabilization device with or without bone grafting. An alloplastic device could either be a Titanium mesh tray or one of various designs of mandibular reconstruction plates (MRP).

Mandibular reconstruction plates (MRP) come in various designs and shapes, the AO reconstruction plate, titanium hollow screw reconstruction plate (THORP) and the titanium functionally dynamic bridging plate system. MRPs are rigid enough to restore mandibular continuity while controlling the spatial orientation of the mandibular segments as well as allowing early function. Another advantage is that the bone graft can be directly secured to the plate by screws. However, stress shielding from the use of MRPs has often been stated to be a concern because bone may undergo resorption if it is not stimulated by a functional load following graft incorporation 68. Several reports document the use of different types of MRPs and their complication rates 69,70,71.

Titanium mesh trays are easily adapted to the required contour to be then filled with a bone graft. It is said to have a modulus of elasticity similar to that of cortical bone. This, along with placement of the bone graft 10 to 15 mm above the titanium tray, allows bone graft function during the healing phase to reduce bone stress shielding. However, the patients are frequently put in maxillomandibular fixation for a period of 1-6 weeks postoperatively, or interarch elastics are used in dentate patients to maintain precise dental occlusal control 72.

Zhou et al38  introduced reverse engineering (RE), computer-aided design (CAD), and rapid prototyping (RP) technique to fabricate customized mandibular titanium trays to precisely restore the mandibular defects. They performed this study on 6 patients with benign lesions affecting the mandible, computer guided segmental resection and immediate reconstruction with 3D prefabricated custom made titanium prosthesis filled with autogenous bone grafts which was attached by extended arms to the residual bone stumps . Wound healing was uneventful in all patients with minimal operative time and excellent facial symmetry. Except in one patient where the titanium tray was removed due to infection and fistula formation dueto stress shielding caused by its regidity and finally replaced by free revascularized fibula flap.

Mini plates are considered available fixation method for the graft either free vascularised or non vascularised. Ferri et al40 and fujiki et al 41 used miniplates as a method of fixation between the transplanted autogenous bone grafts and the native mandibular bone stumps. They recommend such technique as there is no bone stress schielding and do not require hard ware removal on the long terms. Simon et al25,50  used two 2.4 mm plates one superior fixed to the proximal and distal stumps of the alveolar ridges while the other placed inferiorly fixed to the remaining bone segments of the inferior border ,they preferred to use particulate autogenous non vascularised bone grafts and Platlet Rich Plasma (PrP) that were placed into the defect taking support from the 2 plates.

The most common hardware related complications are plate exposure (extrusion), plate-induced infection, screw loosening, screw or plate fracture and temporomandibular joint pain. Plate exposure and infection are commonly related to either insufficient soft tissue closure specially in irradiated patients, or excessive pressure on the overlying skin or mucosa by an improperly shaped or bent plate. Screw loosening may be due to an insufficient number of screws per segment, in the presence of excessive muscular load. Early plate fractures indicate an improperly adapted plate, while a late one, often is a sign of cortical bone resorption around the screws so that the plate is no longer adapted to the bone surface. Distraction of the condyle by an improperly adapted plate during screw tightening, results in significant temporomandibular joint (TMJ) pain.

**Type of bone grafts, Histopathology of the lesion ,Radiation therapy :**

Despite the increasing use of free vascularized bone flaps, non-vascularized autogenous bone grafts still have great support. *Carlson and Marx*65 advocated the use of autogenous non-vascularized grafts, particularly cancellous cellular bone (CCB). They pointed out the main advantages to be, being performed on a delayed basis thus respecting the nature of malignant lesions and radiation tissue injury, minimal donor site morbidity, more anatomic mandibular reconstruction as regards alveolar height and symmetrical arch form, and providing better support for tissue borne or implant supported prosthetic appliances.

Vascularized bone-containing free flaps (VBFFs) are now the gold standard for reconstruction of post-oncologic segmental mandibular defects. According to *Wells* 66, a vascularized graft allows the possibility of immediate reconstruction specially in hypo-vascular irradiated tissue beds. Moreover, the abundant soft tissue in these flaps particularly suit those types of defects in which a large volume of both intra- and extraoral soft tissues are resected. Having performed 210 VBFFs, *Urken* 67reported an overall success rate of 96%, a flap ischemia rate of 8% that was salvageable in 50% of the cases, and an overall postoperative mortality of 1.5%. He placed a total of 360 implants into those patients with an overall success rate of 92%, decreasing to 86% when placed in post-operatively irradiated bone, and to 64% when placed in pre-operatively irradiated bone.

In a study conducted by Van Gemert Et al 73 only 5 (19%) of the 27 irradiated patients had a complication, which is low in comparison to 22 (47%) of the non irradiated patients. The low incidence of complications in irradiated patients in this study may be explained by the fact that almost all irradiated patients had a delayed reconstruction through an extraoral approach. All irradiated patients received HBO2 therapy and intravenous antibiotic therapy continued 10 days postoperatively. Lawson et al63 found that delayed mandibular reconstruction could be performed with 90% success following a full course of radiotherapy. Adamo and Szal74 reported an 81% incidence of complications in previously irradiated patients, of which 63% were major. Moreover, Carlson and Marx65 described comparable success rates in irradiated and non irradiated patients.

 **Site and size of the defect:**

The site of the defect was important factor that affects the success of the grafting procedure. Segmental resection in the anterior mandible causes the muscles of the floor of the mouth and tongue to lose their insertion to the mandible 73 . Lesions crossing the midline involving the mandibular Symphysis together with an intraoral approach appeared significantly associated with failure and major recipient-site complications. The most common complication was intraoral wound dehiscence, often resulting in graft failure. It is very likely that intraoral wound dehiscence and graft failure are related to the intraoral approach and contamination of the wound with oral micro-organisms.

 Concerning the size of the defect ,The results of our search showed that most of the articles recommended the use of vascularised bone grafts for reconstruction of large segmental mandibular defects (> 5cm) specially with adolescent or elder patients who can not withstand several operations and in cases that suffers from impaired vascularity of the soft tissue bed specially after irradiation. Moreover, some publications recommended the use of the non vascularised bone grafts in large segmental defects specially in benign lesions where watertight closure

of the intraoral wound is possible and in cases where the mucosa remains intact;but On the other hand, some authors recommend the use of non vascularised bone grafts for immediate reconstruction of large sized mandibular defects without any fear from failures32.

**Timing of reconstruction ( Immediate versus Delayed):**

The controversy of immediate versus delayed bone grafting of the post-resection defect, is still a subject of great debate. A graft loss rate of 20% after immediate grafting was reported by *Kruger et al* 75; this was much higher than a 3.2% for delayed grafting. *Komisar et al* 76 lost 2 out of 7 (28.5%) immediate bone grafts in their group of patients. *Lawson et al* 77, using various grafting techniques, reported success rates of delayed and immediate grafting to be 91% and 46% respectively. He attributed the poor results of immediate grafting to salivary contamination.

In a prospective study of nine consecutive patients undergoing reconstruction of segmental mandibular defects, no difference between immediate and delayed bone grafting was noted by *Ardary WC* 68 where both groups showed a graft incorporation rate of 100%. It should be noted that all but one of his patients did not suffer from significant soft tissue losses, having had their mandibles resected for benign tumors or trauma. *Kim et al* (8) found no difference in the infection rates between immediate and delayed grafts (26.9 vs. 26.7%), and interestingly as well, they reported a lower revision rate for immediate grafts compared to delayed ones (19.2 vs. 26.7%).

**Recent Advances In Immediate Segmental Mandibular Reconstruction:**

Over the past 20 years, surgeons have adopted computer-aided surgical techniques to assist and guide complex surgical repairs. Computer-aided maxillofacial surgery can be divided into two main categories: computer-aided presurgical planning and image-guided navigational surgery. Presurgical planning software allows the surgeon to import two-dimensional computed tomography (CT) data and generate a precise three-dimensional virtual representation of the skull. The proposed surgical repair can then be performed in a virtual environment prior to the actual procedure.Stereolithographic (hard copy) models can be fabricated from the virtual model to assist with surgical planning and intraoperative repair. The virtual data can also be imported into an intraoperative navigation system which is used to guide the movement of bone segments and application of hardware.

Six publications12,34,39,47,49,51 were identified reporting the use of computer assisted technology for immediate reconstruction of segmental mandibular defects . Levine et al 49  used computer aided design and computer aided manufacturing (CAD/CAM) for fabrication of stereolithographic models, patient specific osteotomy guides, implant guides and dental prosthesis. First ,implants were placed into the fibula then the graft was placed guided by implant supported dental prosthesis. They recommended this technique for single stage mandibular reconstruction .

 In a case series study, Zheng et al 47 conducted a successful immediate reconstruction using computer aided manufacturing of surgical templates that define the resection margins. moreover,fibula cutting and positioning guides were constructed for accurate harvesting of the graft ,results of this study showed satisfactory surgical accuracy but they reported some difficulty in application of fibula cutting templates at the same position of the preoperative virtual planning dueto the cylinder configuration of the fibula.

Again In 2013 Zheng and coworkers43 utilized vascularised fibula flap by the aid of virtual planning including tumour resection, fibula reconstruction, virtual implant and abutment placement into the graft. For restoration of patient facial symmetry the reconstruction plates were prebended on a reconstructed mandibular models. finally, the graft was precisely placed in its ideal position guided by the occlusion using a positioning template molded on stereomodel and prefabricated dental prosthesis.

**Conclusion:**

From this reviewWe can concluded that both vascularized & non vascularised bone grafts could be used with different range of satisfactory results depending on many factors such as defect size,defect site,histopathology of the lesion, fixation methods and radiation therapy.

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