Computer-assisted Secondary Reconstruction of Mandibular Continuity Defects Using Non-Vascularized Iliac Crest Bone Graft Following Oral Cancer Resection

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Abstract: The surgical treatment of oral cancers can lead to continuity defects of the mandible. However, microvascularized free-tissue transfer has several limitations, including issues with morbidity of the donor site, complications and a poorly fitted bone geometry. Thus, non-vascularized iliac crest bone grafting, an established conventional technique, remains a feasible alternative for the reconstruction of mandibular continuity defects following advanced oral cancer resection. The purpose of this study was to retrospectively evaluate treatment outcomes using computer-assisted secondary reconstruction of mandibular continuity defects through non-vascularized iliac crest block grafts over a 5-year period and to explore clinical limitations. A total of 11 consecutive advanced oral cancer patients (6 males and 5 females; mean age, 66.6 years) were included in this study. Participants that received computer-assisted secondary non-vascularized iliac crest bone grafts following advanced oral cancer resection with reconstruction plates ± adjuvant chemoradiotherapy or radiotherapy were examined at least 1 year after the mandibular reconstructions. Patient records, as well as radiological and surgical data, were analyzed. Average cancer follow-up time was 18.0 months, and patients that underwent secondary functional and esthetic reconstruction had an average mandibular defect length of 65.5 mm. Complete bone healing was observed in all patients. However, four patients experienced wound dehiscence and surgical site infection, which required local management for complete wound healing. Adjuvant radiotherapy played a significant role (p < 0.05) in reconstruction site morbidity. In addition, eight patients (72.7%) received subsequent dental implants for oral functional rehabilitation. Our results suggest that non-vascularized iliac crest bone grafts are a reliable treatment option for secondary reconstruction of mandibular continuity defects up to a moderate length in oral cancer patients. However, radiotherapy may confound postoperative complications. Limitations of this technique include that the mandibular defect may be lateral and an extraoral approach is required.

Key words: Computer-assisted surgery, Iliac crest bone, Mandibular defect, Oral cancer, Secondary reconstruction

Introduction

The treatment of advanced oral cancers and several benign tumors, such as ameloblastoma or severe osteomyelitis, commonly includes segmental resection of the mandible, leading to loss of mandibular continuity1-2. These segmental bone defects initially disrupt muscular attachments and impair mastication, speech, and esthetics, which can lead to inadequate lip closure3-5. Thus, functional and esthetic problems may affect oral cancer patients, resulting in a decreased quality of life2-5. Oral and maxillofacial surgeons believe that functional and esthetic reconstruction of segmental bony defects of the mandible is required.

The appropriate timing of reconstruction, both immediate mandibular segmental reconstruction and secondary reconstruction, has remained controversial1,4. Furthermore, several reconstructive bone-transported techniques have been introduced and applied, accompanied by active debate2-5. These bone transplant techniques are classified as vascularized bone flaps and non-vascularized bone flaps. Recently, new techniques have been proposed, including distraction osteogenesis and the use of genetically engineered regenerated mandibular bone3. However, the high costs associated with these newer treatment modalities and lack of appropriate facilities limit their clinical use5-6.

Although vascularized bone flaps such as fibular and scapular free flaps can be used for complete reconstruction of mandibular defects, they have several limitations regarding donor site morbidity and prolonged surgical procedures. In addition, a vascularized fibular free flap (the most commonly used free flap for mandibular continuous defect reconstruction) leads to decreased quality of life due to difficulties with chewing and swallowing5-6. Also, fibular and scapular free flaps may occasionally result in difficulties with dental implant placement and rehabilitation due to their low height compared with conventional less invasive non-vascularized iliac crest bone transplants of three-dimensionally volumetric block bone, leading to decreased bone symmetry6-8. Therefore, the disadvantages of free bone flaps (e.g., scapula and fibula) can be summarized as their small width, vertical, and transversal bone height, which complicate oral rehabilitation using dental implants.

Due to its non-vascularized nature, the success rate of iliac crest bone grafts may decrease with mandibular defect length and total...
area\textsuperscript{3,5}. Furthermore, it is difficult to acquire iliac crest bone with a sufficient three-dimensional (3D) shape for functional and esthetic oral-maxillofacial requirements. Although iliac crest bone is freely pliable, adaptable, and manageable ex vivo intraoperatively as it is non-vascularized, several previous studies have shown the applicability of preoperative computer-assisted precise simulations and surgical preparation using 3D-printed skeletal models, which could support and enhance the 3D customizability of harvested bone (such as non-vascularized iliac crest block bone) and even the intraoperative harvesting design for preparation of the surgical field\textsuperscript{3,5,6,7}. Furthermore, it may be a suitable procedure for small to moderate mandibular discontinuities, in particular, when the esthetics of both the donor and reconstruction site are important or when oral rehabilitation for dental implants is possible\textsuperscript{3,5}. This approach is much less invasive than free bone flaps (e.g., scapula and fibula) and may improve patients’ quality of life\textsuperscript{3,5,6}, but non-vascularized bone grafts are not used when patients lack soft tissue (if no additional flap is raised), and the effect of irradiation on the type of bone transplant remains unclear.

The purpose of this study was to evaluate treatment outcomes of computer-assisted secondary reconstruction of mandibular continuity

Figure 1. Patient Case No. 3. A. Intraoral photo showing advanced oral squamous cell carcinoma of the left oral floor. B. Temporary titanium reconstruction plate (AOCMF; Matrix Mandible Reconstruction plate\textsuperscript{®}; DePuy Synthes, Paoli, PA) is bent and prepared preoperatively with the assistance of a precise preoperative computed tomography (CT)-based surgical simulation using SimPlant Pro software (Materialise, Leuven, Belgium) and three-dimensional (3D)-printed skeletal models. C, D, E) Intraoperative photo showing the advanced oral floor cancer resection with mandibulectomy and radical neck dissection, and complete soft-tissue coverage using temporary titanium reconstruction plate bridging and soft-tissue reconstruction using a pectoralis major myocutaneous flap.

Figure 2. Patient Case No. 3. A. Intraoral photo at 1 year postoperatively. B. Panoramic radiograph at 1 year postoperatively. C. Precise preoperative CT-based surgical simulation using SimPlant Pro software for secondary mandibular reconstruction with the continuity defect of 75 mm. D. 3D-printed skeletal models.

Figure 3. Patient Case No. 3. A. The mandibular reconstruction procedure was surgically re-accessed using the previously used submandibular incision intraorally. B. The bicortical bone grafts were raised in an established manner from the left anterior border of the iliac bone. C. Harvested bicortical iliac crest was as accurate as the preoperative simulation. D. Harvested crestal block bone were further customized with adaptability and fixed with the same titanium screws to the previously bridged mandibular reconstruction plate. The gap between the grafted crestal iliac bone and the residual mandibular edge were occupied with the iliac cancerous marrow particles. E. Panoramic radiograph one-month postoperatively.

Figure 4. Patient Case No. 4. A. Harvested crestal block bone was further customized with adaptability and fixed with the same titanium screws to the previously bridged mandibular reconstruction plate. The gap between the grafted crestal iliac bone and the residual mandibular edge were occupied with the iliac cancerous marrow particles. B. Wound dehiscence of the reconstructed mandibular sites and the surgical site infection (SSI) were observed. (C, D) Resultant boney union and successful soft tissue healing were achieved.
Using non-vascularized iliac crest bone grafts over a 5-year period and to investigate limitations for clinical use in patients with advanced oral cancer and various confounders such as defect size and radiation.

Materials and Methods

Patients

We designed a retrospective clinical study using medical records from a consecutive series of 11 advanced oral cancer patients identified with segmental defects of the mandibular bone who underwent computer-assisted secondary non-vascularized iliac crest bone grafts following advanced oral cancer resection with mandibulectomy defects, neck dissection, and complete soft-tissue coverage using temporary titanium reconstruction plate bridging (AOCMF; MatrixMANDIBLETM Reconstruction Plate System; DePuy Synthes, Paoli, PA) and/or soft-tissue reconstruction (e.g., pectoralis major myocutaneous flap; PMMC) (Table 1, Fig. 1A-E).

Surgical procedures for primary or recurrent advanced late-stage oral cancers and/or lymph node metastasis, radical neck dissection for metastatic lymph nodes, and en bloc complete margin-free cancer ablation surgery were performed prior to this secondary mandibular reconstruction. Age, sex, oral cancer sites, and histological diagnosis are provided in Table 1. Oral cancer stage was classified according to the 2010 criteria outlined by the 7th Edition of the American Joint Committee on Cancer (AJCC) and tumor ablation surgery, including or excluding reconstruction or additional surgeries (Table 1). For the segmental defect of the mandible in tumor ablation surgeries, temporary bridged mandibular reconstruction plates for the segmentally resected mandible were bent and prepared preoperatively using a precise preoperative computed tomography (CT)-based surgical simulation equipped with SimPlant Pro software (Materialise, Leuven, Belgium) and three-dimensional (3D) printed skeletal models. Furthermore, postoperative adjuvant treatments followed the current National Comprehensive Cancer Network (NCCN) guidelines, and regular postoperative clinical follow-ups with functional assessments were performed. Briefly, three patients received chemoradiotherapy consisting of 60 Gy or 66 Gy of irradiation and systemic chemotherapy of cisplatin (CDDP) administered at 100 or 70 mg/m² three times tri-weekly. Two other patients received radiotherapy of 66 Gy.

All 11 patients were treated at the Department of Oral and Maxillofacial Surgery, Shimane University Hospital, Shimane, Japan, from April 2012 to June 2017. Patients that attended more than 12-month follow-up after secondary non-vascularized iliac crest bone grafts were included in this study.

This study was performed in accordance with the Declaration of Helsinki. The President of Shimane University Faculty of Medicine ensured anonymity of all patient data.
Iliac crest bone graft surgical protocols for oral rehabilitation

Regular clinical follow-ups using several radiographical evaluations confirmed no recurrence and/or metastatic lesions after oral cancer surgery and postoperative adjuvant treatments. Our computer-assisted secondary non-vascularized iliac crest bone grafts were planned, and we obtained written informed consent from each patient. The oral care of each patient was well-maintained at our outpatient clinics in collaboration with specialized dental hygienists with experience in supportive care for oral cancer treatment (Fig. 2A, B). Each patient underwent a standard surgical assessment, dental model surgery, and a precise preoperative CT-based surgical simulation using SimPlant Pro® software (Materialise, Leuven, Belgium) and 3D-printed skeletal models (Fig. 2C, D). Defect size and the 3D shape of the iliac crest bone (with accurate size and direction) were simulated preoperatively. The occlusion and maxillomandibular relationships with dentition were considered during this process.

Bicortical bone grafts were raised in an established manner as planned preoperatively from the anterior border of the iliac bone under general anesthesia3,4. The mandibular reconstruction procedure was surgically re-accessed using the same extraoral submandibular incision, and excluded exposure or communication with intraoral reconstructed sites (Fig. 3A). Subsequently, the harvested crestal block bone was further customized with adaptability and fixed with the same titanium screws (DePuy Synthes, Paoli, PA) to the previously bridged mandibular reconstruction plate, which were ideally bent and positioned at the time of cancer surgery (Fig. 3). The gap between the grafted crestal iliac bone and the residual mandibular edge were occupied with the iliac cancerous marrow particles. The surgical sites were meticulously closed in several layers.

Six months following iliac bone graft surgery, each reconstructed mandible was re-evaluated using a standard clinical assessment, dental model surgery, and a precise CT-based dental implant simulation via SimPlant Pro® and/or Nobel clinician® (Nobel Biocare, Göteborg, Sweden) dental implant simulation software for dental implant placement, together with removal of the mandibular reconstruction plates.

Clinical evaluations

Clinical data on abnormal postoperative events were collected from the medical records of evaluations conducted pre-, intra-, and postoperatively. All patients underwent routine pre- and postoperative radiographical examinations. Demographic data and treatment-related information were also collected.

All patients were examined at least 12 months following secondary mandibular reconstruction using the iliac bone. The maintenance of bone continuity and complete consolidation in the absence of infection was confirmed based on intraoperative examination, as well as regular radiographic evaluations such as CT and panoramic radiography. Surgical site infection (SSI) was classified according to the Center for Disease Control and Prevention definition and previous reports19.

For statistical analysis, StatView5 software (SAS Institute, Cary, NC) was used to evaluate statistical differences with respect to the various confounders, and Fisher’s exact test was performed. A p-value < 0.05 was considered statistically significant.

Results

In total, 11 treated patients underwent computer-assisted secondary non-vascularized iliac crest bone graft at an average age of 66.6 years (range, 51-88 years) (Table 2). The mean time between the end of cancer treatment and this surgical procedure was 18.0 months.
wound healing (Fig. 4A-D). No patient required re-reconstructive mandibular surgery using other donor sites.

Neither age, defect length, nor time interval between resection and reconstruction were significantly associated with surgical complications. However, we observed a significant difference ($p = 0.0152$) for irradiated patients, since four of the five irradiated patients (80%) that received postoperative adjuvant chemoradiotherapy or radiotherapy showed dehiscence of the reconstructed mandibular sites and SSIs (Table 2).

All mandibles reconstructed with non-vascularized iliac crest block bone grafts were successful and complete union of the residual mandibles in conjunction with soft-tissue healing was obtained for the 11 patients. This successful bone graft and bone union were confirmed when each patient had their mandibular reconstructive plate removed.

As for oral rehabilitation, eight patients (72.7%) received dental implants (Nobel Biocare-Brånemark MKIII). The average number of implants was 3.4 (range, 2–5) at the time of reconstruction plate removal, 6 months following the bone graft (Fig. 5A-D). These eight patients required vestibular plasty surrounding dental implants and palatal keratinized mucosal grafts at the time of secondary abutment connection surgery, 3 months following the implant healing period (Fig. 6A-C). All dental implants were osseointegrated and remained functional. Finally, dental implants that retained overdenture using the Locator\textsuperscript{TM} attachment (Nobel Biocare) were set for oral functional rehabilitation and esthetic reconstruction in all eight patients (Fig. 6D, E).

A total of two patients did not require dental implants, but had the reconstruction plate removed because the mandibular reconstructive sites were located posteriorly. The remaining patients planned to have dental implant placement, but ultimately only the reconstruction plate was removed as multiple distant metastases were observed at follow-up. As such, 10 of 11 patients were regularly and closely followed at our outpatient clinic; we observed no recurrence or metastasis except for one patient, who developed multiple distant metastases and local recurrence.

**Discussion**

Following segmental mandibular resection to treat advanced oral cancer, esthetics, speech, and mastication are often adversely affected, thereby decreasing patient quality of life.\textsuperscript{1,4,5} Therefore, it is important for oral and maxillofacial surgeons (and is an essential aspect of our treatment policy) to reconstruct the mandible, rehabilitate maxillofacial function, and maintain esthetics in oral cancer patients.\textsuperscript{5} In this study, we determined that our strategic computer-assisted secondary non-vascularized iliac crest bone graft technique for bony continuity and esthetic maintenance was sufficient in our study population. These findings may be explained by characteristics of the recipient site or by the fact that all mandibular defects were small to medium in size and were true lateral defects. These conditions were successfully reconstructed using a sole extraoral approach in accordance with similar clinical reports on secondary non-vascularized iliac crest block bone grafts, where success rates ranged between 46% and 100% by Pogrel MA, et al.\textsuperscript{11} and van Gemert JTM, et al.\textsuperscript{12}.

Pogrel MA, et al.\textsuperscript{11} suggested that non-vascularized crestal bone grafts, which are successful and less invasive, improve contour and bone volume for facial esthetics and subsequent dental implant insertion, and may be the treatment of choice for secondary reconstruction of defects less than 9 cm in length. In addition, lateral mandibular segmental defects may be the best indication for the use of this technique, as opposed to one of the various vascularized free tissue-transferring bone graft techniques, which were the method of choice nearly 20 years ago and are still in accordance with our cancer treatment strategy for mandibular secondary reconstruction. Tidstrom KD, et al.\textsuperscript{13} reported a 100% success rate for 34 patients with delayed mandibular reconstruction at different sites using corticocancellous iliac bone graft blocks in a titanium mesh tray, a similar approach to this report.

Computer-assisted maxillofacial surgery for both primary mandibular reconstruction following advanced oral cancer resection could potentially improve outcomes; this is particularly true for temporal reconstruction plate preparations that consider mandibular function and position, as well as secondary non-vascularized iliac crest block bone harvesting, and preparation to accurately fix the originally positioned reconstruction plate. Improvements are possible given that these types of oral and maxillofacial reconstructive surgeries are challenging. In addition, this surgery was minimally invasive; the operation time was approximately 1.5 h and blood loss was minimal because patients were optimally positioned for restoration of the mandibles, which was evaluated based on accurate computer simulation software and 3D models. The use of 3D CT for maxillofacial reconstruction and virtual planning allows for accurate, individualized assessments, as well as treatment planning.\textsuperscript{5,7,14} One of the primary advantages of computer-assisted surgery is that it can be integrated with other surgical navigation systems to confirm that the devices and surgical implants, such as distractors and reconstruction plates, fit both preoperatively and intraoperatively.\textsuperscript{4,16} In this way, it can be
used to generate an accurate digital environment for next-generation maxillofacial reconstructive treatment, as described recently for maxillofacial trauma and reconstructive procedures that use patient-specific customized plate systems\textsuperscript{[14-16]}. Recipient site complications, including graft revision or removal, range from 20% to 35%, which does not agree with our results\textsuperscript{[10,12,13]}. However, three patients that received adjuvant chemoradiotherapy or radiation therapy according to NCCN guidelines experienced dehiscence of the reconstructed mandibular sites and SSI. We determined that chemoradiotherapy and radiation therapy were significant risk factors for surgical complications. Ultimately, we achieved successful and complete boney union and soft-tissue healing as a result of prompt identification of complications and comprehensive treatment, both locally and through systemic administration of antibiotics. Therefore, careful clinical evaluation is important if a secondary iliac bone graft is planned for post-irradiated patients.

Previous reports of iliac crest bone grafts onto irradiated mandibles remain controversial\textsuperscript{[4,12,15]}. Adamo and Szal\textsuperscript{[19]} reported a complication rate of 81% in previously irradiated patients, of which 63% were major complications. However, Lawson and colleagues\textsuperscript{[10]} observed that delayed mandibular reconstruction could be performed with a 90% success rate following a full course of radiotherapy. Carlson and Marx\textsuperscript{[20]} reported “comparable” success rates in irradiated and non-irradiated patients using cancellous cellular bone grafts in allogeneic bone cibra. However, a limitation of their study was that the number of patients treated was not discussed. The low incidence of complications in irradiated patients in this study may be explained by the fact that all irradiated patients had a delayed, less invasive mandibular computer-assisted reconstruction through an extroral approach, similar to that reported by van Gemert JTM\textsuperscript{[11]}, although our irradiated patients did not receive hyperbaric oxidation (HBO\textsubscript{2}) therapy, as suggested by the same author. Although indications for HBO\textsubscript{2} therapy remain unclear, it is the only modality known to reverse the delayed radiation changes in tissues\textsuperscript{[1,2,20,21]}.

In addition, according to recent clinical reports, the most common complication related to non-vascularized iliac bone grafts is intraoral wound dehiscence, often resulting in graft failure\textsuperscript{[1,2,12]}. It is possible that intraoral wound dehiscence and graft failure are associated with the intraoral approach and contamination of the wound with oral micro-organisms. Thus, we agree that this secondary non-vascularized iliac crest bone graft should be performed using only extroral approaches\textsuperscript{[20,21,12]}. Besides contamination of the wound during surgery, contamination can also occur postoperatively through leakage of saliva into the graft area; therefore, postoperative wound care is important. The presence of dead space and a lengthy surgical procedure could also increase the risk of wound infection and dehiscence. Wound drainage should be applied to reduce dead space, but suction should not be too rigorous. In addition, oral care should be provided by a specialized dental hygienist, in addition to routine wound management.

For dental implants, mandibular reconstruction resulted in patient rigorous. In addition, oral care should be provided by a specialized approach is used.

in oral cancer patients from the late 1980s support the potential of implant-supported approaches compared with conventional, tissue-supported prosthetic dentures\textsuperscript{[1,20,21]}. Strategically placed dental implants are considered a therapeutic option to address, at least in part, both hard and soft tissue defects of the mandible\textsuperscript{[20]}. Dental implant prosthetic rehabilitation is the ultimate goal for patients after oral cancer resection and mandibular reconstruction, and this approach has recently gained attention\textsuperscript{[22]}. As reported here, the majority of the 8 patients (72.7%) underwent dental implant placement, with an average of 3.4 implants at the time of reconstruction plate removal 6 months after bone graft reconstruction in the ideal position. Thus, computer assistance may have contributed to the placement of dental implants for reconstruction with three-dimensionally restricted anatomical sites, in addition to the ideal mandibular reconstruction using non-vascularized crestal bone block with a sufficient height and width for dental implant rehabilitation. All eight patients were well-rehabilitated using Locator attachment implant overdentures, with which oral function (mastication) recovered, as reported previously\textsuperscript{[20,21]}. These patients are easily manageable for close observation of their oral cancer. A functional assessment of our patients, together with longitudinal long-term follow-up evaluation, will be provided in our future report.

Similar to previous clinical reports\textsuperscript{[1,2,20,21]}, we show that peri-implant tissue with appropriate contours generates a self-cleaning environment with a decrease in food debris accumulation, maintaining adequate hygiene in the area. Especially after mandibular reconstruction, bulky soft tissue and/or a shallow vestibular sulcus may contribute to an impaired quality of oral hygiene. In this study, corrective preimplant surgery of the vestibular plasty with palatal keratinized mucosal graft at the time of secondary abutment connection surgery was required in all patients, which would be considered a key strategy in accordance with other reports\textsuperscript{[1,2,20,21]}.

The retrospective design, the small number of patients, and the non-randomized patient selection were limitations of this study. Further clinical studies using computer-assisted secondary non-vascularized iliac crest bone grafts, following advanced oral cancer resection with mandibulectomy defects in advanced oral cancer patients, should be performed to establish an evidence-based protocol for surgical treatment of secondary mandibular reconstructive surgery in advanced oral cancer patients.

In conclusion, the non-vascularized iliac crest bone graft is a reasonably reliable treatment option for secondary reconstruction of mandibular continuity defects up to a moderate length in oral cancer patients. In these cases, microvascular tissue transfer is not required. Non-vascularized iliac bone grafts result in a better contour and bone volume for facial esthetics and subsequent successful dental implant rehabilitation. Radiotherapy could be a strong confounder for postoperative complications such as wound dehiscence and SSI, but could be managed with careful treatment. Necessary constraints may include that the mandibular defect is lateral and that an extraoral approach is used.

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Conflict of Interest
The authors have declared that no conflict exists.

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