

Accepted Manuscript



Donor-site morbidity following osteocutaneous free fibula transfer: longitudinal analysis of gait performance

Riccardo Di Giuli, MD, Matteo Zago, PhD, Giada A. Beltramini, MD, Maria Ludovica Pallotta, MD, Alessandro Bolzoni, MD, Alessandro Baj, MD, Aldo Bruno Gianni, MD, Chiarella Sforza, MD

PII: S0278-2391(18)31195-9

DOI: <https://doi.org/10.1016/j.joms.2018.10.016>

Reference: YJOMS 58502

To appear in: *Journal of Oral and Maxillofacial Surgery*

Received Date: 5 October 2018

Revised Date: 20 October 2018

Accepted Date: 25 October 2018

Please cite this article as: Di Giuli R, Zago M, Beltramini GA, Pallotta ML, Bolzoni A, Baj A, Gianni AB, Sforza C, Donor-site morbidity following osteocutaneous free fibula transfer: longitudinal analysis of gait performance, *Journal of Oral and Maxillofacial Surgery* (2018), doi: <https://doi.org/10.1016/j.joms.2018.10.016>.

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Donor-site morbidity following osteocutaneous free fibula transfer: longitudinal analysis of gait performance.

Riccardo Di Giuli, MD*§, Matteo Zago, PhD*#, Giada A. Beltramini, MD\$, Maria Ludovica Pallotta, MD\$, Alessandro Bolzoni, MD\$, Alessandro Baj, MD&, Aldo Bruno Gianni, MD% (ORCID 000-0002-5983-9674), Chiarella Sforza, MD° (ORCID 0000-0001-6532-6464).

*Drs Di Giuli and Zago equally contributed to this investigation

§Resident, Department of Biomedical Sciences for Health, Università degli Studi di Milano, Milan, Italy;
Resident, Maxillofacial and Dental Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico di Milano, Milan, Italy.

#Postdoctoral Student, Department of Biomedical Sciences for Health, Università degli Studi di Milano, Milan, Italy; Postdoctoral Student, Department of Department of Electronics, Information and Bioengineering (DEIB), Politecnico di Milano, Milan, Italy.

\$Research Associate, Maxillofacial and Dental Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico di Milano, Milan, Italy; Department of Biomedical, Surgical and Dental Sciences, University of Milan, Milan, Italy.

&Adjunct Professor, Maxillofacial and Dental Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico di Milano, Milan, Italy; Department of Biomedical, Surgical and Dental Sciences, University of Milan, Milan, Italy.

%Professor and Unit Head, Maxillofacial and Dental Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico di Milano, Milan, Italy; Director, Department of Biomedical, Surgical and Dental Sciences, University of Milan, Milan, Italy.

°Professor, Department of Biomedical Sciences for Health, Università degli Studi di Milano, Milan, Italy.

MS JOMS-D-18-01239 submitted to the *Journal of Oral and Maxillofacial Surgery* on October 5th, 2018; first revision, October 20th, 2018

Number of Figures: 1

Number of Tables: 5

Number of References: 33

Number of abstract words: 248

Number of text words: 3332

Running title: Donor-site morbidity after free fibula transfer

Key words: Free fibular flap; morbidity; gait analysis; longitudinal; facial reconstruction.

Conflict of interest

The authors have no conflict of interest to declare.

Role of the funding source

No funding sources.

Ethics

The investigation complies with the principles stated in the Declaration of Helsinki (Ethical Principles for Medical Research Involving Human Subjects), adopted by the World Medical Assembly, Helsinki, Finland, June 1964, and as amended most recently by the 64th World Medical Assembly, Fortaleza, Brazil, October 2013. Ethical approval obtained by Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico di Milano, Milan, Italy #427 09 March 2017

Corresponding author:

Prof. Chiarella Sforza

Department of Biomedical Sciences for Health

Università degli Studi di Milano

via Mangiagalli 31

20133 Milano - Italy.

Phone: +39 0250315385 - Fax: +39 0250315387

e-mail: chiarella.sforza@unimi.it

Donor-site morbidity following osteocutaneous free fibula transfer: longitudinal analysis of gait performance.

Number of Figures: 1

Number of Tables: 5

Number of References: 33

Number of abstract words: 248

Number of text words: 3332

Running title: Donor-site morbidity after free fibula transfer

Key words: Free fibular flap; morbidity; gait analysis; longitudinal; facial reconstruction.

Conflict of interest

The authors have no conflict of interest to declare.

Role of the funding source

No funding sources.

Ethics

The investigation complies with the principles stated in the Declaration of Helsinki (Ethical Principles for Medical Research Involving Human Subjects), adopted by the World Medical Assembly, Helsinki, Finland, June 1964, and as amended most recently by the 64th World Medical Assembly, Fontaleza, Brazil, October 2013.

Ethical approval obtained. Details on the title page.

ABSTRACT

Purpose: To evaluate donor site clinical morbidity and changes in kinematic gait parameters after the harvest of a vascularized free fibula flap (VFFF) for facial reconstruction.

Methods: Fourteen patients (50 ± 15 years) were enrolled in a longitudinal study. Every patient underwent a double evaluation performing a pre-surgical and a 6-months post-surgical assessment. Subjective donor-site evaluation was carried out through non-structured clinical questioning about pain, paresthesia, walking ability, restrictions in activity. Further subjective evaluations were assessed through the Western Ontario and McMaster Osteoarthritis Index (WOMAC(®)) and the Point Evaluation System for Lower Extremity Fibulectomy (PESLEF). A clinical evaluation on the donor site assessed muscular deficits, sensibility disturbance and wound healing. Temporal and spatial kinematic parameters were measured through gait analysis during overground walking at a comfortable speed.

Results: Post-surgical clinical examinations detected one patient affected by neurological disorder and three patients with donor-site pain. Ten patients (71%) declared no residual alterations in the operated leg. On average, the WOMAC score was 367/2400 and the PESLEF score was 19/24. Pre-post surgical gait analysis comparison showed no significant differences in gait parameters except for a 6% reduction of the double support phase. Stance values were higher in the operated limb in both evaluations (+1.3% presurgery; +1.8% postsurgery). No alterations were detected in the range of motion of lower limbs joints.

Conclusion: Considering the slight modification of the gait pattern, that is not usually perceived by patients, VFFF harvest was generally associated to successful functional and subjective outcomes of the donor site.

INTRODUCTION

The vascularized free fibula flap (VFFF), first introduced by Taylor et al.¹ in 1975 and subsequently adapted to jaw reconstruction by Hidalgo², is the most reliable and effective way to reconstruct facial composite bone and soft tissue defects³⁻⁶. In the last 40 years several other techniques including plates, local flap and other free flaps have been proposed without achieving the same morphological, aesthetic and functional outcome⁷⁻⁹. The characteristic of the VFFF donor site allowed the development of multiple variables of the flap; it can be harvested in its osteomuscular classic variant or in its only bone composition. Besides, a skin paddle can be associated to provide skin covering of the defect¹⁰. The VFFF can be manipulated through multiple osteotomies to adapt its shape to the bone defect, and its bone thickness consents the positioning of osteointegrated implants for the subsequent dental rehabilitation^{3,11}.

The surgical procedure causes the loss of the normal leg anatomy. Several lower limb muscular insertions take place on the fibula and necessarily partial muscular detachment must be performed¹⁰. Muscular deficits have been described, especially related to flexor and extensor hallucis longus muscles. Tissue stretching can lead to local hypoesthesia and disaesthesia due to minor nerve impairment, whereas major abnormalities can be prevented by sparing the common peroneal nerve by preserving the first six centimeters of the fibula bone¹². Thus, weakness, ankle instability, toe-deformity and difficulties in walking have been described as mixed muscular-nervous consequences of the flap removal^{6,12-15}.

Although the efficacy of the reconstruction has already been demonstrated in multiple publications^{4,5,13}, few investigations described the donor site outcome after the harvest, generally using a qualitative approach based on clinical assessments^{3,6,13,16-18}. A quantitative evaluation after VFFF harvest through computerized gait analysis has been performed by few laboratories, often with non-concordant results due to different study protocols, as summarized in Table 1^{3,10,12,14,19-22}. Most studies collected data only after surgery, with or without the concomitant assessment of a control group. Maurer-Ertl et al.¹² compared the donor limb to the healthy one, while only Lee et al.²² and Macdonald et al.²³ performed a quantitative longitudinal study comparing pre and post surgical gait analyses.

The aim of the current longitudinal study was to quantitatively assess the donor site morbidity after VFFF removal for maxillofacial reconstruction. The patients were evaluated before and six months after the VFFF harvest to enable a correct donor site healing process

and detect any residual functional alteration. Questionnaires, clinical examinations and computerized gait analysis were performed; gait kinematics temporal and spatial parameters were investigated to outline walking pattern differences.

MATERIALS AND METHODS

Study population

At the Maxillo-Facial Surgery unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico of Milan, maxillary composite defects including bone tissue are usually reconstructed with VFFF harvest. In the mainframe of an Italian multicentric collaborative study, 14 patients who underwent VFFF removal and subsequent facial reconstruction consented to participate in the pre and post- surgical analysis. Sample size was estimated according to previous literature data about gait variables measured in patients submitted to VFFF removal vs. healthy controls¹⁴. To obtain an 80% power with an alpha level of 0.05, 10 patients were considered sufficient.

The patients (7 females, 7 males) were aged 23 to 70 years; 13 patients had a mandibular reconstruction, and one a maxillary one; seven of the flaps were osteomyocutaneous, six contained only bone, and one was osteocutaneous (Table 2).

Patients with general conditions not-complying with long surgery-procedures were excluded. Besides, patients with previous or current traumas or important vascular, nervous and skeletal pathologies or abnormalities in their lower limbs were not suitable candidates to VFFF and were not included in the evaluation.

Every patient was evaluated before surgery and 6 months after it. The study followed the principles stated in the Declaration of Helsinki, and it was approved by the local Research Ethics Committee. All patients provided voluntary written informed consent to participate to this study.

Clinical Analysis

Subjective donor-site evaluation was assessed through two validated questionnaires: the Western Ontario and McMaster Osteoarthritis Index (WOMAC(®)) and the Point Evaluation System for Lower Extremity Fibulectomy (PESLEF, Table 3). The WOMAC consists of 24 items divided into 3 subscales: pain in various situations and physical activities, lower limb stiffness and physical impairment in daily life²⁴. Each question is given a 0-100 score, where higher scores denote higher impairment; the total score is up to

2400.

The PESLEF score, modified by the PES score used by Bodde et al.²⁰, evaluates six different areas: pain, paresthesia, gain recovery, activities restrictions, gait impairment and surgical wound²⁰. The patient should indicate the functional impairment with a 0-4 value; the higher the impairment, the higher the score, ranging from a total value of 0 (no problems) to 24 (the worst condition).

Additionally, the patients were asked to answer to a set of non-structured clinical questions before performing the gait analysis. The questions surveyed different areas through restriction in activities and hobbies in everyday life, motor and sensibility functions, pain and complaining about the intervention. A physical evaluation was performed to detect sensibility disturbance, wound alteration, claw-toe deformity and to assess flexor-extensor toe and fingers activity.

Gait Analysis

Data collection was performed at Movement Analysis Laboratory (LAM), Department of Biomedical Sciences, Università degli Studi of Milan. For spatiotemporal gait parameters gathering, a 9-camera optoelectronic movement analysis system (SMART-E, BTS spa, Milano, Italy) was used¹⁹. A set of 29 passive infrared retro-reflexive markers were fixed with adhesive tape on the following anatomical landmarks: glabella, tragus, acromion, C7 spinous process, radial epicondyle, ulnar styloid process, anterior superior iliac spine, S1 spinous process, greater trochanter, medial and lateral femoral epicondyle, tibial tuberosity, medial and lateral malleolus, calcaneus, tip of the foot.

Each subject wore comfortable trainers and thin and adherent clothes to improve marker proximity to the bone landmarks. All kinematic data were collected with a sample frequency of 60 Hz.

The 3-Dimensional reference system was defined as follows: 1) x-axis; parallel to the longitudinal direction of the walking aisle, directed forward; 2) y-axis; orthogonal to the ground, directed upward; 3) z-axis; orthogonal to the sagittal plane, directed right. For each data collection the system was calibrated, with correction of optical and electronic distortions. A preliminary recording of a 5-s static image of the patient standing in orthostatic position with arms slightly abducted and looking forward was made. The patients were then asked to walk overground at their self-selected comfortable walking speed over an 8 m aisle; ten gait trails were consecutively recorded. For each trial, only the central 5 m of the path were analyzed by the optoelectronic system, excluding the initial

and final 1.5 m to eliminate transient acceleration and deceleration phases²⁵. Before data collection each patient performed two gait trials to become familiar with the laboratory environment.

Each film acquisition was followed by the gait cycle definition setting two subsequent ipsilateral heel strikes as extremes. Double support, swing and stance phase were calculated as a percentage of cycle time. Cadency, velocity and stride length were assessed²⁶. Step width was evaluated as the mean sagittal distance between the medial malleoli identified in each acquisition instant. The Range of Motion (RoM) of hip, knee, and ankle flexion-extension was also calculated. Each bilateral parameter (stance, swing, duration of the cycle and flexion-extension RoMs) was analyzed separately in the healthy and operated limb. All calculations were performed using SMART-E Analyzer software.

Statistical Analysis

Mean and standard deviation of pre and post surgical variables were calculated. Given the sample size and the normal data distribution, Student's t test for paired samples was used to compare pre and post surgical unilateral data. For bilateral variables, the 2 way factorial Analysis Of Variance (ANOVA) was used to compare the pre and post surgical assessment (Factor 1) and healthy and operated limb (Factor 2); the time x side interaction was also computed. All tests were carried out with p values <0.05 considered statistically significant. All data are presented as mean and standard deviation.

RESULTS

Clinical analysis

The average WOMAC score was 367 and the PESLEF questionnaire was 19. The non-structured clinical questions found that ten patients (71%) declared no residual alterations in the operated leg (Table 2). Three patients (21%) declared occasional pain related to the operated limb. The pain was referred during activities for patient F2, during pronosupination movements for M4, and to be always present for M5 (WOMAC score 350/500). Patient M6 reported stiffness in the morning after awakening or after inactivity, with a WOMAC score of 160/200. Patient F6 claimed claw toe deformity, albeit no further complaints were reported.

The clinical examinations found muscular impairment in three patients (21%). Patient M5 had an extensor hallucis and digitorum longus muscles deficit (14%). Patient F6 was

affected by extensor digitorum longus deficit and M6 by flexor hallucis longus deficit. Significant paraesthesia was detected on patient M5 (7%). The aesthetic aspect of the wound was generally satisfactory; only one wound dehiscence was reported.

Gait analysis

Quantitative analysis between pre and post-surgical acquisitions showed few alterations in temporal and spatial parameters indicating a mildly affected gait pattern, and only patients with muscular impairment (F6, M5, and M6) had changes in the support phases.

For bilateral variables (Table 4), the analysis of variance found no significant effects of time (pre and post surgical assessment; all p values > 0.05), but showed a statistically significant difference between the healthy and operated limb for stance and swing phases: stance values were higher in the operated limb in both evaluations ($p = 0.002$).

Comparison of lower limbs flexion-extension RoMs showed no significant alterations for hip, knee and ankle joints. In no occasion the time \times side interaction was significant ($p > 0.05$).

The quantitative analysis of unilateral variables detected a significant decrease in the double support phase (pre 28.1%; post 26.3%; t test, $p = 0.05$). All the other comparisons were not significant (Table 5). Figure 1 shows the percentage changes before and after surgery in the healthy and operated limbs: for bilateral variables, all changes were lower than 5%, while larger variations were observed for unilateral ones (double support, 6%; step width, 21%).

DISCUSSION

Walking is a precious and fundamental activity. Being able to move independently is fundamental to achieve independence and to improve and safeguard health status. The aim of the present study was to perform a longitudinal quantitative analysis of mid-term residual gait impairment after VFFF harvest, coupling subjective, clinical and instrumental assessments.

The subjective perception of leg impairment after VFFF was generally low. Ten patients (71%) reported no residual alteration at the donor leg six months after the operation. The questionnaire's assessment showed significant complaints in three patients (M5, M7, F3). M5 presented muscular impairment, paresthesia alongside instability while walking; the

gait analysis of this patient provided alteration supporting his scores at questionnaires and answers at clinical questions. In particular he showed a 4-5% reduction of stance duration and a 7.7% increase in the double support phase.

M7 showed no significant alterations in the gait temporal parameters, but at the time of the evaluation he had recently finished the radiotherapy treatment. After surgery, his hip flexion RoM increased on the healthy side (+10.6%) and decreased on the operated one (-4.4%). F3 reported no deficit at the non-structured clinical questioning, but she indicated problems in all three domains of WOMAC. Her gait analysis showed a 10% increase in the double support phase.

At clinical examination one patient (7%) showed claw toe deformity, a sing reported in several studies with a rate of 0-27%, well in accord with the current findings^{3,6,12,14-18,20}. Pain was referred by three patients (21%), mainly described as a discomfort feeling while performing activities, whereas only one patient reported pain at rest. Pain can be explained by adhesion of the dissected tissues during the healing process and by nerve impairment during the operation. Overall, pain results were satisfactory and 93% of the patients were not taking pain medications. On quantitative gait analysis alterations were detected only in the patients who reported muscular impairment (F3, M2, M5, and M6) with changes in support phases.

Alongside with clinical evaluations, some studies performed instrumental gait analyses comparing the results with a control group^{3,10,14,19,20,21}. These studies did not discriminate potential differences due to patient's habits and systemic illnesses. Most of the patients perform this surgical procedure due to cancer local invasion of the maxillary bones. Tumors in this area are often related with a history of smoke and alcohol which could affect the individual gait ability distorting the comparison with a healthy group¹⁰. A different approach was used by Maurer-Ertl et al.¹² who compared the operated and healthy limb within each patient. Unfortunately, this assessment can offer information only about bilateral gait variables. The current investigation was designed as longitudinal to eliminate every cross-sectional study bias.

Furthermore, most of the studies which performed a gait analysis after VFFF removal made their post-operative evaluation without following a strict temporal criterion but defining a post-surgical moment when all the patients were analyzed^{3,10,12,14,19-21,27}. Despite the advantages in the data collection managing, data are influenced by an evaluation

performed with different healing stages. Indeed, before performing the post-surgical assessment, an appropriate amount of time should be expected to enable the evaluation at a quite stable limb situation. Therefore, we defined the postoperative assessment following two criteria: 1) a fixed postoperative evaluation; 2) a time interval consenting an appropriate leg recovery before performing the assessment. According to Lee et al.²², a 3-months interval could be sufficient to allow a full recovery from the VFFF harvest, even if Feuvrier et al.¹⁴ found significant improvements in temporal gait parameters with a longer follow-up (up to 104 months).

These two criteria led us to choose a 6-months postoperative evaluation in order to assess all the patients at the same stage of the healing process, at a stable leg condition, with a definitive gait pattern, avoiding temporarily discomfort which could affect the data collecting and patients will to join the study. Indeed, patients submitted to radio or chemotherapy could still not have completely recovered even though after six months these alterations should be minimal; in our patient group only two patients underwent radiotherapy (Table 2).

Other two studies performed longitudinal post-surgical evaluations of gait with a fixed follow-up time^{22,23}. Macdonald et al.²³ collected longitudinal data 3 months after surgery in eight patients, and concluded that the surgical procedure was associated with little objective gait impairment. Lee et al.²² acquired 20 patients 1 month postsurgery and 12 of them again 3 months after surgery; 8 patients refused to be analyzed because they felt little discomfort during walking. The authors found a reduction of cadency, speed and stride length after one month albeit in the following evaluation the walking pattern was normal²². Indeed, they may have underestimated possible gait alterations by not evaluating the entire group in the second assessment. According to literature and our findings, the correct restoration of the gait pattern is achieved by training; patients who perform physical rehabilitation obtain faster and better results^{14,15,21,28,29}.

A gait cycle is composed of an alternation of swing and stance phases. The stance phase, defined as the soil contact phase, is divided in heel strike, foot flat, midstance, heel off and toe off. The double support is the phase in which both feet take contact with the floor; it is included between the heel strike and the contralateral toe off. The stance phase is composed by an initial double support phase, a mid-term single support phase and a finally double support phase.²⁶ In the present study, the double support phase significantly decreased after surgery. This decrease could be explained by a combination of residual

muscular impairment and increase of velocity. Accordingly, other investigations detected a double support reduction explained by an insufficient function of the flexor hallucis longus muscle which resulted in anticipated cessation of the preswing phase^{15,21,22}. In our patient group only one patient suffered this alteration (7%) and the analysis of his double support showed a reduction of 11.64% of the pre-operative value against an average decrease of 6.4%.

Furthermore, albeit the velocity was not significantly increased (pre surgery, 1.13 m/s; postsurgery, 1.19 m/s; t test, $p = 0.174$), its change could have influenced the double support measurement. The increase of velocity causes an increase of the swing and a reduction of the double support and stance phases as widely described in literature²⁶. In contrast with our findings, Siegel et al.³⁰ described an increased double support phase in their patient group caused by post-operative leg pain. The discordance could be explained by the little residual leg pain of the present patients as demonstrated by the low percentage taking pain medications (7%).

The comparative analysis between bilateral parameters showed a significant difference in the stance phase between the healthy and operated leg. This divergence was due to a longer stance phase of the operated leg detected in both pre and post-surgical assessments, respectively, of 0.9 and 1.2% (Table 4). The surgical intervention led to a non-significant decrease in both limbs maintaining the asymmetry. Literature does not report clear references to stance asymmetry in healthy subject during gait even if asymmetry in weight loading during standing has been documented³¹. This little variation can be considered physiological, but further assessments in larger groups are necessary. Indeed, no significant asymmetries between the healthy and operated legs were reported in other investigations¹⁴. Rendenbach et al.³² longitudinally analyzed the single leg postural sway in 27 patients before and 8 months after VFFF fibula free flap. Preoperatively, the donor leg values were all somehow larger (range 1.1-1.3%) than those collected in the contralateral limb, thus showing some asymmetry in balance³². After surgery, all values recorded on the donor leg significantly increased, while no variation were observed contralaterally.

In the present study, patients were asked to walk at their preferred velocity while performing the test. No velocity, cadency or stride length alteration were detected, in accord with previous investigations^{12,21,23}. In contrast, other studies found a reduction of velocity^{14,20}, even if Feuvrier et al.¹⁴ claimed that velocity improves with time after surgery. Hadouiri et al.¹⁰ measured a significant reduction in velocity but they used a different

walking test designed for fatiguing the subjects. Bodde et al.²⁰ found an increased variability in stride time when the patients were asked to walk faster or when they were submitted to a double task condition. A similar finding was reported by Feuvrier et al.¹⁴ and ascribed to a more cautious walking pattern, as also reported by Baj et al.¹⁹ for stairs descent. Rendenbach et al.³² observed a significant reduction in lower limb maximum peak power, but did not test gait kinetics. The mild velocity increase detected in our analysis, due to the longitudinal structure of the study, may be explained by a major knowledge of the gait trail in the postoperative assessment jointly to the lack of major gait alterations.

In conclusion, six months after the operation the analyzed patients who underwent VFFF removal suffered little or no alterations of their gait pattern with a mild double support decrease as the only significant alteration. An electromyographic study of the posterior leg muscles could better clarify the flexor hallucis longus muscle impairment. An additional longitudinal study with a larger number of patients could be designed with a two years postsurgical evaluation to verify the total restoration of the gait pattern through the regaining of the pre-operative double support. Furthermore, during the restoration of the normal gait characteristics, there may be different gait pattern categories, beyond differences due to radio-chemotherapy and different surgical techniques³³, which might explain the divergences between studies with similar protocol.

The clinical examination observed that patients were usually unaware of the mild gait alteration and they were generally satisfied about their condition. On these bases we can conclude that VFFF is a safe, effective surgical procedure which leads to minor and not-perceived donor site impairment.

Future investigations should increase the number of patients, assess a longer follow-up and investigate other daily life locomotor activities like stairs climbing¹⁹ and prolonged gait¹⁰.

References

1. Taylor GI, Miller GD, Ham F J: The free vascularized bone graft. A clinical extension of microvascular techniques. *Plast Reconstr Surg* 55: 533–544, 1975.
2. Hidalgo DA: Fibula free flap: a new method of mandible reconstruction. *Plast Reconstr Surg* 84: 71–79, 1989.
3. Lin JY, Djohan R, Dobryansky M, Chou SW, Hou WH, Chen MH, Wei FC: Assessment of donor-site morbidity using balance and gait tests after bilateral fibula osteoseptocutaneous free flap transfer. *Ann Plastic Surg* 62: 246–251, 2009
4. Shroff SS, Nair SC, Shah A, Kumar B: Versatility of Fibula Free Flap in Reconstruction of Facial Defects: A Center Study. *J Maxillofac Oral Surg* 16: 101–107, 2017
5. Taylor GI, Corlet R J, Ashton MW: The Evolution of Free Vascularized Bone Transfer: A 40-Year Experience. *Plast Reconstr Surg* 137: 1292–1305, 2016
6. Urken ML, Buchbinder D, Costantino PD, Sinha U, Okay D, Lawson W, Biller HF: Oromandibular reconstruction using microvascular composite flaps: report of 210 cases. *Arch Otolaryngol-Head Neck Surg* 124: 46–55, 1998
7. Ling XF, Peng X, Samman N: Donor-site morbidity of free fibula and DCIA flaps. *J Oral Maxillofac Surg* 71: 1604–1612, 2013
8. van Gemert J, Holtslag I, van der Bilt A, Merckx M, Koole R, Van Cann E: Health-related quality of life after segmental resection of the lateral mandible: Free fibula flap versus plate reconstruction. *J Cranio-Maxillofac Surg* 43: 658–662, 2015
9. Schardt C, Schmid A, Bodem J, Krisam J, Hoffmann J, Mertens C: Donor site morbidity and quality of life after microvascular head and neck reconstruction with free fibula and deep-circumflex iliac artery flaps. *J Craniomaxillofac Surg* 45: 304-311, 2017
10. Hadouiri N, Feuvrier D, Pauchot J, Decavel P, Sagawa Y: Donor site morbidity after vascularized fibula free flap: gait analysis during prolonged walk conditions. *Int J Oral Maxillofac Surg* 47: 309-315, 2018
11. Sozzi D, Novelli G, Silva R, Connelly ST, Tartaglia GM: Implant rehabilitation in fibula-free flap reconstruction: A retrospective study of cases at 1-18 years following surgery. *J Craniomaxillofac Surg* 45: 1655-1661, 2017
12. Maurer-Ertl W, Glehr M, Friesenbichler J, Sadoghi P, Wiedner M, Haas F, Leithner A, Windhager R, Zwick EB: No adverse affect after harvesting of free fibula osteoseptocutaneous flaps on gait function. *Microsurg* 32: 364-349, 2012
13. Babovic S, Johnson CH, Finical SJ: Free fibula donor-site morbidity: the Mayo experience

- with 100 consecutive harvests. *J Reconstruct Microsurg* 16: 107–110, 2000
14. Feuvrier D, Sagawa Y, Béliard S, Pauchot J, Decavel P: Long-term donor-site morbidity after vascularized free fibula flap harvesting: Clinical and gait analysis. *J Plast Reconstr Aesthet Surg* 69: 262–269, 2016
 15. Ling XF, Peng X: What is the price to pay for a free fibula flap? A systematic review of donor-site morbidity following free fibula flap surgery. *Plast Reconstr Surg* 129: 657-674, 2012
 16. Shpitzer T, Neligan P, Boyd B, Gullane P, Gur E, Freeman J: Leg morbidity and function following fibular free flap harvest. *Ann Plastic Surg* 38: 460–464, 1997
 17. Sieg P, Taner C, Hakim SG, Jacobsen H-C: Long-term evaluation of donor site morbidity after free fibula transfer. *Br J Oral Maxillofac Surg* 48: 267–270, 2010
 18. Zimmermann CE, Börner BI, Hasse A, Sieg P: Donor site morbidity after microvascular fibula transfer. *Clin Oral Invest* 5: 214–219, 2001
 19. Baj A, Lovecchio N, Bolzoni A, Mapelli A, Gianni AB, Sforza C: Stair ascent and descent in assessing donor-site morbidity following osteocutaneous free fibula transfer: A preliminary study. *J Oral Maxillofac Surg* 73: 184–193, 2015
 20. Bodde EWH, de Visser E, Duysens JEJ, Hartman EHM: Donor-site morbidity after free vascularized autogenous fibular transfer: subjective and quantitative analyses. *Plast Reconstruc Surg* 111: 2237–2242, 2003
 21. Chou SW, Liao HT, Yazar S, Lin CH, Lin YC, Wei FC: Assessment of fibula osteoseptocutaneous flap donor-site morbidity using balance and gait test. *J Orthop Res* 27: 555–560, 2009
 22. Lee J-H, Chung C-Y, Myoung H, Kim M-J, Yun P-Y: Gait analysis of donor leg after free fibular flap transfer. *Int J Oral Maxillofac Surg* 37: 625–629, 2008
 23. Macdonald K I, Mark Taylor S, Trites JR, Fung EW, Barnsley PG, Dunbar MJ, Lorne Leahey J, Hart RD: Effect of fibula free flap harvest on the gait of head and neck cancer patients: preliminary results. *J Otolaryngol - Head & Neck Surg* 40 Suppl 1: S34-40, 2011
 24. Salaffi F, Leardini G, Canesi B, Mannoni A, Fioravanti A, Caporali R Reliability and validity of the Western Ontario and McMaster Universities (WOMAC) Osteoarthritis Index in Italian patients with osteoarthritis of the knee. *Osteoarthritis Cartilage* 11: 551-560, 2003
 25. Zago M, Camerota TC, Pisu S, Ciprandi D, Sforza C: Gait analysis of young male patients diagnosed with primary bladder neck obstruction. *J Electromyogr Kinesiol* 35: 69-75, 2017
 26. Whittle MW: *Gait Analysis an introduction*. Oxford: Butterworth-Heinemann, 2007.
 27. Lee EH, Goh JC, Helm R, Pho RW: Donor site morbidity following resection of the fibula. *J*

Bone Joint Surg Br Vol 72: 129–131, 1990

28. Harris BN, Bewley AF: Minimizing free flap donor-site morbidity. *Curr Opin Otolaryngol Head Neck Surg* 24: 447-452, 2016
29. Liu TY, Huang YC, Leong CP, Tseng CY, Kuo YR: Home-based exercise on functional outcome of the donor lower extremity in oral cancer patients after fibula flap harvest. *Biomed J* 36: 90-95, 2013
30. Siegel KL, Kepple TM, O'Connell PG, Gerber LH, Stanhope SJ: A Technique to Evaluate Foot Function During the Stance Phase of Gait. *Foot Ankle Int* 16: 764–770, 1995
31. Stodółka J, Sobera M: Symmetry of lower limb loading in healthy adults during normal and abnormal stance. *Acta Bioengin Biomech* 19: 93–100, 2017
32. Rendenbach C, Kohlmeier C, Suling A, Assaf AT, Catala-Lehnen P, Amling M, Heiland M, Riecke B: Prospective biomechanical analysis of donor-site morbidity after fibula free flap. *J Craniomaxillofac Surg* 44: 155-159, 2016
33. Baj A, Beltramini GA, Massarelli O, Youssef DA, Gianni AB: Minimally Invasive Harvest of Free Fibula Flap. *Plastic Reconstr Surg* 131: 474e–477e, 2013

Table 1. Donor site morbidity: gait analysis studies after VFFF.

Study	Patients	Age (mean, range; years)	Follow up time (mean, range; months)	Study design ¹	Analyzed condition ²	Main results ³
Baj ¹⁹	8 (4 M, 4 F)	55 (17-76)	28 (6-60)	C - CG	Stairs ascent/descent	No major alterations found; in descent ↑ RoM of pelvis inclination
Bodde ²⁰	10 (6 M, 4 F)	58 (19-80)	33 (6-87)	C - CG	Treadmill	↓V; ↑ variability under additional cognitive and visual loads or increased velocity
Chou ²¹	11	52 (38-76)	27 (10-68)	C - CG	SW	↓ DS
Feuvrier ¹⁴	11(7 M, 4 F)	53 (17) ⁴	28 (5-104)	C - CG	Treadmill	↓ V; C; SL; ↑ variability in spatio-temporal variables
Hadouiri ¹⁰	11 (4 M, 7 F)	59 (47-63) ⁵	15 (11-31) ⁵	C - CG	6MWT	↓ V;C; SL; DS; walked distance
Lee ²²	20 (13 M, 7 F)	46 (19-68)	1; 3	L	SW	2 month: ↓ V; C; SL; peak plantarflexion; RoM , months: ↓ peak plantarflexion in swing
Lin ³	7 (5 M, 2 F)	53 (45-68)	34 (15-61)	C - CG	SW	No major alterations found (bilateral VFFF)
Maurer-Ertl ¹²	9 (8 M, 1 F)	33 (18-59)	33 (7-59)	Healthy vs operated leg	SW	No alterations found

¹Study design: L = Longitudinal; C = Cross sectional; CG = Control Group

²Analyzed conditions: 6MWT= Six-Minute Walk Test; SW = Straight Walkway

³RoM = Range of Motion; V = Velocity; DS = Double Support; C = Cadency; SL = Stride Length

⁴Standard deviation

⁵Median, Interquartile range

Table 2. Study population.

Patients	Age (years)	Height (cm)	Weight (kg)	BMI (kg/m ²)	Pathology	Free flap variant ¹	Notes
F1	54	169	51	17.9	Left parasymphysis jaw pseudarthrosis	OC - L	-
F2	38	176	101	32.6	Right parasymphysis jaw keratocyst	B - R	Pain
F3	70	160	58	22.7	Left mandibular ramus SCC ²	OMC - R	-
F4	45	170	75	26.0	Left mandibular ramus keratocyst	B - L	-
F5	53	157	45	18.3	Right mandibular ramus adenoid cystic carcinoma	B - L	-
F6	59	163	56	21.1	Superior maxillary atrophy	OMC mini - L	Extensor hallucis longus deficit
F7	61	147	51	23.6	Right mandibular body mucoepidermoid carcinoma	OMC mini - L	-
M1	64	178	105	33.1	Left mandibular ramus SCC	OMC - R	Radiotherapy
M2	23	171	64	21.9	Right mandibular body keratocyst	B - L	-
M3	27	173	67	22.4	Left retromolar trigone SCC	OMC - R	-
M4	30	158	84	33.6	Right mandibular ramus ameloblastoma recidive	B - L	Pain
M5	61	172	56	18.9	Left mandibular body and mouth floor SCC	OMC - R	Extensor digitorum and hallucis longus deficit – Pain – Paraesthesia Wound dehiscence
M6	59	168	94	33.3	Left retromolar trigone mucoepidermoid carcinoma	B - mini - L	Flexor hallucis longus deficit - Stiffness
M7	59	178	80	25.2	Jaw symphysis and mouth floor SCC	OMC - R	Radiotherapy
<i>Mean</i>	<i>50.21</i>	<i>167.14</i>	<i>70.50</i>	<i>25.04</i>			
<i>SD</i>	<i>15.02</i>	<i>9.03</i>	<i>19.63</i>	<i>5.81</i>			

¹B = bone; OC = osteocutaneous; OMC = osteo-myocutaneous; L = left; R = right;

mini = minimally-invasive technique (Baj et al.³³)

²SCC = squamous cell carcinoma

Table 3. Subjective evaluations assessed through the Western Ontario and McMaster Osteoarthritis Index (WOMAC(®)) and the Point Evaluation System for Lower Extremity Fibulectomy (PESLEF).

Patients	WOMAC				PESLEF	
	Pain (max 500)	Stiffness (max 200)	Physical impairment (max 1700)	Total(max 2400)	Categories' score ¹	Total (max 24)
F1	120	40	190	350	2/2/4/4/2/4	18
F2	75	0	45	120	1/4/1/4/4/4	18
F3	210	120	430	760	1/2/2/4/2/4	15
F4	0	0	0	0	4/3/4/4/4/4	23
F5	15	10	15	40	4/4/4/4/4/4	24
F6	0	30	180	210	4/2/2/4/2/4	18
F7	20	0	0	20	3/4/4/4/4/4	23
M1	95	0	55	150	4/3/2/4/2/3	18
M2	20	0	100	120	3/3/3/4/4/3	20
M3	0	0	35	35	4/4/2/4/2/4	20
M4	130	70	50	250	3/4/2/4/4/4	21
M5	330	145	930	1405	2/2/2/2/2/2	12
M6	0	160	160	320	4/2/3/4/2/4	19
M7	325	135	895	1355	1/3/3/2/2/4	15

¹Pain; Paresthesia; Gait recovery; Activities restrictions; Gait impairment; Surgical wound

Table 4 .Pre- and post surgery gait analysis. Bilateral variables.

Variable	Healthy limb					Operated limb					ANOVA	
	Pre		Post		Δ^1	Pre		Post		Δ^1	H/O ²	Pre/Post ³
	Mean	SD	Mean	SD		Mean	SD	Mean	SD		p	P
Stance (%)	63.6	1.7	62.5	1.9	-1.1	64.5	1.7	63.7	1.9	-0.8	0.002	0.057
Swing (%)	36.4	1.7	37.5	1.9	1.1	35.5	1.7	36.4	1.9	0.9	0.002	0.057
Duration (s)	1.13	0.07	1.11	0.09	-0.02	1.13	0.07	1.11	0.09	-0.02	1.000	0.084
RoM hip F (deg)	41.19	5.04	41.35	4.80	0.16	42.90	2.73	41.85	3.73	-1.05	0.361	0.346
RoM knee F (deg)	68.37	3.45	67.27	5.11	-1.1	70.09	3.49	68.14	6.11	-1.95	0.239	0.471
RoM ankle F (deg)	29.34	4.36	29.19	5.28	-0.15	29.58	4.21	28.36	2.80	-1.22	0.802	0.394

¹ Delta refers to post-pre difference

² P values refer to Healthy-Operated comparison (2-way ANOVA). Values in bold are significant (p < 0.05)

³ P values refer to Pre-Post surgery comparison (2-way ANOVA). Values in bold are significant (p < 0.05)

Table 5.Pre- and post surgery gait analysis. Unilateral variables.

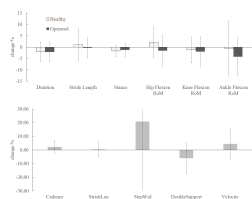
Variable	Pre		Post		Student's t	
	Mean	SD	Mean	SD	Δ^1	P value ²
Velocity (m/s)	1.13	0.11	1.19	0.22	0.06	0.174
Cadency (step/s)	0.89	0.05	0.91	0.08	0.02	0.100
Double Support (%)	28.1	3.4	26.3	3.4	-1.8	0.050
Step width (cm)	7.4	2.9	7.9	3.3	0.5	0.612
Stride length (m)	1.28	0.11	1.29	0.14	0.01	0.742

¹ Delta refers to post-pre difference

² P values refer to pre-post comparison (Student's t test for paired samples). Values in bold are significant ($p < 0.05$)

Figure legend

Figure 1: Percentage changes before and after surgery in the bilateral and unilateral gait variables (mean \pm 1 SD).



ACCEPTED MANUSCRIPT