Two-Stage Osseointegrated Reconstruction of Post-traumatic Unilateral Transfemoral Amputees

Munjed Al Muderis, SQNLDR, MBChB, FRACS, FAOrthA†‡; William Lu, PhD§; Vaida Glatt, PhD¶††; Kevin Tetsworth, MD, FRACS§§

ABSTRACT A new technique called osseointegration was introduced recently by intimately connecting the artificial limb prosthesis to the residual bone, eliminating the problematic socket–residuum interface. The objective here is to describe the two-stage strategy for the osseointegrated reconstruction of amputated limbs and discuss the clinical outcomes of the procedure. This is a prospective case series of 37 post-traumatic unilateral transfemoral amputees with a minimum 2-yr follow-up. Outcome measures included the Questionnaire for persons with a Transfemoral Amputation (Q-TFA), the Short Form Health Survey 36 (SF-36), the 6 Minute Walk Test (6MWT), and Timed Up and Go (TUG) tests. Adverse events including infection, revision surgery, fractures, and implant failures were reported. Clinical outcomes for all outcome measures were significantly improved at follow-up. Twelve participants were wheelchair bound pre-operatively; however, all 12 were able to ambulate after osseointegrated reconstruction. Sixteen patients experienced infection episodes but were managed successfully without the need for implant removal. One periprosthetic fracture occurred due to increased activity, which was revised successfully. These results confirm that the procedure is a suitable alternative for post-traumatic unilateral transfemoral amputees experiencing socket-related discomfort, with the potential to reduce recovery time compared with other treatment protocols.

INTRODUCTION

Amputation of a lower extremity almost inevitably results in major changes in a person’s function, body image, and quality of life.1–3 Lower limb amputation, especially at the transfemoral level, not only adversely affects the vocational capacity of an individual but also their potential to return to active military duty. It is estimated that less than half of the people who require amputations return to work, and the average time to return to work is over 1 yr.2,3 In addition, over 90% of bilateral transfemoral amputees eventually end up confined to a wheelchair due to the difficulty of mobilizing with dual sockets.4 In the United States, there are an estimated 185,000 new amputations every year including military personnel, with an average of more than 500 new amputees every day. Currently, there are 1.9 million people with limb loss living in the United States, and this number is expected to double by 2050.5 The estimated cost for the US Government arising from the treatment and rehabilitation of lower limb amputees is $6.5 billion each year.5

Following amputation, patients require prolonged rehabilitation to fit them with traditional suspended socket prostheses. The higher the level of amputation, the more difficult the fit, and this often results in characteristic complaints of local pain, skin ulceration, and general discomfort.6–9 Patients with a short or inadequate residuum with scarred soft tissues may never be able to use a prosthesis or may choose to go without for most activities. Hoaglund et al surveyed US Vietnam war veterans with amputations and reported a very high prevalence of persistent discomfort and complaints related to use of socket-mounted prosthetics.7 Another survey of 97 patients with a transfemoral amputation (TFA) in Sweden also reported a very high prevalence of problems related to prosthetic use: 72% experienced symptomatic heat and sweating of the residuum, 62% had sores/chafing/skin irritation, 61% had interference with mobility, 51% had pain in the residual when standing or walking, and 44% were uncomfortable sitting with the prosthesis. These patients consistently reported a significantly diminished quality of life when compared with matched controls (normal subjects), with the greatest differences observed in the SF-36.
The typical prosthetic socket used for TFA has also been shown to hinder the range of motion of the involved hip, further contributing to problems when ambulating. Despite extensive and continuing research into socket design and manufacturing, including the use of high-tech labs to optimize prosthetic limb alignment and gait, problems persist. At least one-third of all amputees still encounter socket-related problems including wheelchair-bound patients with short residuum and non-reconstructable limb pathology. This concept has emerged in an attempt to overcome the many issues associated with traditional socket-mounted prosthetics, called osseointegration. This surgical procedure involves the direct attachment of the prosthesis to the skeletal residuum and has already been used with very promising results over the past decade. Several case series have been published that describe these techniques, reporting on their benefits. These studies have demonstrated that this procedure results in major clinical benefits, including improved quality of life, prosthetic use, body image, hip range of motion, sitting comfort, donning and doffing, osseoperception, and walking ability. This has been achieved while maintaining acceptable levels of risk with respect to the associated major complications including implant instability and rates of infection.

This study was conducted to assess the safety and efficacy of this procedure specifically in post-traumatic patients, which have their own unique issues and considerations. The study cohort comprised a subset of unilateral transfemoral amputees that have been reported upon previously in another publication. We hypothesized that these patients would achieve clinical outcomes moderately superior to those reported in the larger study, recognizing the characteristics of this particular cohort of patients.

MATERIALS AND METHODS

This study was designed as a case series using prospectively acquired data. Human Research Ethical approval was granted by the University of Notre Dame, Australia (014153S). Written consent was obtained from all participants before enrollment in the study.

The Osseointegration Group of Australia Accelerated Protocol 1 (OGAAP-1) is a comprehensive, two-stage surgical and accelerated rehabilitation protocol for the osseointegrated reconstruction of amputated limbs. The patients underwent transition to an osseointegrated reconstruction using either the Integral Leg Prosthesis (ILP; Orthodynamics GmbH, Lübeck, Germany) or the Osseointegrated Prosthetic Limb (OPL; Permedica s.p.a, Milan, Italy); both implants are specifically designed for press-fit fixation, allowing bony ingrowth. Selection criteria included age >18 yr, unilateral, transfemoral amputees who had socket-related problems including wheelchair-bound patients with short residuum and non-reconstructable limb pathology. Exclusion criteria included smokers, psychological instability, non-compliance, pregnancy, irradiated affected bone, chemotherapy, immunosuppression, diabetes, and vasculopathy. All patients were enrolled consecutively with consent obtained when identified as suitable during the pre-operative screening procedure.

Pre-operative assessment measures included (1) completing subjective questionnaires (Questionnaire for persons with a Transfemoral Amputation, Q-TFA; Short Form Health Survey SF-36, SF-36) and (2) functional tests including Timed Up and Go (TUG) and the 6 Minute Walk Test (6MWT). Clinical and radiological evaluation included X-rays, computed tomography (CT) scans, and bone mineral density measurements. Critically important, a multidisciplinary team conducted the final screening, which involved pain assessment and psychological and clinical examinations. Patients were advised to follow a prehabilitation program to enhance their potential post-operative recovery. Full disclosure and informed consent were obtained, including a comprehensive discussion of the potential risks and perceived benefits.

The press-fit ILP or OPL implants include an intramedullary component (Fig. 1B), and a transcortaneous dual-cone adapter (Fig. 1C) secured by an internal locking screw (Fig. 1D). The intramedullary part was designed to facilitate immediate mechanical stabilization utilizing a macro-porous surface allowing for bony ingrowth. The transcortaneous dual-cone adapter featured a titanium niobium coating, an alloy known to have bacterial repellent properties, and is highly polished to prevent adhesion to the skin. Insertion of the press-fit implant involved two surgical stages, approximately 4–6 wk apart. Prophylactic intravenous antibiotics using 2 g of cephalozin were administered before each procedure. The first stage involved implantation of the intramedullary stem, preparing the soft tissues with refashioning of the residuum and excision of excess subcutaneous fat. Neuroramas were identified and removed, and the bone prepared to accept the implant. This involved excision of the irregular distal bone and reaming of the intramedullary canal. The intramedullary component was inserted to achieve mechanically stable press-fit fixation, and when necessary, a cross-screw through the femoral neck was inserted for femurs shorter than 16 cm (Fig. 1A). A comprehensive pain management plan was included, as well as a combination of intravenous pain modulators, spinal/epidural medications, and regional nerve blocks. A drain and local anesthetic

**FIGURE 1.** Exploded view of the OPL (Permedica Sociedad por Acciones, Milan, Italy) system showing all implanted components. (A) Optional cross-screw designed to provide additional stability through the femoral neck in short femurs (<16 cm); (B) intramedullary stem featuring a macroporous plasma sprayed titanium coating and proximal fins to provide rotational stability; (C) transcortaneous dual-cone adapter; (D) internal locking screw for the dual-cone adapter. Centimeter (cm).
infiltration device remained in situ. Patients received intravenous and epidural pain medications for the first 3 d post-operation and oral analgesics thereafter. Wound care was minimized to a waterproof dressing on day 1 post-surgery. The drain and local anesthetic infusion catheter were removed on day 2. Patients were mobilizing with crutches or a forearm support frame on day 3 and were discharged home 5–7 d post-surgery. Patients were instructed to continue exercises as an outpatient until the second-stage surgery.

The second stage involved creation of the skin opening and insertion of the transcutaneous dual-cone adapter (Fig. 1C). A guide-wire was used to localize the center of the cannulated end-cap, using an image intensifier. Passing a circular coring device over the guide-wire perforated the skin resulting in a permanent circular opening, and hemostasis was secured before inserting the transcutaneous dual-cone component. This utilized a Morse taper attachment to the intramedullary component and was further secured with a locking screw (Fig. 1D). Post-operative pain management was the same as for the first stage. Wound care involved daily dressing changes for the first 2 wk. Thereafter, patients were advised to wash the implant skin interface with warm tap water and soap and to pat the skin opening dry twice daily. Patients were discharged from hospital 5–10 d post-surgery.

The first phase of rehabilitation was initiated while patients are still hospitalized. On day 3 after the second surgery, patients apply a static axial load of 20 kg twice daily for 20 min. The load is increased each day by 5 kg until it reaches 50 kg or half the body weight. The second rehabilitation phase begun when patients reached the recommended axial loading level and involved the fitting of a rehabilitation prosthesis incorporating a stable locked knee. Patients mobilized using parallel bars until they could balance and felt stable. The third phase started when the patients were safely mobilizing with the rehabilitation prosthesis, and at approximately 14 d, they were then fitted with their definitive prosthesis, including a hydraulic or microprocessor knee with safety mechanisms. For the initial 6 wk, patients were prescribed two crutches when weight bearing; thereafter, a single crutch was used in the opposite hand for an additional 6 wk, and they were allowed unaided weight bearing thereafter. Afterward, further gait training was prescribed that focused on fall prevention and management, balance, walking, and ascending and descending slopes.

Routine follow-up visits were scheduled at 6 wk, and then 3, 6, and 12 mo after the second stage. Additional consultations were scheduled upon request when unforeseen adverse events occurred. The OGAAP-I assessment of potential benefits utilized clinical outcome measures including the Q-TFA, SF-36, TUG, and 6MWT as well as recording adverse events. Comparisons were made between the patients’ pre-operative baseline measures and follow-up data recorded at a minimum of 12 mo after the first stage.

All adverse events were managed and recorded when identified, or at routine follow-up appointments. Refashioning of the residuum was occasionally performed when non-infection-related soft tissue problems were symptomatic at a minimum of 12 mo after the second-stage procedure once tissue healing stabilized. Infections were assessed using an original OGAAP grading system that includes five levels of severity (0–4: no

**FIGURE 2.** Changes from pre- to post-operative values for the following outcome measures: (A) Questionnaire for persons with a transfemoral amputation (Q-TFA) global score; (B) 36-Item Short Form Health Survey (SF-36) physical component summary; (C) 6 Minute Walk Test (6MWT); (D) Timed Up and Go (TUG). All results were statistically significant compared with baseline levels as indicated by an asterisk (*p < 0.05). Error bars indicate a standard error of the mean.
infection, mild soft tissue infection, severe soft tissue infection, bony infection, and implant failure), along with typical incremental treatment actions (oral or parenteral antibiotics, surgical intervention, and implant removal). When infections were suspected; X-rays and swabs were taken for the gram stain and culture tests. Antibiotics were administered based on the level of severity of the infection. The stability of fixation was monitored to detect potential loosening, implant failure, or periprosthetic fractures.

Continuous variables are summarized by the mean and standard deviation, and Kolmorogov–Smirnov test was used to determine the normality of the data. Categorical variables are presented as frequencies and percentages. Analysis of variance (ANOVA) with correlated samples was used to determine differences in each continuous outcome measure, comparing pre-operative with post-operative values (mean ± standard error). Bonferroni corrections were performed to adjust for multiple comparisons. Statistical analysis was performed with Systat (Version 13; Systat, Chicago, IL, USA), a p level of <0.05 was considered significant.

RESULTS
Clinical outcomes were obtained pre- and post-operatively from 24 to 60 mo, with a mean follow-up of 36.38 mo. Compared with the mean pre-operative values with socket prostheses, the mean post-operative values for all outcome measures were significantly improved. Both the post-operative Q-TFA global score (45.27 ± 3.96 to 84.86 ± 3.39, p < 0.0001) and the SF-36 physical component summary (36.97 ± 1.51 to 49.00 ± 1.71, p < 0.0001) were markedly superior to those of the pre-operative values. Both the 6MWT (286.25 ± 21.63 to 412.72 ± 23.69, p < 0.0001) and the TUG (13.86 ± 1.25 to 9.12 ± 0.58, p = 0.0004) were also significantly improved (Fig. 2). Twelve participants were wheelchair bound pre-operatively and could not perform the TUG and 6MWT; however, all 12 were able to do so after osseointegrated reconstruction, and their post-operative values were comparable with those of the prosthetic users who were ambulatory pre-operatively. A total of 21 participants were adverse event-free, but 6 of all patients required elective soft tissue refashioning 12 mo after the second-stage procedure to avoid redundant tissue impingement, skin irritation, and infection. There were 17 episodes of infection in 16 patients: 14 responded to oral antibiotics, 1 patient required intravenous antibiotics, and 2 required surgical soft tissue debridement. Elective refashioning of the soft tissue residuum was performed on a total of 6 patients; 1 periprosthetic fracture occurred due to increased activity (Fig. 3B), which was managed successfully through the application of a trochanteric stabilizing plate (Fig. 3C), which was subsequently removed after the fracture healed (Fig. 3D).

DISCUSSION
Two completely different techniques have been described and used clinically for osseointegration, each with its own merits. Adapting technology initially developed for dental implants, Brånemark performed the pioneering work in this field in Sweden. Promising results have been reported with this screw-type implant that directly attaches the prosthesis to the skeletal residuum. His group uses the OPRA Implant System (Osseointegrated Prostheses for the Rehabilitation of Amputees; Integrum AB, Mölndal, Sweden) that consists of three main components: the fixture, the abutment, and the abutment screw. Treatment involves two operations, with an initial procedure to insert the main intramedullary component and the fixture. The second procedure is delayed for 6 mo, to allow this implant to incorporate fully and bond to bone. This is then followed by a second procedure to create a stoma, a percutaneous opening through which the transcutaneous connection component, the abutment, will then protrude. Only then is prosthetic fitting and gait rehabilitation initiated, resulting in a
very protracted clinical course of definitive reconstruction. In 2014, this group reported on their experience in 55 transfemoral amputated limbs in 51 patients treated over an 8-yr period. They were able to demonstrate statistically significant improvements in both the Q-TFA (global score) and SF-36 (PCS) at 12 and 24 mo, with 92% implant survival at 2 yr. Previous long-term studies have confirmed osseointegrated dental implants can last for greater than 20 yr, with surprisingly few complications considering the relatively hostile environment they inhabit.

In contrast to the screw fixation method offered by the OPRA implant, the second technique uses press-fit macro-porous surface structure implants analogous to modern hip and knee arthroplasty devices. In Germany, Grundei has developed the Endo-Exo-Femurprosthesis (ESKA Implants, Lübeck, Germany) as a modular, unemented, press-fit stem designed specifically for this purpose.26,36 Aschoff has published his results in 37 transfemoral amputees treated over a 10-yr period.26 Unfortunately, this article is largely a descriptive study with no actual outcome measures used to assess patients at any point.

This study from the Osseointegration Group of Australia (OGA) employed two different press-fit devices to perform the osseointegrated reconstruction, using either the ILP or the OPL. These devices are currently in the process of attaining FDA approval but have been widely available in multiple countries including Germany, UK, the Netherlands, New Zealand, and Australia. These devices are available in several versions that are chosen based on the length of the remaining available bone, allowing for a cephalo-medullary extension when the skeletal residuum measures $\leq 16 \text{ cm}$.26 The press-fit design enables osseointegration to take place rapidly in comparison with the screw-fixated design, enabling the gap in between the two stages to be reduced to 4–6 wk as opposed to the 6 mo required by the OPRA Implant System. Recently, OGA further introduced a single-stage surgery protocol, which combined the two-stage procedure into one and reduced the total rehabilitation period to 4–6 wk.37 A study of the single-stage protocol is currently under way with eligible patients being recruited into the study.

A comprehensive analysis of the safety of osseointegration as a two-stage reconstruction using press-fit bone anchored implants was conducted with the OGA in conjunction with another group in the Netherlands who followed a common protocol.25 A total of 86 patients who had at least 24-mo follow-up were included in this study. The median follow-up time was 34 mo (range 24–71 mo). At 24-mo follow-up, 28 (26%) patients had infections on 46 occasions, with 5 (6%) patients requiring surgical intervention. At their final follow-up, 31 (36%) patients (32 implants) had an uneventful course without any complications; 25 (29%) patients (28 implants) had minor complications but no infections; and 24 (28%) patients with infections had a mild episode, non necessitating surgery. Five of the remaining patients had deep infections needing surgical debridement. One patient underwent an exchange of their implant due to aseptic loosening. There was a non-statistically significant association between gender and the risk of any complication (women vs. men OR 1.45 95% CI 0.53–3.96), but a significant association between gender and risk of severe infection with women having a greater than six-fold increase in risk (OR 6.5, 95% CI 1.1–38.15). A BMI $> 25$ was associated with a significant three-fold higher risk of a mild infection (OR 3.47, 95% CI 1.16–10.39). Smokers had a seven-fold higher risk of a recurrent infection (OR 7.5, 95% CI 1.32–42.35). No statistically significant association was observed between other characteristics and the risk of complications. Infection rates in both centers were comparable, with no statistically significant difference observed.32 This multicenter prospective cohort study demonstrated that severe infections resulting in septic implant loosening are rare. Mild infection and irritation of the soft tissue in the skin penetration area are common during the first 2 yr. These complications can be successfully managed using simple measures; however, protocols for adequate surgical management of the peri-implant soft tissue are essential.

The Australian group also recently completed an analysis of outcomes in 50 unilateral transfemoral amputees with a minimum 1-yr follow-up.36 The indication for undergoing osseointegrated reconstruction was almost always related to an inability to effectively use a socket-mounted prosthetic limb, for a variety of reasons; many of these patients were previously wheelchair bound. In this group of challenging reconstruction candidates, the results were nevertheless remarkably consistent and extremely encouraging. Highly statistically significant improvements were demonstrated for all five of the main outcome measures, comparing pre-operative and post-operative values. Both the post-operative Q-TFA global score $(47.82 \pm 2.69$ to $83.52 \pm 2.66$, $p < 0.0001$, Fig. 1A) and the SF-36 physical component summary $(37.09 \pm 1.41$ to $47.29 \pm 1.33$, $p < 0.0001$, Fig. 1B) were markedly superior to those of the pre-operative values. $K$ levels improved in 30 patients and remained unchanged in 20 patients; no patient had a reduction in their $K$ level ($\chi^2=30.32$, df $= 4$, $p = 0.0001$). Both the 6MWT $(281 \pm 19$ to $419 \pm 20$, $p < 0.0001$, Fig. 1C) and the TUG $(14.59 \pm 1.19$ to $8.74 \pm 0.40$, $p < 0.0001$, Fig. 1D), as measures of their mobility, were also significantly improved. A total of 14 participants were wheelchair bound pre-operatively and could not perform the TUG and 6MWT; however, all 14 were able to do so after osseointegrated reconstruction, and their post-operative values were comparable with those of the prosthetic users who were already ambulating pre-operatively.

Despite a 36% (18 of 50) prevalence of superficial soft tissue infection, all of these were successfully managed using a combination of oral or parenteral antibiotics. On only four occasions (in three patients, 6%) was an operative debridement required to manage persistent infection. At a mean follow-up of 21 mo, only 2 of these 50 patients have undergone removal of the implant; in one case, there was a failure of osseointegration related to insertion of an undersized component, and in one case, there was a fatigue failure...
of the implant at 3.5 yr (96% implant survival).\(^{36}\) Both of these were subsequently revised to another osseointegrated reconstruction; none of these 50 patients has reverted to use of a socket-mounted prosthetic limb for any reason.

**CONCLUSIONS**

In these 37 post-traumatic unilateral transfemoral amputees, significant improvements were achieved in all of the outcome measures of health-related quality of life, ambulation ability, and functional levels. These findings are comparable with, or better than, those reported previously by other groups using alternative implants and rehabilitation protocols. Under the OGAAP-1 protocol, the time interval between the initial procedure and fully independent ambulation was approximately 4–5 mo. This contrasts markedly with the protracted interval between the initial procedure and the independent ambulation previously reported for screw-type osseointegration implants, typically requiring as long as 12 mo. The more rapid completion of reconstruction is likely due to a combination of factors, including the decreased interval between stages and the accelerated progression of weight-bearing exercises and rehabilitation. These results confirm that the OGAAP-1 is a suitable alternative for post-traumatic unilateral transfemoral amputees experiencing socket-related discomfort, with the potential to reduce recovery time compared with other staged treatment protocols.

**PRESENTATION**

Presented at the 2016 Military Health System Research Symposium, Kissimmee, FL (abstract number: MHSRS-16-0520).

**REFERENCES**


