■ LOWER LIMB

The Osseointegration Group of Australia Accelerated Protocol (OGAAP-1) for two-stage osseointegrated reconstruction of amputated limbs

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Aims

This study describes the Osseointegration Group of Australia's Accelerated Protocol two-stage strategy (OGAAP-1) for the osseointegrated reconstruction of amputated limbs.

Patients and Methods

We report clinical outcomes in 50 unilateral trans-femoral amputees with a mean age of 49.4 years (24 to 73), with a minimum one-year follow-up. Outcome measures included the Questionnaire for persons with a Trans-Femoral Amputation, the health assessment questionnaire Short-Form-36 Health Survey, the Amputation Mobility Predictor scores presented as K-levels, 6 Minute Walk Test and timed up and go tests. Adverse events included soft-tissue problems, infection, fractures and failure of the implant.

Results

Our results demonstrated statistically significant improvements in all five outcome measures. A total of 27 patients experienced adverse events but at the conclusion of the study, all 50 were walking on osseointegrated prostheses.

Conclusion

These results demonstrate that osseointegrated prostheses are a suitable alternative to socket-fit devices for amputees experiencing socket-related discomfort and that our strategy offers more rapid progress to walking than other similar protocols.

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Amputation of a lower limb results in major changes in a person's function, body image and quality of life.[1-3] It may restrict their ability to gain employment and can leave them dependent upon social services.[4] It is estimated that less than half of those who undergo amputation return to work, and the average time to do so exceeds one year.[4] More than 90% of patients with bilateral above-knee amputations will eventually be confined to a wheelchair due to the difficulty of mobilising with prosthetics on both lower limbs.[5] Despite extensive research into socket design and manufacturing, problems persist[6] with at least one third of all amputees encountering problems at the interface of prosthetic and stump.[5,7]

Over the last two decades the concept of osseointegration has emerged as a potential solution to many issues associated with traditional socket-mounted prostheses.[8-10] By surgically connecting the prosthesis to the residual bone, the problematic interface can now be eliminated. Pioneering work using a screw-type implant adapted from dental implants showed promising initial results.[11] Various studies have demonstrated major clinical benefits from osseointegrated prostheses including improved quality of life,[12] prosthetic use,[12,13] body image,[13] range of movement at the hip,[14] comfort when sitting,[15] fitting and removing prostheses,[12] osseoperception[16] and walking ability[17,18] while simultaneously obtaining implant stability[19] while maintaining acceptable rates of infection.[8,20]

The implants have evolved beyond screw-type fixation to intra-medullary press-fit, highly porous-coated metal alloy devices similar to those used in total hip arthroplasty.[21] This results in a structural and functional connection between the surface of these biocompatible implants and the patient's own bone.[22,23] The device has a portion which is brought out permanently through skin, allowing the prosthesis to be rigidly attached to bone.

Although osseointegration has only recently been approved by the Food and Drug Administration for limited human use in the United States,[24] it has become more established in Australia and Europe over the past decade.

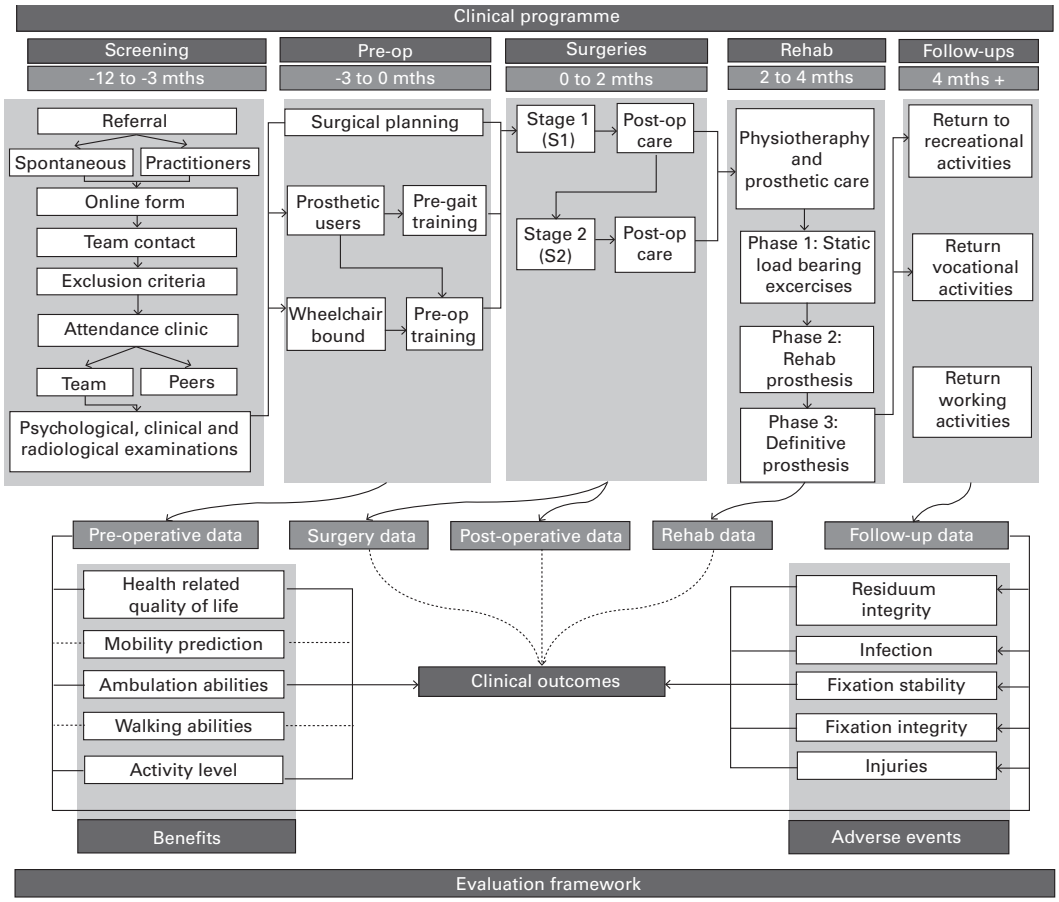

Fig. 1

Diagram of the Osseointegration Group of Australia Accelerated Protocol (OGAAP-1) clinical treatment programme.

Some concerns nonetheless persist with regard to potential adverse events and complications.

The Osseointegration Group of Australia Accelerated Protocol-1 (OGAAP-1) is a programme for the management of patients who have lost lower limbs, with the aim of reducing the overall time required for their definitive reconstruction and rehabilitation. The strategy emphasises an integrated approach encompassing initial screening, pre-operative care, the surgical procedure, rehabilitation, and ongoing post-operative care (Fig. 1). This culminates in surgery with implantation of an osseointegrated device.

The objectives of this study are to describe the OGAAP-1 protocol and to assess its outcomes in a cohort of 50 unilateral trans-femoral amputees.

Patients and Methods

This prospective cohort study had ethical approval from the University of Notre Dame, Sydney, Australia (014153S).

Patients were screened online for eligibility. Inclusion criteria were: aged over 18 years, unilateral trans-femoral amputation and socket or prosthesis-fitting problems. Exclusion criteria were smoking, disabling psychiatric disorder, non-compliant behaviour as demonstrated during the pre-operative screening and evaluation process (e.g., non-compliance with requests for information, inability to show up for scheduled for appointments, failure to honour commitments, inability to adhere to requests to wean off narcotics/abstain from smoking, inability to supply information or documentation as requested, inability to obtain clearance from third-party payers or Worker's Compensation), pregnancy, previous radiotherapy to the affected residual limb, chemotherapy, immunosuppression, diabetes and peripheral vascular disease.

Eligible patients attended a clinic for peer-to-peer counselling, pre-operative baseline recording of outcome measures and clinical and radiological evaluation. The peer-to-peer interaction allowed patients to explore issues related to the surgery and recovery from it. The outcome measures used were the questionnaire for persons with a trans-femoral amputation (Q-TFA);[25] MOS 36-item Short-Form health survey (SF-36);[26] timed up and go (TUG);[27] 6 Minute Walk Test, (6MWT)[28] and the Amputation Mobility Predictor (AMPPRO).[29] Radiological assessment was

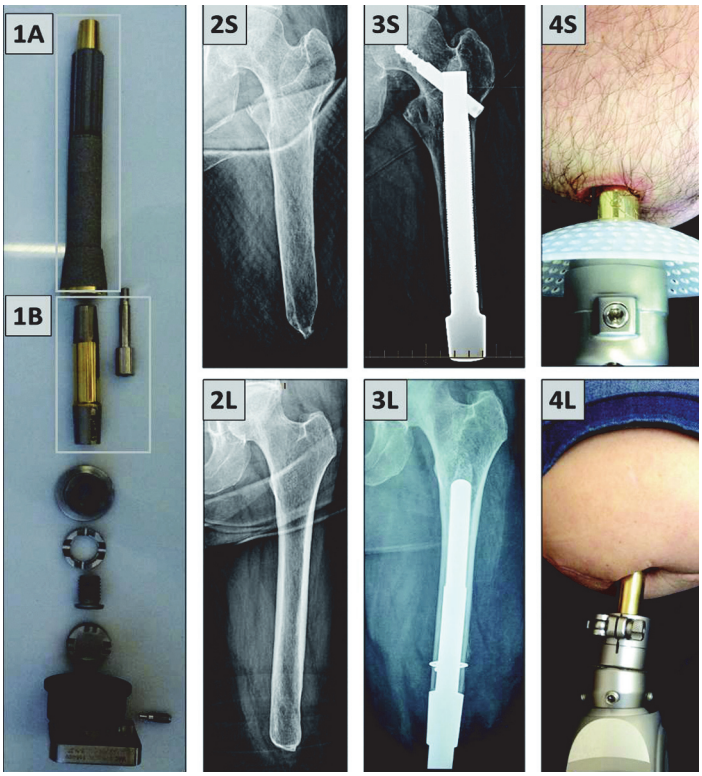

Fig. 2

Osseointegrated Prosthetic Limb (Permedica s.p.a, Milan, Italy) press-fit fixation implant, including the intramedullary part (1a) and transcutaneous dual cone adaptor (1b); Representative radiographs of the proximal femur before (2) and after (3) surgery; skin-fixation interface (4) for participants with short (S) and long residuum (L).

by computed tomography (CT) and bone mineral density measurement. Patients were given a pre-operative physical training programme to enhance their post-operative rehabilitation and informed consent was obtained. Pre-operative training for wheelchair bound patients involved muscle strengthening and visualisation, as well as core strengthening exercises. Prosthetic users were asked to conduct pre-gait training aimed at increasing their range of movement, with a particular emphasis on the hip flexors and adductors.

The patients underwent osseointegrated reconstruction using either the Integral Leg Prosthesis (ILP; Orthodynamic GmbH; Lübeck, Germany) or the Osseointegrated Prosthetic Limb (OPL; Permedica s.p.a; Milan, Italy).

The press-fit ILP/OPL implants include an intramedullary component, and a transcutaneous dual cone adaptor (Fig. 2, far left top and bottom). The intramedullary part was designed with a specific shape, facilitating immediate mechanical stabilisation that incorporates a macro-porous surface allowing for bony ingrowth. The transcutaneous dual cone adaptor enables the attachment of a prosthetic limb. The surface of this adaptor is coated with titanium oxide, an alloy known to have bacterial repellent properties, and is highly polished to prevent adhesion to the skin.[24]

Insertion of the press-fit implant involved two surgical stages, approximately four to eight weeks apart.[21] Prophylactic intravenous antibiotics using two grams of Cephazolin were administered prior to each procedure. The first stage involved implantation of the intramedullary part (Fig. 2, 1a), preparing the soft tissues with refashioning of the stump and excision of excess subcutaneous fat. Neuromas were identified and removed, and the bone prepared to accept the implant. This involved excision of the irregular distal bone, reaming of the intramedullary canal, and locally obtained autologous bone graft when indicated. The intramedullary component was inserted to achieve mechanically stable press-fit fixation and when necessary a cross-screw through the femoral neck was inserted (femurs ≤ 16 cm). A comprehensive pain management plan was included to treat neuromas, as well as a combination of intravenous pain modulators, spinal/epidural medications and regional nerve blocks. A drain and local anaesthetic infiltration device remained *in situ*. Patients received intravenous and epidural pain medications for the first three days post-operative, and thereafter used oral analgesics.

Table I. Patients' demographic information

Patient demographics	
Gender (total)	50
M	34
F	16
Age (yrs)	
Range	24 to 73
Mean	48.4
Amputation side	
Right (Total)	25
M	16
F	9
Left (Total)	25
M	18
F	7
Time from amputation to osseointegration surgery (yrs)	
< 2	11
> 2 to 10	12
> 10 to 20	13
> 20 to 30	8
> 30 to 40	3
> 40 to 65	3
Reason for amputation	
Trauma	32
Blast injury	3
Infection	5
Oncology	8
Congenital	2
Indication for osseointegration surgery	
Wheelchair-bound pre-operatively	14
Direct conversion to osseointegrated implant	5
Short stump and poor socket fit	4
Poor socket fit	4
Socket interface issues (pistoning and skin breakdown, pressure on soft tissues)	1
Socket prosthesis users pre-operatively	36
Socketinterface issue	21
Socket interface issue (pistoning and skin breakdown, pressure on soft tissues) and poor fit	8
Short stump and poor fit	6
Donning and doffing problems related to upper limb injury	1

Wound care was minimised to a waterproof dressing on Day 1 post-surgery. The drain and local anaesthetic infusion catheter were removed on Day 2. Patients were mobilising with crutches or a forearm support frame on Day 3, and were discharged home five to seven days 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 adaptor (Fig. 2, far left bottom). To do this, a guide-wire was used to localise the centre 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 haemostasis was secured before inserting the transcutaneous dual cone component. This utilised a Morse taper attachment to the intramedullary component, and was further secured with a locking screw. Postoperative pain management was the same as for the first stage. Wound care involved daily dressing changes for the first two weeks. 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 five to ten days post-surgery.

Any complaint of pain while weight-bearing was deemed sufficient to suspend further exercise in the rehabilitation program after the second stage. The first phase of rehabilitation is initiated while patients are still hospitalised. On Day 3 after the second stage, patients apply a static axial load of 20 kg twice daily for 20 minutes. The load is increased each day by 5 kg until it reaches 50 kg, or half of their body weight. The second phase started when patients reached the recommended axial loading level, and involved the fitting of a rehabilitation prosthesis incorporating a stable locked knee. Patients mobilised using parallel bars until they could balance and felt stable. The third phase started when the patients were safely mobilising with the

Table II. Clinical outcome measures pre-operatively and minimum of one year post-operatively after the first stage of the surgery with implantation of the metal post

Outcome measure	Units	Pre-operative		Post-operative		p-value, ANOVA
		Mean	SD	Mean	SD	
SF-36 (n = 46 Pre-operative, n = 49 Post-operative)						
Physical Component Summary	points	37.09	9.54	47.29	9.33	< 0.001
Q-TFA (n = 46 Pre-operative, n = 46 Post-operative)						
Global	points	47.82	17.28	83.52	18.04	< 0.001
TUG						
Wheelchair bound (n = 14/50)						
Duration	seconds	-	-	9.00	0.56	n/a
Prosthetic user (n = 36/50)						
Duration	seconds	14.59	5.94	8.74	2.81	< 0.01
6MWT						
Wheelchair-bound (n = 14/50)						
Distance	metres	-	-	411	31.44	n/a
Prosthetic users (n = 36/50)						
Distance	metres	281	93	419	133	< 0.001

SD, standard deviation; ANOVA, analysis of variance; SF-36, Short-Form-36 Health Survey; Q-TFA, questionnaire for persons with a trans-femoral amputation; TUG, timed up and go; 6MWT, 6 Minute Walk Test

Table III. Pre- and post-operative Amputation Mobility Predictor (AMPPRO)[28] scores presented as K-Levels (Fisher's exact test chi-squared, 30.32; degrees of freedom, 4, p = 0.001)

Pre- and post-operative K-levels	Patients (n)
Improved	30
K0 to K2	2
K0 to K3	12
K0 to K4	1
K1 to K3	1
K2 to K3	11
K3 to K4	3
Unchanged	20
K2	2
K3	13
K4	5
Reduced	0

K0 – patient has no ability or potential to ambulate or transfer safely with or without assistance and a prosthesis does not enhance their quality of life or mobility; K1 - patient has the ability or potential to use a prosthesis for transfers or ambulation on level surfaces at fixed cadence - a typical limited or unlimited household ambulator; K2 - patient has the ability or potential for ambulation with the ability to traverse low-level environmental barriers such as curbs, stairs, or uneven surfaces - a typical community ambulator; K3 - patient has the ability or potential for ambulation with variable cadence - a typical community ambulator with the ability to traverse most environmental barriers and may have therapeutic or exercise activity that demands prosthetic use beyond simple locomotion; K4 - patient has the ability or potential for prosthetic ambulation that exceeds basic ambulation skills, exhibiting high impact, stress, or energy levels - typical of the prosthetic demands of the child, active adult, or athlete

rehabilitation prosthesis, and at approximately 14 days they were then fitted with their definitive prosthesis, including a hydraulic knee with safety mechanisms. A laser prosthetic alignment device was used to accurately adjust the prosthetic limb in the sagittal and coronal planes. Alignment was also carefully adjusted to reduce shear and torsional loading on the bone-implant interface. For the initial six weeks, patients were prescribed two crutches when weight-bearing. A single crutch was used in the opposite hand for an additional six weeks and they were allowed unaided weight-bearing thereafter. Afterwards, further gait training was prescribed that focused on fall prevention and management, balance, walking, and ascending and descending slopes.

Routine follow-up was at six weeks and three, six and 12 months post-operatively. Refashioning of the residuum was performed for non-infective soft-tissue problems symptomatic 12 months post-operatively. Infections were graded by our own system of five levels: 0 (no infection); 1 (mild soft-tissue infection/responded to oral antibiotics); 2 (severe soft-tissue infection/required intravenous antibiotics); 3 (bony infection/needed operative debridement) and 4 (implant failure/resulted in removal of the implant).

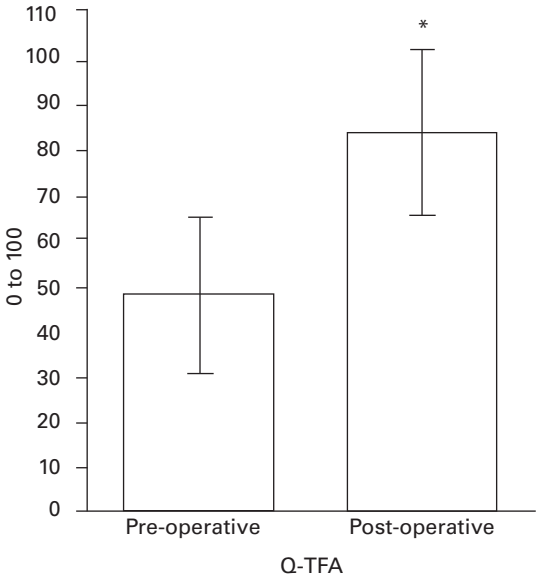

Fig. 3a

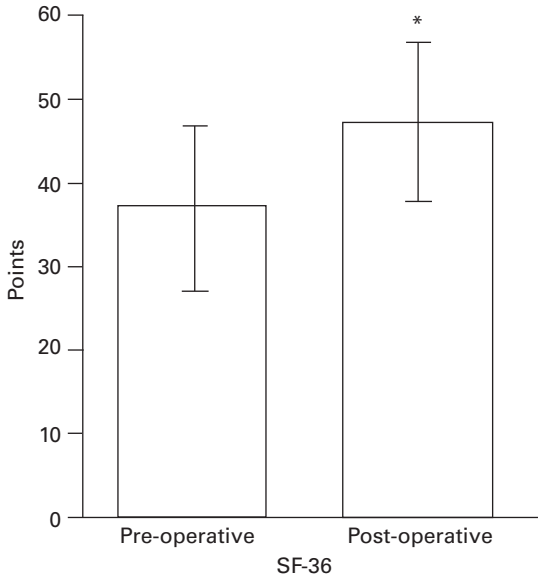

Fig. 3b

Changes from mean pre- to post-operative values at a minimum of one-year follow-up after stage one surgery in (a) Questionnaire for persons with a Trans-Femoral Amputation (Q-TFA) and (b) health assessment questionnaire Short-Form-36 Health Survey (SF-36). Error bars indicate the standard deviation of the mean. Asterisk (*) shows significant ($p < 0.001$ for both, analysis of variance) difference from the pre-operative group.

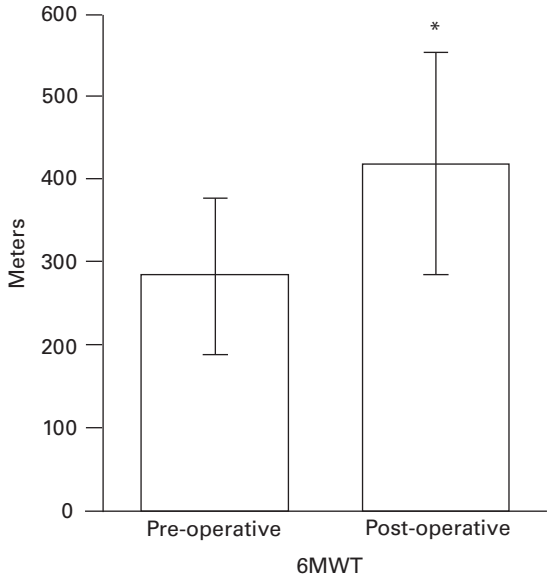

Fig. 4a

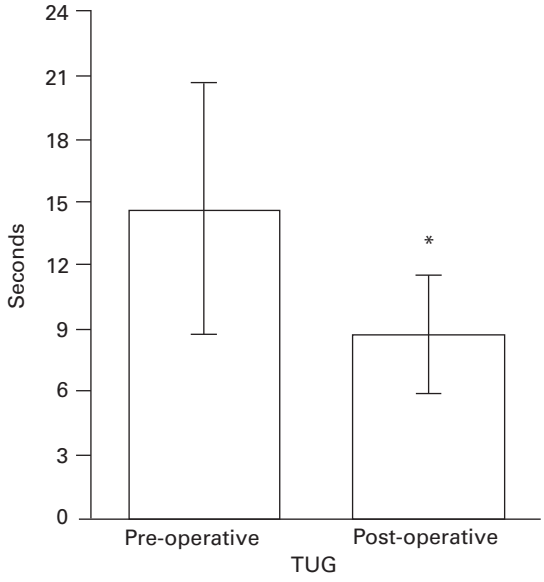

Fig. 4b

Changes from mean pre- to post-operative values at a minimum of one-year follow-up after stage one surgery in (a) 6 Minute Walk Test (6MWT) and (b) timed up and go (TUG). Error bars indicate the standard deviation of the mean. Asterisk (*) shows significant ($p < 0.001$ for 6MWT and $p < 0.01$ for TUG, analysis of variance) difference from the pre-operative group.

Treatment of infetion ranged from oral antibiotic therapy to removal of an infected implant according to the severity of the problem as listed above.[30]

Statistical analysis. The Kolmorogov-Smirnov test was used to test for normality. Analysis of variance (ANOVA) was used to determine differences in continuous outcome measures. Fisher's exact test was used to examine the significance of the contingency of K-levels pre- and post-operative. Bonferroni corrections were performed to adjust for multiple comparisons. Statistical analysis was performed with Systat (Version 13; Systat, Chicago, Illinois) with a p-value < 0.05 considered significant.

Results

Between March 2011 and June 2014, a total of 53 unilateral trans-femoral amputees were treated under this

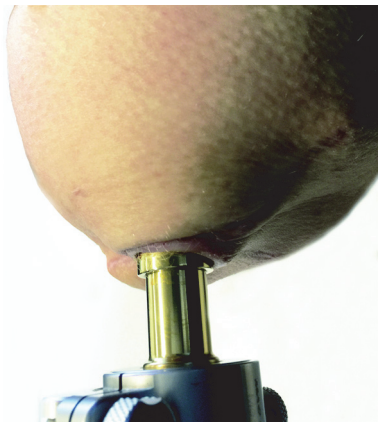

Fig. 5a

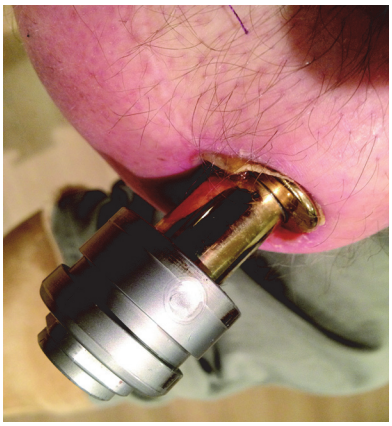

Fig. 5b

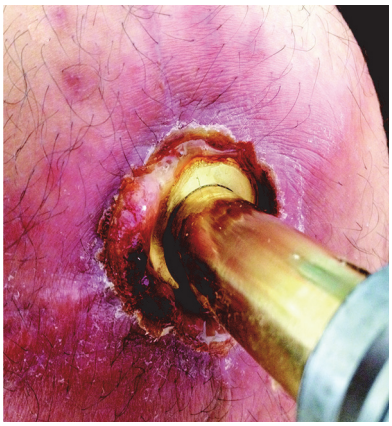

Fig. 5c

Representative images of infection: a) healthy stoma; b) stoma requiring oral antibiotics; c) stoma requiring intravenous antibiotics.

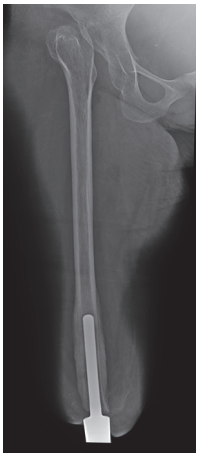

Fig. 6a

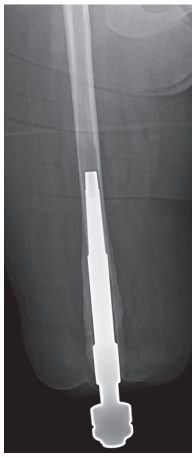

Fig. 6b

Radiographs demonstrating aseptic loosening of an implant custom-made for a patient with tibial hemimelia. The patient's femur was hypoplastic, and required a small diameter of stem. The surface had to be made relatively smooth which led to aseptic loosening; a) loosening two years after implantation; b) the same patient following revision surgery, incorporating a larger stem with more extensive porous coating without any bone loss.

protocol. Their demographic information is presented in Table I.

A total of three patients died from unrelated causes and none were lost to follow-up. Mean follow-up was 21.5 months after the first stage and the time to fully independent walking from the initial procedure was a median 4.5 (2.5 to 5) months.

The mean post-operative values for all five outcome measures were significantly improved from their pre-operative scores (Tables II and III, Figs 3 and 4). All 14 participants that were wheelchair bound pre-operatively could not perform the TUG and 6MWT, but all 14 were able to do so post-operatively. Their post-operative scores were comparable with those of the patients who were walking pre-operatively.

A total of 27 of 50 (54%) patients experienced an adverse event. Soft-tissue refashioning was performed in ten patients to avoid impingement, skin irritation and infection. In addition, 21 patients experienced one or more infections, of whom 13 responded to oral antibiotics alone, five to intravenous antibiotics and three required surgical soft tissue debridement of infected soft tissues (Fig. 5). A total of four patients sustained periprosthetic fractures as a result of falls, three of whom were previously wheelchair-bound with severe osteoporosis. All four fractures were managed by open reduction and internal fixation with a dynamic hip screw and cables as necessary, without interfering with the osseointegration of the implant. Subsequent rehabilitation was by progressive weight-bearing and all fractures healed within three months. Revision of the implant was required in two patients; one due to failure of osseointegration as a result of an undersized device (Fig. 6), and the other as the result of an implant fatigue failure at 3.5 years.

Discussion

Significant improvements were achieved in all five of the outcome measures, findings which are comparable with, or better than, those reported previously by other groups using alternative implants and rehabilitation protocols.[8,18]

Under our protocol the time from surgery to unaided walking was approximately 4.5 months, contrasting markedly with the nine to 12 months seen in previous, screw-fit interventions. [12,31] Press-fit fixation appears to provide adequate immediate stability to allow more rapid rehabilitation, mobilisation, and ambulation, and there may be merit in considering osseointegrated reconstruction as a single procedure.

Despite the complications seen in the cohort, successful reconstruction or revision procedures resulted in all patients continuing to walk on osseointegrated artificial limbs. Importantly, all the infections were confined to soft tissue and no deep bone infection was seen. Few other studies have monitored these adverse events in similar detail and those reporting the results of screw-type implants used a different classification system.[8,20,32] Therefore, comparison is difficult; however, the rates appear to be broadly similar to other published series.[5,33,34]

Our cohort size is similar to previous studies presenting intermediate results of other bone-anchored prostheses.[8,12,18] The main limitation of this study is the short period of follow-up. Other limitations include variability in the duration of use of a prosthesis pre-operatively, the length of the residuum and, most importantly, the prosthetic components used following osseointegrated reconstruction. Some of the clinical improvements observed may relate to the use of superior prosthetic components after osseointegrated reconstruction, such as the microprocessor-controlled knee.

Larger, multicentre studies are required to fully assess the risks and benefits of this approach, but this cohort study demonstrates clear benefits for those trans-femoral amputees who experience problems with traditional, socket-mounted prostheses.

Take home message:

Surgical conversion from a standard socket-style mounting of prosthetic limbs to an osseointegrated reconstruction with a press-fit implant consistently resulted in clinically significant improvements in patient satisfaction, quality of life and functional ability.

Author contributions:

M. Al Muderis: Study design, Patient care and surgical procedure, Manuscript preparation.
K. Tetsworth: Manuscript preparation, Data statistical analysis, Revision and editing of the manuscript.
A. Khemka: Study design, Human research ethics document preparation, Final review of the manuscript.
S. Wilmot: Data collection, Final review of the manuscript.
B. Bosley: Study design, Patient care, Data collection, Final review of the manuscript.
S. J. Lord: Final review of the manuscript.
V. Glatt: Manuscript preparation, Data collection and statistical analysis, Revision and editing of the manuscript.

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