

■ TRAUMA

Periprosthetic osseointegration fractures are infrequent and management is familiar

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Aims

Osseointegrated prosthetic limbs allow better mobility than socket-mounted prosthetics for lower limb amputees. Fractures, however, can occur in the residual limb, but they have rarely been reported. Approximately 2% to 3% of amputees with socket-mounted prostheses may fracture within five years. This is the first study which directly addresses the risks and management of periprosthetic osseointegration fractures in amputees.

Methods

A retrospective review identified 518 osseointegration procedures which were undertaken in 458 patients between 2010 and 2018 for whom complete medical records were available. Potential risk factors including time since amputation, age at osseointegration, bone density, weight, uni/bilateral implantation and sex were evaluated with multiple logistic regression. The mechanism of injury, technique and implant that was used for fixation of the fracture, pre-osseointegration and post fracture mobility (assessed using the K-level) and the time that the prosthesis was worn for in hours/day were also assessed.

Results

There were 22 periprosthetic fractures; they occurred exclusively in the femur: two in the femoral neck, 14 intertrochanteric and six subtrochanteric, representing 4.2% of 518 osseointegration operations and 6.3% of 347 femoral implants. The vast majority (19/22, 86.4%) occurred within 2 cm of the proximal tip of the implant and after a fall. No fractures occurred spontaneously. Fixation most commonly involved dynamic hip screws (10) and reconstruction plates (9). No osseointegration implants required removal, the K-level was not reduced after fixation of the fracture in any patient, and all retained a K-level of ≥ 2 . All fractures united, 21 out of 22 patients (95.5%) wear their osseointegration-mounted prosthetic limb longer daily than when using a socket, with 18 out of 22 (81.8%) reporting using it for ≥ 16 hours daily. Regression analysis identified a 3.89-fold increased risk of fracture for females ($p = 0.007$) and a 1.02-fold increased risk of fracture per kg above a mean of 80.4 kg ($p = 0.046$). No increased risk was identified for bilateral implants ($p = 0.083$), time from amputation to osseointegration ($p = 0.974$), age at osseointegration ($p = 0.331$), or bone density (g/cm², $p = 0.560$; T-score, $p = 0.247$; Z-score, $p = 0.312$).

Conclusion

The risks and sequelae of periprosthetic fracture after press-fit osseointegration for amputation should not deter patients or clinicians from considering this procedure. Females and heavier patients are likely to have an increased risk of fracture. Age, years since amputation, and bone density do not appear influential.

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Introduction

Socket-mounted prostheses have been the traditional rehabilitation solution for lower-limb amputees for at least 500 years.¹ Unfortunately, problems persist. Between one-third and three-quarters of patients develop ulcers, dermatitis

or intolerable perspiration.^{2,3} Mobility and fit are troublesome due to fluctuation in the size of the residual limb⁴ or a feeling of instability from altered proprioception.^{5,6} Most patients require frequent refitting.⁷ Transfemoral amputees often lack confidence when navigating uneven surfaces;

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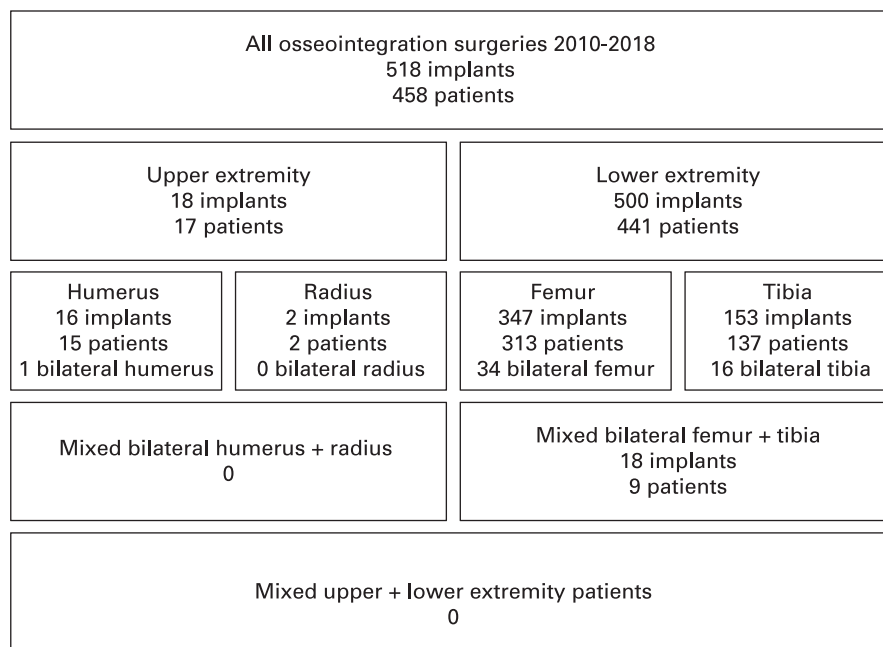


Fig. 1

Anatomical localization of the osseointegration operations for patients with complete medical records.

one-quarter report a poor or extremely poor lifestyle⁸ and 2.2% sustain a fracture in the residual limb within five years of surgery.⁹ Since 1990, the surgical technique of osseointegration, allowing skeletal anchorage of the attachment connecting to a prosthesis, has gained gradual acceptance as an improved option for the rehabilitation of amputees compared with a socket-mounted connection. Patients who adapt from a socket to an osseointegrated prosthesis mobilize quicker and easier and wear their prosthesis more.¹⁰

The widespread adoption of osseointegration, however, has been impeded by concerns among clinicians mostly about two potential complications: infection and periprosthetic fracture. The world's two highest-volume osseointegration groups have reported rates of deep infection of 27%¹¹ and 5%¹² with no reports of infection requiring further proximal amputation or threatening patient survival. Although mentioned briefly elsewhere,¹²⁻¹⁵ the concern of periprosthetic fracture has not received focused attention. This study is the first specifically to investigate the risk of postoperative periprosthetic fracture associated with osseointegration surgery, and the management of these fractures.

Methods

Following ethical approval, a retrospective review of all osseointegration operations performed at four centres between 2010 and 2018 identified 588 evaluable procedures. A total of 518 of these patients had been reviewed within the previous calendar year or were successfully contacted by phone to verify their current status; 70 were unable to be contacted. The anatomical location of the implants is shown in Figure 1. The medical records and radiological data of patients who had a periprosthetic fracture associated with the osseointegrated implant were either

Table I. Demographics of the patients with a periprosthetic fracture and the risk factors for fracture.

Variable	Value (% of 22)
Mean age, yrs (SD, range)	48.3 (13.1; 22.6 to 64.5)
Weight, kg (SD, range)	85.7 (18.9; 56.0 to 120.0)
Male sex, n (% of 22)	13 (59.1)
Left, n (% of 22)	13 (59.1)
Indication for amputation, n (%)	n (% of 22)
Trauma	17 (77)
Untreatable infection after knee arthroplasty	3 (14)
Cancer	2 (9)
Tobacco	5 (22.7)
Diabetes	1 (4.5)
Alcohol > 3/day	2 (9.0)
Frequent falls in socket	6 (27.3)
Previous adult fracture	4 (18.2)
Parental hip fracture	0
Rheumatoid	0
Glucocorticoids	0

reviewed again in the clinic or were interviewed by telephone in order to record their personal and family history as well as their mobility. Their demographic and risk factors including FRAX risks for fragility fracture¹⁶ (Table I) and the history and characteristics of the fracture were evaluated (Table II). The Medicare Functional Classification Level System modifier (K-level)¹⁷ was used to assess mobility due to its familiarity with clinicians who work with amputees and the ease of categorizing without requiring an extended interview or physical examination. The limitations of this system are acknowledged.¹⁸ All implants were introduced with a press-fit technique; 15 fractures occurred in patients with an Osseointegrated Prosthetic Limb (Permedica

Table II. Characteristics of the fracture, treatment and outcome.

Variable	Value, n (% of 22)
Years from amputation to osseointegration	
< 1	4 (18)
1 to 5	1 (5)
6 to 10	6 (27)
10 to 20	8 (36)
20	3 (14)
Months from osseointegration to fracture	
0 to 3	6 (27)
4 to 6	9 (41)
7 to 12	4 (18)
48	3 (14)
Weeks from fracture to fixation	
< 1	20 (91)
> 1	2 (9)
Mechanism of injury	
Ground-level fall	19 (86)
Twist	2 (9)
Kicking	1 (5)
Anatomical location of the fracture	
Neck of femur	2 (9)
Intertrochanteric	14 (64)
Subtrochanteric	6 (27)
Location relative to implant	
> 2 cm proximal of tip	2 (9)
Within 2 cm of tip	19 (86)
> 2 cm distal of tip	1 (5)
Implant used for fixation	
Dynamic hip screw	10 (45)
Locking reconstruction plate	9 (41)
Blade plate	1 (5)
Cannulated screws	1 (5)
Extension nail	1 (5)
Surgeon treating the fracture	
Same as osseointegration	12 (55)
Different surgeon	10 (45)
Patients using prosthesis ≥ 16 hours daily	
Before osseointegration	3 (14)
Currently	18 (82)
Patients with K-level ≥ 2	
Before osseointegration	5 (23)
Currently	22 (100)

Medical Manufacturing, Lecco, Italy) and seven in those with an Integral Leg Prosthesis (Orthodynamic, Lubeck, Germany). The selection of implants reflects a complex decision involving the surgeon's choice and clinical exigency to address the specific needs of each patient.

Statistical analysis

Descriptive statistics were used to summarize patient demographics (percentage, mean, SD, and range as appropriate) and multiple logistic regression analysis was performed of the transfemoral amputees to estimate the relationship among variables; these calculations were performed with Google Sheets (Google LLC, Mountain View, California, USA) using the XLMiner Analysis ToolPak (Frontline Systems, Incline Village, Nevada, USA). Fisher's exact test was used to compare event frequency.

Statistical significance was set at $p < 0.05$. Since all fractures occurred in the femur, a multiple logistic regression analysis was performed specifically of those who underwent transfemoral osseointegration to assess the influence of age at the time of osseointegration, years from amputation to osseointegration, type of implant used for fracture fixation, single- or two-stage surgical protocol, laterality, weight, and sex on the risk of periprosthetic fracture. The 22 patients who experienced a fracture are described in Table I. Their prosthesis use ranged from none to over 20 years, and the reasons for choosing osseointegration included painful intolerance of the prosthesis, severe contact dermatitis, or inability to maintain a secure fit. Preoperative bone mineral density measurement, assessed by dual-energy radiograph absorptiometry (DEXA), was available for 64.0% (222/347) patients who had transfemoral osseointegration including 45% (10/22) of those with a fracture and a separate logistic regression analysis was performed on this subset of patients to evaluate the influence of ipsilateral femoral neck bone density on the risk of fracture.

Results

Fractures occurred exclusively in the femur, 22 in total, giving an overall rate of fracture of 4.2% for all osseointegration operations (518) and 6.3% for femoral osseointegration operations (347). Regarding FRAX specified risk factors (Table I), those who sustained a fracture included a considerable number who reported falling frequently while using or attempting to use their socket prosthesis prior to osseointegration, which is common among amputees.^{19,20} Because nearly all the patients sustained the fracture while still in the relatively acute rehabilitation phase, as discussed later, it was not considered useful to discuss the issue of 'frequent falls' postoperatively in these patients. Smoking was the only other notably prevalent FRAX risk factor.

The time from amputation to osseointegration varied widely (< 1 to > 20 years), and 45% of patients (10/22) had their fracture fixed by a different surgeon from the one that undertook the initial osseointegration procedure (Table II). Otherwise most patients with a periprosthetic fracture could be summarized as: sustaining their fracture within the first year of osseointegration, from a ground-level fall, fracturing in the intertrochanteric region and also within 2 cm of the proximal tip of the implant, with surgical fixation occurring within one week using a common hip-fracture implant (Table II). Despite their fracture, most patients (81.8%, 18/22) currently use their prosthesis without time constraints (≥ 16 hours daily), all remain independently mobile and the K-level declined in none. Their mobility (Figure 2) and hours of using the prosthesis (Figure 3) before osseointegration and at the most recent follow-up are also represented graphically. Patients who reported wearing their prosthesis 'all day' were defined as using it for ≥ 16 hours/day.

The rate of femoral fracture based on the location of the implant is shown in Table III. Although it is highest for patients with implants of both one femur and the contralateral tibia, this difference fell short of significance.

A logistic multiple regression analysis was performed to assess the relative influence of several variables considered as potential risk factors for periprosthetic fracture. Years from amputation to osseointegration ($p = 0.974$), age at osseointegration ($p = 0.331$),

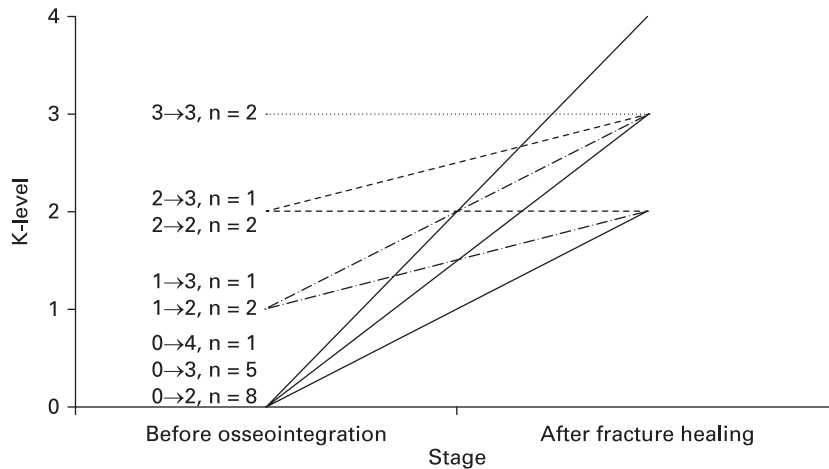


Fig. 2

The mobility (K-level) of patients who sustained a periprosthetic osseointegration fracture is shown before osseointegration and after the care of their fracture was complete. Numerical labels represent pre-osseointegration K-level → current post-fracture K-level, number of patients in this grouping. Notable points: 1) The K-level declined in no patients; 2) all maintained or progressed to a K-level of ≥ 2 (a community ambulator able to traverse curbs and some stairs); 3) even those who were originally confined to a wheelchair (K-level 0) before osseointegration improved to and maintained a K-level of ≥ 2 despite sustaining a fracture.

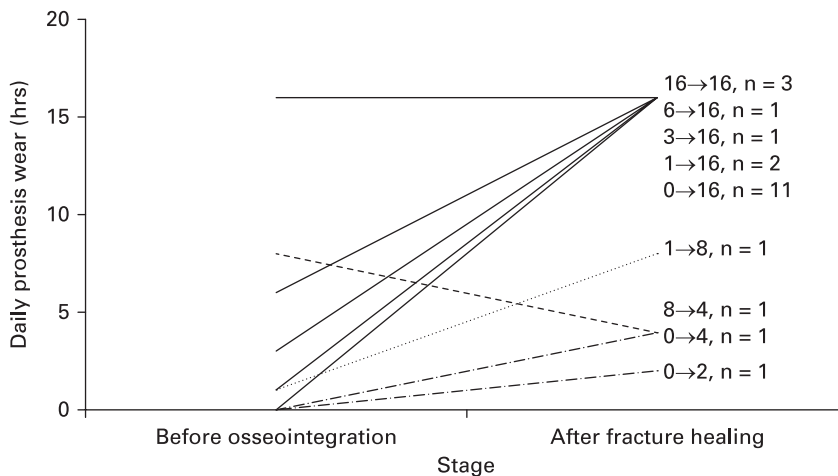


Fig. 3

The amount of time patients reported wearing their prosthesis is shown before osseointegration and after the care of their fracture was complete. Numerical labels represent pre-osseointegration hours → current post-fracture hours, number of patients in this grouping. Notable points: 1) among patients who sustained a fracture, 18/22 (81.8%) wear their prosthesis for ≥ 16 hours/day; and 2) the number of hours before osseointegration and after fracture care declined in only one patient.

Table III. Breakdown of osseointegration fractures by implanted bone.

Implant location	Fracture (implants), n	No fracture (implants), n	Total implants, n (fracture %)
Unilateral femur ^A	17	253	17/270 (6.3)
Bilateral (all)	5	81	5/86 (5.8)
Femur + femur ^B	3	65	3/68 (4.4)
Femur + tibia ^C	2	16	2/18 (11.1)

A vs B vs C; p = 0.083, multiple logistic regression.

A vs B vs C; p = 0.489, Fisher's exact test.

A vs bilateral (all); p = 1.000, Fisher's exact test.

A vs B; p = 0.775, Fisher's exact test.

A vs C; p = 0.337, Fisher's exact test.

B vs C; p = 0.280 Fisher's exact test.

left or right side (p = 0.286), type of implant (p = 0.984), one- or two-stage surgery (p = 0.802), and unilateral/bilateral femoral/mixed femoral and tibial osseointegration (p = 0.083) were not statistically significant predictors of fracture. Since only 222 patients who underwent transfemoral osseointegration had preoperative ipsilateral femoral neck DEXA evaluation (ten fractures), a separate logistic regression was performed on the reduced cohort. No statistical association with fracture was identified (g/cm², p = 0.560; T-score, p = 0.247; Z-score, p = 0.312). Patient factors achieving statistical significance were weight (p = 0.046) and sex (p = 0.007). The mean weight of patients with transfemoral osseointegration was 80.4 kg (SD 17.9) with an overall risk of fracture of 22/347 (6.3%); each kg above 80.4 kg conferred a 1.02-fold

Table IV. Breakdown of femoral osseointegration by sex. Regression analysis identified a 3.89-fold increased risk of fracture for females compared with males ($p = 0.007$).

Sex	Fracture (implants), n	No fracture (implants), n	Total implants, n (fracture %)
Male	13	256	13/269 (4.8)
Female	9	69	9/78 (11.5)

increased risk of fracture (95% confidence interval (CI) 1.00 to 1.05), or 2%. Females were estimated to be at 3.89-fold (95% CI 1.34 to 10.4), or 389% the risk of males (Table IV).

Two patients required further surgery in the management of their fracture, due to inadequate fixation. A 62-year-old man whose intertrochanteric fracture (Figure 4) occurred on falling three months after osseointegration had plate fixation, which was undertaken by a different surgeon, in March 2015. The plate broke in January 2016 probably due to excessive varus malpositioning. The initial surgeon (MAM) revised fixation using a dynamic hip screw and the patient currently uses the prosthesis for ≥ 16 hours daily and mobilizes at K-level 3. A 64-year-old woman sustained a femoral neck fracture (Figure 5) when she fell in May 2018, four years after osseointegration. Five cannulated screws were introduced by a different surgeon giving poor fixation and the following week the screws were repositioned by the initial surgeon (KT) and she now uses her prosthesis ≥ 16 hours daily and mobilizes at K-level 2.

Discussion

The most important finding from this study is that the risk and sequelae of periprosthetic fracture after osseointegration should not deter patients or clinicians from considering this procedure. Periprosthetic fractures in this large cohort of patients with osseointegration occurred at a very low rate overall (22/518, 4.2%), and exclusively in the femur (22/347, 6.3% of femoral implants). The management of the fractures involved techniques and implants common to orthopaedic surgeons familiar with lower-limb trauma care, and patients maintained better mobility than before osseointegration. The vast majority of patients who sustained a fracture (18/22, 81.8%) currently wear their prosthesis ≥ 16 hours daily, whereas few (3/22, 13.6%) did so before osseointegration. A minority (7/22, 31.8%) were K-level ≥ 2 before osseointegration, yet 100% of patients retained a K-level of ≥ 2 after recovering. Most (18/22, 81.8%) had an improved K-level despite the fracture, and no patients had a reduced K-level. Given that the rate of fractures in lower-limb amputees using traditional socket prostheses has been reported to be 2% to 3%,^{9,21,22} osseointegration consistently provides a better quality of life compared with traditional socket prostheses,²³⁻²⁷ and that even after a fracture mobility is likely to remain better compared with a traditional socket prosthesis. Osseointegration can also be expected to confer genuine benefits of greater mobility and enhanced lifestyle without substantially increasing the risk of fracture in the residual limb.

We identified two significant risk factors for fracture after osseointegration surgery: female sex (389% the risk of males, $p = 0.007$) and increasing weight (2% risk per kg above a mean of 80.4 kg, $p = 0.046$). This risk was not associated with other

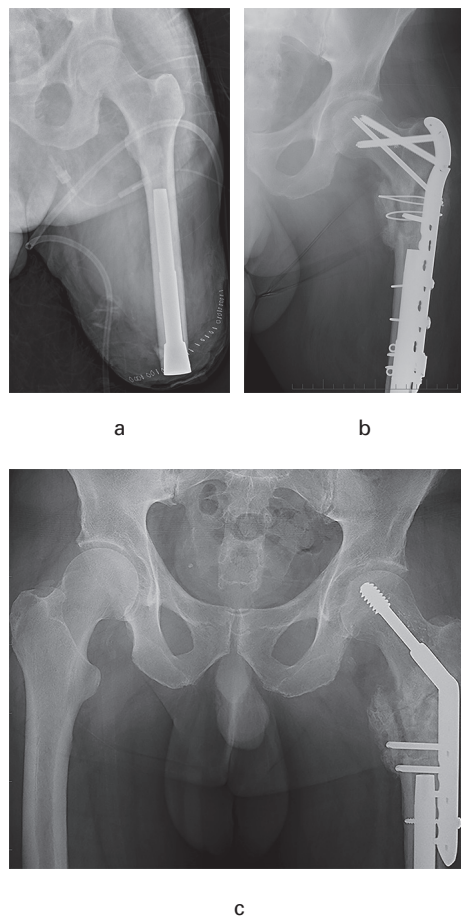


Fig. 4

Anteroposterior radiographs of the left hip and femur (a and b) and pelvis (c) of a 62-year-old man with left transfemoral amputation due to cancer; a) the immediate postoperative appearance (12 years and one month after amputation); b) he sustained an intertrochanteric fracture three months later due to a fall; a different surgeon used the recommended reconstruction plate but it broke ten months later, possibly due to excessive varus positioning; c) revision was undertaken by the initial surgeon (MAM) using a dynamic hip screw and no further care has been required for three years. His K-level improved from 2 before osseointegration to 3 after the care of his fracture, and his prosthesis wear remained unchanged at ≥ 16 hours/day.

factors which were investigated. Because no other publications were identified which investigate the risk of fracture after osseointegration, the rate of periprosthetic fracture after total hip arthroplasty (THA) was used for comparison. For THA, Singh et al²⁸ appear to be the first to investigate the risk of sex on periprosthetic fracture, reporting women to be at an increased risk (hazard ratio (HR) 1.48; 95% CI 1.17 to 1.88); obesity did not increase the risk. In a later meta-analysis, Zhu et al²⁹ estimated the relative risk of female sex at 1.53 but did not comment on weight. Thus, we suggest that women considering osseointegration should be counselled of their relatively increased risk of fracture after a fall. Furthermore, weight is modifiable and despite the fact that patients often report difficulty performing exercise, especially with a socket prosthesis, preoperative counseling gives an opportunity to educate patients that a diet

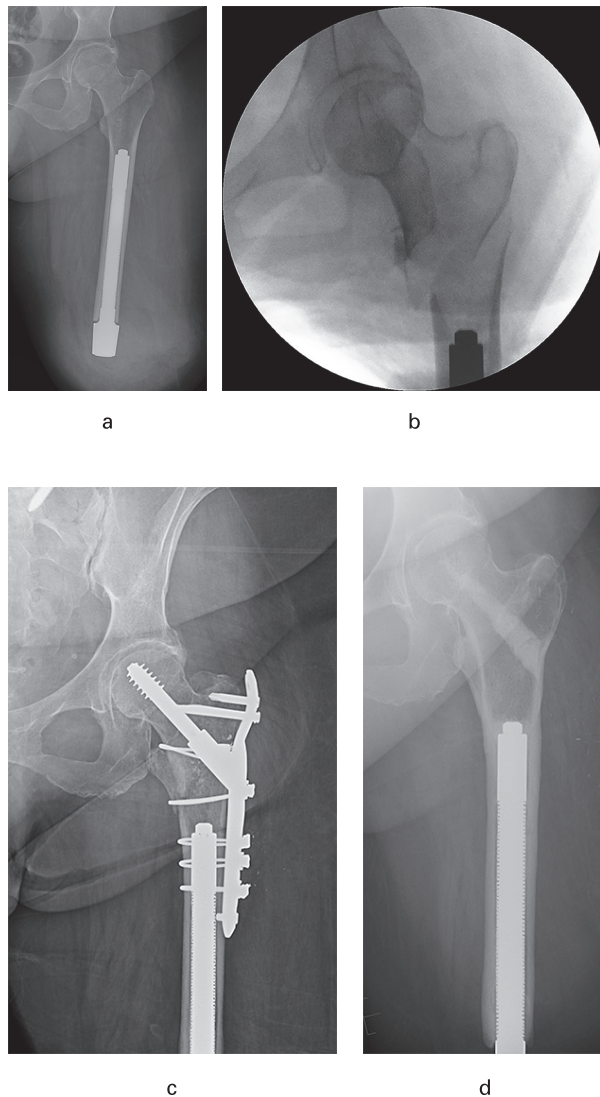


Fig. 5

Anteroposterior radiographs (Figures a, c, and d) and image intensification (b) of a 64-year-old woman who had a left transfemoral amputation for chronic infection after total knee arthroplasty; a) immediate postosseointegration appearance (15 years and two months after amputation); b) she sustained an intertrochanteric fracture eight months later; c) she was treated with a hybrid dynamic hip screw with features of a reconstruction plate; d) there was persistent discomfort and the hardware was removed one year later. She has not needed further care in the subsequent six years. Her K-level improved from 0 before osseointegration to 3 after fracture care, and her prosthesis wear improved from 0 hours with a socket, due to severe silicone and latex allergies, to ≥ 16 hours/day, currently.

rich in protein and low in fats and carbohydrates, even without increased exercise, improves body weight and muscle-to-fat composition.³⁰

Most patients in this study were unilateral transfemoral amputees. There were relatively few bilateral femoral implants and even fewer mixed femoral/tibial implants. The risk of bilateral amputation was assessed, acknowledging the relatively small number of patients. Despite differences in the rates of fracture which were observed, regression analysis and Fisher's exact test

did not achieve significance for association ($p = 0.083$). Although the current data suggest 91.7% instead of 95% confidence that mixed femoral and tibial osseointegration increases the risk of a femoral fracture, surgeons should discuss the possibility of an increased risk of fracture during preoperative counselling, and for such patients to remain especially attentive during rehabilitation to mitigate this risk.

Sensible concerns have been expressed that sudden increased weight-bearing after osseointegration could exceed the strength of the bone in patients whose amputation was long ago, leading to an extended time without anatomical bone loading, or in the elderly and others potentially metabolically at risk for a fragility fracture. Even astronauts have an increased risk of fracture despite excellent health and comparatively short periods of altered weight-bearing.³¹ Fortunately, neither years since amputation ($p = 0.974$), increasing age ($p = 0.331$), nor bone density (g/cm^2 , $p = 0.560$; T-score, $p = 0.247$; Z-score, $p = 0.312$) approached statistical significance for the risk of fracture.

Reports regarding the care of fractures in amputated limbs are scarce, and much of the treatment which is described is outdated, preventing robust comparison of the risk and management strategies of amputees treated with osseointegration and those treated with sockets.³² We identified only one study which allowed at least a limited estimate of the risk of fracture after lower-limb amputation. Nehler et al⁹ reported that four of 172 (2.2%) lower-limb socketed amputees sustained a fracture within a follow-up period of between one and five years. When comparing the risk of fracture between osseointegrated and socketed patients, it is important to remember that typically only approximately half of transfemoral amputees use their prosthesis,³³ often preferring a wheelchair instead. While the use of a wheelchair reduces the risk of fracture, it represents a devastating impairment of mobility and predisposes to other major disability.^{34,35} Most studies describing fractures in socketed amputees are case series, were published before the 1990s, and identify the distal femoral diaphysis as the most common region for fracture. Authors generally recommended casting to avoid surgical complications^{21,22,36} which are currently less problematic.³⁷ In contrast, all fractures in our series occurred in the femoral neck, intertrochanteric or subtrochanteric regions, and 86.4% (19/22) occurred within 2 cm of the proximal tip of the implant, a region generally considered prone to stress risers.^{38,39} It is important to note that unlike fractures around THAs which require removal of the implant due to poor fixation in between 51% and 66% of patients⁴⁰ or distal femoral fractures near total knee arthroplasties which may require revision with a megaprosthesis,⁴¹ none of the patients in our series required removal of an implant. While it is acknowledged that a sample size of 22 patients is not sufficient to make definitive statements, the ability to retain every implant may suggest that strong implant-bone osseointegration occurs quickly, in less than three months, and robustly. It must be noted that retention of the implant with routine fixation of the fracture is not necessarily the recommended strategy for all osseointegration implant designs. Specifically, developers of the Osseointegrated Prostheses for the Rehabilitation of Amputees (OPRA)⁴² and Percutaneous Osseointegrated Prosthesis (POP)⁴³ recommend implant removal, management of the fracture without the implant and possible revision osseointegration following union.

Nearly all fractures in our series (19/22, 86.4%) occurred within the first year, as patients recalibrated their coordination

and proprioception. Given that approximately 20% of patients rehabilitating with socket prostheses fall and sustain injury,⁴⁴ the rate in the lower limb osseointegration patients (4.4% of all lower limb implants (22/500); 6.3% of femoral implants (22/347); 0% of tibia implants (0/153)) does not indicate an increased risk. Surprisingly, three patients sustained a fracture exactly four years after osseointegration, raising concerns of an inherent metabolic or biomechanical cause of this identical timing. One patient slipped on a wet floor at home and fell. The other two fell soon after changing their style of prosthesis, essentially during a period of readjustment of coordination and proprioception. The identical timing of these fractures appears purely coincidental. However, any time a change of prosthesis occurs patients must increase focus to maintain balance and should use a walking aid initially.

The study has limitations. Given its retrospective nature, the most obvious is possible patient-selection bias. Because osseointegration has only recently been introduced, it remains unfamiliar to many surgeons and can be expensive for patients. Nearly all the patients in the current study have financial security as measured by high-level insurance or by independent self-funding resources, which may have reduced the risk of fracture compared with less financially secure patients.⁴⁵ However, most patients were also of Northern European descent, which could increase the risk of fracture of the hip.⁴⁵ Unfortunately not all patients had bone mineral density measurements preoperatively which may have prevented a more reliable and objective assessment of bone health,⁴⁶ although this is not always the case.¹⁶ This study's greatest strength is the large number of patients which were evaluated (518 total implants, 347 femoral, and 153 tibial), representing the world's largest cohort of osseointegrated patients.¹¹



Take home message

- Osseointegration surgery can be expected to confer benefits of improved mobility and enhanced lifestyle; the low-risk of fracture in the residual limb and sequelae of treatment should not deter patients or clinicians from considering this procedure.
- Females and heavier patients are likely to have an increased risk of fracture; bilateral amputation does not definitively increase this risk, and there is probably no risk associated with years since amputation, bone density and staged osseointegration surgery.

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