Review article
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Lower Extremity Osseointegration — A Review of the Current Experiences and Expectations

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Abstract
Transcutaneous osseointegration for amputees (TOFA), an alternative approach to limb-loss rehabilitation, offers an enhanced quality of life and mobility, overcoming some challenges associated with amputation. This review presents evolution, surgical techniques, patient selection principles, and outcomes associated with TOFA. Notable points include the recognition that press-fit osseointegration techniques and implants achieve the quality of life and mobility improvements with a single surgical episode. Infection remains the most common adverse event, but uncommonly requires additional surgery, and rarely requires implant removal. Press-fit osseointegration has proven suitable for rehabilitating a broad range of patients with pelvic, transfemoral, or transtibial amputation performed to manage trauma, cancer, infection, chronic pain, and deformity. This technigue is safe for patients with vascular disease, diabetes mellitus, short residual bones, and osteoporotic residual bones. This article serves as a central resource for understanding the principles and techniques of osseointegration.

Keywords: transcutaneous osseointegration, press-fit osseointegration, amputation, limb-loss rehabilitation.

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Применение метода остеоинтеграции на нижней конечности — современное состояние и перспективы: обзор литературы

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Реферат

Чрескостная остеоинтеграция (ЧО) является одним из методов реабилитации пациентов после утраты конечности, позволяющим повысить качество жизни и мобильность, а также решить некоторые проблемы, связанные с ампутацией. В обзоре освещаются эволюция ЧО, хирургические методы, принципы отбора пациентов и результаты ее применения. Особо следует отметить, что метод остеоинтеграции и press-fit имплантаты позволяют повысить качество жизни и мобильность пациента за одну операцию. На сегодняшний день инфекция остается наиболее часто встречающимся осложнением, которое, тем не менее, редко требует дополнительного хирургического вмешательства и удаления имплантата. Остеоинтеграция с применением press-fit имплантатов успешно используется в реабилитации пациентов, перенесших ампутации на уровне таза, бедра или голени по поводу травмы, онкологического заболевания, инфекции, хронической боли или деформации. Остеоинтеграция безопасна для пациентов с сосудистыми заболеваниями, сахарным диабетом, со сниженной плотностью костной ткани или с короткими фрагментами костей культи.

Ключевые слова: чрескожная остеоинтеграция, press-fit остеоинтеграция, ампутация, реабилитация после утраты конечности.

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INTRODUCTION

Limb amputation remains a significant global health issue. In 2005, approximately 1.6 million people in the United States experienced limb loss, a prevalence of almost 1 in 200 people. This number is expected to double by 2050 [1]. Worldwide, it is estimated that a diabetic patient undergoes a lower extremity amputation every 30 seconds [2]. Traditional socket prostheses (TSP) have been the foundation of limb-loss rehabilitation. Yet, despite advancements in materials like custom-molded carbon fiber and silicone interfaces, TSPs still often have issues such as skin ulceration and poor fit, impacting quality of life (QOL) and mobility [3, 4, 5].

The past 30 years have marked a significant shift in limb-loss rehabilitation with the advent of transcutaneous osseointegration for amputees (TOFA) (Figure 1). This surgical reconstruction implants a permanent metal prosthetic anchor into a patient's residual limb, which then passes transcutaneously to provide a direct skeletal attachment for a terminal prosthesis, such as a leg or arm. TOFA entirely eliminates the need for sockets. This technique has transformed the landscape of limb-loss rehabilitation, offering better QOL and mobility [6]. Osseointegration eliminates many physical and psychosocial challenges associated with TSP, providing benefits such as increased prosthetic wear time [7], improved self-image [6], enhanced stability and mobility [6], osseoperception [8], and greater joint range of motion [6]. On a societal level, press-fit TOFA can also be financially favorable versus TSP, given that many patients can achieve a higher activity level than with TSP, and with only one surgical episode [9].

As the benefits of osseointegration become more popular, an increase in both the number of patients seeking this procedure and surgeons offering it is expected. With the recent surge in literature over the past several years, it is helpful to consolidate and streamline the information to help care providers and patients to better understand the current expectations and limitations of TOFA. This review summarizes TOFA in the following aspects. First — its historical evolution. Second — the surgical and implant techniques, technologies, and principles. Third — the fundamental patient selection considerations. Finally — a review of outcomes and opportunities for amputee cohorts.

The aim of the review — by distilling the collective knowledge, to improve clinician and patient understanding of the technique of transcutaneous osseointegration for amputees.

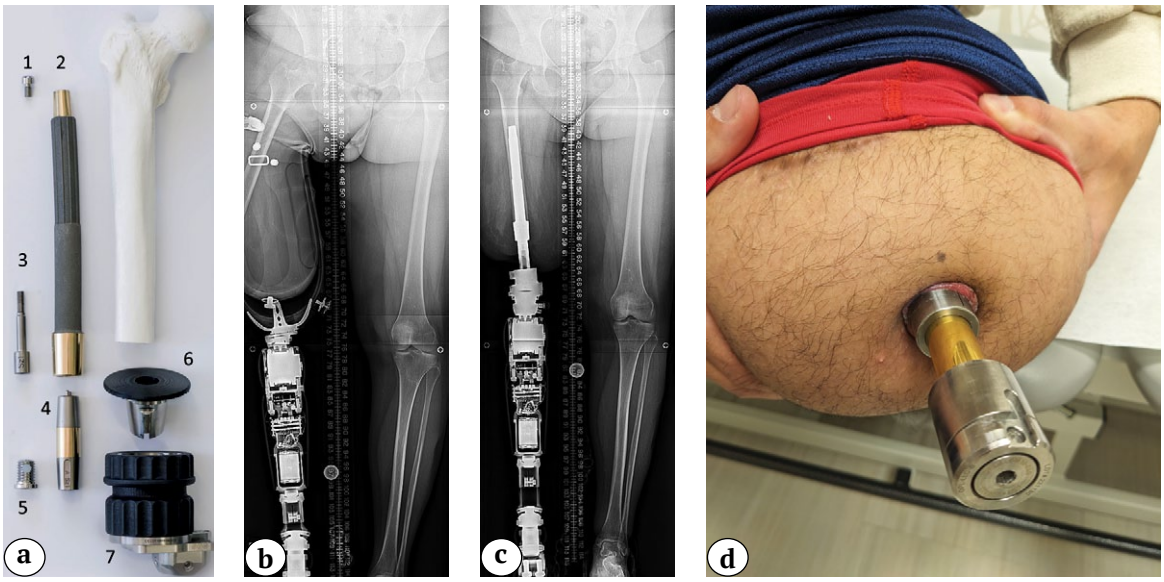

Figure 1. Osseointegrated Prosthetic Limb (OPL) used in the majority of articles reviewed in this manuscript:
a* — exploded view with the componentry arranged at approximately the proximal-distal levels, in which they would reside after being assembled and implanted in a patient who had undergone a femoral amputation (1 — proximal cap screw; 2 — OPL body; 3 — safety screw; 4 — dual cone abutment adapter; 5 — taper base screw; 6 — proximal connector; 7 — prosthetic connector. Components 6 and 7 are one of various styles of mating the dual cone (4) with a prosthetic terminal device);
b — long-standing X-ray of a patient with right transfemoral amputation in the socket prosthesis, identifying the valgus hip position seen in many socket users;
c — long-standing X-ray of the same patient after transfemoral osseointegration, showing the anatomic alignment of the leg;
d — close-up photograph of the transcutaneous portal for the prosthesis. Note the stable skin-implant interface

* Image adapted with permission from Hoellwarth J.S., Tetsworth K., Rozbruch S.R., Handal M.B., Coughlan A., Al Muderis M. Osseointegration for Amputees: Current Implants, Techniques, and Future Directions. *JBJS Rev*. 2020;8(3):e0043. doi: 10.2106/JBJS.RVW.19.00043.

HISTORY OF OSSEOINTEGRATION AND IMPLANT DESIGNS

From a surgical standpoint, perhaps the most striking feature of TOFA is its permanent transcutaneous nature. It is the only orthopedic surgery, and one of the very few surgical techniques overall, where a permanently placed implant passes from the external environment into the body. Given the lack of a biological seal, concerns for infection are understandable.

The concepts, techniques, and technologies of osseointegration are continually evolving. A deep review of the history of osseointegration is provided by J.S. Hoellwarth [10]. Efforts at transcutaneous orthopedic limb care date back at least to the 1500s with the Aztecs, who sometimes used wood dowels to stabilize fractures [11]. The first documented successful treatment of orthopedic pathology with a transcutaneous implant was performed by Joseph François Malgaigne in the 1840s, who used a dual-sided claw clamp to pierce the skin and compress patella fractures [12]. Malgaigne's work emphasized the importance of minimizing skin movement against transcutaneous metal to avoid unwanted reactions. In 1909, Martin Kirschner [13] introduced the Kirschner wire (K-wire), paving the way for techniques and devices such as external fixators by Gavriil Ilizarov [14] and hexapods [15] that remain familiar today. However, these devices are not permanent, being designed for eventual removal.

The modern era of amputated limb replacement began in the 1940s, initially on dogs and later on human amputees, by G. Dümmer in Germany in 1946 [16]. Extensive experimentation was conducted by C.W. Hall, mostly using goats, from 1967 to 1985. His research affirmed the importance of minimizing skin tension against the implant and introduced new surgical and biological principles. These include the potential for skin to bind to and pull implants from bone, the significance of exfoliation in removing desquamated skin, which can compromise the implant's connection to the bone, and the safety of omitting a force dampener between the transcutaneous implant and the bone [17].

The material used for all contemporary TOFA implants is a titanium alloy, specifically Ti6Al4V, chosen because of its strong integration with bone and bioinert behavior with soft tissues, achieving a low clinical infection profile in the right situations [18, 19]. As commercially pure titanium became more readily accessible in the mid-20th century, P.I. Brånemark serendipitously discovered that titanium screws achieved increasingly strong purchase in rabbit bone over time. He subsequently championed the use of titanium in medical care, specifically dental implants through a patient's gingiva, thereby demonstrating titanium's clinical effectiveness as a permanent penetrating implant through soft tissue into bone [20]. It was eventually identified that bone does not grow directly onto the surface of titanium, as it was originally thought due to limitations of imaging techniques, but rather achieves extremely close interdigitation — a sub-micron intermediate layer between the titanium and bone appears to always exist [21]. In 1990, R. Brånemark scaled up his father's design, marking a significant milestone by successfully implanting the first durable, long-term transcutaneous bone-anchored prosthesis in a bilateral transfemoral amputee. Relative stable position of the implant to bone confers a sense of stability to patients, enabling better participation in a wide range of activities. The specific interaction between bone and titanium appears to be non-inflammatory, though the percutaneous opening (termed a "portal") usually will demonstrate some inflammation appearance, which is likely due to unsealed skin edges. While further research is necessary to fully understand the biological interactions between titanium and both bone and skin, the effectiveness of titanium for prosthetic limb anchoring is indisputable.

A thorough review of recent and current implant options is available by J.S. Hoellwarth [22]. The original osseointegration implant featured a screw-type design and was revolutionary. However, its lengthy surgical and rehabilitation requirements were inconvenient. Press-fit alternatives, akin to those used in hip arthroplasty, were eventually developed, achieving TOFA in a single surgical episode with initial time to ambulation as soon as days to weeks after surgery [6, 22, 23, 24, 25]. Press-fit implants are inserted retrograde into the residual bone and axially impacted to achieve an initial scratch fit. Specific technique videos for the femur [26] and tibia [27] demonstrate this in detail. Surgical and rehabilitation techniques continue to evolve, with research aimed towards identifying strategies to minimize infection via better perioperative care, and maximize mobility and performance through improved specific therapy techniques.

The first press-fit TOFA implants were made of cobalt-chrome alloy in Germany in the late 1990s; their use increased in the early 2000s but are generally no longer available [28]. In the early 2010s, titanium implants designed by Al M. Muderis [10] emerged as the highest volume implant option [24]. Particularly with titanium implants, the extensive surface area and surface finishing properties enable robust bone interdigitation, achieving strong fixation [22]. Bone growth through the undulations of the implant helps to achieve long-term stability and strength of the fixation, distributing the force over the surface of the implant on a microscopic scale [29, 30]. Based on skin issues experienced with early press-fit implant

designs, the current paradigm is that the implant should be as smooth as possible where it contacts the skin, to prevent skin adhesion and pain likely related to repetitive tearing from the implant [22]. Press-fit TOFA can be performed in either one or two stages, although currently a single stage is generally utilized. The two-stage procedure involves initial implant insertion procedure and sealing the skin to allow bone ingrowth to occur, with a second surgery 1 to 6 months later to create the transcutaneous portal [6].

PATIENT SELECTION, SURGICAL AND REHABILITATION PRINCIPLES

The initial patient selection criteria for TOFA were cautious. Given the novelty of a permanent transcutaneous implant, the priority was to focus on patients with a low risk of adverse events due to concerns regarding risk of complications, in particular infection [31]. Patients with peripheral vascular disease (PVD) [24], diabetes, skin disease involving the amputated limb [32], osteoporosis [33], or exceeding 100 kg and 70 years of age [34] were excluded. However, as experience with press-fit osseointegration implants increased and consistently good outcomes were achieved, confidence to expand indications for broader patient populations grew.

The authors' current approach to patient selection is as follows. Generally, patients are considered suitable for osseointegration if they are skeletally mature adults who may identify with at least one of three categories: 1) those experiencing pain or mobility dissatisfaction with their TSP; 2) individuals with intact limbs, but suffering from incapacitating pain, deformity, or profound distal weakness, where amputation is deemed likely to improve their functional capacity; 3) recent amputees who prefer osseointegration to traditional prosthetic rehabilitation. There are few absolute and permanent contraindications. Modifiable or temporary contraindications include factors affecting successful bone and wound healing, such as active infections or malignancies. Most patients are suitable candidates upon resolving these issues. Other examples include diabetes mellitus, though patients seem reasonable candidates once consistent glucose control is achieved, approximately HbA1c of 8% or less. Additional contraindications are more generally common to any elective orthopedic surgery. Patients must have stable psychosocial situations, such as the ability to procure and maintain a prosthetic limb following surgery, to uphold reasonable hygiene practices, and to embrace the presence of a transcutaneous implant in their bone. Patients struggling with stable housing, self-harm, or with other signs of poor self-care may not be suitable for osseointegration. Typical preoperative elective surgery medical evaluation is necessary to optimize cardiovascular or other common risks. As with any elective procedure, thorough counseling, shared decision-making, and possible collaboration with additional care providers or patient advocates can help to balance optimizing accessibility versus identifying unsuitable candidates.

Surgical planning for osseointegration, as discussed in depth in the technique videos [26, 27], begins with X-rays in the AP and lateral views and computed tomographic (CT) scans of the affected limb [27]. These are essential for customizing the implant's size, shape, length, and diameter to match the best bone corridor for maximum implant stability [6]. This approach prevents the implant from being too small or too large, which could lead to implant loosening or bone fracture upon insertion [26]. It is imperative to mention that cementing an implant seems to be absolutely inappropriate and will lead to inevitable eventual loosening [35, 36, 37]. Clinical or radiographic determination of the distance to the contralateral knee (for transfemoral patients) or to the floor (for transtibial patients) is critical to plan any potential additional bone resection. Although the prosthetic limb attachment can be lengthened to match the knee or ground, its shortening has a limit, beyond which a revision surgery is necessary. Overall, the bone-implant aspect of TOFA likely is relatively optimized, in that it is well understood how to achieve fast and durable bone ingrowth providing long-term implant stability.

However, the skin-implant interface is less well understood. Many uncertainties remain regarding exactly how to fashion the percutaneous portal, to what extent the soft tissue plays a direct role in long-term infection risk, and what patient factors may present an inherent risk versus should be addressed in patient-specific ways to mitigate risks. Accordingly, there are at least two specific roles a plastic surgeon is directly helpful in TOFA surgery. First, they help with neuroma treatment and/or prophylaxis. Patients who sustain nerve injury or have nerve amputation either traumatically or surgically can develop primary nerve pain, often attributable to a neuroma. Targeted muscle reinnervation and regenerative peripheral nerve interface are two options to both prevent and treat neuroma pain, and both can be performed before, during, or after TOFA [38]. A second specific role for plastic surgery involvement for TOFA is soft tissue contouring and closure. In a traditional amputation, simply achieving closure with no underlying sharp bone or implant is likely generally suitable. Because TOFA has the permanent portal, complex decisions and technical execution of soft tissue work is critical. Excess soft tissue will tend to slide up and down a percutaneous implant and lead to inflammation, which can predispose infection of skin, fat, muscle, or bone. Excessive tension can lead to wound dehiscence at an incision closure or trauma to the portal as the limb moves through its arc of motion. Such potential infectious events are most often seen in the first

several months following TOFA surgery, and wound closure by a reconstructive plastic surgeon is likely to minimize these adverse events [38, 39, 40].

Rehabilitation protocols after osseointegration surgery can vary substantially [6]. Following implant externalization, patients are usually instructed to remain strictly non-weight-bearing for 3 days to 6 weeks, depending on bone quality and overall health. Subsequently, patients begin a progressive loading-protocol, starting with 5 kg to half body weight, and increasing by 5 kg daily or 35 kg per week until they reach full body weight. Some protocols also focus on navigating various terrains and practicing fall prevention. Although rehabilitation protocols may have standard expectations, maintaining a patient-centric rehabilitation process is crucial. This involves making adjustments in response to patient-reported pain or discomfort, tailoring each stage of the process to the patient's unique needs and recovery pace to create the most conducive environment for mobility and gait improvement. Specific research into rehabilitation routines is important to further optimize patient rehabilitation.

FOCUSED OUTCOMES FOR SPECIFIC COHORTS OF INTERESt

Recent reviews by J.S. Hebert et al. [41] and S.K. Kunutsor et al. [42] have highlighted the benefits of osseointegration versus socket rehabilitation for lower extremity amputees: improved mobility, comfort, gait, and prosthetic use, leading to enhanced satisfaction and quality of life. Commonly reported metrics include the 6 Minute Walk Test (6MWT), Timed Up and Go (TUG), walking distance, Short Form 36 (SF-36), Questionnaire for Persons with a Transfemoral Amputation (Q-TFA), and K-level. Osseointegration enables a more natural gait compared to TSP [43], likely due to increased hip range of motion and decreased hip tilt [44]. Subjective measures also report increased comfort of sitting, a commonly reported challenge in patients using TSP, as well as increased daily prosthesis use and easier donning and doffing [45].

The most frequent complication, low-grade soft tissue or superficial infections, was mainly managed with local wound care and oral antibiotics. Advances in techniques, technology, and ongoing research are expected to yield even better functional outcomes and reduce complications. Given the existence of the mentioned reviews, this manuscript will focus on summarizing several important specific cohort studies that are informative to understanding the current TOFA landscape.

The largest civilian study of TOFA in the United States was performed by T.J. Reif et al. [6]. Evaluating 18 transfemoral and 13 transtibial amputees who underwent osseointegration, patients reported significant improvements in prosthesis wear time, mobility, and multiple quality-of-life surveys. With an average follow-up of nearly 2 years, all quality of life domains improved significantly, with increased prosthetic use and comfort and fewer prosthesis-related complications. All patients who were unable to use a TSP prior to surgery were able to ambulate independently with the osseointegrated prostheses. The study also found improvements in overall pain and pain interface, suggesting reduced discomfort enabling enhanced mobility. Although acute complications, such as mechanical issues and soft tissue infections, were noted, all were managed without the need to remove any implants. The study also noted significant improvements in mental health, overall health, physical health, and functionality, as reflected in higher PROMIS scores. These findings, along with patient-reported improvements in activity, self-image, and appearance, reinforce the growing body of literature that osseointegration offers substantial benefits over TSP. One further notable aspect of this article is the relatively large number of tibial amputees represented. There is very little literature describing TOFA for transtibial amputees, even though the procedure can often be exceptionally empowering for them as well as for the transfemoral patients (Figure 2).

While the benefits and potential for more common adverse outcomes such as an infection or a periprosthetic fracture are evident, patients and clinicians must understand the potential risk of the most devastating complications in order to make their best personal decision of whether to undergo TOFA. As with any limb reconstruction surgery, the worst potential situations would likely be to die, have a major systemic complication such as a stroke, or to have a more proximal amputation related to complications of TOFA. J.S. Hoellwarth et al. [46] specifically analyzed those risks in a study of 485 TOFA patients aged 16 to 85, followed for up to ten years. No patients had systemic complications or proximal level amputation. They reported that 19 patients died after having TOFA, but 17 (90%) were unrelated to osseointegration (such as a cancer). This suggests a treatment-related mortality risk of less than 0.4%. Despite the higher mortality risk associated with vascular disease-related amputation or prior infections, the study observed no significant increase in mortality among the 59 patients who required reoperation to manage infections. Factors such as patient weight and sex showed no significant impact on mortality. The study concluded that an all-cause mortality rate of 3.9% and an osseointegration-related mortality rate of 0.4% underscore the procedure's safety. Knowledge of the safety of TOFA can help patients and clinicians to better focus on the more individually relevant benefits and risks without excessive fear of worst case scenarios.

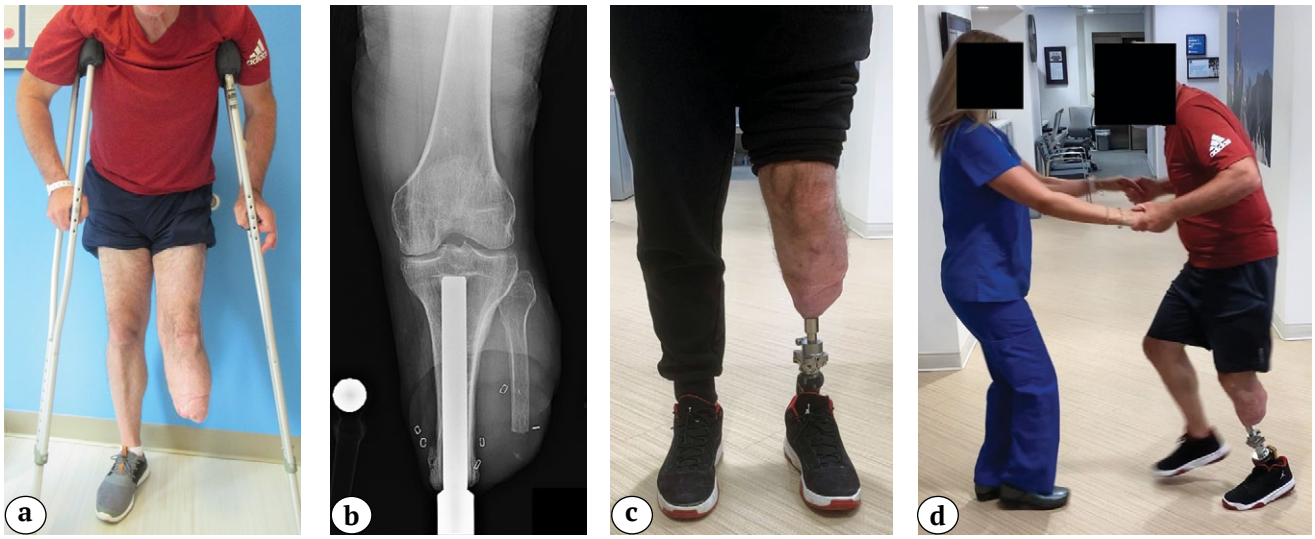

Figure 2. Transtibial osseointegration:
a — preoperative photograph identifies this patient is using two crutches to locomote because of his inability to wear a socket prosthesis due to pain;
b — X-ray in the anterior-posterior view depicting the transtibial osseointegration implant;
c — standing photograph of the patient following transtibial osseointegration;
d — photograph showing the patient feeling comfortable and enthusiastic enough to initiate a dance with the nurse during the postoperative visit. Note that the patient is able to plant on the osseointegrated limb confidently enough to lead his partner while having his intact leg off the ground

Likely due to the transcutaneous nature and permanent exposure of the implant to the external environment, the most common postoperative adverse event related to TOFA is infection. In the previously mentioned study by T.J. Reif et al., out of 31 TOFA patients, 15 experienced 23 soft-tissue infections. Mild signified low-grade soft-tissue infections, which were treated with oral antibiotics. Moderate specified high-grade soft-tissue infections, which were managed with surgical debridement with a retained implant. Severe complications included deep infection or osteomyelitis with bone changes evident on X-rays requiring explantation. Twenty episodes were managed with oral antibiotics, 3 required intravenous antibiotics, 2 of these cases were the same patient who subsequently underwent surgical debridement with implant retention. One patient's infection prompted implant removal with antibiotic therapy followed by reimplantation without additional issues. In an additional study, M. Al Muderis et al. [47] reported outcomes for 86 patients. Twenty-nine patients experienced low-grade soft-tissue infections on 41 occasions, which were managed with oral antibiotics. Two patients developed low-grade soft-tissue infection with significant pain and cellulitis; one was managed with intravenous antibiotics and the other with intravenous antibiotics followed by local debridement. Additionally, 4 patients developed high-grade soft-tissue infection and were treated with surgical abscess drainage and debridement — none of the patients developed bone infection or required explantation. S.H. Alam et al. [48] introduced the first algorithmic approach to preoperative TOFA infection assessment. Peri-implant stump pain was significantly correlated with infection, positive preoperative bacterial culture swab was moderately correlated, and erythema or cellulitis near the transcutaneous region was only mildly correlated. Erythrocyte sedimentation rate greater than 30 was found to be inversely correlated with infection, while C-reactive protein and white blood cell levels were not predictive of peri-TOFA infections. The authors emphasized the limitation of utilizing these common screening labs for TOFA infection.

Infection may also occur from reactivation of previously seeded bacteria, not only from new bacterial ingress from the portal. Patients who had prior amputation can have dormant bacteria that theoretically could become problematic following additional surgery, particularly the insertion of a foreign implant. J.S. Hoellwarth et al. [49] investigated the impact of unexpected positive intraoperative cultures (UPIC) on the occurrence of postoperative infections. In this study, 8 patients with UPIC and 22 patients with negative intraoperative cultures (NIC) were identified. All patients received the routine 24 hours of postoperative antibiotic prophylaxis, with additional antibiotics for UPIC guided by culture results, generally six weeks of oral or intravenous antibiotics. Out of 30 patients, 2 UPIC and 8 NIC patients required antibiotics unrelated to the initial surgery, 1 UPIC patient required debridement and 1 NIC

patient required explantation. The authors concluded that UPIC with subsequent antibiotic therapy did not appear to confer a statistically significant increased risk of infectious-related complications compared to NIC patients. Although more research is required to determine the efficacy and necessity of additional antibiotics following UPIC, patients who are found to have unexpected bacterial presence at index TOFA do not appear to have an increased risk of subsequent infectious concerns.

Periprosthetic fractures (PPF) in osseointegration, while infrequent, pose another concern. Recent studies covering over 500 osseointegrated implants reported PPF rates of 6.3% [50], 7.5% [51], and 10.7% [52]. These fractures occurred exclusively in the femur, near the proximal tip of the implant, most often due to low-impact falls. All the literature has reported that the bone and implant always remain stable for press-fit PPF. Treatment requires a patient-specific approach, often using standard hip fracture management techniques, such as dynamic hip screws or reconstruction plates with a modified traction method. Importantly, PPF do not seem to worsen TOFA outcomes, with all patients maintaining or improving their mobility levels. A study by J.S. Hoellwarth et al. identified PPF risk factors include female sex and weight, while age, time since amputation, and bone density show no significant influence on fracture risk [50]. A separate study by J.S. Hoellwarth et al. [52] demonstrated an innovative technique to reduce the fracture in a TOFA patient. While all current literature reports operative fixation to manage fractures, it is not certain that all patients require surgery to heal well.

A major cohort of patients who may seek TOFA are those whose amputation was performed to manage total knee arthroplasty (TKA) infection. This is particularly compelling because these patients had the knee replacement in order to improve their quality of life and mobility, but as a result of infection have or face transfemoral amputation or knee arthrodesis, both of which are substantially disabling. M.A. Akhtar et al. [25] investigated the experience of TOFA for this specific patient cohort. In a retrospective review of 10 patients who underwent transfemoral amputation (TFA) or knee fusion (KF) following infected TKA, they found that transfemoral osseointegration provides significantly better mobility and quality of life (QOL) compared to KF or TFA with TSP following infected TKA. This study demonstrated that patients with a history of infection can safely undergo osseointegration of the prior infected limb and ought to achieve better outcomes compared to using TSP.

As previously mentioned, traditional contra-indications to osseointegration are often related to factors that impair bone regeneration or wound healing. Historically, patients with skin disease, such as a burn trauma, were excluded from osseointegration [32] even though they often experience more pronounced challenges associated with TSP use [53]. A. Haidary et al. [54] reported on 5 patients with prior burn trauma who underwent osseointegration (8 limbs in total). Pain, psychological depression, skin irritation, and recurrent ulceration were persistent problems prior to surgery, resulting in limited ability to mobilize and wear TSP, as well as in poor mental health. No chronic or recurrent adverse tissue responses occurred despite all patients having burned or grafted skin surrounding the stoma. Three patients required surgical debridement at 3 months, 18 months, and 2 years following osseointegration. One patient eventually had bilateral explantation with subsequent reimplantation. All patients stabilized at a better functional level than prior to TOFA, with improved K-levels. Although several patients did seem to have post-TOFA complications requiring surgical intervention, their increased mobility and willingness to retain their implant and even undergo reimplantation, demonstrates a high level of patient value for the procedure. Importantly, the lack of skin intolerance towards the transcutaneous pin highlights the suitability of TOFA for patients with compromised skin.

To ensure the proper function, stability, and weight-bearing capability of an osseointegration implant, a bone needs to grow and mesh with the titanium implant. This requirement might raise concerns for patients with low bone mineral density (BMD) or poor bone quality as measured by dual-energy X-ray absorptiometry (DEXA). A study by J.S. Hoellwarth et al. [55] compared DEXA values of 9 patients before and five years after osseointegration. The study found that while non-amputated limbs had an expected decrease of BMD, osseointegrated limbs increased in BMD, indicating that osseointegration might help reduce the rate of BMD loss or even improve BMD. Notably, patients with overt local disuse osteoporosis showed significant improvement in their BMD. The study concludes that patients with low BMD can be safely considered for osseointegration and that it may slow the decline or even improve their amputated limb BMD.

An additional concern is whether there is a minimum bone length to achieve stable osseointegration. There is no apparent consensus on what defines a short limb, but standard press-fit implants are 14 cm long. There are two strategies reported by two different groups. One strategy as reported by J.S. Hoellwarth et al. [56] is to lengthen a bone prior to osseointegration. In that study, 10 patients were lengthened by an average of 52 mm, requiring about a year from starting lengthening to the TOFA surgery. All patients achieved independent ambulation without any apparent compromise to implant stability, but the multiple surgeries and protracted period tempered patient satisfaction. An alternate option, also reported by J.S. Hoellwarth et al. [56], is simply directly performed

TOFA for residual bones as short as 5-6 cm (Figure 3). They reported no association between residual bone length and post-TOFA reoperation rates, including such issues as aseptic loosening, periprosthetic fractures, or infections. A true minimum bone length remains uncertain, and greater experience will likely eventually help elucidate possible factors contributing to a potential limit.

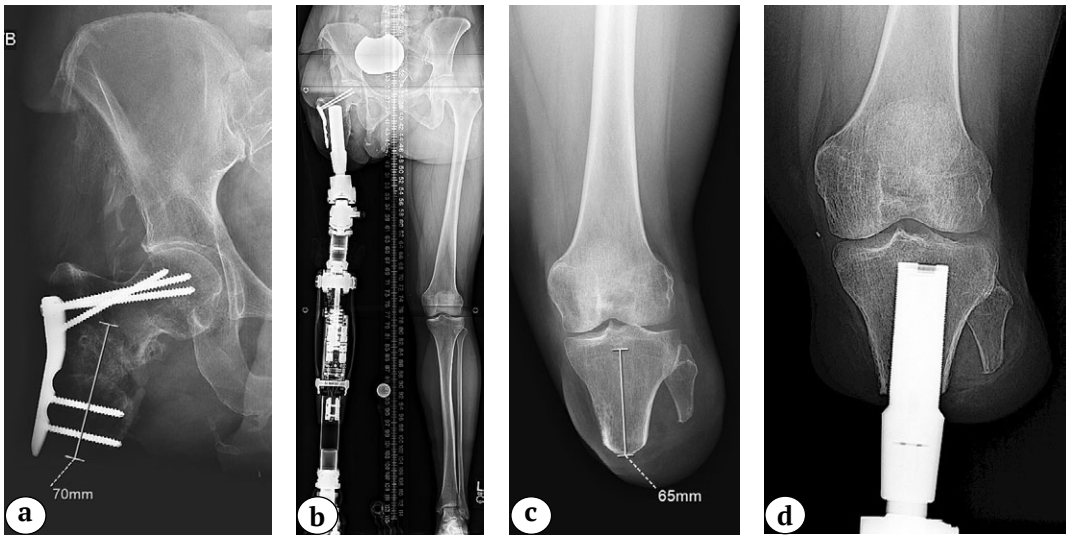

Figure 3. Short residual bone for osseointegration:
a — X-ray in the anterior-posterior view of the right femur identifying almost no bone beyond the lesser trochanter. She was a functional hip disarticulation patient due to the inability to wear a socket;
b — this patient had partial hardware removal with simultaneous osseointegration, achieved excellent fixation and now ambulates without an assistive device;
c — X-ray in the anterior-posterior view of the left tibia for a patient with minimal bone distal to the tibial tubercle. His residual limb was too short to use tibia-level prosthesis and he was considering transfemoral amputation prior to consultation for osseointegration;
d — the patient also achieved ambulation without an assistive device with a press-fit osseointegration implant

The management of painful deformity is another area where osseointegration appears to provide a paradigm shift, specifically complex regional pain syndrome type 1 (CRPS1). Given its unclear etiology, there remains controversy whether incessant rehabilitation efforts are appropriate, or whether an amputation is more enabling for severely affected patients with recalcitrant pain. J.S. Hoellwarth et al. [57] reported on a series of three patients with severe unremitting CRPS1, recalcitrant to conservative interventions and with persistent disabling pain, who underwent amputation and osseointegration. Two of these patients had simultaneous amputation with osseointegration whereas one patient already had previous amputation. All patients experienced reduced pain and pain interference. Within 3 months, two patients ambulated independently; within 6 months, all three patients ambulated independently. At the most recent follow up, one patient reported the ability to walk 5 km distances multiple times a week, navigate hills, climb stairs, and walk with items held in both hands. Another patient reported being able to walk unaided on various terrains such as sand and water, and to climb stairs. The third patient, who initially progressed similarly to the others, experienced a decline in his progression following an unapproved surgical procedure, which disrupted prior nerve work; although his pain then interfered with his performance, he remained ambulatory but required two crutches. Interestingly, the patients who had both procedures done at the same time had better outcomes, however, more research is necessary to determine if an association exists. The role of TOFA for patients with complex pain requires further exploration, in particular the potential rehabilitation strategies to optimize postoperative performance [58, 59].

CONCLUSIONS

Transcutaneous osseointegration for amputees has proven a highly enabling surgical reconstruction for patients who have had or are considering amputation. Despite initial slow adoption, attention and interest are rapidly increasing. Single-surgery press-fit TOFA allows a more streamlined recovery than the traditional two-stage protocols. Particularly exciting is the recent

literature recognizing that rather broad spectrums of amputee patients are likely suitable to benefit from TOFA. It seems reasonable that in the near future, TOFA can become a primary option for the rehabilitation of amputees, similar to the role arthroplasty has served for patients with arthritic joint pain.

DISCLAIMERS

Author contribution

All authors made equal contributions to the study and the publication.

All authors have read and approved the final version of the manuscript of the article. All authors agree to bear responsibility for all aspects of the study to ensure proper consideration and resolution of all possible issues related to the correctness and reliability of any part of the work.

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Заявленный вклад авторов

Все авторы сделали эквивалентный вклад в подготовку публикации.

Все авторы прочли и одобрили финальную версию рукописи статьи. Все авторы согласны нести ответственность за все аспекты работы, чтобы обеспечить надлежащее рассмотрение и решение всех возможных вопросов, связанных с корректностью и надежностью любой части работы.

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