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Emerging Value of Osseointegration for Intuitive Prosthetic Control after Transhumeral Amputations: A Systematic Review

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Background: Upper extremity limb loss profoundly impacts a patient's quality of life and well-being and carries a significant societal cost. Although osseointegration allows the attachment of the prosthesis directly to the bone, it is a relatively recent development as an alternative to conventional socket prostheses. The objective of this review was to identify reports on osseointegrated prosthetic embodiment for transhumeral amputations and assess the implant systems used, postoperative outcomes, and complications.
Methods: A systematic review following PRISMA and AMSTAR guidelines assessed functional outcomes, implant longevity and retention, activities of daily living, and complications associated with osseointegrated prostheses in transhumeral amputees.
Results: The literature search yielded 794 articles, with eight of these articles (retrospective analyses and case series) meeting the inclusion criteria. Myoelectric systems equipped with Osseointegrated Prostheses for the Rehabilitation of Amputees implants have been commonly used as transhumeral osseointegration systems. The transhumeral osseointegrated prostheses offered considerable improvements in functional outcomes, with participants demonstrating enhanced range of motion and improved performance of activities compared with traditional socket-based prostheses. One study demonstrated the advantage of an osseointegrated implant as a bidirectional gateway for signal transmission, enabling intuitive control of a bionic hand.
Conclusions: Osseointegrated prostheses hold the potential to significantly improve the quality of life for individuals with transhumeral amputations. Continued research and clinical expansion are expected to lead to the realization of enhanced efficacy and safety in this technique, accompanied by cost reductions over time as a result of improved efficiencies and advancements in device design.
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INTRODUCTION

The human arm and hand are critical structures for intelligent interaction and engagement with our surrounding environment. Their function is nearly indispensable for fulfilling the basic needs of various daily activities, social interactions, and delicate manipulations of any kind.[1,2] Although the hand only contributes 1% of the human body weight, a significant portion of anatomical sensorimotor cortex is dedicated to the upper extremity. Accordingly, the loss of the upper extremity is a debilitating condition for a patient and results in a disfigured body image and partial or full loss of an individual's autonomy, contributes to potential social withdrawal, and has a significant overall impairment in quality of life.[3] The number of people affected by upper extremity loss was estimated to be approximately 41,000 patients living in the United States alone (data estimate from 2005), and this high number of patients

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highlights the importance of providing appropriate care for amputations and advancing functional restoration of the hand.[4,5]

Although no consensus exists on the best reconstructive technique after transhumeral amputation, prosthetic devices have gained a primary role.[6] With ongoing advancements in microsurgical techniques and biomedical engineering, prosthetic technology has greatly improved, presenting a clinically viable option for the restoration of motor control in the human arm.[7] Although the bionic replacement of hand function is a remarkable achievement and continues to advance, it is important to note that these technologies have not yet matched the seamless and intuitive control inherent in the biological human hand.[8] Existing devices have significant limitations including durability, stability of electromyographic readings, prosthetic fitting, and lack of sensory feedback.[9]

Many existing limitations of transhumeral prostheses have been improved by one of the surgical solutions originating from dental medicine: osseointegration (OI) dental implants.[10] This surgical technique is designed to stabilize and directly attach a prosthesis to the bone. The OI technique was introduced by Brånemark et al,[11] who developed the integration of titanium and bone tissue from dental implants, and the concept was adapted to introduce OI for reconstruction of the upper and lower extremities. In 1990, the first osseointegrated prosthesis for transfemoral amputations was implanted in a 25-year-old patient. Since this initial case, the OI technique has been subsequently refined and improved.[12] More precisely, OI within the extremity involves implanting a titanium device into the residual axial bone, and an abutment stem emanates from the skin to connect with an external prosthesis. In this way, the biomechanical stability, alignment, and osseoperception of the implant-prosthesis-limb system and the decoding of electromyographic readings in certain bioprosthetic systems can be enhanced and capitalized. OI transhumeral prostheses allow for better weight distribution; more precise prosthetic positioning, for example, the entire glenohumeral joint remains free to move in space; and greater improvements within the freedom for ranges of motion. Signal stability and also reliability of control add another beneficial aspect to such bone anchored devices[13] (Fig. 1). Nevertheless, there remain limitations and unknowns in OI prostheses, such as the inherent risk of transcutaneous infections, inter- or periprosthetic fractures, and osteomyelitis.[14]

This systematic review is conducted with the objective of assessing functional outcomes, implant survival rates, activities of daily living (ADL), and complications among patients who have undergone OI following transhumeral amputation. The study aims to compare the outcomes achieved with OI-powered prostheses to those with conventional socket-based prosthetic fixation. Furthermore, the senior authors offer their consensus on the surgical approach, drawing from their extensive experience in the field.

Takeaways

Question: The study aims to address the benefits of osseointegrated prostheses for individuals with transhumeral amputations, compared with traditional socket prostheses in terms of functionality, quality of life, and complication rates.

Findings: The study found that myoelectric systems with Osseointegrated Prostheses for the Rehabilitation of Amputees implants were commonly used for transhumeral osseointegration, offering significant functional improvements over traditional prostheses. This included enhanced range of motion and better performance in daily activities.

Meaning: Osseointegrated prostheses represent a promising advancement that could substantially enhance the quality of life for those with upper extremity amputations, with the potential for more intuitive prosthetic control and increased functionality.

MATERIALS AND METHODS

The work has been reported in line with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and Assessing the Methodological Quality of Systematic Reviews (AMSTAR) Guidelines.[15,16] institutional review board approval and informed consents were obtained from the academic institution (reference number EK Nr: 1299/2021 and 2274/2020) for the presentation of the single case report. No institutional review board approval was required for systematic review because all the reported data were acquired from the available published literature. We conducted a comprehensive literature search of the electronic databases MEDLINE (PubMed), Embase, and Cochrane Library from their inception up to August 2023, using appropriate medical subject headings (MeSH). The following Boolean phrase was used to systematically search the current literature: (osseointegration) AND ((humerus) OR (shoulder) OR (upper limb) OR (upper extremity)). References of each included article were checked to screen for additionally potentially relevant studies.

Eligibility Criteria

Studies were included that (1) investigated the use of osseointegrated prostheses after transhumeral amputation; (2) reported functional outcomes [eg, range of motion (ROM), ADL], complication rates (eg, infection, skin breakdown), and survival rates of the prostheses; (3) included human subjects; and (4) were published in peer-reviewed journals. We excluded studies that (1) were animal studies; (2) investigated nonosseointegrated prostheses; (3) included nontranshumeral amputations; (4) were biomechanical testing studies; (5) did not report functional outcomes, complication rates, or survival rates; or (6) were conference abstracts, reviews, or editorials.

Study Selection

Two reviewers (V. T. and R. G.) independently screened the titles and abstracts of all the articles retrieved by the

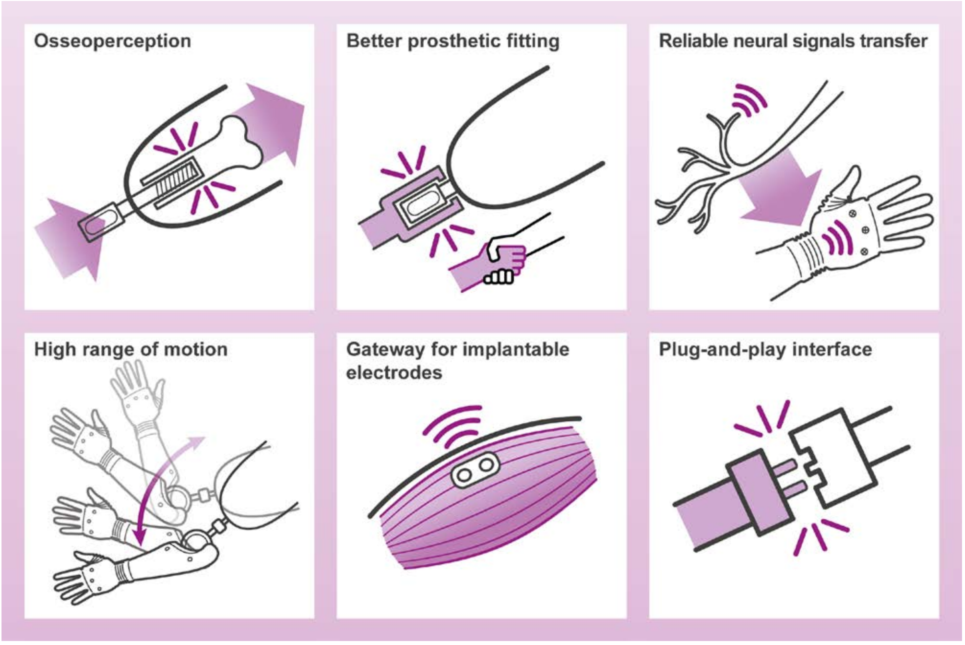

Fig. 1. Advantages of osseointegrated prostheses. Osseoperception: direct attachment to the bone enhances the wearer's perception of the prosthesis, offering an advantage over traditional socket fittings. Prosthetic fitting: the bone anchor allows for a stable connection during a variety of movements, reducing the risk of electrode displacement and movement disruption seen with socket systems. Neural signal transfer: osseointegrated implants serve as a mechanical conduit, facilitating the bidirectional travel of signals through the wires to and from the prosthesis. ROM: osseointegrated prostheses enable a greater ROM due to fewer restrictions compared with socket fittings. Implantable electrodes: the osseointegrated abutment provides a secure point for implantable electrodes, an option not available with socket-fitted prostheses. Plug-and-play interface: osseointegration simplifies the process of attaching and detaching the prosthesis, thanks to a user-friendly interface. © Aron Cserveny. https://www.sciencevisual.at.

search strategy. Any discrepancies between the reviewers were resolved by discussion and, if necessary, by a third reviewer who double checked the selection criteria (K. R. E.). Subsequently, the complete texts of potentially qualified articles underwent a meticulous review process, overseen by the same two reviewers, and adhering closely to the aforementioned eligibility criteria. This stringent review process aimed to ensure the inclusion of articles that met the established criteria and standards. To maintain transparency and provide a clear overview of the study selection process across all databases, we adopted the utilization of a PRISMA flow diagram, which serves as an organized visual representation documenting the path of article selection.

Data Extraction

Data were extracted from the included studies using a standardized data extraction form. The following data were extracted: author(s), year of publication, study design, sample size, patient demographics (age, gender), type of amputation, type of prosthesis, duration of follow-up, functional outcomes (eg, ROM, ADL), complication rates (eg, infection, skin breakdown), and survival rates.

Quality Assessment

Methodological quality of included studies was assessed independently by two separate authors (V. T. and R. G.). The risk of bias was analyzed for each study, with the Methodological Index for Nonrandomized Studies (MINORS) criteria.[17] The MINORS tool is a validated instrument designed to assess the methodological quality of nonrandomized studies. The maximum score for noncomparative studies is 24.

RESULTS

A total of 794 articles were identified through the electronic database search. After removing duplicates and screening the titles and abstracts, 25 articles were considered potentially relevant for full-text review (Fig. 2). After assessment of the full-text articles, eight studies met the inclusion criteria and were included in the systematic review (Table 1).

The included studies were conducted between 2010 and 2022. The sample sizes of the studies ranged from one to 16 participants, with a total of 47 participants across all studies. Most of the studies used a case report/case series design, whereas a few utilized a retrospective design and one, a prospective design.

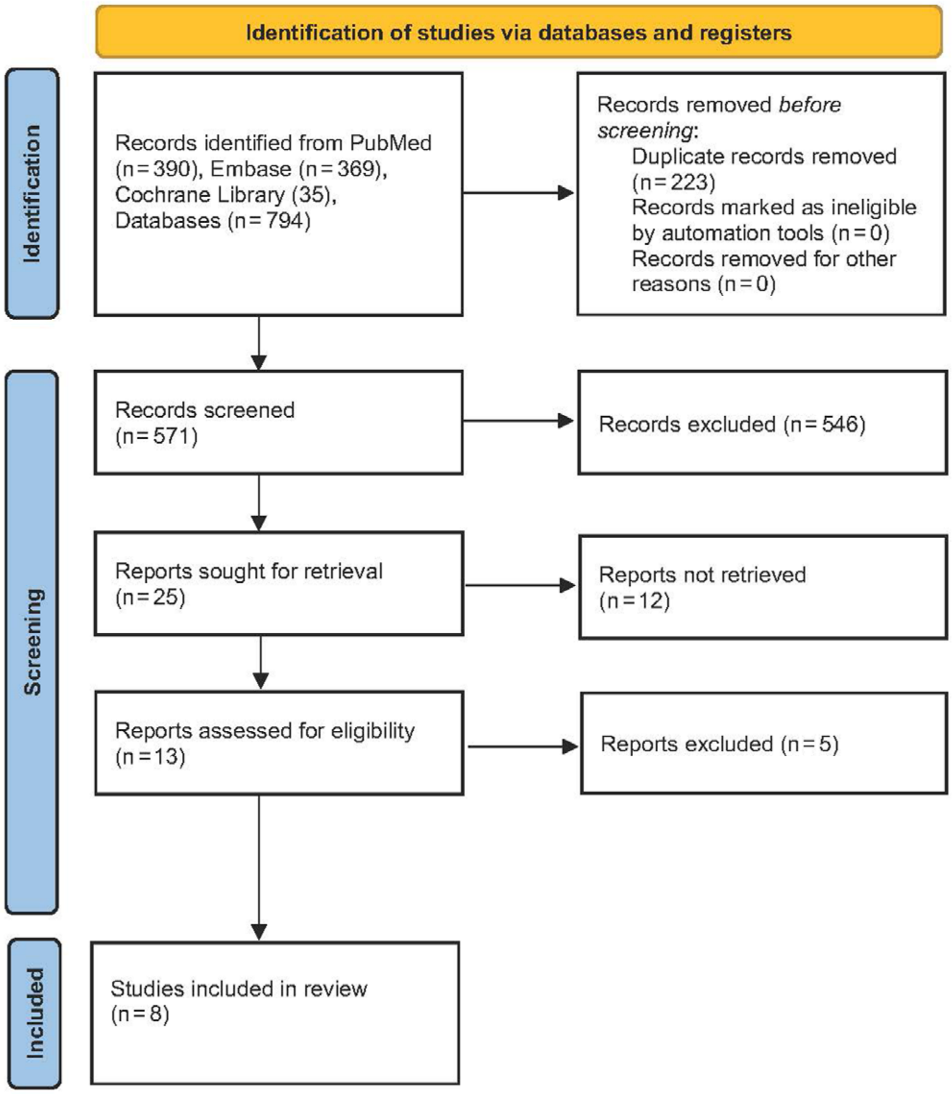

Fig. 2. PRISMA 2020 flow diagram for new systematic reviews that included searches of databases and registers only.

Different types of osseointegrated prostheses were investigated across the included studies. The most commonly used osseointegrated prostheses included the myoelectric system. The most used implant was Osseointegrated Prostheses for the Rehabilitation of Amputees (OPRA) with a total of 34 (four of which were e-OPRA), subcutaneous implant-supported attachment (SISA) was used in two limbs, and intraosseous transcutaneous amputation prostheses (ITAP) was used in one.

A variety of outcome measures were assessed in the included studies. Functional outcomes, including the ROM and ADL, were commonly evaluated. Quality-of-life measures, such as Southampton Hand Assessment Procedure, Box and Block Test, visual analog scale, Disabilities of the Arm, Shoulder and Hand, were also used. Other outcomes of interest included time of prosthesis use, prosthesis abandonment, number of procedures, prosthetic-related complications, and patient satisfaction.

The findings from the included studies indicated that osseointegrated prostheses in transhumeral amputation offer significant improvements in functional outcomes. Most of the studies showed participants demonstrating an enhanced ROM and improved performance of activities compared with traditional socket-based prostheses. Quality-of-life measures consistently showed positive outcomes, with individuals reporting better physical and psychosocial well-being following OI.

Risk of Bias and Study Quality Assessment

The risk of bias assessment for the studies was performed using MINORS criteria.[17] MINORS scores ranged from 11 to 16, with an average score of 13.1. The major deficiencies were the lack of an adequate control group and a contemporary group. All studies showed a clearly stated aim, appropriate endpoints, and a small loss at follow-up.

Table 1. Studies

Authors, Year	Study Design	Sample Size (Limbs, n)	Age (y)	Etiology of Amputation	Time between Amputation and S1 (y)	Type of Implant	Type of Prosthesis	Follow-up (y)	ROM (Shoulder)	ADL	Complications	Surgical Procedures (n)
Sabharwal et al, 2022[18]	Prospective	10	35.4 ± 13.4	Trauma (10)	8.7 ± 5.1	Not reported	Myoelectric (10)	Not reported	Not reported	Not reported	Not reported	Not reported
Ortiz-Catalan et al, 2020[19]	Case series	4	45.25 ± 1.3	Tumor (1), trauma (3)	7.5 ± 5.6	e-OPRA	Myoelectric (4)	7	Not reported	Higher trust in prosthesis, improved daily life activities	Sepsis (1), electrodes removed due to infection (1)	2
Vincitorio et al, 2020[20]	Case report	2	27	Trauma (2)	3	OPRA	Myoelectric	2	Full	Self-sufficient daily activities	Not reported	3
Ricardo et al, 2020[21]	Case report	1	51	Trauma (1)	1	OPRA	Hybrid	7	Flexion 148 degrees, abduction 142 degrees*	Normal work routine of 8 h/d	Not reported	2
Stenlund et al, 2019[22]	Retrospective	11	49.4 ± 16.3	Trauma (9), tumor (2)	17.5 ± 10	OPRA	Cosmetic (3), body-powered (1), myoelectric (7)	9	Flexion: 150 degrees ± 12.5, extension 65 degrees ± 9.1, abduction 154 degrees ± 9.7, adduction 25 degrees ± 5.3	Not reported	Not reported	2
Salminger et al, 2018[23]	Case series	2	40 ± 10	Trauma (2)	0.7, 23	SISA	Myoelectric (2)	1.5	Ad/abduction 92 degrees/191 degrees, flexion/extension 170 degrees/172 degrees, rotation 77 degrees/115 degrees†	Not reported	Seroma formation (1)	2
Tsikandylakis et al, 2014[24]	Retrospective	16	42 (19–69)	Trauma (14), tumor (2)	9 (1.5–33)	OPRA	Body-powered, cosmetic, and myoelectric	8 (2–19)	Not reported	Not reported	Cutaneous infection (5),‡ skin reaction (8), incomplete fracture (8), defective bony canal at s2 (3), avascular skin flap necrosis (3), and deep implant infection (1)	2
Kang et al, 2010[25]	Case report	1	48	Trauma (1)	Not reported	ITAP	Myoelectric	2	Not reported	Ability to swim in public pools	Not reported	1

*Seven-year follow-up with OI prostheses (2019).
†Absolute values for patient 1/patient 3.
‡In total, 15 infections were observed in five patients.
S1, surgery 1; S2, surgery 2.

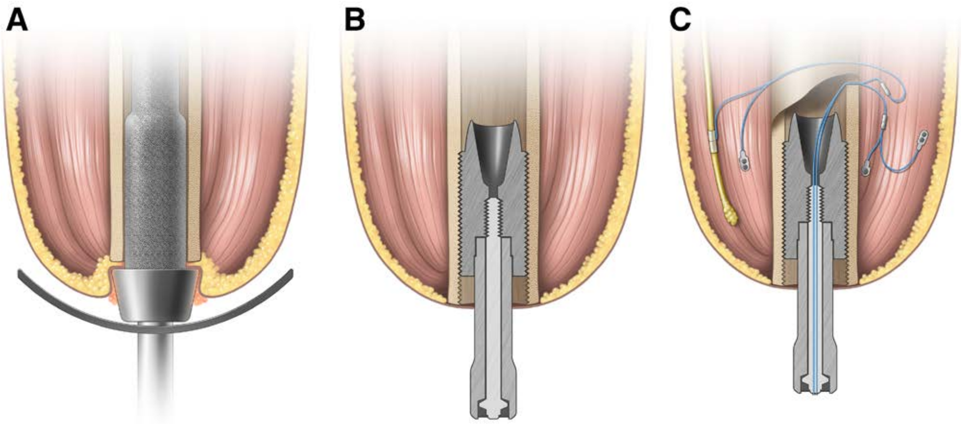

Fig. 3. Differences between press-fit and screw-fit implant technologies. A, Press-fit technology which is used for SISA and ITAP implants. The implantation of press-fit system may result in excessive formation of granulation tissue at the skin–implant interface leading to risk of chronic infection and eventually implant mobility. In contrast, the implantation of screw-fit system, that is, OPRA (B and C), requires thinning out of the subcutaneous fat tissue layer covering the periosteum, or replacing it using a split-thickness skin graft, and ensures tight adherence of the skin–bone interface avoiding chronic wound formation. Additionally, the screw-fit e-OPRA system (C) provides a gateway for epimysial or cuff electrodes to exit the abutment. © Aron Cserveny. https://www.sciencevisual.at/

DISCUSSION

The functional restoration of upper extremity loss significantly impairs a patient's quality of life. Recently, bionic reconstruction has advanced as a clinically valid approach to restoring certain hand functions lost with the loss of an upper extremity.[6] Although technological advances in bioengineering have outpaced the biological capacity of the human body to transfer commands to or from the high-fidelity electrodes of the prosthetic device, a robust and patient-friendly biomechanical fixation of the prosthesis remains a high priority in prosthetic embodiment.[7] Conventional socket fitting for a prosthesis has multiple limitations in terms of electrode alignment, coupled with unstable fixation typically utilizing straps, which significantly contributes to a decreased willingness of patients to use a prosthesis in their everyday activities and, consequently, prosthesis abandonment.[9] In this systematic review, we highlight the advantages and analyze the complications of an alternative approach for prosthesis fixation in transhumeral amputations: OI.

All patients (47) from the included studies, regardless of the implant system OPRA, SISA ITAP used for OI, showed improved ADL, ROM, and patients' satisfaction with the prosthesis. However, the biomechanical implantation differences between screw-fit (OPRA and e-OPRA) or press-fit (ITAP and SISA) systems may also contribute to different clinical outcomes in terms of the risk of skin infection (Fig. 3). The skin–bone interface in press-fit systems contains a thick subcutaneous fat tissue layer, leading to an increased risk of chronic wound infection. In contrast, the screw-fit system involves thinning out or replacing the skin adjacent to the periosteum with a split-thickness skin graft, which provides robust adherence to the bone and helps prevent excessive granulation tissue formation.[26] Other differences include the requirements for minimal bone length and the gateway ability of the e-OPRA for epimysial and cuff electrodes (Fig. 3). The ideal transhumeral stump should enable a reliable and rotationally stable connection to the prosthesis without restricting ROM in the shoulder joint. One of the main advantages of the osseointegrated prosthesis fixation is a better freedom of the shoulder movements and the lack of a restriction of the contralateral straps fixating the prosthetic device. This was supported by the evidence of an improved ROM of the shoulder compared with the prior use of the socket fitting by reduced prosthesis use restriction from $62.18 \pm 15.19\%$ to $2.51 \pm 2.49\%$ in patient 1 and from $42.55 \pm 6.56\%$ to $9.23 \pm 14.89\%$ in patient 2, as reported by Salminger et al.[23] Additionally, an improved ROM of the shoulder was reported by Ricardo et al[21] from flexion of 60 degrees and abduction of 55 degrees using a traditional prosthesis to flexion of 148 degrees and abduction of 142 degrees using an osseointegrated prosthesis. Ultimately, a better fitting of the osseointegrated prosthesis resulted in better patient satisfaction and integration of the prosthetic device into the daily life activities, as reported by all eight studies included in this review. Moreover, a recent patient perspective study by Resnik et al[27] reported that more than 20% of patients with unilateral amputations are willing to consider OI surgery to gain better prosthetic control. The results of the included studies do not only emphasize a more durable and reliable fixation of the prosthetic device compared with the conventional socket fitting but also report on the improvement in terms of comfort from the patients' perspective.

As the advantages of OI in prosthetic control become increasingly evident, it is important to be aware of the complications and adverse effects of OI. One major risk is the potential for periprosthetic fractures, which can require additional surgical intervention and ultimately lead to the failure of the osseointegrated gateway. Although only one of the included studies reported an incidence of incomplete fractures after OI, with a rate of 44% (eight of 18 patients),[24] these fractures did not compromise the primary stability of the fixture and did not necessitate additional surgical management. In contrast, fractures associated with OI in the lower extremity were reported at a lower rate of 4.4% (22 of 500 lower limb implants), requiring surgical management with dynamic hip screws (10) or reconstruction plates (9).[28] Importantly, OI-associated fractures, regardless of their location, did not necessitate the removal of implants. Other complications reported in the studies included seroma formation, cutaneous infections, skin reactions, and avascular skin flap necrosis.[19,23,24] The incidence of infectious complications for 5 years was 38%, but none of the patients required surgical interventions, and the infections were resolved conservatively as reported by Tsikandylakis et al.[24] One patient experienced major complication, such as sepsis, as reported by Ortiz-Catalan et al.[19] These complications led to a prolonged in-patient stay, additional surgery, and the subsequent removal of the implant. Thus, it is worth noting that the inclusion of the modular neural interface system in the e-OPRA system carries an additional risk of infection.[19] One study reported on the implant's cumulative survival rate at 2 and 5 years that was 83% and 80%, respectively, in which three patients underwent surgical explantation and one of three underwent a successful replantation.[24] Given the significant role of armed conflict in contemporary history, it is imperative to address the sequelae of war-related injuries through efficient, low-complication surgical strategies.[29] Amid increasing rates of amputation, there is a growing emphasis on postoperative care that extends beyond mere limb replacement with prosthetics.[30–32] In this realm, the OI method stands out as a potentially viable long-term rehabilitation strategy for individuals who have undergone upper limb amputations.

From a surgical perspective, it is important to highlight the minimal length of the humerus bone required for OI. Given the novelty of OI in the upper extremity, there are currently only anecdotal reports in the literature regarding the critical length of the humerus needed for successful OI.[24] In the authors' experience (K.R.E., I.L.V., J.M.S., and O.C.A.), the critical length for a humeral bony stump that is acceptable for transhumeral OI is estimated to be around 8 cm, which is necessary to accommodate the fixation stem of the indwelling portion of the OPRA OI prosthesis. Conversely, the ITAP implant, being a press-fit system, generally requires a longer bone for optimal fit. Nevertheless, our unpublished data suggest that in rare cases, even with a humerus length as short as 6 cm, it is possible to achieve bone lengthening using the iliac crest for transhumeral OI with the OPRA system. In this article, we present a representative case, demonstrating a patient who underwent two procedures (1) the placement of the abutment and (2) targeted muscle reinnervation. This case shows the patient achieving active prosthetic use, with sufficient deltoid support for movement and stabilization of the joint, maintained complication-free for a follow-up period of up to 24 months (Fig. 4).

One of the integral challenges for myoelectric prosthesis embodiment is how to conduct myoneural signals to the device. This can be achieved by myoneural signal amplification in surgical procedures such as targeted muscle reinnervation or regenerative peripheral nerve interface.[33–37] These approaches allow for hyperreinnervation of a target muscle and muscle tissue via surgical nerve rewiring, resulting in amplification of myoelectrical signals from the reinnervated muscles that can be decoded using electromyography (EMG) signal capture software and hardware for bioprosthetic function.[38–40] With the rise of implantable EMG electrodes, there is a need for reliable signal transmission to enhance bioprosthetic function.[41] Although osseointegrated implants provide a robust biomechanical fixation of the prosthesis itself, they can also act as a viable option for the bidirectional transmission of neural signals. Although percutaneous wires for signal transmission might be at high risk of cutaneous infection,[42] OI provides an enclosed communication channel with minimal risk of infection between the EMG electrodes and the prosthetic device. The experimental and clinical studies reported on reliable use of the osseointegrated implant as a housing or gateway for different types of neural interfaces.[43,44] Recently, it has been shown to offer more precise and reliable control than surface electrodes, regardless of limb position and environmental conditions, and with less effort.[45]

Apart from the high volume of motor input, emerging evidence indicates the pivotal role of sensory feedback in the control of dexterous hand movements.[46,47] Thus, the restoration of sensory feedback by transmitting sensory signals from the device to the patient can improve prosthetic control. However, this remains a major challenge in bionic reconstruction. A recent report on osseointegrated prosthetic embodiment showed a promising alternative beyond improved biomechanical fixation. It also provided an ultimate gateway for transferring neural signals in a bidirectional manner from implantable EMG electrodes to the machine and eliciting sensations by electrical stimulation of the major peripheral nerves via cuff electrodes.[19] Therefore, the osseointegrated prosthesis provides a viable option for biomedically stable fixation and a gateway for bidirectional signal transmission for intuitive control of a bionic hand.

This article presents several limitations that should be acknowledged. First, the inclusion of a small number of procedures in the study represents a significant limitation. This limited sample size may restrict the generalizability of the findings and introduce potential biases. Future studies should include larger sample sizes to strengthen the evidence base and draw more robust conclusions. Second, the use of various study designs among the included studies introduces heterogeneity, which can pose challenges in effectively comparing and synthesizing the results. The lack of standardized protocols across studies further emphasizes the need for more consistent approaches in future research to enhance the reliability of the findings. Furthermore, there is a clear predominance

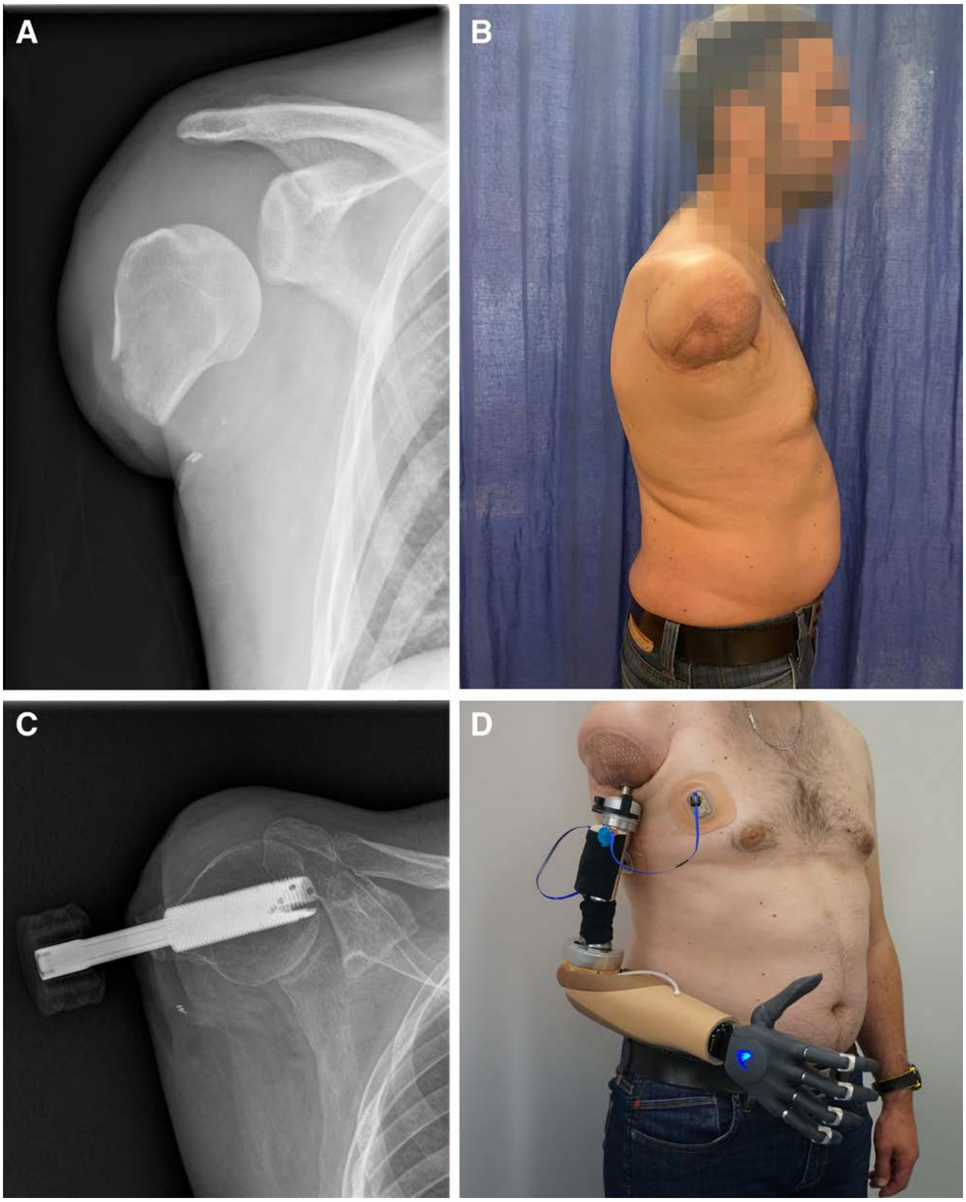

Fig. 4. Case presentation of a 36-year-old man after successful transhumeral osseointegration using OPRA system. A–B, Preoperative patient representation with an x-ray image showing 6 cm of remained humerus. C–D, A 16-week postoperative presentation. The x-ray image of the abutment and successful integration of the myoelectrical prosthesis.

of myoelectric systems with OPRA implants, potentially introducing a bias toward a specific type of prosthetic system. Another limitation is the limited information regarding the overall incidence or severity of complications associated with osseointegrated prostheses. A more comprehensive assessment of complications and their management is crucial for a clearer understanding of the risks and challenges associated with this technique. Future studies should emphasize thoroughly investigating and reporting complications to facilitate informed decision-making. Additionally, future research should focus on patient-reported outcome measures to precisely evaluate the impact of osseointegrated prostheses on quality of life. Incorporating patient-reported outcome measures in studies would provide valuable insights into how the quality of life is improved with this particular type of prosthesis.

CONCLUSIONS

In conclusion, the systematic review consistently demonstrated significant improvements in functional outcomes, quality of life, and user satisfaction with OI prostheses following transhumeral amputation, compared with traditional socket-based prostheses. OI resulted in enhanced ROM, improved stability, and superior prosthetic control. However, the careful monitoring and management of potential complications, including infection and implant failure, are crucial. Osseointegrated prostheses offer a promising solution for individuals with transhumeral amputations, enhancing their functional abilities and overall quality of life. Further research is needed to evaluate long-term outcomes and optimize candidate selection criteria.

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DISCLOSURE

The authors have no financial interest to declare in relation to the content of this article.

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All data needed to evaluate the conclusions in this article are presented. Additional data related to this article may be requested from the authors.

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ETHICAL APPROVAL

Reference number EK Nr: 1299/2021 and 2274/2020.

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