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Extracorporeal Shockwave Therapy (ESWT)—A Novel Method for Transferring Oral Implant Primary Failures to Final Clinical Success: A Test Case Report Followed up for More Than 6 Years

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Purpose: To evaluate the feasibility of reversing a primary failure through therapeutic mechanical stimulation induced by transcutaneous application of acoustic waves (extracorporeal shockwave therapy [ESWT]) in the peri-implant tissues. ***Materials and Methods:*** This clinical report evaluates the outcome of a new protocol proposed to treat a primary failure (loosened oral implant): application of three cycles of ESWT (one session per week for 3 consecutive weeks) with an equivalent positive energy of 0.18 mJ/mm^2 (therapeutic dose: 2,000 pulses, 8 Hz, 4.0 bar). Standardized intraoral radiographs and CBCT scans were taken, the implant stability quotient (ISQ) was determined, and clinical evaluations were performed. ***Results:*** It was possible to verify a progressive increase in ISQ values after the ESWT protocol: 17 initially, 46 at 2 months, and 68 at 4 months. This led to successful implant prosthetic rehabilitation (35 Ncm). Follow-up evaluations at 6 years confirm that the new bone-implant interface is preserved and that ESWT is a safe, noninvasive treatment. ***Conclusions:*** In the context of the new dynamic model of osseointegration (the foreign body equilibrium), this represents the first report of a host-implant equilibrium reestablished after an early implant failure process. However, more studies are needed to determine both the medical device and the most effective therapeutic range for clinical applications of this technology in oral implantology. *Int J Oral Maxillofac Implants 2024;39:922–930. doi: 10.11607/jomi.10820*

Keywords: case report, ESWT, oral implant, osseointegration, osteoimmunology, primary failure

An early or a primary implant failure is a clinical scenario that arises from a lack of osseointegration and when osseointegration is assumed to never have been reached. It is commonly diagnosed when an implant is spinning while attempting to place the definitive prosthesis. The frequency of this scenario is low, reported in the range of 0% to 2% in most clinical reports.[1] Early implant failure may be linked to immunologic or genetic variables or be associated to surgical trauma or different types of patient disease.[2] However, clinically, early failures are not related to infection,[3] as the possible diagnosis of peri-implantitis applies after the implant's first year in service.[4] The majority of histologic findings indicate that primarily failed implants are surrounded by a connective tissue capsule.[5]

Scientifically documented reasons for such primary failures are currently lacking.[1,6] In this sense, the early failure is an anomaly that represents a challenging puzzle to be solved. Today, a new immunologic theory of osseointegration,[7] based on the new field of osteoimmunology, not only provides an alternative cellular and molecular explanation to primary failures,[8] but also opens up the possibility of developing new therapeutic strategies focused on the peri-implant osteoimmunology of the host,[9] such as the possible immunomodulation of osseointegration through extracorporeal shockwave therapy (ESWT),[10] developed from a noninvasive form of treatment for musculoskeletal disorders, developed from extracorporeal shockwave lithotripsy.[11]

Orthopedic surgeons have used ESWT treatment to refixate orthopedic implants over a long period of time.[12,13] Additionally, ESWT has been used as an effective strategy to promote quality of healing in patients with delayed fractures and non-unions.[14] Inspired by their findings in orthopedics, two orthopedic surgeons (M.B. and L.P.) were invited attempt to investigate whether ESWT would be a suitable treatment for primarily loose oral implants. The ESWT technique has been applied in dentistry before, in extracorporeal lithotripsy of salivary stones,[15] in painful myogelosis of the masseter muscle,[16] and in orthodontics,[17,18] and all cases achieved positive

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results. Further, because shockwaves are also known to have a bactericidal effect on periodontal pathogens and have potential for biofilm disruption, ESWT has been proposed as an emerging treatment for peri-implantitis and periodontal-associated diseases.[19,20]

ESWT works by rapidly emitting acoustic waves (shockwaves) in a very short period, generating transient pressure changes that propagate through the tissues where they are applied. ESWT are subdivided into two types: focused shockwave therapy (FSWT), characterized by generating a pressure field that converges to reach maximal energy deeper in body tissues, and radial shockwave therapy (RSWT), described by the diverging pressure field and a more superficial aspect. Recent studies have shown that the mechanisms of action for ESWT could be related to a polarity shift in the macrophage phenotype from the pro-inflammatory M1-macrophage to the anti-inflammatory and pro-regenerative M2-macrophage, especially for low-energy ESWT.[10,21,22] In fact, shockwave-induced immunomodulation has been proposed to have potential as a noninvasive physical therapy to regulate macrophage functions related to wound healing.[23]

The aim of the present study is to investigate whether ESWT could be used safely to stabilize primarily loosened oral implants. The present investigation is related only to one patient who was followed up for more than 6 years to investigate whether the possible initially formed repair bone was maintained over time.

MATERIALS AND METHODS

This case report examined the outcomes of an ESWT protocol on a loose implant treated at the Oral Surgery and Implant Dentistry Centre (Marchesani Oral Surgery and Implant Dentistry Center, Concepción, Chile) in July 2017. This study is based on an ethical approval for the "use of ESWT in patients with oral implant failure" that was obtained from the University of Concepción, Chile (protocol C.I.Y.B, no. 01/17). Planning was carried out in accordance with CARE guidelines,[24] and data were collected from patient files according to the World Health Organization.

For the ESWT protocol, the patient was instructed to fill out a standardized questionnaire with important aspects of her systemic condition, medications, and oral history. After being instructed carefully and in detail about the ESWT protocol, the patient signed an informed consent. This patient met the following criteria for ESWT application: absence of contraindications such as acute infection and malignant tumor in the treatment area, pregnancy, and severe coagulopathy.[25] The patient was then clinically and radiographically examined following a standardized protocol. Any

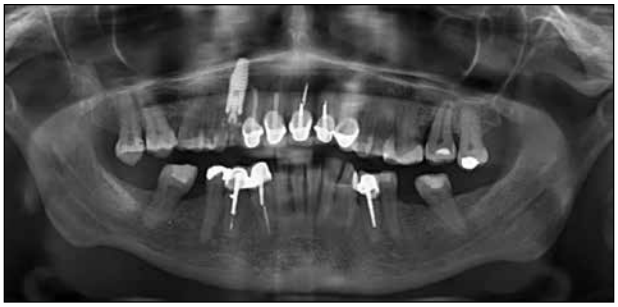

Fig 1 Panoramic radiograph taken immediately after surgery and provisionalization.

ESTW application complaints were immediately noted. In addition, the patient was instructed to attend close follow-up examinations at regular intervals and/or in the occurrence of any complication. In all follow-up visits, the implant stability quotient (ISQ) was measured, and standardized intraoral radiographs, panoramic radiographs, and CBCT images were taken following the standardized protocol.

The patient came to the present authors' center for emergency dental prosthetic rehabilitation after a complicated anterior crown fracture, which had an extensive restoration, on the maxillary right canine. She was 45 years old, allergic to penicillin, nonsmoker, and without any known secondary disease. The patient suffered from periodontal disease, calculus, and ill-fitting restorations. Because she was in a lot of pain and the tooth could not be saved (vital tooth with a palatal subcrestal crown fracture projection to the root), and there was no infection or inflammation of the local tissues, an atraumatic extraction and immediate implant placement in the fresh extraction socket was performed by an experienced surgeon (F.M.). The implant insertion torque progressed as follows: 20, 25, 30, 35, and 40, finally reaching an excellent primary stability (45 Ncm) along the palatal socket wall, anchoring the implant apex (Tapered Internal Plus, 4.6 × 15 mm, BioHorizons) close to the cortical aspect of the maxillary palatine process, in the triangle of bone. Bicortical stabilization and a subcrestal position were achieved, with an ISQ of 65 (ISQ SmartPeg Type 32, Osstell). In addition, a bone graft (Puros Cortical Particulate Allograft, 0.5 cc, Zimvie) and a resorbable collagen membrane (CollaGuide, Riemser) were placed into the residual gap around the immediate fresh socket as a complementary guided tissue regeneration procedure in a Type I defect, which is a routine procedure recommended on pristine tooth sockets to overcome the distance between the implant and the surrounding bone in the coronal area.[26] Finally, an immediate restoration/provisionalization was performed (Fig 1); it was placed within 48 hours after implant placement but not in occlusion with the opposing

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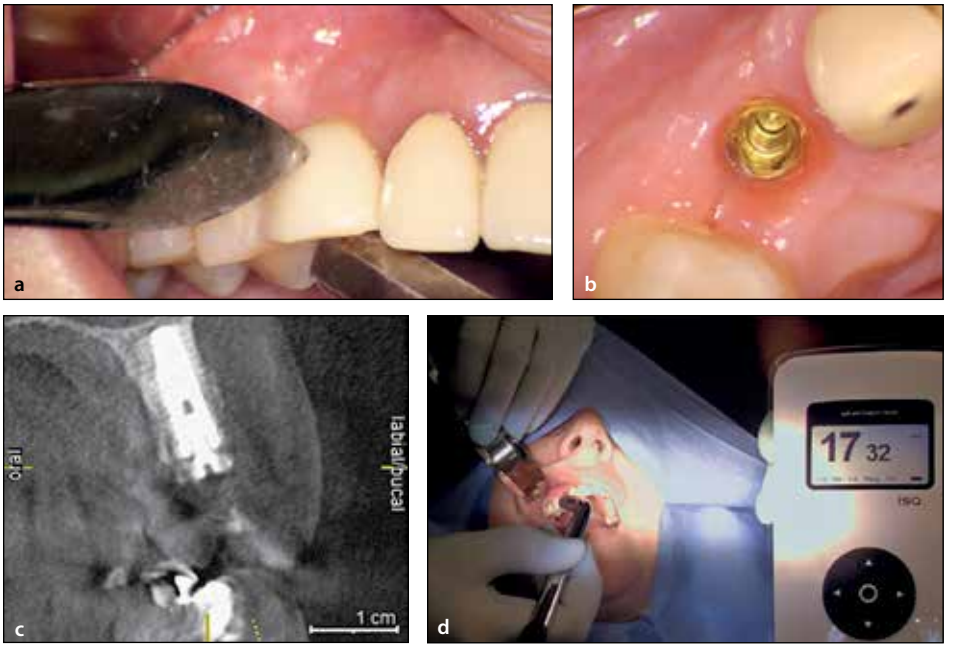

Fig 2 Primary failure assessment about 5 months after surgery, before the rehabilitation stage. *(a)* Two metal instruments applied pressure, and mobility of the implant-temporary crown was noted. *(b)* The integrity of the implant-abutment connection was confirmed. *(c)* A CBCT examination did not reveal any signs of complications, and bone loss was not seen around the implant. *(d)* The ISQ value was very low (17/32), which was directly correlated with the clinical implant movement.

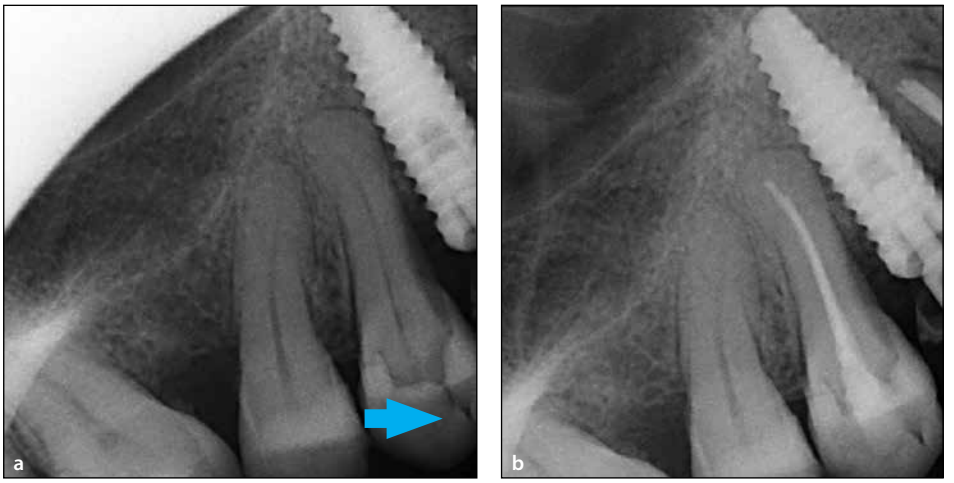

Fig 3 Endodontic treatment of the maxillary right first premolar. *(a)* The tooth presented irreversible pulpitis (without any signs of infection) related to a fractured restoration *(blue arrow)*. *(b)* Absence of periapical lesion.

dentition[27] (PEEK Temporary Cylinder, Hexed, 4.5 mm, BioHorizons). At the same time, the patient was referred to a periodontist and a prosthodontist to treat her general oral condition.

About 5 months after surgery and before the rehabilitation stage, implant loosening was confirmed (Fig 2). Discernible mobility of the implant-temporary crown was noted when applying pressure with the ends of two metal instruments (see Fig 2a). Pain at the apical implant region was also related, but no infectious-inflammatory alteration (such as edema, pus, or bleeding) was observed around the implant. Further, no deeper probing depths were detected around the implant, and there were no visible graft remnants. As a first measure, the absence of occlusal contacts with the opposing dentition was verified (nonfunctional provisional). In addition, the integrity of the implant-abutment connection was confirmed (see Fig 2b). A CBCT examination was performed to complement the clinical evaluation, and neither revealed any signs of complication; in fact, an absence of bone loss around the implant was reported by the oral and maxillofacial radiologist (see Fig 2c). Additionally, endodontic treatment of the adjacent maxillary right first premolar was indicated, as it presented irreversible pulpitis (without any signs of infection) related to an old and deep fracture of a direct mesio-occlusal composite resin restoration (Fig 3). As a precaution, the endodontists prescribed prophylactic antibiotic coverage (azithromycin 500 mg, once daily for 3 days). The clinical situation was explained to the patient, and ESWT was proposed to avoid removing the implant. The patient agreed and signed an informed consent.

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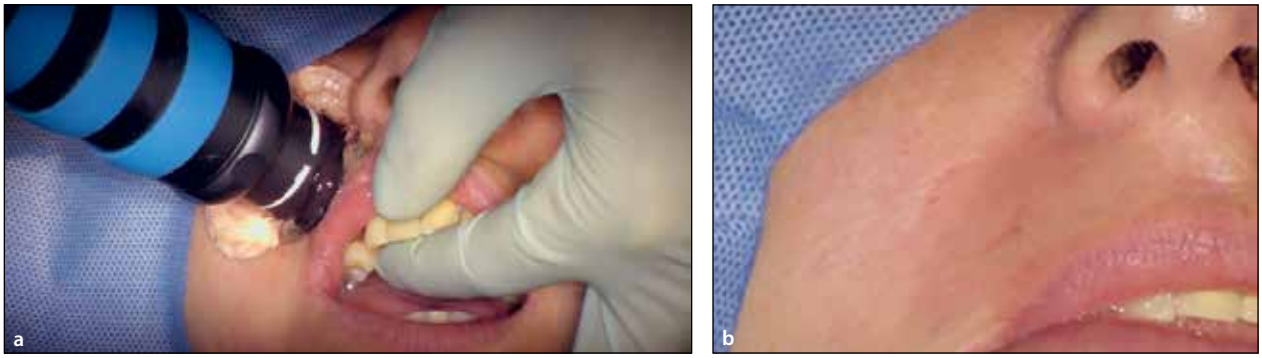

Fig 4 *(a)* For ESWT application, it is necessary to locate the target (bone triangle) precisely, for which the skin area was demarcated with a colored mark. A conductive gel is placed for intimate contact with the device. *(b)* Skin remains intact after ESWT application. Three cycles of ESWT were performed in total. Cycles were performed by L.A.

One month later and after studying the case, an RSWT protocol was proposed by orthopedic surgeons (L.P. and M.B.) due to its effectiveness and safety in the treatment of fractured non-unions of superficial bones. In turn, the ESWT device was provided by a local company (Leoni Medical). Because ISQ is a quantitative method to evaluate osseointegration and at the risk of removing/unscrewing the implant, the primary failure was assessed by measuring the ISQ value.[28] The ISQ value was very low (17/32), which was directly correlated with the clinical implant movement (see Fig 2d). The patient felt pain when spinning the implant, reporting a pain level of 8 on a visual analogue scale (VAS), within a range from 1 = no pain, to 10 = worst pain. Therefore, under local anesthesia (infraorbital nerve block) and after removing the provisional, the patient received ESWT on her peri-implant–affected tissues. A healing abutment was subsequently placed to avoid hitting the provisional with the ESWT device (Swiss DolorClast Master, EVO BLUE handpiece, 15-mm applicator, EMS) in the therapeutic sessions.

Three ESWT cycles were applied in total, focused on the triangle of bone, with one session per week for 3 consecutive weeks (Fig 4). For each treatment session, ESWT therapeutic settings comprised 2,000 shockwaves at a frequency of 8 Hz and 4.0 bar of pressure. In addition, a previous analgesic dose was applied in the same sessions: 1,000 shockwaves at a frequency of 13 Hz and 1.5 bar of pressure, for the patient's tolerance to the therapeutic micro-impacts of the device. According to the ESWT device manufacturer, the equivalent positive energy (ED+) for 1.5 bar and 4.0 bar is 0.02 mJ/mm^2 and 0.18 mJ/mm^2, respectively.

This dual modality was proposed because the effect of shockwaves is predominantly analgesic at a low energy (bar, mJ/mm^2) with a high application frequency, and is more osteogenic with higher energy and lower application frequency (Hz). The chosen setting for ESWT was based on experience in adult orthodontic patients (energy flux density of 0.19 to 0.23 mJ/mm^2),[17,18] and the amount of 2,000 shocks per session was also proposed in accordance with previous experience and protocols suggested by most manufacturing companies.[29] In turn, the rationale for using ESWT at a certain cycle for a certain time is that multiple-session RSWT treatments have been shown to result in a cumulative clinical effect, especially one RSWT session per week for 3 consecutive weeks.[30] It should be noted that the radial pressure wave equipment has a slight disadvantage: Because the wave is generated pneumatically, there may be an annoying vibration for the patient. Currently, the use of piezoelectric generation focal shockwaves is much more comfortable for the patient.[17,18]

Interestingly, in the following weeks of treatment, the pain level when manipulating the implant decreased, with VAS scores of 3 and 0 in the second and last ESWT sessions, respectively. The provisional was later repositioned after completing all ESWT cycles at the patient's request.

RESULTS

Eight weeks after ESWT, the implant stability had progressed, and the implant no longer seemed loose. In fact, the measurement showed an increased ISQ value (46/59). Therefore, a standardized intraoral radiograph was taken to compare with one taken 2 months prior, and a slight increase was seen in the peri-implant radiopacity at the interproximal bone crest level (Figs 5).

Sixteen weeks after ESWT, a high ISQ value (68) was measured, exceeding the measurement obtained at implant placement and indicating treatment success (Fig 6a). Although radiography cannot be used to prove osseointegration, the high ISQ value acted as confirmation of osseointegration, and L.A. proceeded with the rehabilitation stage (Figs 6b and 6c). New CBCT scans

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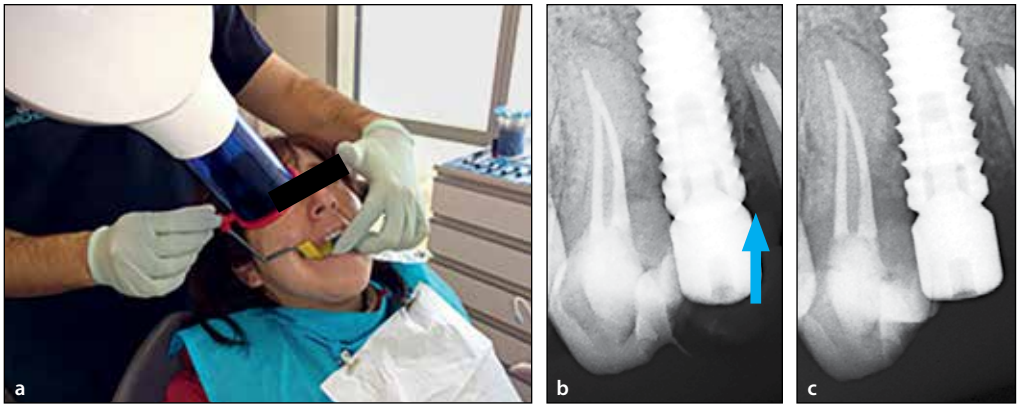

Fig 5 *(a)* A standardized intraoral radiograph was taken using the parallel technique. *(b)* Initial radiograph. *(c)* The radiograph taken 2 months later shows a subtle increase in radiopacity at the mesial bone crest *(blue arrow)*.

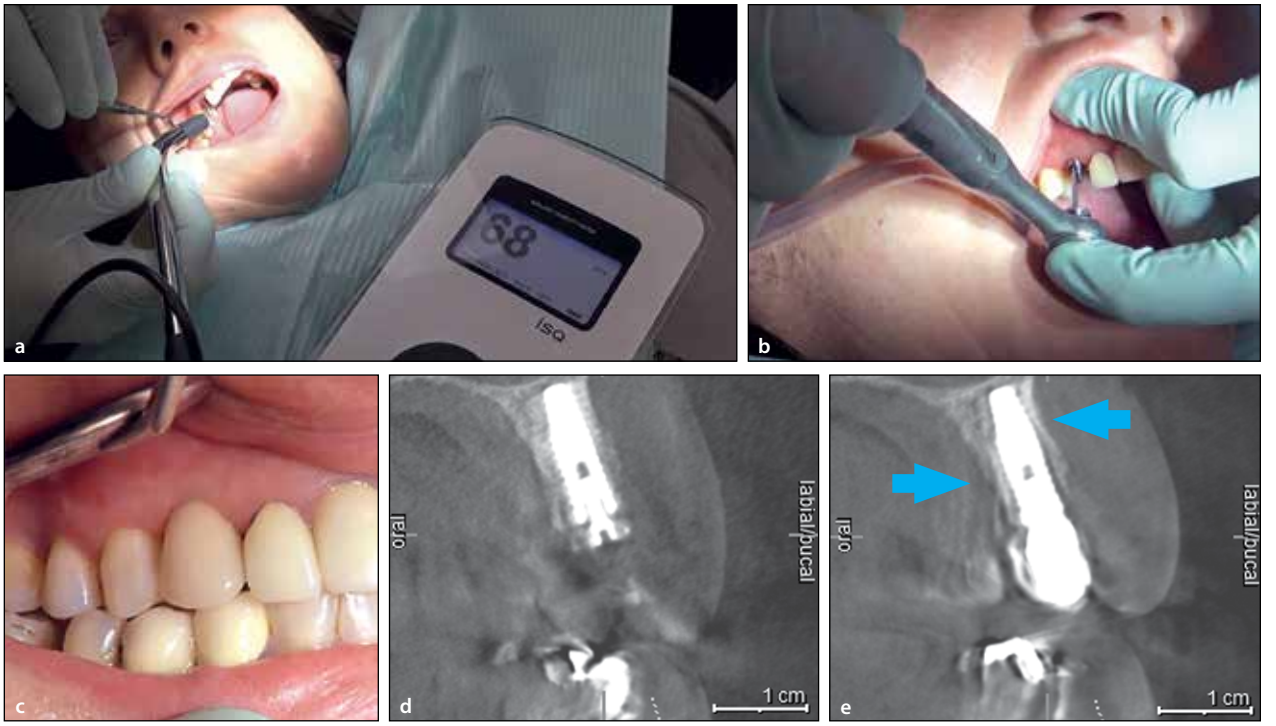

Fig 6 Sixteen weeks after ESWT. *(a)* Clinical follow-up. A high ISQ value was measured, indicating treatment success. *(b and c)* The rehabilitation stage proceeded after the high ISQ value. *(d and e)* CBCT scans were taken. Compared to the original CBCT scan *(d)*, the follow-up scan *(e)* shows that an overgrowth of the buccal and palatal cortical aspect occurred *(blue arrows)*.

were performed to complement the clinical evaluation at 4 months, showing remodeling. Interestingly, an overgrowth of the buccal and palatal cortical aspects appears to have occurred when compared to the previous CBCT (Figs 6d and 6e). A bone reaction to shockwave trauma described by orthopedic researchers is an intense apposition of new bone at the lesion site, with a considerably thickened cortical layer.[31]

At the final, 6-year follow-up, CBCT showed that the buccal cortical plate was maintained (Fig 7a), and there was soft tissue stability around the implant (Fig 7b). Even more, there were no complications.

DISCUSSION

To the present authors' knowledge, this case report represents the first report of a host-implant equilibrium reestablished through the use of ESWT after an early failure process of an immediate implant with provisionalization and nonfunctional loading, as confirmed by ISQ measurement and CBCT more than 6 years after treatment. Although some failing implants may have been rescued by unloading and allowing a period of healing, these cases are associated with ISQ values of 49 to 58 and failure risk of 18.2%.[32] In a follow-up study

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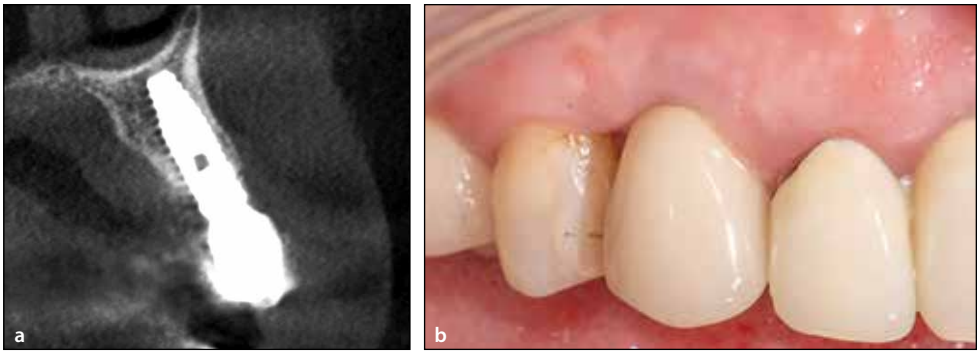

Fig 7 Six years after ESWT. *(a)* CBCT showed that the buccal cortical plate was maintained. *(b)* Soft tissue stability was seen around the implant. No complications occurred.

on implants placed in extraction sockets subjected to immediate/early loading, one implant rescue was demonstrated through ISQ measurements: During the first 6 weeks, the ISQ value dropped significantly from 67 to 53, but after implant unloading, the ISQ recovered to a value of 72 after 6 months.[32] However, it is known that ISQ measurements < 45 are indicative of implant failure,[33] and oral implants with an ISQ < 40 in the early healing stages after primary stability, or after initial bone remodeling and new bone growth have occurred, are irretrievably lost, and it is not possible to save them. In fact, a histologic study showed that these clinically mobile implants do not have bone present in close contact, and instead there is dense connective tissue with few cells.[28]

Therefore, to disrupt the fibrous tissue encapsulation and to renew the healing process, a shockwave treatment protocol was adapted for this type of condition. Shockwave therapy has the potential to induce osteogenic differentiation of mesenchymal cells, which is also reflected in clinical reports on its positive effects in situations such as delayed fracture healing (non-union)[34,35] and the refixation of loosening orthopedic titanium implants.[12,13] Recent histologic studies in animals have shown that this anabolic bone response through ESWT could be beneficial in bone defects reconstructed with a titanium scaffold and to improve screw fixation and osseointegration.[36–38] How was it possible to increase the ISQ in the present case report? Biophysical stimulation through ESWT can stimulate the positive regulation of proangiogenic growth factors and thus the process of vascularization, osteogenesis, and bone formation. In particular, the highly vascularized periosteum represents a vital prerequisite for successful fracture repair by providing cortical blood supply and serving as a source of osteogenic cells.[39] This could be related to the implant refixation and the maintenance of the buccal cortical plate at the 6-year follow-up in the present study, a critical finding considering that alveolar ridge remodeling occurs after tooth extraction and implant placement.[40] Nevertheless, there is evidence that vascularization is only one piece of the puzzle in the much more complex process of bone regeneration.[39] In fact, favorable osteogenesis, angiogenesis, and osteoimmunology around implants play a critical role in desirable osseointegration.[41]

In this context, a new line of research has proposed that osseointegration is regarded as a foreign body reaction equilibrium that is achieved after a dynamic osteoimmunomodulatory event. In this regard, it is understood that an efficient and timely switch from M1 to M2 macrophage phenotype (a nomenclature that described polar-opposite proinflammatory and repair activities, reflecting Th1/Th2-type responses that are independence from T cells) is the basis for the concept of osteoimmunomodulation.[8] Therefore, the study of osseointegration today is challenging, as the understanding of the osteoimmunology of the host must be unified with the ability of the titanium surface to continue serving as an immunomodulator, promoting the M2-macrophage polarization.[42–45] In support of this, recent quantitative polymerase chain reaction and histologic animal model studies have shown that the osteoimmune cellular components are constantly adapting to the changing environment. Therefore, the immune and healing responses are not only transient one-time reactions.[8] Furthermore, breakthrough technologies (such as flow cytometry) and high-throughput single-cell RNA sequencing studies have provided a complete picture of the alveolar bone's immunomodulatory microenvironment, its diverse cellular heterogeneity, and the characterization of the osteoimmune responses modulated by titanium properties at an unprecedented level of detail; these create a comprehensive landscape that facilitates new insights into the complex cell environment involved in maintaining the tissue–implant interface in the long term.[8,46–48]

On the other hand, the prolonged presence of inflammatory M1 macrophages can exacerbate tissue damage (local imbalance) and prevent biomaterial integration, resulting in a fibrous encapsulation.[8] Interestingly, histologic characteristics of primary failures range

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from implants surrounded by a connective tissue capsule with a great number of inflammatory cells to a heterogeneous interface, representing time stages of the failure process.[5] Similarities to the histologic stages of an ongoing foreign body reaction (FBR) to a biomaterial (including chronic inflammation, excessive granulation, collagen fiber deposition, and fibrous tissue formation) are a product of a persisting inflammatory microenvironment.[49] A prolonged presence of M1 proinflammatory polarization can be induced by the collection of both pathogen- and damage-associated molecular patterns (PAMPs and DAMPs, respectively). Therefore, the inflammatory potential can be multiplied due to the synergistic activation of proinflammatory pathways of septic and aseptic nature, and thus implant failure does not always need to have a septic background.[8]

In the present case report, it is not clear whether an infection or aseptic loosening occurred, or a combination of both. Although the patient did not present signs of infection, an initial subclinical infection cannot be ruled out. Indeed, the potential for bacteria to cause clinical problems before osseointegration is complete has been described in cases of oral implants placed without simultaneous antibiotic coverage, increasing implant failure rates. In the present case report, the endodontists indicated prophylactic antibiotic coverage (azithromycin 500 mg, once daily for 3 days), which is a common practice of more than one-third (39.3%) of clinicians trying to resolve symptomatic irreversible pulpitis in a permanent tooth without any signs of systemic infection.[50] Nevertheless, the effects of antibiotic prophylaxis on osteoimmune processes are unknown. In fact, recent contradictory findings in mice suggest that antibiotic prophylaxis could deregulate osteoimmune wound healing induced by implant placement and attenuate the alveolar bone–implant interface.[51] In this sense, a bactericidal effect of ESWT on the eventual presence of periodontal pathogens also cannot be ruled out,[19,20] and with this the decrease of a proinflammatory M1 environment through the induction of PAMPs.

Aseptic mechanisms could be related to the clinical handling from the surgeon and prosthodontist.[8] Although the present case was performed by an experienced surgeon (F.M.) under a strict protocol, which minimizes this risk factor, it is necessary to address underlying molecular aspects. Surgery can damage the tissue and lead to sterile inflammation. Additionally, pattern recognition receptors (PRRs) can be activated by nonmicrobial signals associated with recognizing intracellular contents released from damaged and necrotic cells,[52] which increases the levels of DAMPs and can lead to the increasing levels of PAMPs. In turn, cell-free DNA levels could be increased because of the accumulation of DAMPs and PAMPs, a key promoter in the progress of alveolar bone inflammation.[53] Macrophages, which are primarily localized in the tissue, play a pivotal role in sensing DAMPs through PRRs and can also detect and respond to resolution-associated molecular patterns (RAMPs) and specific proresolving mediators during sterile inflammation, which regulate the balance between inflammatory and resolving processes. However, even if the importance of sterile inflammation is considerable, most studies on inflammation focus primarily on pathogen responses.[54] In fact, it seems that DAMPs/PRRs pathways are essential components in the dynamic titanium osseointegration process in mice. In a recent study in mice, inhibition of HMGB1 proteins or RAGE receptors impaired osseointegration, leading to an FBR.[55] DAMPs can also be the product of implant/prosthetic remains, with several potential sources of ions and particles in dental implantology. Additionally, the presence of organic and inorganic contaminants on some surfaces and the possible exposure of less stable elements after surface modification procedures can also trigger an aseptic inflammatory response.[8] Although the patient reported herein does not present systemic pathologies, local conditions could coexist. Studies have identified senescent cells and the senescence-associated secretory phenotype (SASP) as critical in the regenerative process after injury. A key function of SASP is the recruitment of immune cells to the injury site and the subsequent clearance of senescent cells, among which are macrophages.[56]

During recent years, a growing number of studies are pointing to the immunomodulation capacity of shockwaves, specifically their potential as a noninvasive physical therapy to exert direct modulation on macrophage functions related to wound healing.[23] M1 macrophages are closely related to inflammation, and reduced M1 presence has been observed to attenuate FBR.[57] Stimulation of human monocyte-derived macrophages with ESWT has been shown to cause significant inhibition of some M1 marker genes (CD80, COX2, and CCL5) in M1 macrophages and a significant synergistic effect for some M2 marker genes (ALOX15, MRC1, and CCL18) in M2 macrophages.[58] Further, a recent study in rats highlighted the beneficial properties of ESWT to causally intervene in the fibrotic process related to a FBR. After inserting silicone devices, the results showed a significant decrease in the genetic expression of CD68 (expressed on the surface of macrophages) and CCL2 (cytokine secreted by monocytes and T cells), which are associated with an inflammatory reaction, as well as a significant decrease in TGFb-1 expression, a well-known profibrotic protein. Interestingly, it was observed that a single ESWT application was capable of decelerating capsule formation when compared to multiple ESWT, which degrades fibrotic tissue.[59] This last point supports the indication of orthopedic surgeons (M.B. and

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L.P.) for the present case and the application of three ESWT cycles, once a week for 3 consecutive weeks.

After this clinical experience, the present authors believe that the opportunity to transmit mechanical energy through shockwaves gives rise to a new dental application with many advantages (such as its noninvasiveness, safety, and cost-effectiveness) over traditional treatments for such cases, such as surgical implant removal and possible reimplantation. Specifically, the possibility that the transition between the M1 inflammatory phase and the M2 anti-inflammatory phase can be guided through mechanotransduction makes ESWT a promising therapeutic alternative to improve clinical success in oral implants.[60] ESWT is a therapeutic approach based on the new understanding of osseointegration as a "foreign body reaction where interfacial bone is formed as a defense reaction to shield off the implant from the tissues."[61] In light of this case report, it is believed that an immune-driven process was reestablished, leading to new bone formation around the implant surface rather than a pure anabolic bone response[62]—that is, it may have been an immunomodulation of osseointegration through extracorporeal shockwave therapy.[10]

CONCLUSIONS

The use of ESWT in oral implantology could be a novel immunomodulatory strategy focused on the osteoimmunology of the host to treat primary failures and maintain a foreign body equilibrium in the long term. In the future, it is necessary to carry out animal studies to understand the relationship between these externally applied signals and oral peri-implant cellular function. Furthermore, it is vital to determine the most effective amount of energy to apply and its frequency through clinical trials. So far, no side or adverse effects have been observed from this treatment.

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REFERENCES

1. Chrcanovic BR, Albrektsson T, Wennerberg A. Reasons for failures of oral implants. J Oral Rehabil 2014;41:443–476.
2. Kochar SP, Reche A, Paul P. The etiology and management of dental implant failure: A review. Cureus 2022;14:e30455.
3. Esposito M, Hirsch JM, Lekholm U, Thomsen P. Biological factors contributing to failures of osseointegrated oral implants. (I). Success criteria and epidemiology. Eur J Oral Sci 1998;106:527–551.
4. Lindhe J, Meyle J, Group D of European Workshop on Periodontology. Peri-implant diseases: Consensus report of the Sixth European Workshop on Periodontology. J Clin Periodontol 2008;35(suppl 8):282–285.
5. Esposito M, Thomsen P, Ericson LE, Lekholm U. Histopathologic observations on early oral implant failures. Int J Oral Maxillofac Implants 1999;14:798–810.
6. Kang DY, Kim M, Lee SJ, et al. Early implant failure: A retrospective analysis of contributing factors. J Periodontal Implant Sci 2019;49:287–298.
7. Albrektsson T, Dahlin C, Reinedahl D, Tengvall P, Trindade R, Wennerberg A. An imbalance of the immune system instead of a disease behind marginal bone loss around oral implants: Position paper. Int J Oral Maxillofac Implants 2020;35:495–502.
8. Albrektsson T, Tengvall P, Amengual L, Coli P, Kotsakis GA, Cochran D. Osteoimmune regulation underlies oral implant osseointegration and its perturbation. Front Immunol 2023;13:1056914.
9. Albrektsson T, Tengvall P, Amengual-Peñafiel L, Coli P, Kotsakis G, Cochran DL. Implications of considering peri-implant bone loss a disease, a narrative review. Clin Implant Dent Relat Res 2022;24:532–543.
10. Amengual-Peñafiel L, Jara-Sepúlveda MC, Parada-Pozas L, Marchesani-Carrasco F, Cartes-Velásquez R, Galdames-Gutiérrez B. Immunomodulation of osseointegration through extracorporeal shock wave therapy. Dent Hypotheses 2018;9:45–50.
11. Auersperg V, Trieb K. Extracorporeal shock wave therapy: An update. EFORT Open Rev 2020;5:584–592.
12. Loske AM (ed). Extracorporeal shock wave therapy, shock wave and high pressure phenomena, bone healing. In: Medical and Biomedical Applications of Shock Waves. Springer International, 2017:222.
13. Gstoettner C, Salminger S, Sturma A, et al. Successful salvage via re-osseointegration of a loosened implant in a patient with transtibial amputation. Prostet Orthot Int 2020;45:76–80.
14. Willems A, van der Jagt OP, Meuffels DE. Extracorporeal shock wave treatment for delayed union and nonunion fractures: A systematic review. J Orthop Trauma 2019;33:97–103.
15. Iro H, Schneider HT, Födra C, et al. Shockwave lithotripsy of salivary duct stones. Lancet 1992;339:1333–1336.
16. Kraus M, Reinhart E, Krause H, Reuther J. Low energy extracorporeal shockwave therapy (ESWT) for treatment of myogelosis of the masseter muscle. Mund-Kiefer Gesichtschir 1999;3:20–23.
17. Falkensammer F, Rausch-Fan X, Schaden W, Kivaranovic D, Freudenthaler J. Impact of extracorporeal shockwave therapy on tooth mobility in adult orthodontic patients: A randomized single-center placebo-controlled clinical trial. J Clin Periodontol 2015;42:294–301.
18. Falkensammer F, Schaden W, Krall C, Freudenthaler J, Bantleon HP. Effect of extracorporeal shockwave therapy (ESWT) on pulpal blood flow after orthodontic treatment: A randomized clinical trial. Clin Oral Investig 2016;20:373–379.
19. Elisetti N. Extracorporeal shock wave therapy (ESWT): An emerging treatment for peri-implantitis. Med Hypotheses 2021;150:110565.
20. Venkatesh Prabhuji ML, Khaleelahmed S, Vasudevalu S, Vinodhini K. Extracorporeal shock wave therapy in periodontics: A new paradigm. J Indian Soc Periodontol 2014;18:412–415.
21. Lv F, Li Z, Jing Y, Sun L, Li Z, Duan H. The effects and underlying mechanism of extracorporeal shockwave therapy on fracture healing. Front Endocrinol (Lausanne) 2023;14:1188297.
22. Simplicio CL, Purita J, Murrell W, Santos GS, Dos Santos RG, Lana JFSD. Extracorporeal shock wave therapy mechanisms in musculoskeletal regenerative medicine. J Clin Orthop Trauma 2020;11(suppl 3):s309–s318.
23. Holsapple J, Cooper B, Berry S, et al. Low intensity shockwave treatment modulates macrophage functions beneficial to healing chronic wounds. Int J Molecular Sciences 2021;22:1–18.
24. Riley DS, Barber MS, Kienle GS, et al. CARE guidelines for case reports: Explanation and elaboration document. J Clin Epidemiol 2017;89:218–235.
25. Schmitz C, Császár NB, Milz S, et al. Efficacy and safety of extracorporeal shock wave therapy for orthopedic conditions: A systematic review on studies listed in the PEDro database. Br Med Bull 2015;116:115–138.
26. Caplanis N, Lozada JL, Kan JY. Extraction defect assessment, classification, and management. J Calif Dent Assoc 2005;33:853–863.

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27. Aparicio C, Rangert B, Sennerby L. Immediate/early loading of dental implants: A report from the Sociedad Española de Implantes World Congress consensus meeting in Barcelona, Spain, 2002. Clin Implant Dent Relat Res 2003;5:57–60.
28. Scarano A, Carinci F, Quaranta A, Iezzi G, Piattelli M, Piattelli A. Correlation between implant stability quotient (ISQ) with clinical and histological aspects of dental implants removed for mobility. Int J Immunopathol Pharmacol 2007;20(suppl 1):33–36.
29. Schmitz C, Császár NB, Milz S, et al. Efficacy and safety of extracorporeal shock wave therapy for orthopedic conditions: A systematic review on studies listed in the PEDro database. Br Med Bull 2015;116:115–138.
30. Ke MJ, Chen LC, Chou YC, et al. The dose-dependent efficiency of radial shock wave therapy for patients with carpal tunnel syndrome: A prospective, randomized, single-blind, placebo-controlled trial. Sci Rep 2016;6:38344.
31. Delius M. Twenty years of shock wave research at the Institute for Surgical Research. Eur Surg Res 2002;34:30–36. doi:
32. Sennerby L, Meredith N. Implant stability measurements using resonance frequency analysis: Biological and biomechanical aspects and clinical implications. Periodontol 2000 2008;47:51–66.
33. Suzuki JB, Misch CE. Periodontal and maintenance complications. In: Resnik RR, Misch CE (eds). Misch's Avoiding Complications in Oral Implantology. Mosby, 2018:771–826.
34. Mittermayr R, Haffner N, Feichtinger X, Schaden W. The role of shockwaves in the enhancement of bone repair—From basic principles to clinical application. Injury 2021;52(suppl 2):s84–s90.
35. Lv F, Li Z, Jing Y, Sun L, Li Z, Duan H. The effects and underlying mechanism of extracorporeal shockwave therapy on fracture healing. Front Endocrinol (Lausanne) 2023;14:1188297.
36. Koolen MKE, Pouran B, Öner FC, Zadpoor AA, van der Jagt OP, Weinans H. Unfocused shockwaves for osteoinduction in bone substitutes in rat cortical bone defects. PLoS ONE 2018;13:e0200020.
37. Koolen MKE, Kruyt MC, Zadpoor AA, Öner FC, Weinans H, van der Jagt OP. Optimization of screw fixation in rat bone with extracorporeal shock waves. J. Orthop Res 2018;36:76–84.
38. Jafarpour Mahalleh A, Mesgarzadeh AH, Jarolmasjed S, et al. Extracorporeal shock wave therapy as a helpful method for rapid osseointegration of dental implants: Animal study. Biomimetics (Basel) 2023;8:137.
39. Menger MM, Laschke MW, Nussler AK, Menger MD, Histing T. The vascularization paradox of non-union formation. Angiogenesis 2022;25:279–290.
40. Araújo MG, Wennström JL, Lindhe J. Modeling of the buccal and lingual bone walls of fresh extraction sites following implant installation. Clin Oral Implants Res 2006;17:606–614.
41. Zhou A, Yu H, Liu J, et al. Role of Hippo-YAP signaling in osseointegration by regulating osteogenesis, angiogenesis, and osteoimmunology. Front Cell Dev Biol 2020;8:780.
42. Trindade R, Albrektsson T, Tengvall P, Wennerberg A. Foreign body reaction to biomaterials: On mechanisms for buildup and breakdown of osseointegration. Clin Implant Dent Relat Res 2016;18:192–203.
43. Li Q, Shen A, Wang Z. Enhanced osteogenic differentiation of BMSCs and M2-phenotype polarization of macrophages on a titanium surface modified with graphene oxide for potential implant applications. RSC Adv 2020;10:16537–16550.
44. Zhang Y, Cheng X, Jansen JA, Yang F, van den Beucken JJJP. Titanium surfaces characteristics modulate macrophage polarization. Mater Sci Eng C Mater Biol Appl 2019;95:143–151.
45. He Y, Gao Y, Ma Q, Zhang X, Zhang Y, Song W. Nanotopographical cues for regulation of macrophages and osteoclasts: Emerging opportunities for osseointegration. J Nanobiotechnology 2022;20:510.
46. Li J, Zhao C, Xu Y, et al. Remodeling of the osteoimmune microenvironment after biomaterials implantation in murine tibia: Single-cell transcriptome analysis. Bioact Mater 2022;22:404–422.
47. Lin W, Li Q, Zhang D, et al. Mapping the immune microenvironment for mandibular alveolar bone homeostasis at single-cell resolution. Bone Res. 2021;9:17.
48. Shirazi S, Ravindran S, Cooper LF. Topography-mediated immunomodulation in osseointegration; ally or enemy. Biomaterials 2022;291:121903.
49. Chen Y, Sun W, Tang H, et al. Interactions between immunomodulatory biomaterials and immune microenvironment: Cues for immunomodulation strategies in tissue repair. Front Bioeng Biotechnol 2022;10.820940.
50. Agnihotry A, Gill KS, Stevenson Iii RG, et al. Irreversible pulpitis—A source of antibiotic over-prescription? Braz Dent J 2019;30:374–379.
51. Ahmad W, Pishevar N, Cochrane LJ, et al. Antibiotic prophylaxis dysregulates dental implant placement surgery-induced osteoimmune wound healing and attenuates the alveolar bone-implant interface in mice. J Clin Periodontol 2023;50:1670–1684.
52. Chen GY, Nuñez G. Sterile inflammation: Sensing and reacting to damage. Nat Rev Immunol 2010;10:826–837.
53. Huang H, Yang R, Shi B. The potential role of cfDNA-related innate immune responses in postoperative bone loss after alveolar bone grafting. Front Immunol 2023;13:1068186.
54. Koncz G, Jenei V, Tóth M, Váradi E, Kardos B, Bácsi A, Mázló A. Damage-mediated macrophage polarization in sterile inflammation. Front Immunol 2023;14:1169560.
55. Biguetti CC, Cavalla F, Silveira EV, et al. HGMB1 and RAGE as essential components of Ti osseointegration process in mice. Front Immunol 2019;10:709.
56. Elder SS, Emmerson E. Senescent cells and macrophages: key players for regeneration? Open Biol 2020;10:200309.
57. Liu Y, Segura T. Biomaterials—Mediated regulation of macrophage cell fate. Front Bioeng Biotechnol 2020;8:609297.
58. Sukubo NG, Tibalt E, Respizzi S, Locati M, d'Agostino MC. Effect of shock waves on macrophages: A possible role in tissue regeneration and remodeling. Int J Surg 2015;24(Pt B):124–130.
59. Fischer S, Mueller W, Schulte M, et al. Multiple extracorporeal shock wave therapy degrades capsular fibrosis after insertion of silicone implants. Ultrasound Med Biol 2015;41:781–789.
60. Amengual-Peñafiel L, Brañes-Aroca M, Marchesani-Carrasco F, Jara-Sepúlveda MC, Parada-Pozas L, Cartes-Velásquez R. Coupling between osseointegration and mechanotransduction to maintain foreign body equilibrium in the long-term: A comprehensive overview. J Clin Med 2019;8:139.
61. Albrektsson T, Chrcanovic B, Jacobsson M, Wennerberg A. Osseointegration of implants—A biological and clinical overviem. JSM Dent Surg 2017;2:1–6.
62. Amengual-Peñafiel L, Córdova LA, Constanza Jara-Sepúlveda M, Brañes-Aroca M, Marchesani-Carrasco F, Cartes-Velásquez R. Osteoimmunology drives dental implant osseointegration: A new paradigm for implant dentistry. Jpn Dent Sci Rev 2021;57:12–19.

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