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Original Article

Internal fixation with biodegradable high purity magnesium screws in the treatment of ankle fracture

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ABSTRACT

Background: Metal plates and screws are widely used as internal fixations in the treatment of ankle fracture. However, there are many disadvantages such as "stress shielding" effect and the need for secondary surgical removal, which potentially affected the blood supply around the fracture site. In recent years, many studies confirmed that the biodegradable high purity magnesium (Mg) screws exhibited sufficient mechanical strength with adequate degradation rate for effective bone healing, avoiding the need for implant removal operations.
Method: We conducted a prospective study on patients with ankle fractures treated at Affiliated Zhongshan Hospital of Dalian University between January 2020 and January 2021. Twenty-four patients (twelve patients for each group) with ankle fractures were treated with high purity Mg screws or conventional titanium alloy plates and screws. Hematological examinations were performed in the early postoperative period, X-ray examinations were performed in the long-term postoperative follow-up. Postoperative complications, including infection, failure of internal fixation and malunion, were recorded during the follow-up. The visual analogue scale (VAS) was used to evaluate postoperative pain perceived by the patients, and the American Orthopedic Foot and Ankle Society (AOFAS) ankle-hindfoot scoring system was used to evaluate their postoperative ankle function.
Results: All patients achieved good fracture alignment, and imaging examination showed that the biodegradable high purity Mg screws degraded gradually without breakage or displacement. None of the patients experienced infection, failure of internal fixation, malunion or other complications in both groups.
Conclusion: The results showed that biodegradable high purity Mg screws could be effectively used in the clinical treatment of ankle fractures, ensuring safety and satisfactory postoperative functional recovery.
The translational potential of this article: The biodegradable high purity Mg screws could provide sufficient mechanical strength and fixation stability for ankle fracture. Our study extended the clinical application of the biodegradable high purity Mg screws for fracture.

1. Introduction

Ankle fracture is commonly seen in clinical practice. Although the ankle joint is smaller, it bears greater load than the hip and knee joints. Due to its proximity to the ground, the ankle joint struggles to effectively cushion the stress, making the treatment of ankle fractures more complex than other parts of the body [1–3]. The internal and external surfaces of the ankle joint form a mortise, and the morphological changes of the mortise can reduce the contact area of the tibiofemoral joint. Ultimately, such imbalance leads to traumatic arthritis. For stable fractures with displacement less than 2 mm, conservative treatment with plaster fixation is indicated [4]. In order to achieve precise anatomical repositioning, open reduction and internal fixation are always recommended clinically [5,6]. The bone plate system is commonly

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used to fix ankle fractures, but it can result in large incisions and trauma, potentially affecting the blood supply around the fracture site and impeding fracture healing. The metal screws are also widely used internal fixations in clinical practice, but there are still disadvantages such as "stress shielding" effect and the need for secondary surgical removal [7,8]. These plates and screws are mostly made of titanium (Ti) alloy. However, the Young's moduli of Ti alloy is often higher than that of human bone (10–30 GPa), which is a major cause of the known stress shielding effect and lead to implant loosening or refracture around the implant [9]. In addition, the second operation has always been performed where the scar and soft tissue adhesions formed. Therefore, it berries higher risks compared to the initial operation, which may cause pain, infection and wound dehiscence [10]. Besides, biologically inert Ti alloy materials are inactive and the releasing toxic ions can cause pain or discomfort [11]. Today, biodegradable implant materials could offer a solution to the aforementioned problems.

With the development of biodegradable metallic materials, Mg alloy screw has been adapted in clinical practice [12]. Mg is an important element in human metabolism [13]. It participates in multiple enzyme-catalysed reactions and maintains the normal physiological function of the skeleton. High purity Mg is light in mass with a density of 1.74 g/cm^3, which is close to natural bone (1.8–2.1 g/cm^3), making it more suitable as an implant material. Moreover, the mechanical properties of Mg-based implants are compatible with human bones, which could effectively reduce the "stress shielding" effect between bone and implant materials [14]. In the meanwhile, numerous studies have indicated the good biocompatibility and bone regeneration promotion effect of Mg [15]. The elevation of extracellular Mg was founded to influence vital biological activities in bone repair [16]. Mg could induce local neurons to produce CGRP, which in turn promotes bone healing [17]. Considering the beneficial effects of Mg^{2+}, preclinical studies of Mg-based orthopedic implants were applied and reported [18–20].

MAGNEZIX®CS is a compression screw developed by Syntellix AG, which is the first Mg alloy implant approved for human. It has been utilized in preliminary clinical studies for correcting bunion deformity osteotomy [21]. Researchers in China have developed a patented Mg alloy Mg-3Nd-0.2Zn-0.5Zr (JDBM) and have further improved its biocompatibility and corrosion resistance through a calcium phosphate (Ca–P) coating. During the one-year follow-up of JDBM screws in the treatment of medial malleolar fractures, none of the 9 cases experienced infection, failure or other complications [22,23]. However, the presence of high concentrations of chloride ions in the environment of the human body could exacerbate the Mg corrosion or degradation in the body, leading to health concerns about the increasing complexity of alloy elements and compositions [24]. In recent studies, researchers have focused on improving technologies to reduce the impurity elements (such as Fe, Ni and Cu) or surface treatment technologies, which could effectively enhance the Mg corrosion resistance [25,26]. Therefore, there has been a proposal to simplify chemical compositions while still achieving the same effects, a trend for future R&D of biodegradable materials.

In 2013, biodegradable high purity Mg screws were used for the first time in preclinical cases in China (as shown in Fig. 1). In 2019, China's National Medical Products Administration (NMPA) approved the 99.99 % high purity Mg screws for multicenter clinical trials to register Class III medical devices. In 2020, this high purity Mg screws were certified with CE mark. In our previous studies, the biodegradable high purity Mg screws were applied to fix the bone flap and achieved satisfactory results in the prevention of bone flap displacement [27]. The released Mg ion were found to promote osteogenic. Moreover, high purity Mg was then designed as large-size weight-bearing screws for the fixation of femoral neck fractures in goats. The biodegradable high purity Mg screws exhibited sufficient mechanical strength with adequate degradation rate for effective bone fracture repair [28]. The ultimate tensile strength, the yield strength, and the elongation at break of high purity Mg (99.99 wt %) in this study were about 164.1 MPa, 118.5 MPa, and 17.2 %, which was basically consistent with previous report [29]. The reported results indicated that the biodegradable high purity Mg screws could be extended for applications in multiple types of fracture fixation. In order to evaluate the stress shielding effect, we performed a mechanical test to compare the elastic properties of Ti alloy and as-extruded pure Mg prior to this study. Then, the finite element analysis was used to verify the feasibility of high purity Mg screws in the treatment of ankle fracture and the results were shown in Fig. 2. The maximum stress acting on the screw was concentrated on the contact area between the screw and the bone. The maximum stress was 59.5 MPa, which was less than the yield strength of the high purity Mg. Therefore, we speculated that it was feasible to treat the ankle fracture with high purity Mg screws. In this study, we applied biodegradable high purity Mg screws for ankle fractures in comparison to conventional Ti alloy plates and screws. The study aimed to explore the therapeutic efficacy of the high purity Mg screws in clinical application.

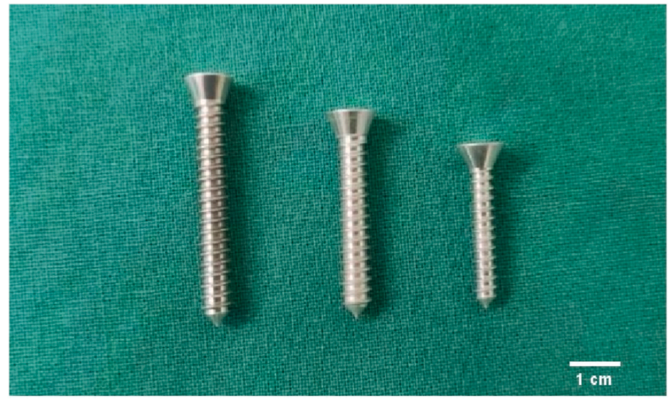

Fig. 1. Biodegradable high purity magnesium screws.

2. Materials and methods

2.1. Mechanical study

The RFDA-HTVP1750-C (IMCE, Belgium) was utilized to conduct the elastic modulus test. Samples of Ti alloy and as-extruded high pure Mg were machined and ground to dimensions of 50 mm × 10 mm x 5 mm, followed by a mechanical polishing process to achieve a mirror-like finish. Subsequently, the samples were placed in a graphite furnace under an argon gas atmosphere. The Young's modulus of the samples was calculated based on the bending vibration analysis, which was induced by a pulse driver. Three samples were measured for each material. The results showed that the Young's moduli of Ti alloy and high purity Mg were 108.55 ± 1.83 GPa and 44.75 ± 0.66 GPa respectively.

2.2. Preoperative planning

The purpose of this work is to predict the therapeutic effect of high purity Mg screw in the treatment of ankle fracture. The CT images of the ankle were taken and saved in the form of DICOM files. The data was imported to the Mimics Research 21.0 software to obtain a 3D model. Then the reconstructed model was imported into 3-Matic (The Materialise Group, Leuven, Belgium) software for optimization processing. The model of the screw was then imported and positioned appropriately. The FEA models were meshed with tetrahedral elements and the convergence test was performed to verify that element discretization was sufficiently fine for the stress analysis using ANSYS Workbench software (version 16.0, ANSYS, Canonsburg, PA, USA). It was assigned a Young's modulus of 18 GPa and Poisson's ratio of 0.3 to represent the bone, while a Young's modulus of 44.8 GPa and Poisson's ratio of 0.35 to represent the high purity Mg screw. The underside of the foot was fixed

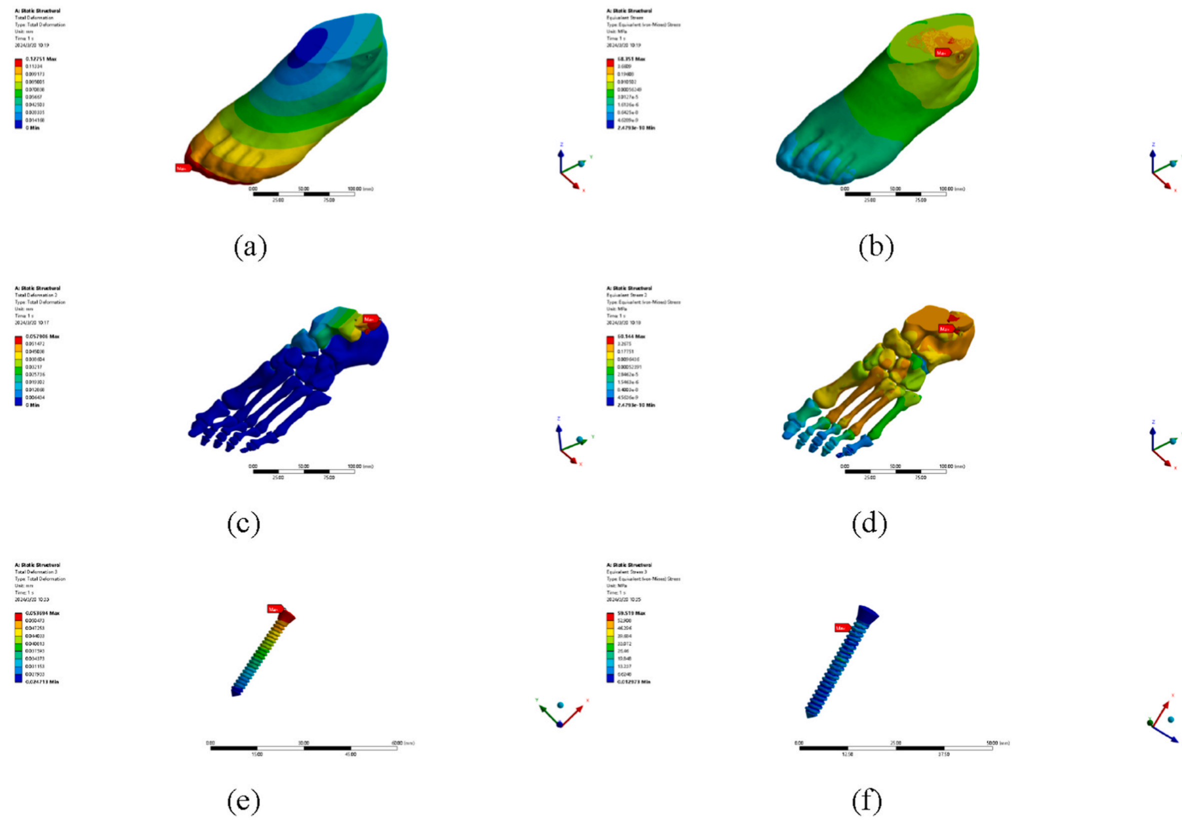

Fig. 2. FEA was performed for an assembly of the high purity Mg screw and lateral malleolar to obtain the interface mechanical parameters such as total deformation and maximum von Mises stress. (a–b) the assemble model; (c–d) the bone; (e–f) the high purity Mg screw.

and the forces on the upper part was the 375N, which was acting downward on one foot when the person (weight 75 kg) was standing.

2.3. General information

We conducted a prospective study to compare the effect of the biodegradable high-purity Mg screws and the Ti alloy plates and screws in the treatment of ankle fractures. The study was approved by the Ethics Committee of Affiliated Zhongshan Hospital of Dalian University (No. 2013-006). The patients were selected according to pre-determined inclusion and exclusion criteria. Patient inclusion criteria: (1) radiographically confirmed ankle fracture; (2) no contraindication to open reduction and signed informed consent for the study; (3) absence of contraindications to implantation (4) approval from the hospital ethics committee. Patient exclusion criteria: (1) old fractures and open ankle fractures; (2) severe comminuted fractures; (3) combined with special type of ankle fracture, such as Pilon, Maisonneuve, etc.; (4) combined with serious cardiovascular and cerebrovascular diseases, liver and kidney function disorders, and other underlying diseases; (5) combined with mental illness or poor compliance; (6) combined with malignant tumors; (7) patients with a history of severe allergies or known allergy to metals; (8) combined with severe osteoporosis; (9) the body weight of the patient was more than 75 Kg. All the patients were assessed for study eligibility and the diagnosis was confirmed by the senior orthopaedic surgeon. A total of 24 patients (13 males and 11 females) participated and randomized to the two groups, with 12 patients (7 males and 5 females) receiving treatment with biodegradable high-purity Mg screws and 12 patients (6 males and 6 females) receiving treatment with Ti alloy plates and screws. The demographic and clinical characteristics between the two groups were similar ($p > 0.05$) (Table 1). Each patient who participated in the study signed the informed consent.

Table 1
General information of the patients.

Variable	Group Mg(n = 12)	Group Ti(n = 12)	p-Value
Age(years±SD)	45.67 ± 13.68	44.17 ± 17.38	0.816[a]
Sex(M/F)	7/5	6/6	1[b]
Side(R/L)	6/6	6/6	1[b]
Fractures site(n)			0.458[b]
Medial mallelus	5	3	
Lateral malleolus	1	4	
Bimalleolar	3	4	
Lateral and medial malleolus	2	2	
Lateral and posterior malleolus	1	2	
Trimalleolus	3	1	

M male, F Female, R right, L left.
[a] Two independent sample t-test.
[b] Chi-square test (Fisher).

2.4. Implants

The biodegradable high purity Mg screws were designed jointly with Dongguan Yi'an Technology Company. The purity of the Mg screws was 99.99 % (wt.%) and the chemical composition was analyzed by glow discharge mass spectrometry (GDMS). The detailed composition was listed in Table 2. The biodegradable high purity Mg screws were fully threaded with a diameter of 4 mm and a length of 30–50 mm. The tail end of the screws was processed with a line-shaped and non-penetrating sink hole, which was beneficial to the holding and precession of high-purity Mg screws. The angle between the nut and the screw body is 22–30°. 12 of these patients were treated with titanium compression screws or screw-plate system (4.0 mm or 4.5 mm partial thread cannulated screws) and the remaining 12 patients were treated with

Table 2
Analyzed chemical compositons (ppm wt) of high purity Mg screw.

Composition	Fe	Ni	Cu	Zn	Mn	Ca	Si	Na	Al	Pb	Ti	Sn	Mg
High purity Mg	0.5	0.3	0.12	1.2	0.11	0.31	0.67	0.37	0.25	4.3	0.01	<0.01	Bal.

bioabsorbable high purity Mg screws.

2.5. Preoperative preparation and surgical methods

Admitted patients were temporarily immobilized with a limb stent and received symptomatic treatment. Preoperative routine examinations and ultrasound were conducted to exclude the possibility of deep vein thrombosis. X-ray and CT three-dimensional reconstruction of the affected limb were performed to provide imaging reference for fracture repositioning. Intravenous antibiotics were injected 30 min before surgery to prevent infection. After anesthesia, the affected thigh was tied with a balloon tourniquet. The routine surgical area was disinfected, draped, and the tourniquet was inflated to stop bleeding. Depending on the fracture site, a medial longitudinal incision was made to expose the medial malleolus, and a posterior-lateral incision was made to expose the lateral and posterior malleolus. The skin incision should be taken care to protect the superficial gastrocnemius nerve. Then the subcutaneous soft tissue was separated to expose the fracture, and the soft tissue embedded in the fracture end was debrided carefully. For bimalleolar fracture, it's recommended to first reduce and fix the lateral malleolus fracture to facilitate the reduction of the internal malleolus fracture. For trimalleolar fractures, the posterior malleolus was fixed first, followed by the reduction and fixation of the medial and lateral malleolus fractures.

All fractures were fixed with biodegradable high purity Mg screws or Ti alloy plates and screws. Fibula fractures were rigid fixed with Ti alloy plates with or without Ti alloy lag screws, or with only high purity Mg screws. Medial malleolar fractures were fixed with one to three 3.5-mm Ti alloy cancellous screws or high purity Mg screws. Displaced posterior fragments were fixed with one to two 3.5-mm cancellous screws or high purity Mg screws. C-arm fluoroscopy confirmed satisfactory alignment of the fractures. Correct anatomical repositioning was demonstrated in three ways: (1) Equal and symmetrical joint gaps inside, outside, and above the talus. (2) The normal distance of the inferior tibiofibular union was maintained (3) The arc formed by the lateral talus and the tip of the fibula was intact. The incision drainage was performed after surgery and the incision was sutured layer by layer. The operative time and bleeding volume were recorded. All patients were operated by the same team of surgeons.

2.6. Postoperative treatment

After the operation, the ankle joint was fixed in a functional position with an ankle brace or plaster brace. All patients were treated with broad-spectrum antibiotics for 3 days to avoid infection, and the drainage tube was removed according to the drainage situation. The sterile dressing was changed regularly, and the stitches were removed about 14 days after surgery. The patients were instructed to perform functional exercises. Non-weight-bearing passive ankle activities were started 3 days after the operation, and functional exercises of the partially weight-bearing ankle joint were started 4–6 weeks after operation. After fracture healed, full weight-bearing walking was allowed.

2.7. Observation indicators and evaluation criteria

Postoperative anteroposterior and lateral ankle radiography examinations were performed to evaluate the fracture healing. Early postoperative hematological examinations, including blood routine, CRP, SAA and serum Mg concentration were performed prior to surgery (PTS), 1–2 postoperative days (PODS) and at 2nd, 4th, 8th, 12th,24th and 48th weeks after surgery. The visual analogue scale (VAS) was used to evaluate postoperative pain experienced by the patients, and the American Orthopedic Foot and Ankle Society (AOFAS) ankle-hindfoot scoring system was used to evaluate the ankle function of the patients after the operation. The VAS and AOFAS scores at the final follow-up were used for statistical analysis to determine the recovery of the included patients. During the follow-up period, complications such as infection, failed internal fixation, and malunion were carefully recorded.

2.8. Statistic analysis

The data of this study were analyzed and processed using SPSS 21.0 statistical software. The data were presented as mean and standard deviation. The ANOVA was used for comparison of serum Mg, WBC, SAA and CRP levels between high pure Mg group and Ti alloy group. Statistical difference was determined at $P < 0.05$.

3. Result

3.1. Finite element analysis

The results showed that the total deformation of the assemble model was 0.1275 mm and the maximum von Mises stress was 68.351 MPa (Fig a–b). It was also observed that the deformation of bone was 0.058 mm and the maximum stress was 60.144 MPa which was concentrated at the junction of the screw and bone (Fig c–d). The deformation and stress of the bone was less than the assemble model under the action of gravity. It indicated that the deformation and stress of the skin was bigger than the bone. The deformation of the screw was 0.053 mm, which was less than the value of the skin and bone. It was speculated that the screw had a good fastening effect. In addition, the maximum stress of the screw was 59.519 MPa, which was less than the yield strength of the screw (Fig e–f). Therefore, it was speculated that the high purity Mg screw could fix the ankle bone effectively. The results were shown in Fig. 2.

3.2. Intraoperative conditions

All the patients' ankles were anatomically repositioned and firmly fixed intraoperatively with biodegradable high purity Mg screws or Ti alloy screw-plate system. The types of fractures observed intraoperatively were consistent with the preoperative judgment.

3.3. General conditions of surgical patients

The patients in high purity Mg screws group were followed up for a mean of 146.0 ± 14.5 weeks and Ti alloy screws group for a mean of 76.0 ± 24.5 weeks. The incisions of all the cases were healed by first intention. After the operation, the fracture in both groups showed good alignment. During the following-up, none of the patients showed complications such as infection, internal fixation failure, fracture displacement or malunion. The results of hematological examinations of the two groups were shown as Figs. 3–4.

3.4. Long term follow-up

All the patients were followed up for a long time. CT had better observation effect, but it was expensive with a long waiting time, so X-ray was the main method of follow-up examination in this study. X-ray examination showed that the fracture healing of the patients was good, and the high purity Mg screws did not fall off or break during the whole

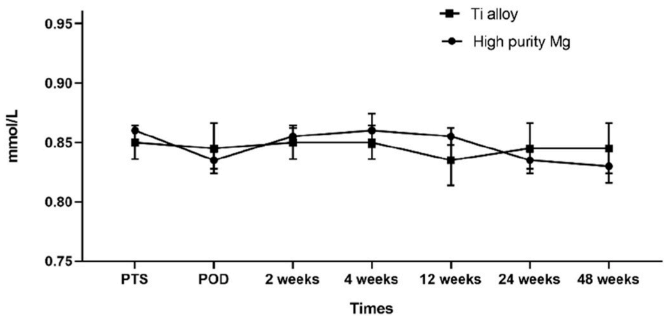

Fig. 3. Changes of the concentration of Mg^{2+} in blood after operation in both groups.

follow-up process. In the high purity Mg screws group, slight radiolucent zones around the high purity Mg screws were observed under radiography postoperatively, which shrank gradually as time prolonged. This phenomenon was consistent with other research teams [30,31]. The underlying cause of these radiolucent zones was related to hydrogen formation and non-mineralized bone tissue [32,33]. In this study, the radiolucent zones of the X-ray films were used to indirectly represent the gas production with the degradation of the high purity Mg screws. The results showed that the high purity Mg screws began to degrade after implantation. The area of the radiolucent zones reached the maximum at about 2 weeks after implantation, and decreased gradually.

3.5. VAS score and AOFAS score

11 of the patients had no obvious pain at 3 months after surgery, and 1 patient reported pain relief at 6 months after surgery in the high purity Mg group. One patient in the Ti group felt continuous pain after surgery, and the pain symptoms disappeared after implant removal. At the last follow-up, the mean VAS score was similar between the two groups. The ankle function improved gradually after the operation. The details are shown in Table 3.

3.6. Typical cases

Case 1. A 31-year-old male patient was admitted to the hospital with complaint of "trauma-induced left foot pain for 3 days." He was diagnosed as lateral malleolus fracture of left ankle and underwent open reduction internal fixation with two biodegradable high purity Mg screws. The radiographs of the ankle joint after treatment were depicted in Fig. 8. Radiolucent zones around screws could be observed the day after surgery. The fracture healed 24 weeks postoperative and the radiolucent zone decreased significantly 92 weeks postoperative (Fig. 5D and E). At 152 weeks after operation, the degradation of high purity Mg screws were almost completed (Fig. 5F). The radiolucent zone was non-mineralized bone tissue surrounded by osteosclerotic zone from CT image (Fig. 5G).

Case 2. A 29-year-old female patient complained of right ankle pain and limited mobility after 5 days after falling and was diagnosed of right trimalleolar fracture. Open reduction and internal fixation of right ankle fracture was performed with biodegradable high purity Mg screws. The imaging examinations before and after the operation were presented in Fig. 6. Pictures (D-Q) displayed the X-ray of the right ankle joint. The results indicated that the fracture arrangement was satisfactory. The fracture completely healed 12 weeks after surgery. The radiolucent zones were observed around the high purity Mg screws and shrank gradually. At the last follow-up, the high purity Mg screws were hardly noticeable.

Case 3. A 67-year-old male patient was admitted to the hospital with complaints of right ankle pain and limited activity for 12 h after trauma. He was diagnosed as " lateral malleolus fracture of right ankle" and underwent open reduction internal fixation with Ti alloy plates and screws. The imaging examinations before and after treatment were shown in Fig. 7. Fig. 7F was a frontal view of right ankle joint two years after surgery, the Ti alloy screws and plate were removed with good bone healing. The radiolucent zone could also been observed where the white arrow indicated. The joint space of the ankle became narrow at the last follow-up.

Case 4. A 31-year-old female patient was admitted to the hospital due to "right ankle swelling after trauma and limited activity for 5 h". She was diagnosed of " right trimalleolar fracture". The patients underwent an open reduction internal fixation using Ti alloy screws and plate. The imaging examinations before and after treatment are shown in Fig. 8.

4. Discussion

The treatment of ankle fractures is always dependent on the mechanism of injury, the pattern of fracture and the soft tissue conditions. The ankle fractures need anatomical repositioning and appropriate internal fixation to ensure early movement. Effective fixation is one of the fundamental principles to ensure the early activity of the joint. In fact, cancellous screws and tension band fixation were both good choices for the fixation of the medial malleolus. In the treatment of the lateral malleolus fracture, small plates and screws are used, such as one-third tubular plates, 2.7/3.5-mm cortical screws or 4.0-mm threaded screws. Furthermore, the posterior malleolus is best stabilised with screws or anti-glide plates. Plate fixation might provide more rigid stabilization than screw fixation, however it required relatively larger

Table 3
Postoperative functional score.

Time	AOFAS score		VAS score	
	Mg group	Ti alloy group	Mg group	Ti alloy group
3 months	77.75 ± 4.06	79.75 ± 3.46	2.18 ± 1.68	1.98 ± 1.86
6 months	91.00 ± 5.80	92.10 ± 4.50	2.16 ± 0.98	2.05 ± 0.77
12 months	95.00 ± 5.15	94.60 ± 5.65	0.54 ± 0.68	0.79 ± 0.38
24 months	97.00 ± 5.15	96.70 ± 5.05	0.34 ± 0.18	0.51 ± 0.38

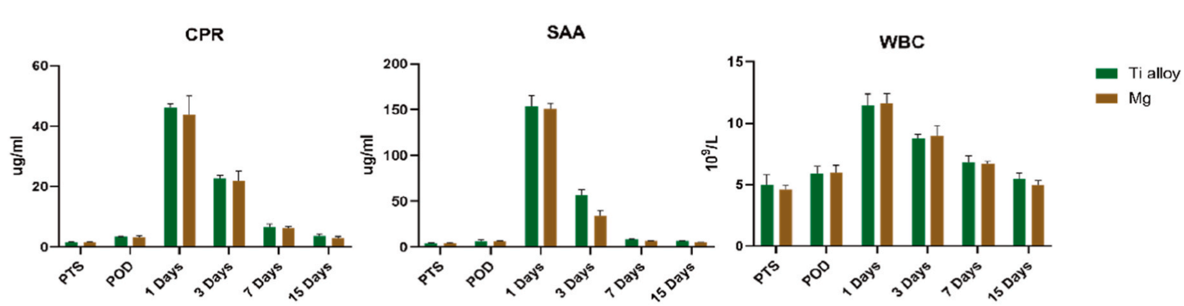

Fig. 4. The concentration of inflammatory factors after operation in both groups.

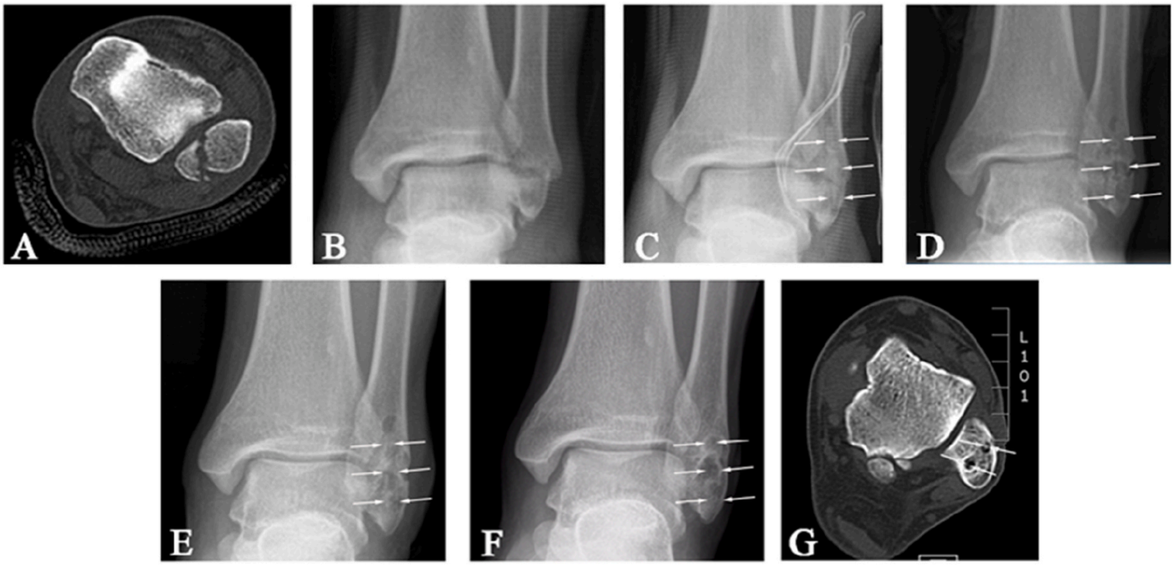

Fig. 5. Preoperative and postoperative radiographs of a 31-year-old man patient with left Lateral malleolar fracture. (A–B) image of the patient before operation; (C) the fracture was fixed with two bioabsorbable high pure Mg screws; (D) the fracture healed 24 weeks postoperative; (E) the radiolucent zone decreased significantly 92 weeks postoperative; (F–G) The degradation of high pure Mg screws were almost completed 152 weeks postoperative. The radiolucent zone was non-mineralized bone tissue surrounded by osteosclerotic zone.

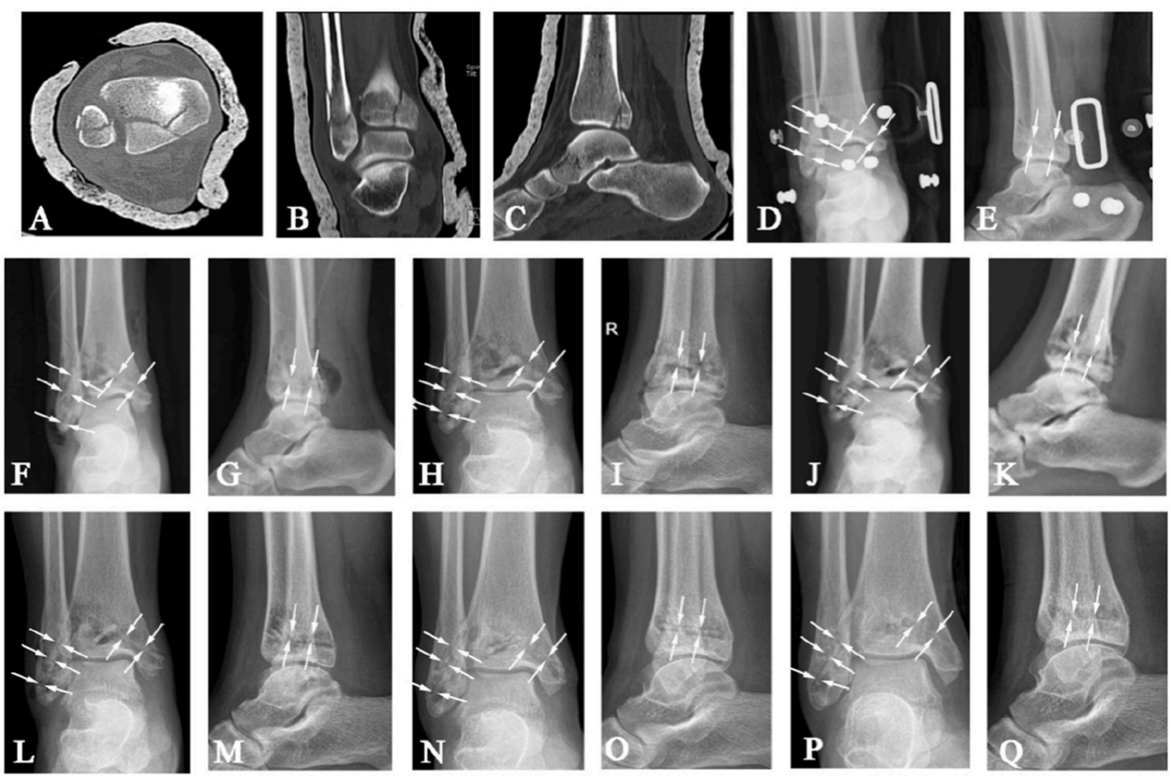

Fig. 6. Preoperative and postoperative radiographs of a 29-year-old female patient with a right trimalleolar fracture. (A–C) CT image of 29-year-old female patient preoperative; (D–E) the fracture fixed with four bioabsorbable high purity Mg screws; (F–G) At 2 weeks follow-up, the radiolucent zones were observed around the screws postoperative; (H–I) the radiolucent zones decreased gradually 4 weeks postoperative; (J–K) 12 weeks postoperative; (L–M) the ankle fracture was united, and the radiolucent zones was significant decrease at 12 weeks follow-up; (N–O) At 50-weeks follow-up, the radiolucent zones reduced significantly. (P–Q) The high purity Mg screws and the radiolucent zones were hardly noticeable at 91 weeks follow-up postoperative.

incisions and extensive exposure, increasing the risk of scarring or infection [34]. These plates and screws are always made of Ti alloy. The elastic modulus of Ti alloy is much higher than that of human bone tissue, which will lead to the occurrence of "stress shielding" [35]. Biodegradable high purity Mg screws had been used in preclinical cases in China for more than ten years and achieved satisfactory results in the fixation of the bone flap in the treatment of femoral head necrosis [36]. In this study, the Young's moduli of high purity Mg screws is 44.75 ± 0.66 GPa, which is much closer to that of human bone and provides a lower stress shielding than Ti alloy bone plates and screws.

Fig. 7. Preoperative and postoperative radiographs of a 67-year-old male patient with right ankle joint fracture. (A) The imaging examination before operation; (B) the day after the operation; (C) 5 weeks after operation; (D) 7 weeks after operation; (E) 88 weeks after operation; (F) Ti alloy screws and plates were removed 88 weeks after operation.

Fig. 8. Preoperative and postoperative radiographs of a 31-year-old female patient with right ankle joint fracture. (A) The imaging examination before operation; (B) The fracture fixed with Ti alloy screw-plate system the day after surgery; (C) The fracture had healed completely 52 weeks after operation and the fracture bone was reconstructed well; (D) the screws and plate were removed 73 weeks after surgery.

Bioabsorbable high purity Mg screws have the potential advantages of eliminating the need for removal and decreasing irritation caused by Ti alloy bone plates and screws. Mg ions could also promote osteogenesis and angiogenesis, while inhibiting osteoclast activity and inflammation [37]. In this study, FEA was performed on the ankle joint to simulate the implantation of one high purity Mg screws and analyze the stress distribution of the entire ankle joint after the implantation. It manifested that the initial strength of high purity Mg screws could effectively fix the ankle fracture. Therefore, a prospective study was conducted to compare the effect of the biodegradable high purity Mg screws and the Ti alloy plates and screws in the treatment of ankle fracture. To better investigate the efficacy of the high purity Mg screws compared with that of other existing techniques, different types of ankle fractures were included.

Considering Mg^{2+} would be released into the blood with degradation of high purity Mg screws, the blood Mg^{2+}concentrations were monitored 48 weeks postoperative. Results showed that the serum Mg^{2+} concentrations of all patients with different number of high purity screws fluctuated in the normal range during the following-up ($P < 0.05$). In our study, the inflammation index WBC, SAA and CRP in both groups started to decrease 3 days after the operation. All cases showed good wound healing without infection, which could be rated as Grade A 14 days after the operation. When interacted with body fluids after implantation, the high purity Mg screws would transform into Mg $(OH)_2$ and hydrogen (H_2) gas during degradation which would gradually be absorbed by the surrounding tissue. In previous studies, hydrogen played an important role in regulating gene expression, reducing oxidative stress, and inhibiting the expression of pro-inflammatory cytokines [35]. Studies have also shown that Mg^{2+} ions can induce the differentiation of mesenchymal stem cells (MSCs) into bone tissues, including bone and cartilage, which played an important role in preventing osteoarthritis [38–40]. In our study, there were no instances of aggravated osteoarthritis in the Mg group compared to Ti alloy group during three years' follow-up. Therefore, the high purity Mg screws might prevent traumatic arthritis to a certain extent when used in the treatment of ankle fractures.

In this study, we observed the fixation effects of high purity Mg screws compared to Ti alloy screws in the treatment of 24 patients with ankle fracture. The results showed that all the patients acquired good fracture alignment without delayed healing. The mean healing time was similar between the two groups. According to the VAS score, pain could be divided into different categorizes of pain-free, mild, moderate and severe, corresponding to scores of 0, 1–3, 4–6 and 7–10 respectively. The higher the score, the more severe the pain was. Postoperative functional recovery was evaluated by the ankle and hindfoot function score (AOFAS), which had a total score of 100 points, with ratings of excellent: 90–100 points; good: 75–89 points; acceptable. 50–74 points; poor: less than 50 points. In this study, 11 of the patients in the Mg group reported no evident pain at 12 weeks after surgery and 1 patient reported that the pain disappeared at 24 weeks after surgery in high purity Mg screws group. In Ti alloy group, one patient experienced continuous pain after surgery, and the pain symptoms disappeared after the removal of the implant. None of the patients in either group reported pain at the last follow-up. The ankle function improved gradually after operation in both groups. Consequently, the biodegradable high purity Mg screws achieved similar effect as Ti alloy screw-plate system in the treatment of ankle fractures.

In the high purity Mg screws group, slight radiolucent zones around the high purity Mg screws were observed under radiography post-operatively. The radiolucent zones began to appear after the high purity Mg screws implanted and reached the maximum at about 2 weeks after surgery. After that, the radiolucent zones shrank gradually as time prolonged. This might be related to the accumulation of corrosion products which slowed down the degradation of the high purity Mg screws. Once the formation rate was less than the diffusion rate of H_2, the radiolucent zone would decrease gradually [41]. At the final follow-up, the slight radiolucent zones could be observed in both the high purity Mg screws group and the Ti alloy group, which might be related to local osteodystrophy. In this study, the high purity Mg screws disappeared 116 ± 24.8 weeks after implantation when used for ankle fracture and the extraction operation were avoided. Although the mechanical properties of the high purity Mg screws would gradually decrease, none of the patient experienced infection, failure of internal fixation, malunion or other complications. The results showed that biodegradable high purity Mg screws could be effectively used in the clinical treatment of ankle fractures, ensuring safety and satisfactory bone healing. In our previous study, we had obtained favorable clinical outcomes by using biodegradable high purity Mg screws for femoral head necrosis and bone flap fixation. This study expanded the clinical application of biodegradable high purity Mg screws and applied them in the treatment of ankle fractures for the first time. To ensure the safety and effectiveness of treating ankle fractures with high purity Mg screws, all the patients were evaluated over a 36-months follow-up until the screws were decreased completely. However, there were also some limitations. Firstly, only 24 patients were enrolled in this study for security purposes and some types of ankle fractures were not concluded. Secondly, it is impossible to calculate the degradation rate of the high purity Mg screws accurately when applied for ankle fractures due to the lack of clinical data such as CT. Thirdly, because a large number of in vitro and in vivo studies have shown that Mg contributes to osteogenesis, we did not evaluate the bioactive function, such as healing enhancement of the high purity Mg screws when used for ankle fracture.

5. Conclusion

This study demonstrated the advantages of using biodegradable Mg screws for ankle fracture compared with Ti alloy plates and screws. Both groups experienced complete healing of ankle fractures without complications such as nonunion or delayed union. The high purity Mg screws degraded gradually after implantation in the body, eliminating the need for implant removal operations. This study makes biodegradable high purity Mg screws a promising alternative in orthopedic surgery.

Declaration of competing interest

The authors have no conflicts of interest relevant to this article.

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