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Original Article

Effect of a synthetic osteoconductive bone graft substitute with zeta potential control (geneX®ds) in the treatment of intertrochanteric fracture: A single center experience of 115 consecutive proximal femoral nail antirotations

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ABSTRACT

Introduction: Although various clinical applications of geneX®ds have been reported, no study has reported the clinical application of geneX®ds in osteoporotic hip fracture. The present study aimed to identify the clinical effect of the application of geneX®ds in elderly patients with intertrochanteric fracture treated using proximal femoral nail antirotation (PFNA).

Materials and methods: From March 2014 to October 2017, 233 patients with intertrochanteric fracture (65 men and 168 women) were enrolled in this study. All patients received surgical treatment using PFNA. Patients were classified into two groups: those in whom geneX®ds which is synthetic osteoconductive bone graft substitute with the unique property of Zeta Potential Control (ZPC®), was use, and those in whom it was not. We compared the preoperative details and surgical outcomes, including radiologic outcome (postoperative reduction, tip apex distance, sliding distance of the helical blade, union, and union time) and clinical outcomes (Harris Hip Score and the walking ability at the last follow-up) between the groups.

Results: In patients with unstable fracture who achieved anatomical or extramedullary type of reduction, the average sliding distance at 1, 3, and 12 months was 4.9 mm, 7.5 mmm and 8.1 mm in the geneX®ds group and 7.5 mm, 10.8 mm, and 12.1 mm in the no geneX®ds group, respectively. There were significant differences in the sliding distance at 1, 3, and 12 months between these two groups.

Conclusion: The use of this synthetic osteoconductive bone graft substitute with zeta potential control may have positive effect on the controlled sliding of the helical blade and the healing of intertrochanteric fracture.

1. Introduction

Proximal femoral nail antirotation (PFNA, Synthes, Paoli, Switzerland) has been wildly accepted as a good surgical option for the treatment of intertrochanteric fracture with osteoporosis [1–3]. However, the best available treatment for the osteoporotic intertrochanteric fracture is still a topic of debate, because relatively high rate of failures including loss of fixation, cut-out or cut through of the helical blade, excessive sliding, and nonunion are reported in unstable fractures [4–6]. Since these failures in unstable fractures are known to be associated with lack of an adequate posteromedial buttress to support compression and severe osteoporosis, the importance of anterior cortical apposition and an effort to augment the poor bone quality of osteoporotic patients with intertrochanteric fracture has been emphasized in many literature [7–9].

Previously some augmentation techniques including polymethylmethacrylate (PMMA) cement and resorbable calcium phosphate have been successfully used for structural augmentation of unstable intertrochanteric fracture [10–12]. However, these techniques have not gained wide acceptance or reported consistent surgical outcomes. GeneX®ds (Biocomposites, Wilmington, NC) is a

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recently developed resorbable, fully synthetic osteoconductive bone graft substitute that contains calcium sulfate and beta-tricalcium phosphate. It is engineered with the unique property of Zeta Potential Control (ZPC®), which provides the graft material with a controlled, reproducible, negative surface charge that attracts the key proteins and bone forming cells to its surface [13–15].

Although various clinical applications of geneX®ds have been reported, there has been no literature that has reported the clinical application of geneX®ds in osteoporotic hip fractures. Thus, the aim of the present study was to identify the clinical effect of the application of geneX®ds in elderly patients with intertrochanteric fracture treated using PFNA. We hypothesized that the application of geneX®ds would improve union rate and surgical outcomes and shorten the union time in elderly patients with intertrochanteric fractures.

2. Materials and methods

2.1. Study population and definitions

This study followed the guidelines of the Declaration of Helsinki and the guideline for Korean Good Clinical practice (KGCP), and institutional review board approval was obtained (H-1812-009-074). This retrospective cohort study was based on consecutively collected data from a data base in a tertiary university hospital. From March 2014 to October 2017, 315 patients underwent surgeries for the treatment of intertrochanteric fractures in the author's institution. The inclusion criteria were patients with low-energy hip fractures who received surgical treatment using PFNA. We excluded those patients who had follow-up for less than 6 months, were younger than 65 year old, had surgical treatment using long PFNA, and had hip fracture due to a high-energy injury including falling from a height, vehicle accident, and crushing injury (Fig. 1).

Clinically, a low-energy hip fracture is defined as a fracture that occurs as a result of a minimal trauma, such as a fall from a standing height or less. Radiologically, unstable fractures are defined as fractures that have a large posteromedial defect, lateral wall fracture, reverse oblique fracture, and fractures with subtrochanteric extension. However, all reverse oblique fractures and fractures with subtrochanteric extension were excluded in the present study because long PFNA was used for the treatment of these fractures [16–19]. The definition of tip apex distance (TAD) was adopted from Baumgaertner's definition which is the sum of distance between the tip of the helical blade and the apex of the femoral head, as measured on the anterior-posterior view and on the lateral view considering the radiographic magnification [20].

2.2. Surgical technique

All operations were performed with the patients in a supine position on a standard fracture table with traction under general or spinal anesthesia. Before internal fixation, closed reduction was carried out under fluoroscopic guidance. When the closed reduction was unacceptable, indirect reduction techniques using various instruments, including the long Kelly, Kidney clamp, and Hoffman retractor were applied. On a coronal fluoroscopic image, we tried to place the medial cortex of the proximal fragment anatomically or slightly medial to the medial cortex of the distal fragment. We regarded achieving anatomical reduction or mild extra-medullary type of reduction on Lorenz image as the most important factor to avoid fixation failure in unstable intertrochanteric fractures. When the intramedullary type of reduction was identified, we inserted the Kidney clamp into the fracture site to lift the proximal fragment anteriorly for anatomical or extramedullary type of reduction (Fig. 2). Anatomical or extramedullary type of reduction was considered as satisfactory reduction and intramedullary reduction was considered as unsatisfactory reduction [21,22]. PFNA was inserted according to the manufacturer's instruction through the standard lateral approach. Then, a guidewire was inserted in the center of the femoral head and reaming for the insertion of the helical blade was performed. After inserting the needle underneath the guidewire for injection of geneX®ds into the femoral head where the helical blade will be inserted and some part of the fracture site, 5 cc of geneX®ds was injected (Fig. 3). The helical blade was placed in the center within the femoral head, and the tip-apex distance was 25 mm or less. The lateral end of the helical blade was placed just lateral to the lateral cortex of the femur so as not to

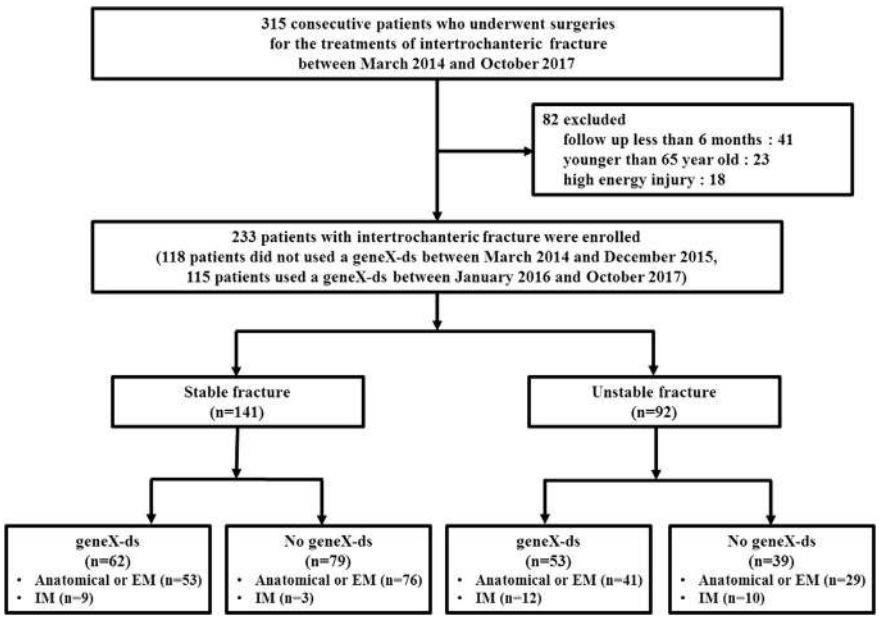

Fig. 1. Flow chart of the study.

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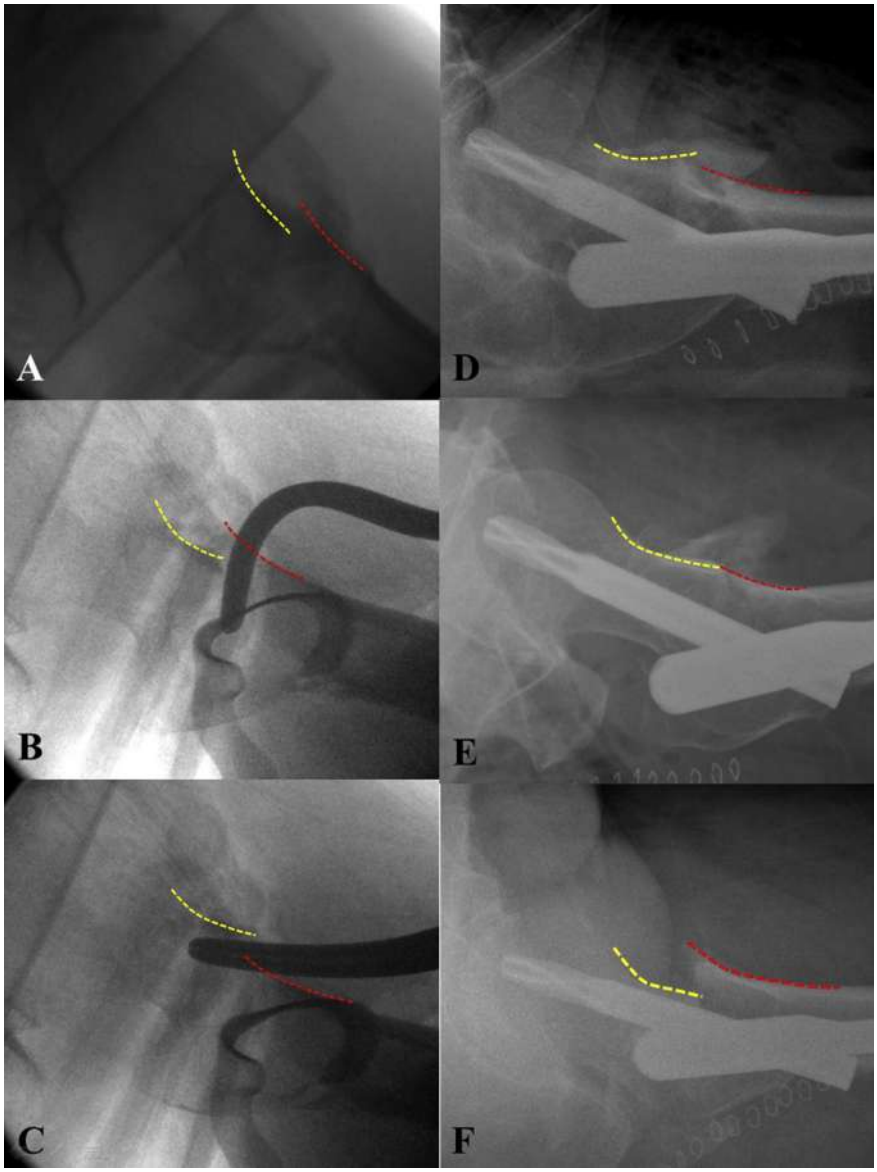

Fig. 2. (A) Intramedullary type of reduction. (B, C) Kidney clamp insertion into the fracture to lift the proximal fragment anteriorly. (D) Extramedullary type of reduction. (E) Anatomical reduction. (F) Intramedullary type of reduction.

hinder sliding of the helical blade according to Abram's concept [23]. Finally, a distal locking screw was inserted.

2.3. Assessment of outcome measures

The following data were collected to compare the preoperative details of elderly patients with intertrochanteric fracture: type of fracture (stable or unstable fracture), use of geneX®ds, sex, age, affected side, body mass index (BMI), bone mineral density (BMD; lumbar and femur), American society of Anesthesiologists (ASA) class, presence of lateral wall fracture, basicervical fracture, pre-injury mobility score, and follow-up period. All cases were classified according to the fracture type (stable and unstable fracture) and the use of geneX®ds and then each preoperative detail was compared.

Postoperative reduction, tip apex distance (TAD), sliding distance of the helical blade at 1, 3, and 12 months, union, and union time from the surgery were evaluated to assess radiologic outcomes. Postoperative reduction was classified into anatomical, extramedullary type, and intramedullary type. Facture union was defined as full, painless weight bearing with a bridging callus across at least three cortices on anteroposterior and lateral views of the femur [13]. We considered a fracture nonunion when a definite fracture gap could be seen at a minimum of 9 months after injury without visible, progressive signs of healing for 3 months. Fracture nonunion, cut-out or cut-through of the helical blade, and significant back-out or loosening of the helical blade without definite evidence of union were considered as failure. To minimize measurement errors, two orthopedic surgeons who did not participate in the operations independently measured the radiologic values and the averages of each value were used for the analyses.

Harris Hip Score and the walking ability at the last follow-up visit were evaluated to assess clinical outcomes. Walking ability was graded from 0 to 9 using the mobility score of Parker and Palmer, which reflects the sum of the ability to walk indoors and outdoors and to participate in social activities.

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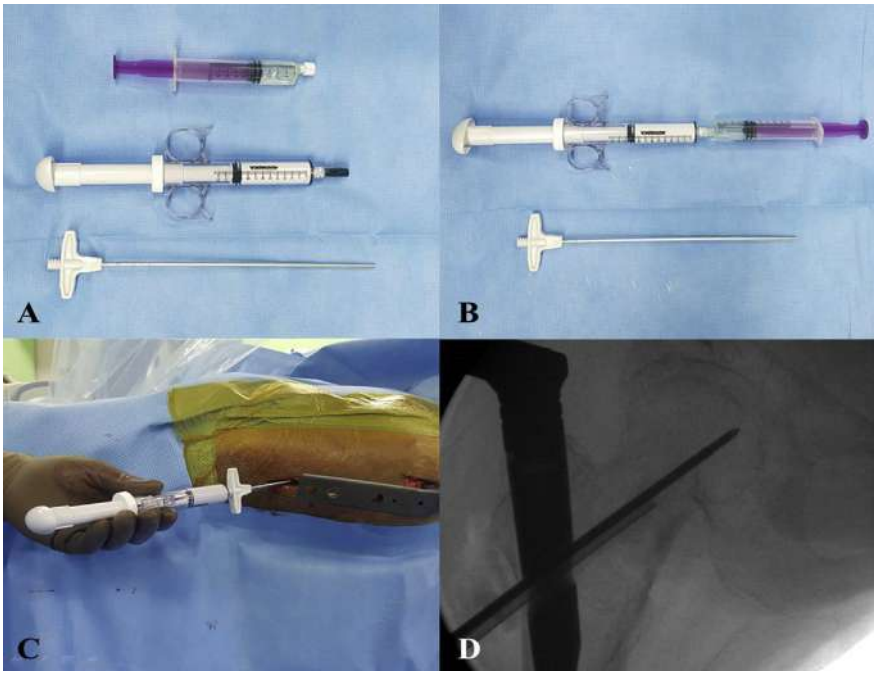

Fig. 3. (A) Preparation of geneX®ds injection. (B) Mixing the powder and the liquid. (C, D) 5 cc of geneX®ds injected into the femoral head where the helical blade will be inserted and some part of the fracture site through the guide wire.

2.4. Statistical analysis

We compared the preoperative details and surgical outcomes of the groups using Pearson's Chi-square test or Fisher's exact test for categorical variables, and the independent Student's test or Mann-Whitney U-test for continuous variables, where appropriate. Risk factors for the nonunion of an intertrochanteric fracture were identified using a multiple logistic regression model. The following covariates were included: age, sex, fracture type (stable or unstable), the use of geneX®ds, BMI, BMD (femur), ASA class, lateral wall involvement, basicervical fracture, preinjury mobility score, postoperative reduction, and TAD. The intra- and interobserver reproducibility of the LLD measurements was evaluated by the intra-rater correlation coefficient (ICCs). The results were interpreted as follows: >0.8 = almost perfect agreement, 0.7–0.8 = strong, 0.5–0.6 = moderate, 0.3–0.4 = fair, and 0–0.2 = poor. The SPSS software package (version 21.0; SPSS Inc, Chicago, IL, USA) was used for all statistical analyses. Statistical significance was set at $p < 0.05$.

3. Results

Two hundred thirty-three patients (65 men and 168 women) met the above criteria. Their mean age was 80.0 years (range; 66–94 years). There were 141 stable fractures and 92 unstable fractures. GeneX®ds was consecutively injected in 115 patients. The comparison of preoperative demographics between patients in whom geneX®ds was used and in whom it was not used is presented in Table 1. There was no significant difference in sex, age, affected side, BMI, BMD (L-spine, femur), ASA classification, lateral wall fracture, basicervical fracture, preinjury mobility score, and follow-up period between the two groups (Fig. 1).

Bone union was confirmed in 227 patients (97.4%) and the average union time in all patients enrolled in the present study was 18.7 weeks. Comparison of postoperative outcomes of all patients who used and did not use geneX®ds is shown in Table 2. There was no significant difference in postoperative reduction, TAD, sliding distance at 1, 3, and 12 months, HHS at the last follow up, mobility score at the last follow up, union, and union time between the patients with stable fracture in whom geneX®ds was used and in whom it was not. In the unstable fracture group, postoperative reduction, TAD, sliding distance, HHS at the last follow up, mobility score at the last follow up, union, and union time did not differ significantly either. However, the average sliding distance at 1, 3, and 12 months was 5.4 mm, 8.2 mm, and 9.1 mm in the geneX®ds group and 7.7 mm, 10.8 mm, and 12.4 mm in the no geneX®ds group, respectively, and significant differences in sliding distance at 1, 3, and 12 months were identified. Since there was no loosening of the helical blade in the femoral head in the union group, change of TAD in follow-up X-rays was not identified. In patients with unstable fractures who achieved anatomical or extramedullary type of reduction, the average sliding distance at 1, 3, and 12 months was 4.9 mm, 7.5 mm, and 8.1 mm in the geneX®ds group and 7.5 mm, 10.8 mm, and 12.1 mm in the no geneX®ds group, respectively. There were significant differences in the sliding distance at 1, 3, and 12 months between these two groups. However, regardless of postoperative reduction, there was no significant difference in sliding distance between the geneX®ds group and no genex®ds group in patients who achieved intramedullary type of reduction 1 (Table 3). Inter-rater correlation coefficient was 0.821 for TAD ($p < 0.001$), 0.920 for sliding distance at 1 month ($p < 0.001$), 0.916 for sliding distance at 3 months ($p < 0.001$), 0.902 for sliding distance for 12 months ($p < 0.001$), 1.000 for union ($p < 0.001$), and 0.812 for union time ($p < 0.001$).

The results of the unadjusted and adjusted logistic regression analyses are presented in Table 4. In the unadjusted models using univariate analysis, low BMD of the femur and intramedullary type of reduction were significantly associated with nonunion of intertrochanteric fractures (OR = 0.375; 95% CI = 0.177 to 0.796, OR = 51.333; 95% CI = 6.079 to 433.487, respectively). The adjusted model using multivariate logistic regression analysis

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Table 1
Comparison of preoperative demographics between all patients with intertrochanteric fracture who used and did not used a synthetic osteoconductive bone graft substitute with Zeta Potential (geneX®ds).

Variables	Stable fracture (n = 141)			Unstable fracture (n = 92)		
	geneX®ds	No geneX®ds	p-value	geneX®ds	No geneX®ds	p-value
Number (n, %)	62 (44.0)	79 (56.0)	–	53 (57.6)	39 (42.4)	–
Female (n, %)	46 (74.2)	57 (72.2)	0.786	35 (66.0)	30 (76.9)	0.257
Age (years)	80.1 ± 6.8 (67–93)	78.7 ± 5.9 (70–93)	0.180	81.0 ± 6.4 (66–94)	80.7 ± 5.8 (67–94)	0.817
Affected side (Rt.)	30 (48.4)	46 (58.2)	0.245	22 (41.5)	15 (38.5)	0.768
BMI (kg/m2)	22.2 ± 4.0 (12.9–37.8)	23.2 ± 4.8 (15.8–38.9)	0.202	22.6 ± 3.4 (16.9–31.6)	22.4 ± 3.0 (17.8–28.3)	0.790
BMD						
L-spine	−2.4 ± 1.3 (−4.6–1.0)	−2.8 ± 1.3 (−4.9–2.1)	0.226	−2.2 ± 1.6 (−5.8–2.0)	−2.2 ± 1.4 (−4.9–0.3)	0.917
Femur	−2.0 ± 1.3 (−5.9–2.7)	−2.7 ± 1.0 (−4.4–−0.6)	0.456	−2.8 ± 1.2 (−5.5–0.4)	−3.1 ± 0.9 (−4.9–−1.4)	0.272
ASA classification						
I, II	26 (41.9)	43 (54.4)		17 (32.1)	11 (28.2)	
III, IV	36 (58.1)	36 (45.6)	0.141	36 (67.9)	28 (71.8)	0.690
Lateral wall involvement (n, %)	1 (1.6)	0 (0.0)	0.257	11 (20.8)	12 (30.8)	0.273
Basicervical fracture (n, %)	16 (25.8)	13 (16.5)	0.173	0 (0.0)	0 (0.0)	–
Preinjury mobility score	7.7 ± 1.5 (4–9)	7.7 ± 1.5 (4–9)	0.992	7.6 ± 1.6 (3–9)	7.6 ± 1.6 (4–9)	0.894
Follow-up period (months)	10.5 ± 4.0 (6–25)	11.8 ± 7.2 (6–24)	0.218	9.6 ± 4.2 (6–23)	11.7 ± 6.6 (6–24)	0.060

Values are presented as mean ± standard deviation (range), or number (%).
BMI; Body mass index, BMD; Bone mineral density, ASA; American Society of Anesthesiologists.

Table 2
Comparison of postoperative outcomes of all patients with intertrochanteric fracture who used and did not used a synthetic osteoconductive bone graft substitute with Zeta Potential (geneX®ds).

Variables	Stable fracture (n = 141)			Unstable fracture (n = 92)		
	geneX®ds (n = 62)	No geneX®ds (n = 79)	p-value	geneX®ds (n = 53)	No geneX®ds (n = 39)	p-value
Postop. reduction (n, %)						
Anatomical or EM	54 (87.1)	71 (89.9)		41 (77.4)	29 (74.4)	
IM	8 (12.9)	8 (10.1)	0.606	12 (22.6)	10 (25.6)	0.464
TAD (mm)	19.3 ± 3.9 (13–26)	18.8 ± 3.5 (13–27)	0.497	18.3 ± 2.5 (14–23)	18.0 ± 2.3 (13–21)	0.584
Sliding distance (mm)						
At 1 month	3.7 ± 3.8 (0–14)	3.9 ± 3.8 (0–15)	0.693	5.4 ± 3.8 (0–16)	7.7 ± 4.2 (0–16)	0.008
At 3 month	5.7 ± 5.3 (0–24)	5.7 ± 3.6 (2–16)	0.950	8.2 ± 4.8 (2–20)	10.8 ± 5.8 (2–30)	0.020
At 12 month	6.7 ± 6.6 (0–34)	7.4 ± 4.5 (3–28)	0.471	9.1 ± 5.9 (2–24)	12.4 ± 6.6 (2–32)	0.013
HHS at the last f/u	82.2 ± 10.5 (61–98)	84.2 ± 8.7 (62–95)	0.214	78.1 ± 9.9 (52–95)	77.8 ± 12.0 (52–95)	0.920
Parker and Palmer mobility score at the last f/u	7.0 ± 1.7 (4–9)	7.3 ± 1.8 (3–9)	0.407	6.5 ± 1.6 (3–9)	6.5 ± 1.8 (3–9)	0.811
Union (n, %)	61 (98.4)	77.9 (98.7)	0.863	52 (98.1)	36 (92.3)	0.177
Union time (weeks)	16.2 ± 3.9 (12–24)	16.1 ± 5.3 (12–32)	0.872	19.1 ± 4.8 (12–36)	21.0 ± 5.4 (12–32)	0.122

Values are presented as mean ± standard deviation (range), or number (%).
EM; Extramedullary, IM; Intramedullary, TAD; Tip apex distance, HHS; Harris hip score.

Table 3
Comparison of sliding distance of all patients with intertrochanteric fracture who used and did not used a synthetic osteoconductive bone graft substitute with Zeta Potential (geneX®ds).

Sliding distance (mm)	Stable fracture (n = 141)			Unstable fracture (n = 92)		
	geneX®ds (n = 62)	No geneX®ds (n = 79)	p-value	geneX®ds (n = 53)	No geneX®ds (n = 39)	p-value
POD 1 month						
Anatomical or EM	2.4 ± 2.4 (0–10)	2.1 ± 2.1 (0–10)	0.522	4.9 ± 3.7 (0–16)	7.5 ± 4.4 (0–16)	0.008
IM	7.6 ± 3.9 (3–12)	12.0 ± 3.0 (9–15)	0.105	7.3 ± 4.0 (3–14)	9.4 ± 4.1 (3–14)	0.242
POD 3 month						
Anatomical or EM	3.9 ± 3.2 (0–12)	3.9 ± 2.7 (0–12)	0.429	7.5 ± 4.5 (2–20)	10.8 ± 6.2 (2–30)	0.013
IM	10.7 ± 3.4 (7–16)	14.0. ± 2.0 (12–16)	0.149	10.8 ± 5.2 (3–18)	12.1 ± 5.0 (5–18)	0.541
POD 12 month						
Anatomical or EM	4.4 ± 3.5 (0–13)	4.8 ± 3.4 (0–13)	0.444	8.1 ± 5.4 (2–23)	12.1 ± 6.7 (2–32)	0.008
IM	12.9 ± 6.1 (7–32)	18.0 ± 6.1 (14–25)	0.331	12.3 ± 4.7 (3–24)	14.4 ± 7.0 (5–24)	0.474

Values are presented as mean ± standard deviation (range).
POD; postoperative day, EM; Extramedullary, IM; Intramedullary.

showed that a low BMD of the femur and intramedullary type of reduction were significantly associated with nonunion of intertrochanteric fractures (OR = 6.565; 95% CI = 1.694 to 25.441, OR = 0.008; 95% CI = 0.000 to 0.155, respectively) Significant associations between nonunion of intertrochanteric fractures and the use of geneX®ds were not identified in both statistical analyses.

4. Discussion

The purpose of this study was to assess the clinical effects of the application of geneX®dss which is a recently developed resorbable, fully synthetic osteoconductive bone graft substitute, in elderly patients with intertrochanteric fractures treated with a PFNA. We compared the clinical outcomes between 115 consecutive patients

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Table 4
Unadjusted and adjusted logistic regression analysis for nonunion of intertrochanteric fracture.

Variables	No.	No. of nonunion (%)	Univariate		Multivariate	
			Unadjusted Odds Ratio (95%CI)	P value	Adjusted Odds Ratio (95% CI)	P value
Age	–	–	1.073 (0.958–1.202)	0.223	–	–
Sex						
Male	78	1 (1.3)	1 (reference)			
Female	155	7 (4.5)	3.642 (0.440–30.139)	0.231	–	–
Type of fracture						
Stable fracture	141	2 (1.4)	1 (reference)			
Unstable fracture	92	6 (6.5)	4.849 (0.957–24.569)	0.057	–	–
Use of geneX-ds						
No geneX-ds	118	6 (5.4)	1 (reference)			
geneX-ds	115	2 (1.7)	0.181 (0.065–1.672)	0.181	–	–
BMI (kg/m2)	–	–	0.1009 (0.850–1.198)	0.920	–	–
BMD (Femur)	–	–	0.375 (0.177–0.796)	0.011	0.241 (0.087–0.664)	0.006
ASA class						
ASA I or II	97	2 (2.1)	1 (reference)			
ASA III or IV	136	6 (4.4)	2.192 (0.433–11.100)	0.343	–	–
Lateral wall fracture						
No lateral fracture	209	6 (2.8)	1 (reference)			
Lateral wall fracture	24	2 (8.3)	3.076 (0.585–16.171)	0.185	–	–
Basicervical fracture						
No basicervical fracture	204	6 (2.9)	1 (reference)			
Basicervical fracture	29	2 (6.9)	2.444 (0.469–12.729)	0.288	–	–
Pre-injury mobility score	–	–	0.136 (0.506–1.097)	0.136	–	–
Postoperative reduction						
Anatomical or EM	199	1 (0.5)	1 (reference)		1 (reference)	
Intramedullary	34	7 (20.6)	51.333 (6.079–433.487)	<0.001	94.016 (8.541–1034.857)	<0.001
TAD	–	–	0.890 (0.696–1.138)	0.352	–	–

Values are presented as mean ± standard deviation (range), or number (%).
BMI; Body mass index, BMD; Bone mineral density, ASA; American Society of Anesthesiologists, EM; Extramedullary.

who were treated with a PFNA in combination with geneX®ds and 118 patients who were treated with PFNA alone. BMD and postoperative reduction were independent risk factors associated with nonunion in this study and the clinical outcomes did not show the evidence that geneX®ds could improve the rate of union and clinical outcomes, and shorten the union time. However, the sliding distance was significantly shorter in patients with unstable fractures when the anatomical or extramedullary type of postoperative reduction was achieved.

It has been more than a decade since the injectable bone substitutes were first introduced for the surgical treatment of orthopedic trauma and various bone substitutes have been widely used over recent years. Many reports have shown that they can be useful for the augmentation of metaphyseal fractures when a bone defect is present and randomized studies have verified the clinical effect of these, especially in tibial plateau fractures [24–26]. Mattsson et al. [11] demonstrated that a sliding screw system with augmentation using calcium phosphate for the surgical treatment of trochanteric fracture was significantly more stable and the patients had less pain, and the quality-of-life variables were more favorable compared with controls in their prospective, randomized multicenter study. However, information on how and when these bone substitutes might be clinically effective is still limited.

GeneX®ds was introduced as a synthetic bone graft material with a unique bi-phasic composition manufactured through a proprietary process ZPC® (Zeta Potential Control), which confers the product with a reproducible negative surface charge. This property stimulates bone cell activity, accelerating bone formation and fusion by harnessing key proteins, directing osteoblast adhesion, and proliferation for rapid osteogenesis [14,27]. Zhang et al. [28] and Yang et al. [29] reported that geneX®ds is a useful alternative to PMMA in vertebroplasty for vertebral compression fractures in a calf and a sheep model, respectively. Zhan et al. [30] reported good biocompatibility, strong bone inducibility, little loss of vertebrae height and Cobb angle, and satisfactory results without any complication after using geneX®ds for vertebroplasty in 38 patients. Despite the unique property of geneX®ds regarding its zeta potential control and related expectation about improvement of new bone formation, there is no clinical study related to the use of geneX®ds in hip fracture surgery.

Against the author's hypothesis at the beginning of the study, we could not demonstrate that geneX®ds improved the union rate and shortened the union time in elderly patients with intertrochanteric fractures. Further, there was a small difference in the average sliding distance and the range of sliding distances in patients with unstable fractures in both groups was similar, even though significant difference between the two groups was identified. However, authors do not believe that these results simply showed that there is no positive effect regarding fracture healing in patients with intertrochanteric fractures. Many previous studies have reported that surgical outcomes of intertrochanteric fractures improved dramatically since the newly designed PFNA and helical blade were introduced. While the failures requiring reoperation such as a cutting out of the femoral head were reported to be as high as up to 16% with screw devices [31,32], failures were reported to be around just 6% or less with PFNA and the present study also showed only 6 cases (2.6%) of failure after surgery. This means that the implant factor related to improved surgical outcomes became much stronger than in the past to demonstrate significant improvement regarding bone union after the surgical treatment of intertrochanteric fractures. Thus, we think that further study with larger sample size should be needed to evaluate the clinical effect of geneX®ds more specifically.

Another important factor related to successful outcome after intertrochanteric fracture surgery is postoperative reduction, which multiple regression analysis in the present study already showed. Unstable type of intertrochanteric fractures, which have posteromedial defects are known to have a higher possibility of failure after surgery when anatomical or extramedullary type of reduction in Lorenz view cannot be achieved because there of the

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lack of anterior cortical bone to bone buttress effect. Our study showed that sliding distance at 1, 3, and 12 months follow-up in the geneX®ds group was significantly shorter than that in the no geneX®ds group when anatomical or extramedullary reduction was achieved postoperatively. However, when intramedullary type of reduction was achieved, there was no difference in sliding distance regardless of the use the geneX®ds. We believe that this may be because postoperative reduction was a strong factor associated with surgical outcome, and it would be difficult to identify the positive effect of geneX®ds under the poor postoperative reduction. We could not find any difference in sliding distance in patients with stable fractures either. We think that this is because good bone to bone contact plays more important role than geneX®ds in the bone healing process. Nevertheless, we believe that the fact that geneX®ds decreased the sliding distance at 1, 3, and 12 months in unstable fractures with good postoperative reduction in the present study shows that it may have positive potential for improvement of bone healing.

Previous researchers have been worried about the complications of geneX®ds. Friesenbichler et al. [33] reported that 5 of the 31 patients (16%) had complications, including 3 cases of sterile inflammation adjacent to the geneX®ds and 2 cases of delayed wound healing with local pain after surgery. Based on their experience, they suggested that this type of bone substitute should not be used in the treatment of bony defects. However, Phillip et al. commented on this report via a letter to the editor stating that their data appear presumptuous, and do not support that strength of the outcomes and that geneX®ds is cleared as a Class II medical device by the FDA, CE marked in accordance with the Medical Devices Directive 93/42/EEC, and complies with all safety and biocompatibility requirements. Thus, they suggested that geneX®ds is a safe and effective bone void filler when used in accordance with their Instructions For Use [34]. In the present study, any complications, including infection, sterile inflammation, delayed wound healing, wound dehiscence, and local pain related to geneX®ds were not identified.

There are some limitations in the present study. First, this was a retrospective study. However, we conducted a comparative study based on prospectively collected data of 115 consecutive patients treated by a single experienced surgeon in single institute, with a larger sample size that used by previous studies. In particular, to the best of our knowledge, this is the first study regarding the effect of geneX®ds on the outcome of intertrochanteric fracture surgery. Second, 6 cases of failure seem to be too little to assess the clinical effect of geneX®ds on fracture healing of intertrochanteric fractures. In addition, the numbers of patient who achieved intramedullary type of reduction in both groups were too small to conduct a comparative analysis, even though the non-parametric analysis showed that there was no significant difference between the two groups. As mentioned earlier, we believe that the low rate of surgical failure and small number of poor reduction case can be associated with improvement of recent surgical implants and surgeon's effort to achieve satisfactory reduction of fractures. Thus, further clinical studies with a larger sample size are required to show the advantage of geneX®ds for the treatment of intertrochanteric fractures. Third, there could be errors in the measurement of the sliding distance. To minimize these errors, two orthopedic surgeons who had never participated in surgeries independently measured the sliding distance and the average sliding distance of two measurements was used for analysis. The inter-rater correlation coefficient also showed good or excellent agreement. Fourth, we could not consider the cost benefit of geneX®ds. Since we only focused on radiological and clinical effects of geneX®ds in the present study, further study regarding the cost effectiveness of geneX®ds is needed.

5. Conclusion

Although the findings of the present study did not show that geneX®ds can improve the union rate and shorten the union time in patients with intertrochanteric fractures, geneX®ds decreased the sliding distance in unstable fractures when good postoperative reduction was achieved. Our findings suggest that the use of a synthetic osteoconductive bone graft substitute with zeta potential control may have a positive effect on the controlled sliding of the helical blade and the fracture healing of intertrochanteric fractures.

Conflict of interest

None.

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