의학석사 학위논문

골수내정 교체 및 보강 금속판을 이용한 비정형 대퇴골 골절 수술 후 불유합의 치료

Management of atypical femoral fracture nonunion using nail exchange with augmentative plate

울 산 대 학 교 대 학 원

의 학 과

김 도 헌

골수내정 교체 및 보강 금속판을 이용한
비정형 대퇴골 골절 수술 후 불유합의 치료

지도교수 김 지 완

이 논문을 의학석사 학위논문으로 제출함

2024 년 8 월

울 산 대 학 교 대 학 원
의 학 과
김 도 헌

김도헌의 의학석사 학위논문을 인준함

심사위원 이 범 식 인

심사위원 김 지 완 인

심사위원 김 철 호 인

울 산 대 학 교 대 학 원

2024 년 8 월

영문요약

Background

Management of nonunion in atypical femoral fractures (AFF) poses significant challenges. This study investigates the outcomes of nail exchange and augmentative plating in treating AFF nonunion, aiming to define effective management strategies.

Methods

A retrospective analysis was conducted on 10 female patients treated for AFF nonunion with nail exchange and augmentative plating at a single center from January 2018 to December 2022. Criteria for exchange nailing included broken nails or varus malreduction > 5 degrees, while augmentative plating targeted cases with mechanical instability shown by peri-implant X-ray loosening signs. Preoperative bone turnover markers (BTMs) were evaluated to measure bone remodeling suppression, with surgical techniques focusing on fracture reduction, fixation stability, and addressing biological impairment. The effectiveness of screw fixation in plating measured by the number of cortices purchased by the screw, malalignment correction via neck-shaft angle (NSA) adjustments, and improvements in ambulatory function using the Koval score were key outcome measures.

Results

The combined surgical approach demonstrated significant success, achieving bone union in all 10 patients within an average timeframe of 21.4± 7.4 weeks. A notable observation across all cases was the prevalence of loosening signs, indicative of the mechanical instability challenges inherent in AFF nonunion. Mechanical stability was enhanced by securing an average of 4.8±3.2 and 4.6±2.5 cortices in proximal and distal fragments, respectively, through augmentative plating. Among the cases, six exhibited varus malalignment which was successfully corrected, bringing postoperative NSA in line

with the contralateral side. Additionally, the analysis revealed that in most patients not using bisphosphonate or denosumab, preoperative BTMs were normalized, suggesting that suppression of bone remodeling, a concern with long-term antiresorptive therapy, could be recovered prior to surgery. The Koval score decreased from an average of 4.2 preoperatively to 1.6 one year post-surgery, indicating a considerable recovery in walking ability.

Conclusion

Correcting malalignment and employing augmentative plating for rigid fixation proved highly effective in treating AFF nonunion, achieving notable success in bone union. This strategy is critical for managing complex cases, showcasing its potential as a key treatment modality.

차 례

서론

Osteoporosis is a disease characterized by low bone mass and microarchitectural deterioration of bone tissue, leading to enhanced bone fragility and a consequent increase in fracture risk, as defined by the WHO. Osteoporosis is a major health problem in the elderly population. It poses a serious concern due to its association with an increased risk of fractures, typically involving the wrist, vertebrae, and hip. Among these, hip fractures are particularly concerning given their high morbidity, mortality, and consequent high cost to medical services.

Normal bone turnover involves a balance of bone formation (osteoblasts creating bone) and bone resorption (osteoclasts destroying bone); however, an imbalance (when bone resorption exceeds bone formation) can lead to bone loss and potential fractures

Osteoporosis medications that increase bone formation (anabolic agents) or reduce bone resorption (anti-resorptive agents) have been developed and are in use (Table 1).

Table 1. Type of osteoporosis medication

Type	Mechanism of action	Drugs (Route)
Bisphosphonate	Activated osteoclasts dissolve bisphosphonate-laden hydroxyapatite crystals during bone resorption, leading to the ingestion of bisphosphonates. Impaired lipid synthesis in osteoclasts subsequently promotes their apoptosis	Alendronate (Oral) Ibandronate (Oral, IV) Risedronate (Oral) Zoledronic acid (IV)
RANK-L inhibitors	A monoclonal antibody, binds to RANK-L, thereby preventing its interaction with the RANK receptor on osteoclasts. This action reduces the formation and activity of osteoclasts	Denosumab (SC)
SERMs	Mimics the natural effects of estrogen, gradually reversing resorption of bone that occurs after menopause	Raloxifene (Oral) Bazedoxifene (Oral)
Parathyroid hormone analog	Intermittent exposure to PTH activates osteoblasts more than osteoclasts, resulting in a net increase in new bone formation	Teriparatide (SC)
Anti-sclerostin antibody	A humanized monoclonal antibody that targets and inhibits sclerostin, a negative regulator of bone formation, increasing bone formation and decreasing bone resorption	Romosozumab (SC)

Among them, bisphosphonate and denosumab have been widely used as pivotal therapeutic agents in the management of osteoporosis.[1, 2] There is significant evidence that both drugs effectively increase bone mineral density (BMD) and reduce the incidence of fractures associated with osteoporosis.[3, 4] However, atypical femoral fractures have been reported following long-term use of bisphosphonate (BP) and denosumab.[5-7] Oversuppression of bone turnover may inhibit the bone remodeling process, leading to the accumulation of trabecular microfractures and weakening of bone strength. Although the treatment of atypical femoral fractures with full-length intramedullary cephalomedullary nail has been proposed, complications such as delayed union and nonunion have been reported, leading to unsatisfactory outcomes.[8-10] The complex pathophysiology underlying AFF nonunion, possibly stemming from suppressed bone remodeling and microdamage accumulation, underscores the intricacies of managing these fractures.

Recently, evidence regarding the treatment approach for atypical femoral fracture nonunion is scarce and limited[11-13] While a case-control study has documented the use of blade plate in revision surgery, [12] research utilizing nail exchange with augmentative plates remains scarce, according to current knowledge. This study aims to shed light on the treatment of AFF nonunion using nail exchange and augmentative plates, intending to contribute valuable clinical insights into effective management strategies for this challenging condition.

연구방법

The study design and protocol were approved by our institutional review board, and informed consent was waived. The author retrospectively reviewed medical records of patients who underwent revision osteosynthesis for atypical femoral fracture nonunion at Asan Medical Center between January 2018 and December 2022. Initially, 12 patients were considered for inclusion; however 2 patients who underwent revision surgery with a blade plate were subsequently excluded, resulting in a total of 10 patients being included in the study. All patients were female and had been referred from other hospitals following the failure of their initial surgical treatments.

The author collected demographic data including age, gender, body mass index (BMI), Charlson Comorbidity Index (CCI)[14], and ambulatory function assessed by Koval score[15] (Table 2)

Table 2. Koval score

Grade	Performance status
1	Independent community ambulator
2	Community ambulator with cane
3	Community ambulator with walker/crutches
4	Independent household ambulator
5	Household ambulator with cane
6	Household ambulator with walker/crutches
7	Nonfunctional ambulator

Patient characteristics including BMD, and BP or denosumab history, along with its duration were identified. Long-term treatment was defined as receiving treatment for over three years, as previously described.[16] The author also investigated the number and the specifics of the initial osteosynthesis surgeries undertaken at referring hospitals before the patients were admitted to our institution.

Upon reviewing the initial radiographic images acquired before our surgical intervention, the researcher confirmed that all fractures conformed to the 2013 American Society for Bone and Mineral Research (ASBMR) Task Force criteria for atypical femur fractures(Table 3).[17] These criteria include characteristic radiological features such as a transverse or short oblique fracture line, a medial spike, focal lateral cortical thickening, and no or minimal comminution. All fractures were subtrochanteric fractures, located proximal to or within 5 cm distal to the lesser trochanter, and resulted from minimal trauma, defined as a slip, or fall from a standing height or less.[18]

Table 3. Major and minor features for diagnosing atypical femoral fractures

All major features, accompanied by non or some of the minor features, are required to diagnose atypical femoral fractures.

Major features	**Minor features**
No history of trauma, or associated with low-energy trauma	Localized periosteal thickening of the lateral cortex
Fracture located anywhere from distal to the lesser to proximal to the supracondylar area	Generalized thickening of the femoral cortices
Transverse or short oblique fracture configuration	Prodromal symptoms
Noncomminuted fracture	May be associated with bilateral fractures or symptoms
Medial spike in complete fractures; incomplete fractures involve only the lateral cortex	Evidence of delayed fracture healing
	Comorbid conditions or the use of some medications*

* Examples of comorbid conditions and medications are rheumatoid arthritis, rickets and osteomalacia, renal osteodystrophy, and the use of bisphosphonates, glucocorticoids, or proton pump inhibitors.

The recorded factors of revision surgeries included operating time, the number of augmentative plates used, the number of cortices engaged by screws in each proximal and distal fragment, whether exchange nailing was performed, and the type of bone graft used; iliac bone harvest, bone material collected during reaming, bone morphogenic protein 2 (BMP2, Norvosis, CGBio, Seoul, Republic of Korea) or a combination thereof.

Surgical procedures

In cases of nonunion accompanied by a broken nail or a malreduction indicated by a varus deformity exceeding 5 degrees, exchange nailing with correction was performed (Fig. 1). After removal of the previous nail, debridement and decortication of the nonunion site were performed. A new entry point with 'piriformis fossa' was guided and reamed, with or without reduction of the mal-alignment with bone holding clamps. Sometimes, creating a new piriformis entry allowed for automatic correction of 'varus malalignment'. Instances showing loosening or pull-out of proximal or distal screws were addressed by repositioning or reinserting to ensure secure fixation. The femur was subjected to maximal intramedullary reaming to accommodate the thickest nail feasible. In one case, where the removal of existing screws in the femoral head resulted in an excessively large space, raising concerns about the fixation strength of the revision hip screw or blade, cement augmentation was applied (Fig. 2).

For cases with minimal or no deformity, augmentative plating was performed without the need for exchange nailing (Fig. 3). In cases where nonunion demonstrated mechanical instability with signs of loosening on the x-ray, augmentative plating was conducted.[19] This procedure involved the use of one or two 3.5mm locking compression plates (DePuy Synthes®, West Chester, PA, USA) via a single lateral incision made at the level of the nonunion. Plates of adequate length, each with at least three holes for each fragment, were selected and bent to match the contour of the proximal femur. An incision starting at the tip of the greater trochanter was made proximally and extended distally. The tensor fascia lata was incised, followed by an L-shaped cut in the vastus lateralis, which was then elevated. The insertion point for the plate, located 3-4 cm proximal to the vastus ridge, was pinpointed. A distal skin incision aligned with the plate's distal end was then made, and both the fascia lata and vastus lateralis were gently separated. Depending on the existing nail's location, cortical or locking screws with feasible fixation angle were inserted, either unicortically or bicortically, maximizing the number possible.

Although most patients were elderly, autologous iliac bone grafting was performed, it should be noted that in the author's country, the Reamer/Irrigator/Aspirator (RIA) system, an alternative device for bone harvesting, is not approved for use. However, in cases with multiple comorbidities or a prior history of ipsilateral iliac bone grafting, bone debris generated during revision reaming was supplemented with BMP-2. In instances where nail exchange was not carried out, BMP-2 was solely utilized for bone grafting (Fig. 4).

Medical treatment and evaluation of bone turnover marker

After the initial consultation at the outpatient clinic for revision surgery, patients immediately discontinued the use of BP or denosumab. Supplementation with Ca and vitamin D was continued or started. Following the revision surgery, teriparatide was recommended for patients with osteoporosis, except in those with a history of cancer or chronic renal disease, or in cases immediately following the discontinuation of denosumab. This decision was made because transitioning from denosumab to teriparatide significantly declined BMD in the proximal femur and increase of bone turnover markers. This effect is thought to be related to the 'rebound phenomenon of multiple spine fractures'.[20]

Bone turnover markers were measured at the time of admission for revision surgery. These included serum Calcium (Ca, normal range 8.2 to 10.8 mg/dL), Phosphorus (P, normal range 2.5 to 4.5 mg/dL), 25(OH) vitamin-D (Vit. D, normal range 30 to 48.1 ng/mL), parathyroid hormone (PTH, normal range 8 to 76 pg/mL), C-terminal telopeptide (CTX, as bone resorption marker, normal range 0.177 to 1.015 ng/mL), and osteocalcin (OC, as bone formation marker, normal range 15 to 46 ng/mL).

Rehabilitation protocol

Wheelchair ambulation commenced on the first day postopertively. By the following day, patients were encouraged to engage in weight-bearing ambulation as tolerated. However, ambulation was postponed to 3 or 4 days postoperation due to pain in cases where an iliac bone harvest was performed. Routine follow-up appointments with radiographic evaluation were scheduled at 4, 12, and 24 weeks after surgery, with subsequent appointments every 8 weeks until bone union was confirmed.

Radiologic evaluation

The radiological variables were documented, including pre-operative neck-shaft angle (NSA) (Fig. 5),[21] post-operative NSA, contralateral naive NSA, anterior and lateral fracture gaps of the nonunion site, signs of loosening such as broken nail, a hollow sign around the nail and loosening of proximal or distal screws. Additionally, the time to union were recorded. Bone union was defined by the formation of bony bridges involving three or four cortices on anteroposterior (AP) and lateral radiographs.[22]

No patients were lost to follow-up or deceased before a determination regarding the fracture union was made.

결과

The patient demographics are summarized as presented in Table 4. The average age of the 10 women patients was 73 years (range, 60-83), with an average CCI of 4.3 (range, 3-6). The mean follow-up period was 19.5 months (range, 12-33). At the time of diagnosis with AFF, seven out of ten patients had been on long-term antiresorptive osteoporosis medication: six were using BP and one was on denosumab, with an average medication duration of 6.5 years (range, 3-10 years). Of the three patients without a history of osteoporosis medication, one was treated with steroids and methotrexate for 10 years for rheumatoid arthritis (Case 10).

The choice of osteoporosis medication post-AFF diagnosis was determined by the physicians at the initial treating hospital, while the selection of osteoporosis medication following revision osteosynthesis was performed at a referred hospital. Among the six patients diagnosed with AFF while on BP, three switched to teriparatide upon discontinuation of BP and continued teriparatide after revision osteosynthesis. Two patients, due to economic reasons, refused teriparatide and only stopped BP; one of these later started teriparatide injections after the revision osteosynthesis. The remaining patient on BP switched to denosumab, not recommended by the ASBMR, and was subsequently switched to a selective estrogen receptor modulator (SERM) after revision osteosynthesis at our institution.

The patient receiving denosumab treatment at the time of AFF diagnosis continued the medication for one additional dose (lasting six months) post-diagnosis, then halted it. Post-revision osteosynthesis, and after a sufficient wash-out period of denosumab, teriparatide was initiated as the treatment.

Of the three patients without a history of osteoporosis treatment at the time of AFF diagnosis, one received teriparatide up to and following the secondary surgery, while another, not qualifying for osteoporosis, did not receive any osteoporosis medication. However, the last patient began BP treatment after AFF surgery and was switched to teriparatide on revision osteosynthesis.

The average vitamin D level was 28.2 ng/mL (range, 17.3-46.9), with two patients exhibiting levels below 20 ng/mL, indicative of deficiency and the other three had insufficiency (20-30 ng/mL) (Table 5). The mean osteocalcin level was measured at 19.4 ng/mL (range, 2.3-41.5), with four out of eight patients showing levels below the normal range, including two who continued bisphosphonate or denosumab treatment post-diagnosis of AFF. The average CTX level was observed to be 0.228 ng/mL (range, 0.09-0.406), with three patients presenting levels beneath the normal threshold, coincidentally the same individuals who persisted with bisphosphonate or denosumab use.

Among the 10 patients who underwent revision surgery, 8 received their second surgery, while the remaining 2 patients, having undergone two unsuccessful surgeries elsewhere, were referred to us for a third surgery. One patient underwent surgery with a blade plate at another institution, while nine received long intramedullary nailing at other institutions before being referred to our hospital. In proximal fixation, a cephalomedullary screw or blade was used in five cases, of which two had screws that were too short, resulting in a tip-apex distance (TAD) of more than 25mm (Case 1, 5). Two cases were secured with two reconstruction screws, and another used two standard interlocking screws. The last one case did not include a proximal screw during prophylactic nailing for an incomplete fracture, leading to varus collapse, progression to a complete fracture, and eventually nonunion. The average time from the surgery at another institution to surgery at our center was 15.1 months (range, 9-29).

The mean NSA of the contralateral femur was 130.1°±2.9° and the mean pre-operative NSA was 123.8°± 5.1° (Table 6). The difference was 6.3°± 4.3°. In six patients, malreduction with a varus deformity exceeding 5 degrees was observed. The mean lateral gap on the total hip AP radiograph was 5.4±3.6mm and the average anterior gap was 3.8±2.9mm.

All 10 patients exhibited mechanical instability, indicated by implant loosening or metal breakage (Table 7). In all nine cases where a nail was used in the previous surgery, a hollow sign around the nail was observed. Two cases, which utilized standard interlocking screws and did not secure the screw, were accompanied by progressing varus deformity. Out of these nine cases, eight exhibited a hollow sign around the proximal screws, and seven showed a hollow sign and/or screw pull-out around the distal interlocking screws. In the case with a blade plate fixation, hollow signs were observed around the blade and two proximal screws, with additional findings of two distal screws broken.

The average surgical time for the 10 cases was 157 minutes (range, 80-262 minutes). In four cases that exhibited normal alignment or minimal varus malalignment and no hardware failure, augmentative plating was performed without the need for nail exchange. The average surgical time for these cases was 98 minutes (range, 80-115). In the remaining six cases, characterized by varus malalignment or the presence of a broken nail or screw, exchange nailing with a new entry point was performed, followed by augmentative plating. The average operation time for these cases was 196 minutes (range, 159-262). The mean post-operative NSA was 129.6° ± 3.7°, with a difference from the contralateral NSA of -0.5° ± 2.8°, indicating successful correction of varus malalignment (Table 6).

In augmentative plating, an average of 1.6 plates were used per case: two plates were used in six cases, and one plate was used in four cases. The number of cortices engaged by screws through the plate averaged 4.8 ± 3.2 (range, 1.5-12) in the proximal fragment and 4.6 ± 2.5 (range, 1.5-8) in the distal fragment.

All patients received bone grafts: five underwent autogenous bone grafting from the ilium, and in two patients, bone debris from reaming was mixed with BMP2 for grafting without further autogenous bone harvest. Among those who did not undergo nail exchange, BMP2 alone was used for bone grafting in three of the four cases.

All 10 patients achieved bone union without secondary intervention, with an average duration of 21.4 ± 7.4 weeks (range, 12-33 weeks) (Table 8). The preoperative Koval grade, which averaged 4.2 (range, 3-6), improved to an average of 2.5 (range, 1-6) at 6 months post-surgery and further progressed to an average of 1.6 (range, 1-3) at 1 year post-surgery, indicating significant improvement in performance status. One patient developed a urinary tract infection as a postoperative complication; no other major complications were reported.

Table 4. Patient demographics and history of osteoporosis medication

Case	Sex	Age	BMI	CCI	Previous osteoporosis medication	Medication duration (months)	Osteoporosis medication after fracture	Osteoporosis medication after revision
1	Female	82	24	6	Bisphosphonate	58	Denosumab	Raloxifene
2	Female	83	20	4	Bisphosphonate	66	Teriparatide	Teriparatide
3	Female	81	25	5	None		Teriparatide	Teriparatide
4	Female	80	27	4	Bisphosphonate	72	None	None
5	Female	68	31	5	None		Bisphosphonate	Teriparatide
6	Female	63	27	3	Denosumab	36	Denosumab	Teriparatide
7	Female	60	24	3	Bisphosphonate	120	Teriparatide	Teriparatide
8	Female	71	27	4	Bisphosphonate	120	None	Teriparatide
9	Female	79	16	5	Bisphosphonate	72	Teriparatide	Teriparatide
10	Female	63	21	4	None, Steroid 10yrs		None	None
Mean		73	24	4.3		78		

Table 5. Patient bone turnover markers (BTMs)

Case	Vitamin D (ng/mL)	Osteocalcin (ng/mL)	Decreased in Osteocalcin	CTX Level (ng/mL)	Decreased in CTX
1	34.6	19.3	No	0.095	Yes
2	26.2	41.5	No	0.398	No
3	46.9	12.7	Yes	0.197	No
4	18.9	2.3	Yes	0.16	No
5	22	15.8	No	0.09	Yes
6	36.3	14.95	Yes	0.089	Yes
7	23.6	12.5	Yes	0.389	No
8	17.3	36.1	No	0.406	No
9					
10					
Mean	28.2	19.4		0.228	

Table 6. Radiological variables, Characteristics about surgery

Case	Pre-operative NSA	Contralateral NSA	Varus alignment	Exchange nailing	Post-operative NSA	Number of plates used	Number of purchased cortices at the proximal fragment	Number of purchased cortices at the distal fragment	Bone graft
1	128	129	No	No	128	2	12	6.5	BMP2 1cc
2	126	129	No	No	126	2	6.5	8	BMP2 1cc
3	130	134	No	No	130	2	5.5	8.5	BMP2 3cc
4	132	133	No	No	132	2	7	5	Autogenous bone graft
5	118	124	Yes	Yes	122	1	1.5	1.5	Autogenous bone graft
6	121	128	Yes	Yes	132	1	3	2.5	Autogenous bone graft
7	121	130	Yes	Yes	128	1	2	2	Reaming debris + BMP2 3cc
8	121	130	Yes	Yes	134	1	2	3	Reaming debris + BMP2 3cc
9	117	132	Yes	Yes	132	2	4	4	Autogenous bone graft
10	124	132	Yes	Yes	131	2	4	5	Autogenous bone graft
Mean	123.8	130.1			129.6	1.6	4.8	4.6	

Table 7. Loosening signs and gap of nonunion site

Case	Loosening sign around nail	Loosening sign of proximal screw(s)	Loosening sign of distal screw(s)	Lateral gap (mm)	Anterior gap (mm)
1	Yes	Yes	Yes	7	2
2	Yes	Yes	Yes	3	2
3	Yes	Yes	Yes	2	2
4	Yes	Yes	Yes	3	1
5	Yes	Yes	No	3	2
6	Yes	Yes	No	5	9
7	Yes (blade plate)	Yes	Yes	8	2
8	Yes	Yes	Yes	5	6
9	Yes	No	Yes	14	8
10	Yes	Yes	Yes	4	4
Mean				5.4	3.8

Table 8. Time to union, Pre & Post-operative functional score

Case	Time to union (weeks)	Pre-operative Koval score	Post-operative 6 months Koval score	Post-operative 1 year Koval score
1	12	6	2	2
2	24	5	3	1
3	28	3	2	2
4	13	3	3	3
5	33	6	2	2
6	18	3	1	1
7	26	3	3	1
8	13	4	1	1
9	28	6	2	2
10	19	3	6	1
Mean	21.4	4.2	2.5	1.6

고찰

The comprehensive outcomes from this study underscore the effectiveness of augmentative plating and bone grafting, with or without exchange nailing, in achieving highly successful outcomes for patients with AFF nonunion.

In the treatment of nonunion, three key factors must be considered: fracture reduction, fixation stability, and biological impairment. Among these, mechanical instability was observed in all cases. To overcome this, the method of plate augmentation was chosen, resulting in excellent outcomes.

Until now, the treatment of AFFs has primarily focused on addressing the biological impairment due to bisphosphonate through bone grafting for biologic augmentation.[23-25] However, according to the results of this study, radiological signs indicating mechanical instability, such as implant failure, implant or screws loosening and pull-out, were observed. As is already recognized, the period required for bone union in AFFs is extended compared to regular fractures. Initial studies indicate that the primary healing rate after cephalomedullary nailing is 68.7%, with an average time to union of 10.7 months.[26] Additionally, another study found that 69.7% of cases achieved bone union within six months, whereas issues related to healing, such as delayed union or nonunion, were observed in 30.3% of cases.[27] After identifying risk factors that influence nonunion, it is expected that the current bone union rates have significantly increased. However, it remains imperative that the implant must withstand weight-bearing and maintain proper fixation of the femur until bone union is achieved. For femoral shaft or subtrochanteric fractures with nonunion, options like exchange nailing with a larger diameter or plate augmentation are common. However, if initial nailing fails, showing loosening in nails and screws, the efficacy of repeating nailing for enhancing supra-isthmic fixation is doubtful. Recent studies suggest better outcomes with plate augmentation or a combination of nail exchange and plate augmentation over nailing alone.[28] This evidence reinforces our approach, emphasizing the importance of augmentative plating. Mechanically, nails are robust against axial and bending forces but less resistant to torsion.[29] Research indicates that rotational instability impairs bone healing.[30] Plate augmentation significantly enhances rotational stability compared to intramedullary nailing alone. This underscores plate augmentation's effectiveness in boosting rotational stability, offering a biomechanical basis for its success in treating nonunions and supporting the superior results achieved through augmentative plating.

The second factor is reduction. Reduction is a pivotal factor in all fractures, but it is especially critical in AFFs, where varus reduction or distraction is a recognized risk factor for nonunion. [26, 27] Consequently, correction of malalignment is deemed necessary.[31, 32] In this study, six instances showed varus alignment exceeding 5 degrees, necessitating an adjustment. To amend varus reduction to a neutral or slight valgus alignment, the entry point for a double-bended nail was relocated from the tip of the greater trochanter to the piriformis fossa. This alteration effectively restored alignment, achieving a correction of varus alignment with a difference between the contralateral and postoperative NSA of -0.5° ± 2.8°. The new entry point avoids overlapping with the previously reamed hole and utilizes the medial cortex of the greater trochanter as a barrier against lateral slippage of the reamer or nail, thus ensuring the maintenance of proper alignment. Existing research, particularly by Kim et al. [11], has explored the use of a blade plate for treating failed osteosynthesis in AFFs, reporting an 85.7% success rate and bone union within an average of 8.4 months for 12 out of 14 patients. Despite this outcome, the technique presents significant disadvantages, including periosteal stripping, devascularization, and a heightened risk of postoperative bleeding and infection due to the requirement for larger incisions. [19] Notably, its use as a load-bearing device restricts early post-surgical ambulation, which is especially problematic given the predominantly elderly demographic of AFF patients,[23] with an average age of 73 years in the study. This limitation, coupled with the ASBMR's recommendation for preferring intramedullary reconstruction with full-length nails to reduce the risk of peri-implant fractures,[17, 33] underscores the undesirability of blade plating.

The final and third critical factor involves the bone biology perspective, essential in the healing process of AFFs. Despite guidelines recommending the discontinuation of BP or denosumab, three patients persisted with their use, underscoring a notable lack of awareness and signaling the need for greater attention from surgeons. BTMs normalized in most cases, excluding these three patients, indicating a probable recovery of over-suppression of bone remodeling, by the time of nonunion surgery. Although BTMs turned to normal, but atrophic nonunions frequently necessitate bone grafting; in this study, 50% of patients underwent bone grafting using BMP-2 alone or in conjunction with reaming bone debris, without autogenous bone harvest. this technique may serve as a good alternative for elderly patients or those lacking suitable bone graft sites due to previous revision surgery.

It's crucial not to solely focus on the aspect of biologic suppression, which is thought to contribute to the occurrence of AFF and subsequent nonunion. As demonstrated by the BTM results at the time of the revision surgery and our surgical outcomes, adhering to the fundamental principles of fracture reduction and rigid fixation can lead to successful results. The effectiveness of the surgical technique underscores the significance of achieving rigid fixation in revision surgery for AFF nonunion. This is in line with previous studies, D. Jayaramaraju et al., who highlighted the necessity of securing strong mechanical stability to facilitate optimal healing in nonunion cases within the subtrochanteric region of the femur[34]

Thus, the findings from this study provide strong evidence that a tailored approach incorporating augmentative plating and bone grafting, with or without exchange nailing, offers a viable and effective solution for managing AFF nonunions, leading to highly successful outcomes even in complex cases.

Limitations

This study, being a retrospective, single-center analysis involving a small cohort of 10 individuals, faced limitations such as potential observer bias and challenges in making statistical comparisons due to the absence of a control group. These challenges are further compounded by the inherently low prevalence of AFF and the rarity of cases progressing to nonunion. Despite these limitations, to the best of our knowledge, there have been no previously published studies on the outcomes of revision osteosynthesis using augmentative plates following failed osteosynthesis of AFFs.

결론

The integrated strategy of correcting malalignment and applying augmentative plates for rigid fixation marks a substantial improvement in addressing nonunion in atypical femoral fractures. This approach has shown a high success rate in attaining bone union, underscoring its potential as a crucial treatment option for these intricate scenarios. Based on the outcomes and discussions presented, it's evident that prioritizing both biomechanical stability and addressing the underlying bone biology are key to effective treatment, even in the face of challenges such as biologic suppression from medication or the complexities of treating an elderly patient population.

참고문헌

1. Hollick RJ and Reid DM. Role of bisphosphonates in the management of postmenopausal osteoporosis: an update on recent safety anxieties. *Menopause international* 2011; 17: 66-72.

2. Miyazaki T, Tokimura F and Tanaka S. A review of denosumab for the treatment of osteoporosis. *Patient preference and adherence* 2014: 463-471.

3. Dell RM, Greene D, Anderson D, et al. Osteoporosis disease management: what every orthopaedic surgeon should know. *JBJS* 2009; 91: 79-86.

4. Simpson E, Martyn-St James M, Hamilton J, et al. Clinical effectiveness of denosumab, raloxifene, romosozumab, and teriparatide for the prevention of osteoporotic fragility fractures: a systematic review and network meta-analysis. *Bone* 2020; 130: 115081.

5. Odvina CV, Zerwekh JE, Rao DS, et al. Severely suppressed bone turnover: a potential complication of alendronate therapy. *The Journal of Clinical Endocrinology & Metabolism* 2005; 90: 1294-1301.

6. Javaid M, Handley R and Costa M. Clinical management and pathogenesis of atypical fractures of the femur. *The Bone & Joint Journal* 2017; 99: 291-294.

7. Selga J, Nuñez J, Minguell J, et al. Simultaneous bilateral atypical femoral fracture in a patient receiving denosumab: case report and literature review. *Osteoporosis International* 2016; 27: 827-832.

8. Grady MK, Watson JT and Cannada LK. Treatment of femoral fracture nonunion after long-term bisphosphonate use. *Orthopedics* 2012; 35: e991-e995.

9. Jeong S-Y, Hwang K-T, Oh C-W, et al. Mid-term outcomes after the surgical treatment of atypical femoral fractures: minimum three-year follow-up. *The Bone & Joint Journal* 2021; 103: 1648-1655.

10. Koh A, Guerado E and Giannoudis P. Atypical femoral fractures related to bisphosphonate treatment: issues and controversies related to their surgical management. *The bone & joint journal*

2017; 99: 295-302.

11. Kim S, Rhyu K and Lim S. Salvage of failed osteosynthesis for an atypical subtrochanteric femoral fracture associated with long-term bisphosphonate treatment using a 95° angled blade plate. *The Bone & Joint Journal* 2018; 100: 1511-1517.

12. Lim H-S, Kim C-K, Park Y-S, et al. Factors associated with increased healing time in complete femoral fractures after long-term bisphosphonate therapy. *The Journal of Bone and Joint Surgery American Volume* 2016; 98: 1978.

13. Prasarn ML, Ahn J, Helfet DL, et al. Bisphosphonate-associated femur fractures have high complication rates with operative fixation. *Clinical Orthopaedics and Related Research®* 2012; 470: 2295-2301.

14. Charlson M, Szatrowski TP, Peterson J, et al. Validation of a combined comorbidity index. *Journal of clinical epidemiology* 1994; 47: 1245-1251.

15. Koval KJ, Aharonoff GB, Rosenberg AD, et al. Functional Outcome After Hip Fracture: ffect of General Versus Regional Anesthesia. *Clinical Orthopaedics and Related Research®* 1998; 348: 37-41.

16. Weil YA, Rivkin G, Safran O, et al. The outcome of surgically treated femur fractures associated with long-term bisphosphonate use. *Journal of Trauma and Acute Care Surgery* 2011; 71: 186-190.

17. Shane E, Burr D, Abrahamsen B, et al. Atypical subtrochanteric and diaphyseal femoral fractures: second report of a task force of the American Society for Bone and Mineral Research. *Journal of bone and mineral research* 2014; 29: 1-23.

18. Sasaki S, Miyakoshi N, Hongo M, et al. Low-energy diaphyseal femoral fractures associated with bisphosphonate use and severe curved femur: a case series. *Journal of bone and mineral metabolism* 2012; 30: 561-567.

19. Kim J-W, Oh C-W, Park K-H, et al. The role of an augmentative plating in the management of femoral subtrochanteric nonunion. *Archives of Orthopaedic and Trauma Surgery* 2023: 1-9.

20. Leder BZ, Tsai JN, Uihlein AV, et al. Denosumab and teriparatide transitions in postmenopausal osteoporosis (the DATA-Switch study): extension of a randomised controlled trial. *Lancet* 2015; 386: 1147-1155. 2015/07/07. DOI: 10.1016/S0140-6736(15)61120-5.

21. Kay RM, Jaki KA and Skaggs DL. The effect of femoral rotation on the projected femoral neck-shaft angle. *Journal of Pediatric Orthopaedics* 2000; 20: 736-739.

22. Whelan D, Bhandari M, McKee M, et al. Interobserver and intraobserver variation in the assessment of the healing of tibial fractures after intramedullary fixation. *The Journal of Bone & Joint Surgery British Volume* 2002; 84: 15-18.

23. Barquet A, Mayora G, Fregeiro J, et al. The treatment of subtrochanteric nonunions with the long gamma nail: twenty-six patients with a minimum 2-year follow-up. *Journal of orthopaedic trauma* 2004; 18: 346-353.

24. de Vries JS, Kloen P, Borens O, et al. Treatment of subtrochanteric nonunions. *Injury* 2006; 37: 203-211.

25. Kang SH, Han SK, Kim YS, et al. Treatment of subtrochanteric nonunion of the femur: whether to leave or to exchange the previous hardware. *Acta Orthopaedica et Traumatologica Turcica* 2013; 47: 91-95.

26. Cho JW, Oh CW, Leung F, et al. Healing of Atypical Subtrochanteric Femur Fractures After Cephalomedullary Nailing: Which Factors Predict Union? *Journal of orthopaedic trauma* 2017; 31: 138-145. 2016/12/24. DOI: 10.1097/bot.0000000000000743.

27. Lim HS, Kim CK, Park YS, et al. Factors Associated with Increased Healing Time in Complete Femoral Fractures After Long-Term Bisphosphonate Therapy. *J Bone Joint Surg Am* 2016; 98: 1978-1987. DOI: 10.2106/JBJS.15.01422.

28. Kook I, Oh CW, Shon OJ, et al. Comparing outcomes of plate augmentation, nail exchange, and nail exchange with plate augmentation in the treatment of atrophic femoral shaft nonunion after intramedullary nailing: a multicenter retrospective study. *Arch Orthop Trauma Surg* 2024; 144: 1259-1268. 2024/02/19. DOI: 10.1007/s00402-023-05183-4.

29. Park K, Kim K and Choi YS. Comparison of mechanical rigidity between plate augmentation leaving the nail in situ and interlocking nail using cadaveric fracture model of the femur. *Int Orthop* 2011; 35: 581-585. 2010/03/10. DOI: 10.1007/s00264-010-0983-y.

30. Grundnes O and Reikeras O. Effects of instability on bone healing. Femoral osteotomies studied in rats. *Acta Orthop Scand* 1993; 64: 55-58. 1993/02/01. DOI: 10.3109/17453679308994529.

31. Giannoudis PV, Ahmad MA, Mineo GV, et al. Subtrochanteric fracture non-unions with implant failure managed with the "Diamond" concept. *Injury* 2013; 44: S76-S81.

32. Krappinger D, Wolf B, Dammerer D, et al. Risk factors for nonunion after intramedullary nailing of subtrochanteric femoral fractures. *Archives of Orthopaedic and Trauma Surgery* 2019; 139: 769-777.

33. Jeong SY, Hwang KT, Oh CW, et al. Mid-term outcomes after the surgical treatment of atypical femoral fractures : minimum three-year follow-up. *The bone & joint journal* 2021; 103-b: 1648-1655. 2021/11/02. DOI: 10.1302/0301-620x.103b11.Bjj-2021-0416.R1.

34. Jayaramaraju D, Nandakumar S, Agraharam D, et al. Subtrochanteric Femur Nonunion-Chasing the elusive An analysis of two techniques to achieve union: nail-plate fixation and plate-structural fibula graft fixation. *Injury* 2024: 111462.

그림

Figure 1. Case #6. A 63-year-old female patient. A. Initial radiographs display a right subtrochanteric atypical femoral fracture. B. Postoperative x-ray reveals fixation with an intramedullary nail, showing varus and flexion malalignment. C. An 8-month postoperative x-ray indicates further progression of varus, medial side bone loss at the proximal nail, and proximal screw pull-out, with an absence of callus formation. D. Intraoperative fluoroscopic images demonstrate the restoration of alignment, achieved

with clamps and a new entry point at the piriformis fossa. E. Revision surgery entailing exchange nailing, augmentative plating, and autogenous bone grafting corrected the varus malalignment. F. Bone union was achieved 4 months post-surgery.


Fig. 2A
Fig. 2B
Fig. 2C

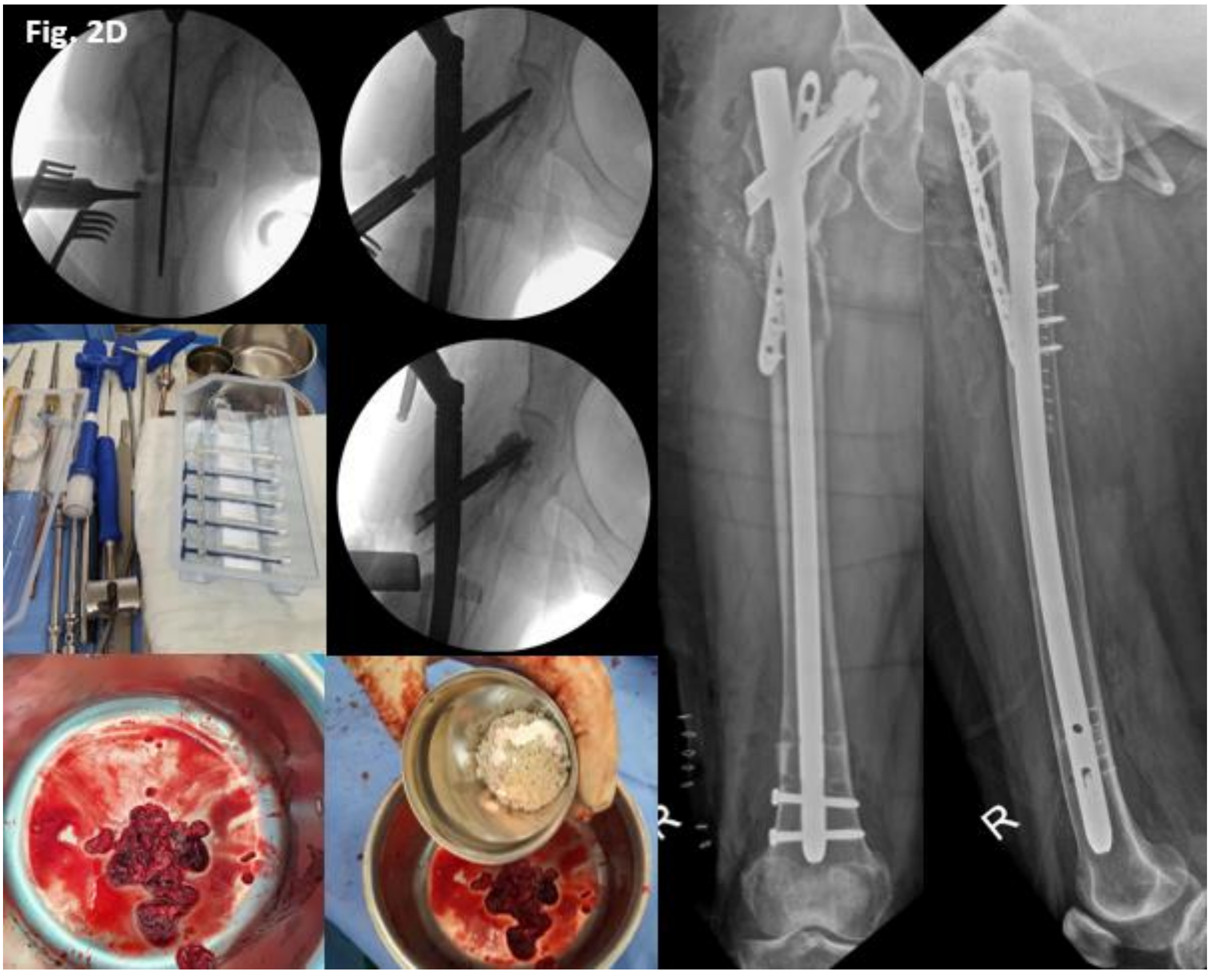
Fig. 2D
R
R

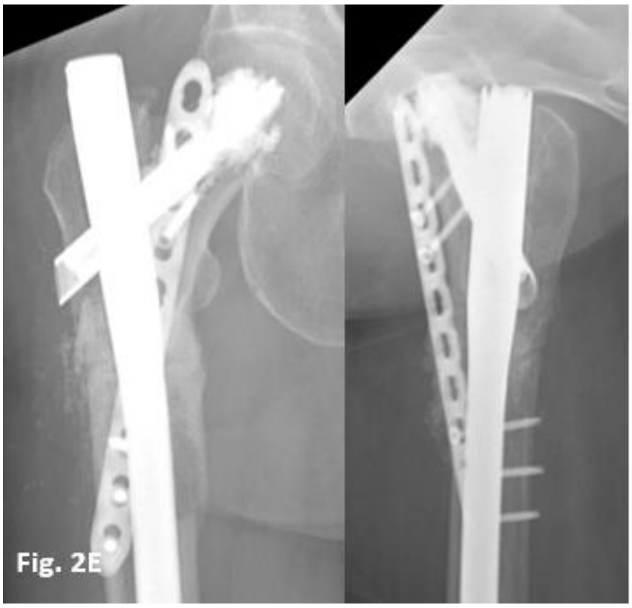
Fig. 2E


Fig. 2F

Figure 2. Case #8. A 71-year-old female patient with a history of 10-year bisphosphonate use presented with a right subtrochanteric fracture. B. Initial treatment involved nailing, but resulted in varus mal-reduction. C. Fifteen months later, radiographs revealed nonunion and signs of loosening around the nail, proximal, and distal screws. D. Revision osteosynthesis was undertaken, involving exchange nailing with a new entry point at the piriformis fossa, augmentative plating, and grafting with reaming debris and BMP2. Additionally, cement augmentation through a blade was utilized to enhance proximal stability. E. A radiograph taken 3 months post-revision demonstrated bone bridging across the anterior, medial, and lateral aspects of the nonunion site. F. Bony consolidation was successfully achieved 5 months after operation.

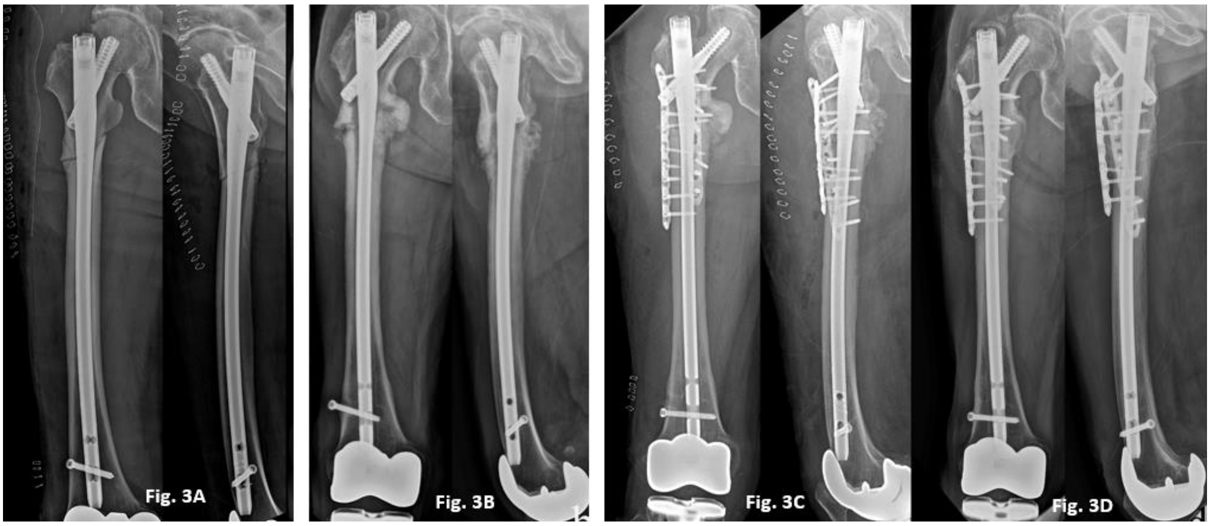

Figure 3. Case #1. An 82-year-old female patient. A. Postoperative radiographs demonstrate a well-reduced atypical femoral fracture stabilized with a cephalomedullary nail, but the hip screw appears short. B. Radiograph at 14 months postoperatively reveals callus formation with a persistent lateral gap, a hollow sign around the proximal nail and hip screw, and distal screw pull-out. C. Stability enhancement was achieved using dual plating with 3.5mm LCP plates, accompanied by BMP2 grafting. D. The 3-month postoperative x-ray shows consolidation of the callus and complete bone union.


Fig. 4A
Fig. 4B
R
Fig. 4C
Fig. 4D
R
Fig. 4E
R

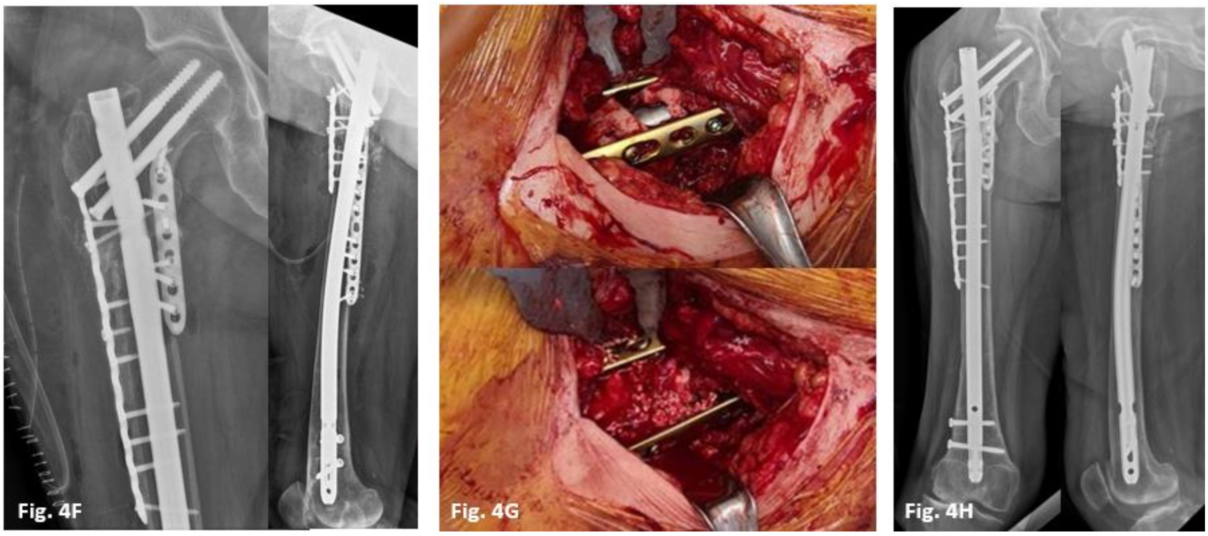

Figure 4. Case #3. An 81-year-old female patient A. Initial x-ray with a right subtrochanteric atypical femoral fracture. B. Postoperative x-ray illustrates a well-reduced fracture stabilized with a cephalomedullary nail. C. Radiographs taken 8 months post-surgery display a hollow sign around the nail and proximal screw, with an absence of callus formation. D. Exchange nailing with larger diameter and autogenous bone grafting were performed 8 months after the initial surgery. E. An x-ray 7 months following the second surgery reveals newly developed a hollow sign around the nail, proximal, and distal screws, along with widening of the medullary canal of the femur shaft, yet no significant bridging and only a tiny callus present. F. Revision surgery entailing double augmentative plating and tightening of the hip screw was undertaken. G. An intraoperative image exhibits a bone defect at the anterior aspect of the nonunion site, which was filled with BMP 2. H. Bone union was successfully achieved 7 months after the revision osteosynthesis.

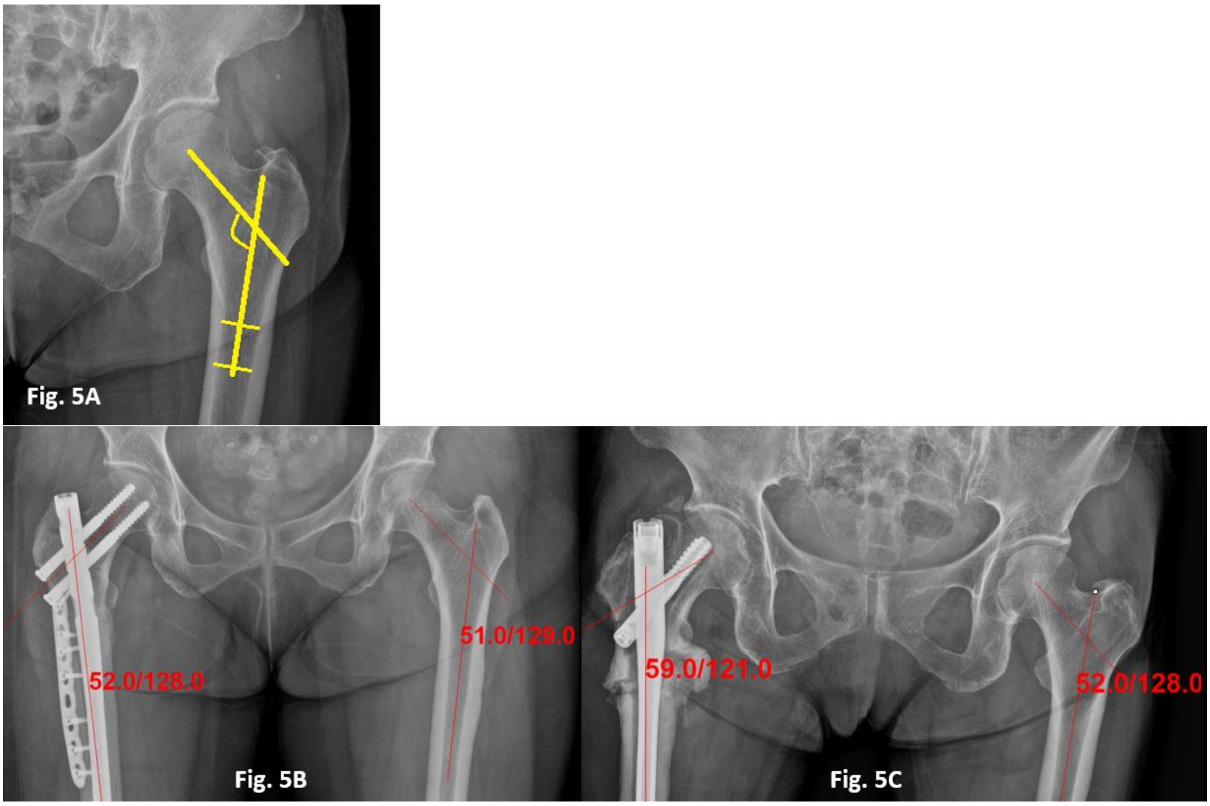

Figure 5. A. The femoral neck-shaft angle is defined by the angle between the longitudinal femoral shaft axis and the femoral head-neck axis. A line that bisects the femoral neck through the center of the femoral head defines the axis of the femoral neck, and two bisections of the femoral shaft at different locations determine the longitudinal femoral shaft axis. B. Case #1. Radiograph taken before surgery at referred hospital shows a pre-operative NSA of 128 degrees and a contralateral naive NSA of 129 degrees, indicating normal alignment. C. Case #6. Radiograph taken before surgery at referred hospital shows varus malalignment. The pre-operative NSA is 121 degrees, and the contralateral naive NSA is 128 degrees, indicating a 7-degree difference. This case requires malalignment reduction through nail exchange.

국문요약

배경

비정형 대퇴골 골절 수술 후 발생한 불유합은 치료가 어려우며 이에 대한 연구 또한 제한적인 상태이다. 본 연구의 목표는 비정형 대퇴골 골절 불유합 치료에서 골수내정 교체와 보강 금속판을 이용한 수술의 결과를 조사하여 효과적인 치료 방침을 세우는 것이다.

방법

2018년 1월부터 2022년 12월까지 단일 기관에서 비정형 대퇴골 골절 불유합에 대해 골수내정 교체와 보강 금속판을 이용하여 치료받은 10명의 여성 환자를 대상으로 후향적 분석을 수행하였다. 골수내정이 부러졌거나 5도 이상의 내반 변형이 있을 경우 골수내정 교체를 시행하였고, X-ray 상 임플란트 주변의 해리 징후가 관찰되어 기계적 불안정성이 의심되는 경우 금속판 보강을 시행하였다. 골 리모델링 억제 정도를 확인하기 위해 수술 전 골대사 표지자를 측정했으며, 수술 시에는 골절 정복, 튼튼한 고정에 중점을 두었고, 생물학적 손상 해결을 위해 뼈 이식을 하였다. 주요 결과지표로 금속판 고정력 확인을 위한 나사가 관통한 피질골 수, 부정 정렬 교정 여부 확인을 위한 수술 전후 경부-골간 각도(Neck-shaft angle, NSA) 차이, 수술 전후 보행 기능의 개선 정도를 파악하기 위한 Koval 점수를 측정하였다.

결과

평균 21.4±7.4주 이내에 이러한 수술 방법을 통하여 10명의 환자 모두에서 성공적으로 골유합을 달성하였다. 모든 사례에서 기계적 불안정성 문제를 나타내는 해리 징후가 관찰되었다. 보강 금속판을 통해 근위 및 원위 골편에서 각각 평균 4.8±3.2 및 4.6±2.5 피질골을 고정하여 기계적 안정성을 향상시켰다. 내반 부정정렬이 있던 여섯 명의 환자

에서 수술 후 경부-골간 각도가 건측에 맞게 성공적으로 교정되었다. 또한, 대부분의 비스포스포네이트 또는 데노수맙을 사용하지 않은 환자에서 수술 전 골대사표지자가 정상화되어, 장기간의 항흡수 치료로 인한 골 리모델링 억제가 수술 전에 회복될 수 있음을 시사했다. Koval 점수는 수술 전 평균 4.2에서 수술 1년 후 1.6으로 감소하여 보행 능력의 상당한 회복을 나타냈다.

결론

부정정렬 교정을 위한 골수내정의 교체와 강력한 고정을 위한 보강 금속판 사용은 비정형 대퇴골 골절 수술 후 불유합 치료에 매우 효과적임을 입증하였고, 이러한 복잡한 사례에 대한 주요 치료 방법으로서 잠재력을 보여주었다.