

Full Paper

Effects of multi-modal exercise and nutritional intervention nursing on microcirculation function and functional recovery in elderly patients with fracture

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Received: 22 July 2025 / Accepted: 10 September 2025 / Published: 15 September 2025

Abstract: The effects of multi-modal exercise and nutritional intervention combined with etoricoxib on bone metabolism markers and functional recovery in elderly patients with fracture will be studied. Eighty elderly patients with fracture admitted to the hospital from April 2023 to April 2024 were selected for the trial. They were randomly divided into group A (n = 40) and group B (n = 40). All patients were given etoricoxib and conventional nursing while group A was also given multi-modal exercise and a structured nutritional intervention (targeting protein, calcium, and vitamin D intake). The bone metabolism markers, functional disability (Oswestry Disability Index), serum matrix metalloproteinase-3 (MMP-3) and cyclooxygenase-2 (COX-2) levels and quality of life were compared between the two groups. Results showed that microvascular blood perfusion and average velocity of blood cell movement levels increased in both groups after the intervention but were significantly higher in group A than in group B. After 1, 2 and 4 weeks of intervention, Oswestry Disability Index scores were lower in group A than in group B. After intervention, serum MMP-3 and COX-2 levels were lower in both groups than before intervention, and lower in group A than in group B. After intervention, all health survey short form scores were higher in both groups than before intervention, with group A being higher than group B (all $P < 0.05$). Thus, the multi-modal exercise and nutritional intervention combined with etoricoxib have a significant effect on the improvement of bone metabolism markers and functional recovery in elderly fracture patients, while they negatively regulate MMP-3 and COX-2 levels and also improve the quality of life.

Keywords: elderly patients with fracture, etoricoxib, multi-modal exercise, nutritional intervention

INTRODUCTION

Fracture is one of the most common orthopaedic diseases in the elderly patients, who suffer from bone pain, swelling and restricted movement, which can lead to disability in severe cases and

pose a great threat to their physical and mental health and quality of life [1]. Etoricoxib is one of the non-steroidal anti-inflammatory drugs with a highly selective inhibitory effect, which is more effective and safer in fracture, especially in elderly patients with fracture, and has the advantage of reducing the risk of complications [2]. In addition, an active and effective nursing intervention programme based on pharmacological treatment is important for promoting the functional recovery in fracture patients. Early and effective exercise and nutritional intervention can facilitate the recovery of function, improve posture and balance and maintain bone stability, thus contributing to early recovery [3]. Previous studies have also demonstrated that structured exercise intervention can significantly increase bone mineral density and reduce fracture risk in older adults [4]. Furthermore, integrating exercise with appropriate nutritional strategies has been shown to maintain bone health and improve metabolic status [5, 6]. However, little research has been reported on the use of multi-modal exercise and nutritional intervention in elderly patients with fracture. In this paper we investigated the effects of multi-modal exercise and nutritional intervention combined with etoricoxib (a selective COX-2 inhibitor used off-label for fracture-related pain) on bone metabolism markers and functional disability in elderly patients with fracture.

MATERIALS AND METHODS

General Data

Eighty elderly patients with fracture admitted to the hospital from April 2023 to April 2024 were selected for the trial. They were divided into group A (n = 40) and group B (n = 40) by computerised random number method. Group A consisted of 24 males and 16 females, aged 61-82, (mean 70.52 ± 6.24), whose course of disease was 3-11 years, (mean 6.15 ± 1.07 years). Group B consisted of 26 males and 14 female, aged 60-84 (mean 70.61 ± 6.29), whose course of disease was 3-12 years (mean 6.18 ± 1.09 years). The differences in the above information between the two groups were small ($P > 0.05$) and could be compared at follow-up. Inclusion criteria: (1) All subjects met the diagnostic criteria for fracture as established in the Guidelines for the diagnosis and treatment of osteoarthritis [7]; (2) All were diagnosed by X-ray examination; and (3) Age ≥ 60 . Exclusion criteria: (1) Patients were accompanied by severe impairment of vital organ function; (2) Patients with combined major infections, immune disorders or malignancies; (3) Patients were accompanied by spine and hip trauma, tuberculosis or tumours; and (4) Patients with combined mental abnormalities. All participants provided written informed consent before participation.

Methods

All patients were given etoricoxib (a selective COX-2 inhibitor used off-label for fracture-related pain) (Jiangsu Hengrui Pharmaceuticals Co., China), which was administered orally after meals at a dose of 0.1 g/time, 2 times/day. Group B was given routine nursing including health education, psychological guidance and proper instruction on hot water fumigation before bedtime. In group A, in addition to the same treatment as group B a multi-modal exercise and nutritional intervention were also given:

(1) *Muscle training.* For those with standing dysfunction, they were instructed to perform supine training, dorsiflex the ankle bone, tense the quadriceps, lift the patella vertically upwards, place a soft pillow between the spine and hips, and the subject was told to keep pressing harder. In addition, a soft pillow was placed under the affected spine and hip, the ankle was dorsiflexed, the lower leg was kept straight and the pillow was pressed downwards with constant pressure. These movements were repeated 5 times, maintaining each time for 6 sec. The subject was assisted to maintain the spine and hip in various angles of flexion and to complete 10 intervals of isometric resistance training in flexion and extension, 10 sec./time, with a 30-sec. break for alternating angles. For those with a fair spine and hip condition, the subject was instructed to train in a sitting position, maintaining a straight upper body and flexing and extending the spine and hip as much as possible. Then the position was changed to supine, the ankle dorsiflexed, straight leg raised 60°, slowly lowered, the spine and hip flexed at an angle of 90°. Then the feet were flattened and the lower leg of the affected spine and hip slowly lifted off the floor and lowered at the same speed. The spine and hip were bent and the ankle dorsiflexion was maintained, the heel kicking to strike the hip as far as possible. These movements were repeated 5 times, maintaining each time for 6 sec.

(2) *Joint mobility training.* For those with standing dysfunction, they were assisted to assume a supine position and trained with the continuous passive motion machine by first fixing the affected limb to the machine and then determining the range of bone movement according to the subject's specific situation and ability to tolerate it, 15 min./time, 3 times/day. For those who could stand, they were instructed to assume a spine and hip flexion position, hold the spine and hip and popliteal fossa with both hands until there was a pulling sensation and then stop forward flexion, slowly touch the heel with both hands and pull the hamstring. The above movements were repeated for 6 sec./time, 3 times/day. Both groups were continuously intervened for 4 weeks.

(3) *Nutritional intervention.* In addition to the standard hospital diet, Group A received a targeted nutritional support protocol supervised by a clinical dietitian. This included a daily oral nutritional supplement to provide high protein (1.5-2.0 g/kg/day) and adequate calories to support collagen synthesis and prevent muscle loss. Additionally, all patients in Group A received daily calcium (1000-1200 mg) and vitamin D3 (800-1000 IU) supplementation to meet bone mineralisation requirements. Individualised dietary counselling was provided to reinforce intake of protein-rich and calcium-rich foods throughout the 4-week intervention period.

Ethical Statement

This project was approved by the Ethics Committee of Lixin County People's Hospital with project no. LXP2022-003 on March 5, 2022. All participants were informed of the contents of this study, which comply with the Declaration of Helsinki.

Evaluation indicators

(1) A dual-channel laser Doppler PF 6000 (Perimed AB, Sweden) was used to assess the bone metabolism markers of the subjects. The relevant indicators included microcirculatory blood

perfusion (MBP), average velocity of blood cells (AVBC) and concentration of moving blood cells (CMBC). The timing of the assessment was 1 day before and 4 weeks after intervention.

(2) The Oswestry Disability Index (ODI) [8] was used to assess the functional disability of the subjects. It is a questionnaire that covers 10 areas, i.e. pain, ability to live, weight bearing, sitting, standing, walking, travel, impact on sleep, sex and social life, with a score of 0 to 5 points in each area and a total score of 0 to 50 points. Higher scores indicate greater bone dysfunction. The timing of the assessment was 1 day before and 1, 2 and 4 weeks after intervention.

(3) Serum levels of matrix metalloproteinase-3 (MMP-3) and cyclooxygenase-2 (COX-2) were measured by enzyme-linked immunosorbent assay. All subjects gave 3 ml of venous blood before the morning meal 1 day before and 4 weeks after intervention, and the serum was centrifuged at 3000 r/min. for 10 min. Serum levels of MMP-3 and COX-2 were measured using enzyme-linked immunosorbent assay (ELISA) kits (MMP-3 ELISA kit and COX-2 ELISA kit; Shanghai Xuanya Biotechnology Co., China), according to the manufacturer's instructions. Quality of life was assessed using the Medical Outcomes Study 36-Item Short Form Health Survey (SF-36) [9]. There were 8 dimensions of emotional/physical functioning, somatic pain and social functioning. All dimensions are scored on a percentage scale and the scores were positively related to quality of life.

Statistical Methods

Data were analysed using SPSS 24.0 software. The measurement data were described by $\bar{x} \pm s$ and t-test was performed. The statistical data were described as [n, (%)] and the χ^2 test was performed. $P < 0.05$ means the difference was statistically significant.

RESULTS

Comparison of Bone Metabolism Markers

After intervention, MBP and AVBC levels are higher in both groups than before intervention, with the values in Group A being higher than in Group B (all $P < 0.05$) (Table 1).

Table 1. Comparison of bone metabolism markers between groups A and B (%)

	MBP		AVBC		CMBC	
	Pre-inter- vention	Post-inter- vention	Pre-inter- vention	Post-inter- vention	Pre-inter- vention	Post-inter- vention
Group A	8.04±1.30	9.33±1.42*	10.87±2.25	13.16±2.51*	78.54±14.21	82.05±15.73
Group B	8.02±1.28	8.70±1.36*	10.90±2.27	12.01±2.45*	78.60±14.18	80.96±15.26
t-value	0.069	2.026	0.059	2.074	0.019	0.315
P-value	0.945	0.046	0.953	0.041	0.985	0.753

* $P < 0.05$ compared to pre-intervention.

Comparison of ODI Scores

After 1, 2 and 4 weeks of intervention, Group A has lower ODI scores than Group B (all $P < 0.05$) (Table 2).

Table 2. Comparison of ODI scores between groups A and B (Mean $\pm$ SD)

Group	Pre-inter- vention	After 1 week of intervention	After 2 weeks of intervention	After 4 weeks of intervention
Group A	37.01 $\pm$ 5.19	25.20 $\pm$ 4.09	20.74 $\pm$ 3.74	16.48 $\pm$ 3.11
Group B	37.07 $\pm$ 5.24	30.75 $\pm$ 4.62	26.28 $\pm$ 4.16	21.72 $\pm$ 3.88
t-value	0.051	5.689	6.263	6.665
P-value	0.959	<0.001	<0.001	<0.001

Comparison of Serum MMP-3 and COX-2 Levels

After intervention, serum MMP-3 and COX-2 levels decrease in both groups and are significantly lower in group A compared to group B (all $P < 0.05$) (Table 3).

Table 3. Comparison of serum MMP-3 and COX-2 levels

	MMP-3 (μ g/L)		COX-2 (ng/L)	
	Pre-inter- vention	Post-inter- vention	Pre-inter- vention	Post-inter- vention
Group A	126.33 $\pm$ 12.48	67.29 $\pm$ 6.24*	23.59 $\pm$ 4.61	9.47 $\pm$ 1.25*
Group B	126.41 $\pm$ 12.50	81.40 $\pm$ 7.09*	23.71 $\pm$ 4.68	11.49 $\pm$ 1.80*
t-value	0.029	9.448	0.116	5.830
P-value	0.977	<0.001	0.908	<0.001

* $P < 0.05$ compared to pre-intervention

Comparison of Quality of Life

After intervention, all SF-36 scores are higher in both groups than before intervention, and are higher in group A than in group B (all $P < 0.05$) (Table 4).

Table 4. Comparison of quality of life (Mean $\pm$ SD)

		Physiological functions		Physiological intelligence		Somatic pain		Vitality	
		Pre-inter- vention	Post-inter- vention	Pre-inter- vention	Post-inter- vention	Pre-inter- vention	Post-inter- vention	Pre-inter- vention	Post-inter- vention
Group A		63.11±	80.52±	66.07±	81.20±	64.19±	79.75±	65.98±	80.94±
		4.92	5.81*	4.28	6.04*	4.87	6.01*	4.67	6.28*
Group B		63.20±	76.40±	66.23±	76.29±	64.54±	74.58±	66.12±	75.48±
		4.97	5.23*	4.35	5.27*	4.92	5.47*	4.70	6.03*
t-value	-	0.081	3.333	0.166	3.774	0.320	4.024	0.134	3.966
P-value	-	0.935	0.001	0.869	<0.001	0.750	<0.001	0.894	<0.001
		Social function		Emotional function		Mental health		Overall health	
		Pre-inter- vention	Post-inter- vention	Pre-inter- vention	Post-inter- vention	Pre-inter- vention	Post-inter- vention	Pre-inter- vention	Post-inter- vention
Group A		66.97±	81.50±	66.98±	82.05±	67.42±	82.05±	69.10±	81.27±
		4.58	5.47*	4.87	5.91*	4.29	6.03*	4.53	6.10*
Group B		67.12±	74.69±	67.12±	74.77±	67.61±	76.48±	69.17±	76.10±
		4.64	5.10*	4.94	5.26*	4.35	5.67*	4.50	5.23*
t-value		0.146	5.759	0.128	5.820	0.197	4.256	0.069	4.069
P-value		0.885	<0.001	0.899	<0.001	0.845	<0.001	0.945	<0.001

* P < 0.05 compared to pre-intervention

DISCUSSION

Fracture is one of the degenerative arthritic diseases and its pathogenesis may be related to factors such as ageing, bone overuse, inflammation and metabolic abnormalities [10]. However, there are still controversies about the specific pathogenesis of fracture, and therefore there is no uniform clinical treatment protocol. Etoricoxib is one of the most commonly used drugs for fracture treatment, and as one of the new non-steroidal anti-inflammatory drugs, it exerts strong anti-inflammatory and analgesic effects [11]. However, the treatment period of fracture is often long, and it is difficult to achieve a more satisfactory outcome with drug therapy alone, so supplementing drug therapy with active and effective nursing intervention is the key to improving the treatment outcome and prognosis.

The experimental results in this paper demonstrate that MBP and AVBC levels are higher in both groups after intervention. The values are also higher in group A than in group B. This is similar to the study reported by Wang Zhentao et al. [12], suggesting that the intervention protocol in group A has a certain effect on bone metabolism markers in elderly patients with fracture. This is likely that the multi-modal exercise and nutritional intervention can reduce fluid shear stress between blood and vascular endothelium, which in turn regulates the release of vasodilator and inflammatory

cytokines, improves endothelial function and ultimately promotes the recovery of bone metabolism markers [13].

In addition, after 1, 2 and 4 weeks of intervention, group A has lower ODI scores than group B. This is corroborated in the study reported by Chen Hongbo et al. [14], reflecting that the intervention protocol in group A is effective in reducing functional disability and improving physical function in elderly fracture patients. Our findings are in line with an earlier clinical report [15] which showed that combined exercise and nutritional approaches play a key role in rehabilitation after hip fracture by promoting physical function recovery and bone stability. The reason for this is that multi-modal exercise and nutritional intervention can improve blood circulation in the affected limb through muscle training and posture and balance training, thereby improving endurance and muscle strength and bone stability, which in turn can promote good recovery of spine and hip function and improve treatment outcomes [16].

Furthermore, MMP-3 is a key enzyme involved in the degradation of the extracellular matrix including cartilage collagen and proteoglycans, which play a crucial role in the pathological process of fracture and joint destruction [17]. COX-2, on the other hand, is an inducible enzyme in charge of the synthesis of prostaglandins, which are central mediators of inflammation and pain [18]. After the onset of fracture, the local inflammatory response often leads to a significant upregulation of these two mediators. The results of this paper show that the serum MMP-3 and COX-2 levels in both groups were lower than those before intervention, and group A has even lower levels than group B, fully confirming that the intervention protocol in group A can effectively inhibit inflammatory response and reduce extracellular matrix degradation, thereby contributing to the healing process and functional recovery.

The positive effect of our multi-modal exercise intervention aligns with a recent randomised controlled trial from Japan, which found that structured home-based exercise significantly improved outcomes in elderly fracture patients [19]. The multi-modal exercise and nutritional intervention seem to effectively delay the destruction of the soft matrix of the bone and reduce pain, while efficiently unblocking blood vessels and improving microcirculation, thus reducing the inflammatory response [20]. The results in this paper also show that all SF-36 scores are higher in both groups after intervention, and they are higher in group A than in group B. This indicates that the intervention programme in group A significantly improves the quality of life of elderly fracture patients. The multi-modal exercise and nutritional intervention thus seem to effectively improve bone peripheral blood circulation, promote venous and lymphatic return to the bone, achieve significant improvement of the local microenvironment, enhance muscle strength and promote the recovery of bone balance and stability, creating favourable conditions for the improvement of quality of life. A recent systematic review and meta-analysis also reported that multicomponent exercise combined with nutritional supplementation can improve frailty and overall quality of life in community-dwelling older adults [21]. This further supports the effectiveness and generalisability of our multi-modal intervention protocol.

Throughout the 4-week intervention period, no significant adverse events related to the

multimodal exercise programme (such as new falls, exacerbated pain or musculoskeletal injury) or the nutritional supplementation (such as gastrointestinal discomfort or hypercalcemia symptoms) were reported in Group A. This suggests that the prescribed regimen, administered under professional supervision, was well-tolerated by the elderly fracture patients in our study. The use of etoricoxib, while effective for pain management, carries known potential risks (e.g. cardiovascular and gastrointestinal complications). However, its application in this context was short-term and monitored in alignment with its common use for acute pain in such clinical scenarios. However, the absence of reported etoricoxib-related adverse effects in our study should be interpreted with caution due to the relatively short duration of intervention and specific case characteristics.

CONCLUSIONS

The multi-modal exercise and nutritional intervention protocol presented in this study demonstrates significant clinical utility for optimising the recovery of elderly patients with fractures. Our findings provide robust evidence that can directly guide clinical practice, firstly by offering a practical, non-pharmacological strategy to mitigate inflammation (as evidenced by reduced MMP-3 and COX-2 levels) and improve functional outcomes, key factors in healing and preventing secondary fractures. Secondly, the protocol effectively addresses the critical issue of functional decline and quality of life in this vulnerable population. The intervention is feasible to implement under the guidance of clinical nurses and physiotherapists, suggesting that its integration into standard post-operative and rehabilitative care can lead to improved patient outcomes, reduced complication rates, and potentially shorter hospital stays. Therefore, we recommend that clinicians consider adopting such a comprehensive rehabilitative approach to enhance the overall management and prognosis of elderly fracture patients. Future research should focus on several areas: firstly, investigating the long-term effects (e.g. 6 or 12 months) of this multimodal intervention on functional recovery and fracture recurrence rates. Secondly, exploring its efficacy in other common fracture types (e.g. hip fractures) would be valuable. Lastly, conducting a cost-effectiveness analysis would provide crucial evidence for broader clinical implementation and health policy decision-making.

ACKNOWLEDGEMENTS

The authors thank the staff of Lixin People's Hospital for their support and assistance during the study.

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