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Volume 50, Number 3, June 2026

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Aims and Scope

Annals of Rehabilitation Medicine (*ARM*) is the official journal of the Korean Academy of Rehabilitation Medicine. It is an international, peer-reviewed open access journal, which aims to be a global leader in sharing up-to-date knowledge dedicated to the advancement of care and enhancing the function and quality of life of persons with various disabilities and chronic illnesses. As the official journal of one of the largest societies of rehabilitation medicine in Asia and Oceania, more than 3,500 physiatrists regularly receive this journal's table of contents via email, and the number is continually increasing. This journal is endorsed by the International Society of Physical and Rehabilitation Medicine (ISPRM) and the Asia-Oceanian Society of Physical and Rehabilitation Medicine (AOSPRM). International members comprise approximately half the editorial board, conducting peer-reviews of submitted manuscripts or acting as handling editors by assigning peer-review tasks to other reviewers.

The journal encompasses all aspects of physical medicine and rehabilitation, including basic, translational, clinical, and policy research, as well as rehabilitation education. Research areas covered by this journal include rehabilitation for brain disorders, spinal cord injuries, neuromuscular diseases, and dysphagia; cancer, cardiopulmonary, geriatric, pain & musculoskeletal, and pediatric rehabilitation; electrodiagnosis, orthosis & prosthesis, physical therapy, and sports medicine; and other emerging fields in rehabilitation medicine.

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Hormonal Shifts and Structural Strain: A Literature Review of Menopause and Perimenopause in Relation to Overuse Injuries and Stress Fractures

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Musculoskeletal injury risk in midlife women has traditionally been attributed to estrogen decline, but this narrow focus overlooks the broader biomechanical, neuromuscular, and structural changes associated with menopause. Estrogen plays a multisystem role in maintaining trabecular bone integrity, collagen turnover, and neuromuscular coordination. Its abrupt loss causes bone demineralization (2%–5% annually in early menopause), impairs tendon repair, and contributes to sarcopenia. Fluctuating estradiol levels during perimenopause may transiently increase ligament laxity, further destabilizing joints. Common injuries such as Achilles and rotator cuff tendinopathies, plantar fasciitis, and stress fractures are amplified by low bone mineral density, prior fracture history, aromatase inhibitor use, and rapid increases in physical activity. Although early initiation of hormone replacement therapy reduces fracture risk by 20%–40%, it is not appropriate for all patients due to contraindications and individualized risk–benefit profiles. Non-hormonal strategies—including resistance training, nutritional optimization, and early screening with dual-energy X-ray absorptiometry and peripheral quantitative computed tomography—remain underutilized, particularly among marginalized populations. This structured narrative review synthesizes evidence from endocrinology, biomechanics, and musculoskeletal epidemiology to evaluate limitations in current research, including reliance on observational data, homogeneous cohorts, and technocentric approaches with limited generalizability. Future efforts should prioritize personalized, hormone-informed exercise prescriptions, biomarker-guided monitoring, and community-based prevention strategies. The prevailing estrogen-centric paradigm may benefit from a broader multidisciplinary framework integrating biological, mechanical, and social determinants of injury risk. We propose a hormone–tissue–load mismatch model that reframes menopause as a modifiable biomechanical window for injury prevention.

Keywords: Menopause, Perimenopause, Stress fractures

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INTRODUCTION

Overuse injuries and stress fractures are prevalent musculoskeletal conditions, often resulting from repetitive mechanical loading that exceeds tissue repair capacity [1]. Among midlife women, the incidence of these injuries is influenced by the physiological changes associated with menopause and perimenopause, periods marked by profound hormonal and structural alterations. The perimenopause phase is reported to last for an average of 4–7 years, though it can last up to 14 years, and the average age of menopause is 51–52 years in the US [2]. Perimenopause, which can last 4 years, is characterized by fluctuating estrogen and progesterone levels, followed by an abrupt decline post-menopause. These hormonal shifts significantly impact bone integrity, muscle mass, and connective tissue properties, predisposing women to biomechanical vulnerabilities [3]. Unlike prior reviews that focus primarily on bone mineral density (BMD) or fracture outcomes, this review critically examines how endocrine-driven tissue vulnerability interacts with mechanical loading to precipitate overuse injuries before overt osteoporosis develops.

Estrogen is critical in maintaining bone homeostasis by modulating osteoclast and osteoblast activity. Postmenopausal estrogen deficiency accelerates bone resorption resulting in an average annual BMD loss of 2%–3% annually during early menopause, with cumulative losses approximating 10% over the first five years. Studies report that nearly 20% of total lifetime bone loss occurs in this early postmenopausal period [4]. Trabecular bone, found in high-stress regions such as the tibia and pelvis, is particularly affected, resulting in compromised load-bearing capacity and increased susceptibility to stress fractures. These biomechanical changes coincide with lifestyle factors such as increased physical activity among midlife women seeking cardiovascular and weight control benefits, which, paradoxically, can elevate injury risk if not appropriately managed. Epidemiological data indicate that the prevalence of stress fractures in postmenopausal women engaged in recreational or endurance activities is nearly double that observed in premenopausal counterparts [5]. Given the growing participation of women over 40 in recreational sports and structured exercise programs, understanding the interplay between hormonal decline and musculoskeletal vulnerability is clinically significant [6].

Tendon elasticity and collagen synthesis are also diminished under hypoestrogenic conditions, leading to an increased risk of tendinopathies and other overuse syndromes. In midlife and older women, such overuse injuries and stress fractures not only affect physical function but also contribute to long-term morbidity, including chronic pain and reduced quality of life [7]. This review critically examines the current evidence linking menopausal and perimenopausal hormonal shifts to structural strain, overuse injuries, and stress fractures with emphasis on underlying mechanisms, risk factors, and preventive strategies.

METHODS

This review was conducted as a structured narrative review to analyze current evidence and identify mechanistic and clinical gaps. Electronic searches were performed in PubMed, Scopus, and Web of Science using combinations of the terms: menopause, perimenopause, estrogen, stress fracture, overuse injury, tendinopathy, bone microarchitecture, and sarcopenia. Inclusion criteria comprised English-language human studies published between 2010 and 2025, with priority given to randomized controlled trials (RCTs), longitudinal cohort studies, biomechanical analyses, and high-resolution imaging studies. Exclusion criteria included case reports, non-peer-reviewed sources, and studies without sex-specific data. Evidence quality was appraised qualitatively based on study design, population relevance, and methodological transparency.

Conceptual framework: hormone–tissue–load mismatch

We introduce the hormone–tissue–load mismatch model, which posits that menopausal injury risk emerges not solely from estrogen deficiency, but from a temporal mismatch between declining tissue resilience (bone, tendon, muscle) and maintained or increased mechanical loading. During perimenopause, fluctuating estradiol (E2) alters ligament compliance and neuromuscular control, while early postmenopause accelerates microarchitectural bone loss and sarcopenia. When physical activity intensifies without adaptive recovery capacity, repetitive sub-threshold loads accumulate, culminating in overuse injury or stress fracture.

Hormonal changes in menopause and perimenopause

Menopause results in a significant decline in circulating levels of estrogen and progesterone. In addition to changes in follicle-stimulating hormone (FSH) and luteinizing hormone (LH) levels, there is a substantial decrease in the amount of estrogen produced during menopause [8]. Estrone (E1), derived from

peripheral aromatization of androstenedione, becomes the predominant, but significantly less potent, estrogen [9]. Estriol (E3) remains negligible outside of pregnancy. Progesterone, dependent on corpus luteum activity, ceases following ovulatory failure, leading to neuroendocrine and musculoskeletal changes. E1 without the presence of progesterone may cause endometrial hyperplasia with/despite an overall low estrogen tone [10].

Menopause derived estrogen deficiency has pronounced systemic consequences. However, it's most clinically relevant consequences for this review relate to the musculoskeletal system. Reduced estrogen signaling alters bone remodeling through increasing osteoclast activity and reducing osteoblast function. This leads to accelerated bone loss and impaired microdamage repair. In parallel, declines in collagen synthesis and tendon elasticity reduces the mechanical resilience of connective tissues. Sarcopenia and impaired neuromuscular control diminish load absorption [11]. Collectively, these changes reduce the capacity of bone, tendon, and muscle to tolerate repetitive loading, increasing susceptibility to overuse injuries and stress fractures during the menopausal transition [12].

Estrogen also plays a vital role in bone metabolism. Estrogen receptor alpha (ERα), which dominates in cortical bone, regulates osteoblast and osteoclast activity. Estrogen receptor beta (Erβ) in trabecular bone has modulatory effects, and G-protein coupled estrogen receptor 1 (GPER1) ensures the survival of osteocytes via non-genomic signaling [13]. With estrogen loss, osteoclastogenesis increases due to high receptor activator of nuclear factor kB ligand (RANKL) and low osteoprotegerin, while osteoblastogenesis drops due to impaired Wnt/β-catenin signaling and raised tumor necrosis factor alpha (TNF-α) and interleukin-6 (IL-6) levels [14]. Trabecular bone score (TBS) loss of around 6.3% within the first five years post menopause [15]. Overall, these receptor-level changes will manifest as accelerated osteoporosis, increasing the fragility of the joints.

Beyond bone, estrogen deficiency degrades ligaments and tendons due to loss of ERβ signaling, elevated matrix metalloproteinases-1 and -3 (MMP-1/3), and reduced elastin, destabilizing joints [16]. Muscles suffer from reduced satellite cell activation, advancing sarcopenia. Neuromuscular junctions lose acetylcholine receptor stability, slowing contraction and proprioception [17]. These molecular changes present clinically with slower tendon healing, joint instability, and increased overuse injury. Apart from the molecular level, Perimenopause also features hormonal fluctuations rather than a steady decline. E2 may spike to 300 pg/mL, while FSH stays >25 IU/L due to inhibin B loss. These surges can temporarily increase ligament laxity, heightening joint instability risk. Postmenopause, E2 stabilizes below 20 pg/mL, leading to progressive degradation of muscle and connective tissue, increasing risks for tendinopathy, rotator cuff tears, and stress fractures [18].

The hormonal shifts of menopause represent a systemic endocrine failure with biomechanical consequences. Disruption of ER signaling, inflammation, and tissue architecture explains the elevated risk of fractures and injuries [19]. Hormone therapy is time-sensitive, with early initiation preserving bone health, whereas late use offers minimal benefit. Future therapeutic strategies should prioritize targeting selective ER modulation for musculoskeletal protection while minimizing cancer risk as it has agonist and antagonist activities [20].

To synthesize these endocrine and metabolic mechanisms into clinically relevant musculoskeletal outcomes, Table 1 summarizes key hormonal and physiologic changes observed during menopause and perimenopause, their effects on bone, tendon, and muscle tissue, and corresponding preventive strategies relevant to rehabilitation and injury prevention.

Structural and biomechanical consequences of menopause and perimenopause in relation to overuse injuries and stress fractures

Estrogen decline boosts bone resorption, outpacing formation. Within the first 3–10 years post-menopause, trabecular bone loses 2%–3% annually, while cortical bone declines by about 1% annually. Sites rich in trabecular bone, such as the vertebrae, hips, and distal tibia, are most vulnerable. Concurrently, cortical thinning and porosity reduce stiffness and load capacity, raising fracture risk [21]. Low estrogen levels also impair bone repair by preventing adequate remodeling of microcracks, a natural result of loading, by reducing remodeling activation. This leads to incomplete resorption and delayed mineralization. Unrepaired microdamage weakens trabecular structure and cortical strength, increasing fracture risk. In addition, osteocytes become less responsive to strain, further limiting adaptive remodeling [22]. As a result of all these changes, stress fractures are more likely to occur under loads that would otherwise be well tolerated.

Estrogen deficiency also weakens tendons and ligaments by decreasing collagen synthesis, fibril regulation, and hydration. These changes reduce tensile strength and elasticity. Furthermore, increased advanced glycation end products (AGEs) stiffen collagen, impairing load distribution and increasing ten-

Table 1. Hormonal and metabolic changes in menopause: musculoskeletal effects and preventive strategies

Hormonal/physiologic change	Bone outcome	Tendon/ligament outcome	Muscle/neuromuscular outcome	Practical preventive strategy
Declining estradiol (E2) → ↑RANKL, ↓OPG, impaired remodeling	Rapid bone loss; ↑cortical porosity; ↓bone strength and fatigue resistance → ↑stress fracture risk	↓Collagen synthesis, ↓hydration, altered fibril structure → stiffer tendon, slower healing	↓Satellite cell activity and protein synthesis → sarcopenia, ↓shock absorption	Progressive load increases (≤10%–15%/wk); deload weeks; strength training 2–3×/wk; protein 1.0–1.2 g/kg/day; Ca 1,000–1,200 mg/day; replete vitamin D; DXA±TBS
Perimenopausal hormonal fluctuations (variable E2/progesterone)	Variable bone turnover; early microarchitectural decline may precede DXA change	Periods of ↑laxity/compliance → joint instability	Variable neuromuscular control and coordination	Neuromuscular training; balance/proprioception; hip/core stabilization; reduce impact during symptom flares; cross-training
Low progesterone/anovulation	Indirect effects on bone via altered turnover	Possible impaired connective tissue recovery; altered pain perception	Sleep disturbance, fatigue → worse motor control	Treat vasomotor symptoms; optimize sleep; schedule high-load sessions during best recovery periods; emphasize rest days
Aging+estrogen deficiency → ↑inflammation, endothelial dysfunction	Reduced bone quality; slower fracture healing	↑Tendinopathy risk from impaired perfusion and repair	↓Aerobic capacity, slower reaction time, ↓motor unit performance	≥150 min/wk moderate aerobic activity; address CV risk; tendon rehab with eccentric/heavy slow resistance; longer rehab timelines
Advanced glycation end products (AGEs) (↑ with age, insulin resistance)	Altered bone material properties; ↑fragility at similar BMD	Stiffer collagen → ↑microtear risk	Reduced tissue elasticity; altered gait/loading	Weight management; glycemic control; diet quality; progressive loading; avoid sudden plyometrics if deconditioned
Medication-induced estrogen depletion (e.g., aromatase inhibitors)	Accelerated bone loss; ↑fracture risk	May worsen tendinopathy symptoms	Myalgias, weakness → ↓stability and activity	Baseline DXA±TBS; earlier repeat screening; osteoporosis prophylaxis per guidelines; supervised exercise; nutrition optimization
Low baseline BMD/prior fracture	Lower fatigue failure threshold; recurrent fractures	Secondary gait changes ↑tendon load	Fear-avoidance → deconditioning and poor mechanics	Individualized loading limits; low-impact conditioning; gradual return to impact; PT-guided protocols
Low energy availability/under fueling	Impaired bone formation; ↑stress fracture risk	Poor collagen synthesis and repair	Fatigue, weakness, altered biomechanics	Adequate calories; protein; Ca/vitamin D; screen for RED-S/disordered eating

OPG, osteoprotegerin; DXA, dual-energy X-ray absorptiometry; TBS, trabecular bone score; CV, cardiovascular; BMD, bone mineral density; PT, physical therapy; RED-S, relative energy deficiency in sports.

dinopathy risk. Diminished lower tissue elasticity also increases injury risk by raising skeletal strain [23].

Menopausal-induced sarcopenia can also lead to losses in muscle strength, altered gait mechanics, and amplified bone fragility. Reduced type II fibers and neuromuscular control impairs shock absorption and leads to gait changes, which include shorter strides, wider steps, and greater hip abductor use. Kyphosis from vertebral fractures shifts the center of gravity forward, overloading the lower limbs. Ground reaction force redistribution adds stress to already weakened bones, promoting stress fractures [24]. Together, compromised bone, tissue repair, and neuromuscular changes create a structurally vulnerable system. Preventive strategies must focus on bone, muscle, and biomechanical support during menopause [25].

Overuse injuries in menopausal and perimenopausal women

Overuse injuries rise during menopause due to hormonal decline, structural weakening, and biomechanical changes. Tendinopathies, especially Achilles and rotator cuff injuries, are the most common. Achilles tendons face repetitive eccentric load plus poor collagen synthesis, leading to stiffness and microtears.

Rotator cuff tendons with high functional demand suffer matrix and vascular changes leading to chronic tendinopathy and partial tears [26]. Plantar fasciitis, linked to foot muscle weakening, arch collapse, and altered gait, is frequent. Poor shock absorption and tendon compliance cause microdamage to the plantar fascia, leading to chronic inflammation and degeneration [27].

Sarcopenia caused by estrogen loss reduces type II fibers, weakening joint stabilization and shock absorption. Concurrently, estrogen withdrawal disrupts tenocyte metabolism and extracellular matrix (ECM) turnover, leading to reduced collagen and hydration, increasing AGEs and tendon stiffness. Mechanical loading further activates ECM, interleukin-1 beta (IL-1β), and matrix metalloproteinase-9 (MMP-9), which break down collagen and induce tendon apoptosis. Together, these changes slow down the healing process and promote degeneration [28]. Years of cumulative loading work and exercise, combined with poor vascularity, low cell proliferation, and impaired matrix deposition, means that repetitive stress now exceeds repair capacity and can progresses to chronic injuries. Clinically, this explains why menopausal women tend to have more tendinopathies that are either chronic, recurrent, and/or resistant. The interaction of hormonal, neuromuscular, and molecular changes significantly raises the risk of Achilles tendinopathy, rotator cuff tears, and plantar fasciitis. These reduce mobility and increase fracture risk and disability. Effective prevention, therefore, requires a focus on muscle preservation, tendon resilience, and hormone support during and after menopause [29].

Stress fracture epidemiology in midlife and older women

Stress fractures are significantly more prevalent in midlife and older women compared to premenopausal counterparts, largely due to estrogen decline and age-related structural changes. Large-scale analyses demonstrate that women over 50 experience markedly higher rates of lower-extremity stress fractures involving the tibia, metatarsals, and proximal femur than men or younger women [30]. In perimenopausal cohorts, fracture incidence (including low-energy fractures) ranges from 5.6% to 8.5% over 2–3.6 years with common sites being the wrist (37%), ankle (12%), hands, feet, ribs, and hip [31]. Women sustaining perimenopausal fractures exhibit a 5.8% lower lumbar spine BMD and 4.6 lower femoral BMD compared to non-fracture controls [32].

Postmenopausal women with metatarsal stress fractures have significantly lower dual-energy X-ray absorptiometry (DXA) scores compared with premenopausal women despite similar body mass index (BMI) and vitamin D status, confirming a direct link between menopausal status and skeletal fragility [33]. Key risk factors include low BMD (each 1-standard deviation decrease in spinal or femoral BMD raises risk by 1.4–1.6-fold), absence of hormone therapy (relative risk [RR] 1.5–2.2 for osteoporotic fractures), prior fractures (hazard ratio [HR] 1.25–1.33), chronic illness (RR 1.4–1.6), smoking (RR 1.8), and high alcohol intake (odds ratio [OR] ~1.45) [31,34,35]. Mechanistically, estrogen withdrawal accelerates trabecular bone and compromises microdamage repair, lowering fracture thresholds under repetitive loads, even before osteoporosis becomes overt [36]. These combined effects highlight the importance of targeted preventive measures during the menopausal transition.

Bone quality vs. quantity

Although areal BMD quantifies mineral content, menopause induces severe bone quality deterioration that functionally undermines skeletal integrity. Estrogen loss triggers rapid cortical porosity through intracortical remodeling. Studies of populations in Australia showed an annual porosity increases of about 0.44% in premenopause, 0.80% during perimenopause, and 1.40% postmenopause; this cortical change accounted for nearly 80% of appendicular bone loss despite modest trabecular declines (~0.17%–0.31% bone volume fraction [bone volume/total volume] per year) [37]. High-resolution peripheral quantitative computed tomography (pQCT) studies confirm cortical porosity is a dominant determinant of bone strength in postmenopausal women (semi-partial $R^2 \approx 0.22$ at the tibia) and predicts nonvertebral fracture risk, independent of BMD and Fracture Risk Assessment Tool (FRAX) scores [38]. Cortical thinning and area loss further compound fragility, especially when advanced tools show porosity contributions beyond what FRAX or Garvan captures [39].

Concurrently, trabecular architecture deteriorates after age 50, characterized primarily by the loss of connectivity and trabecular number rather than simple thinning. This leads to the production of discontinuous rod-like structures with fewer load-bearing elements [40]. In vivo comparisons demonstrate postmenopausal women experiencing 3%–8% declines in cortical tissue mineral density alongside increased porosity, regardless of ethnicity [41]. These fine structural deficits–such as cortical porosity, sparse trabecular nodes, and reduced tissue density–compromise both mechanical strength and microdamage repair. This sharply reduces failure thresholds under repetitive stress, even when BMD remains above osteoporotic thresh-

olds. Advanced microarchitecture measures thus add critical prognostic value beyond BMD alone [42]. Put simply, even women with normal BMD scores have higher fracture risks if the microarchitecture is compromised, demonstrating the need for more imaging or biomarkers.

Interaction with physical activity

Midlife women frequently increase exercise, like weight-bearing or high-impact activities, for weight control and metabolic benefit. Although resistance and impact training can stimulate osteoblast activity, preserve bone mass, and lower osteoporosis risk (in postmenopausal women, regular exercise reduced incident osteoporosis by ~17%; HR 0.83; 95% confidence interval [CI] 0.71–0.97) [43]. Abrupt intensification of loading during accelerated bone loss can overwhelm diminished microdamage repair capacity. Stress fractures often arise in postmenopausal women who initiate vigorous regimens without gradual progression when coupled with low BMD, protein or calcium inadequacy, or sarcopenia [44].

Estrogen deficiency impairs targeted bone remodeling while amplifying cortical porosity and trabecular weakening. As a result, even moderate repetitive stresses—such as increased running mileage—can exceed the fatigue thresholds of weakened bone. A survey in female runners (mean age ~35–54) identified that osteopenia (OR 4.14), previous tendon injuries (OR 1.49), running >20 miles/week (OR 1.74–1.77), and amenorrhea/bracketing menstrual disturbances (RR≥2) raised stress-fracture risk significantly [45]. Sarcopenia further limits dynamic load absorption, shifting stress to compromised bone. Thus, while physical activity remains essential, an optimal strategy during menopause is centered around progressive loading, strength training, nutritional support, and careful monitoring to avoid exceeding the bone's reduced fatigue resistance threshold.

Additional risk factors

Additional risk factors that compound stress fracture risk in midlife women include nutritional deficits and medication exposures that exacerbate bone fragility. Inadequate calcium intake (below the recommended 1,000–1,200 mg/day) and vitamin D deficiency–common in older women due to reduced dietary absorption, limited sun exposure, obesity, or drug interactions–trigger secondary hyperparathyroidism. The resulting metabolic cascade elevates bone turnover, impairs mineralization, and weakens proximal muscles, which increases fall and fracture risk [46]. Although calcium and vitamin D supplementation improves serum levels, large-scale analyses suggest minimal fracture reduction benefit, prompting critical re-evaluation of universal supplementation policies.

Estrogen-depleting medications such as aromatase inhibitors (AIs) (e.g., anastrozole, letrozole, exemestane) dramatically increase fracture risk beyond what is expected from menopause alone. Meta-analyses encompassing nearly 100,000 women show pooled RR of osteoporotic fractures ~1.35 (95% CI 1.29–1.42) and vertebral fractures RR ~1.83 during AI therapy compared to tamoxifen or no AI use [47]. Observational data report fracture risks in AI-treated women up to 40% higher (HR ~1.40) than tamoxifen users, though elevated baseline BMI and BMD may mitigate observed fracture incidence in some cohorts [48].

AI therapy accelerates bone loss by an additional 2%–3% annually in trabecular-rich regions and increases cortical porosity through unchecked remodeling in estrogen-deprived bone [49]. Combined, nutritional insufficiency and AI-induced estrogen deprivation imposes a dual insult: diminished bone mass, degraded microarchitecture, compromised mineralization, and slowed microdamage repair. This synergistic effect sharply lowers skeletal fatigue resistance, contributing to a higher incidence of stress fractures and fragility fractures in menopausal and perimenopausal women. Since AI therapy has been seen to increase risks of fracture through various pathways, women on these medications should be screened earlier and more aggressively for earlier intervention.

Role of estrogen and hormone therapy in injury prevention

Hormone replacement therapy (HRT), consisting of estrogen with or without progestogen, has been demonstrated in multiple RCTs and meta-analyses to significantly reduce fracture risk and increase BMD in postmenopausal women. A meta-analysis of 28 trials (33,426 women) found HRT reduced total fracture risk by 26% (RR ~0.74; 95% CI 0.69–0.80), hip fracture by ~28%, and vertebral fracture by ~37% compared to placebo or no therapy [50]. In the Women's Health Initiative (WHI) trial, combined conjugated equine estrogen and medroxyprogesterone acetate decreased risk of any fracture by ~24% (HR 0.76; 95% CI 0.69–0.83), hip fractures by ~30% (HR 0.66; 95% CI 0.45–0.98) and wrist/vertebral fractures with similar reductions, while raising total hip BMD by ~3.7% over three years versus 0.14% in the placebo group [51]. Benefits appear strongest when HRT is initiated before age 60 or within 10 years of meno-

pause onset; fracture protection diminishes when started later than 60, and the anti-fracture effect wanes after cessation [51].

Prospective cohort data (OSTPRE, Finnish study; n≈7,217 women age 47–56) similarly report ~31%–38% reduction in any fracture and distal forearm fractures with HRT use (adjusted HR ~0.67 and 0.53, respectively) over five years [52]. Systematic reviews indicate vertebral fracture reductions of approximately 33% especially in women younger than 60 or with osteoporosis and non-vertebral fractures by ~27% (RR 0.73; 95% CI 0.56–0.94), though efficacy declines in older age groups (≥60) [53]. In frail elderly women (≥75 years), HRT increased lumbar spine BMD by ~4.3% and total hip by ~1.8% over nine months with substantial reductions in bone-turnover markers [54]. Overall, estrogen-based HRT clearly enhances bone quantity (BMD) and microarchitectural stability, translating into 20%–40% reductions in vertebral, hip, and overall fractures when started early in menopause. However, declining benefit with delayed initiation, and risk considerations (e.g., thromboembolism, cardiovascular and breast cancer risk), require individualized risk-benefit assessment before prescribing HRT [55].

Non-hormonal interventions

Exercise programs combining impact (e.g., jumping, step aerobics) and resistance training (e.g., weight-lifting, vest-jump work) produce modest but clinically meaningful gains in BMD for postmenopausal women: meta-analysis showed that moderate intensity resistance training was superior in improving lumbar spine bone mineral density (LS BMD) and femoral neck bone mineral density (FN BMD) compared to the control group (as per usual daily life), with a statistically significant difference ($p<0.05$) [56]. One RCT in breast cancer survivors found resistance+impact training preserved spinal BMD (-0.47% vs. -2.13% in controls) and attenuated elevated bone turnover markers (osteocalcin, deoxypyridinoline). Meta-analyses indicate that combined and multicomponent exercise yields the most consistent benefit at both the spine and hip, though the quality of evidence is rated low to moderate [57].

Nutritional strategies also play a key adjunct role. Adequate daily intake of calcium (1,000–1,200 mg), vitamin D (600–800 IU), protein (1.0 g/kg/day), magnesium, vitamin K_2, and antioxidants like vitamin E correlate with better BMD maintenance and lower fracture risk in postmenopausal populations [58]. Vitamin K_2 supports osteocalcin carboxylation and bone mineralization, while phytoestrogens and phytates may modestly inhibit osteoclastic resorption and contribute to bone preservation [59].

Collectively, evidence supports strategically dosed, multi-modal exercise programmes–incorporating weight-bearing and resistance training several times a week–along with nutrition strategies emphasizing adequate protein and diverse micronutrients. These non-hormonal approaches help to maintain bone density, improve muscle function, reduce fall risk, and indirectly lower stress-fracture and osteoporotic injury risk in menopausal and perimenopausal women [60].

Clinical implications and future directions

Screening and monitoring bone health during menopause and perimenopause are critical to reducing fracture risk and preventing overuse injuries. DXA remains the gold standard for BMD assessment, typically performed at the lumbar spine and femoral neck [61]. Studies show that each standard deviation decrease in BMD at these sites increases fracture risk by 1.4 to 1.5 times, and women in the lowest quartile of spinal BMD face nearly three times the fracture risk compared with those in the highest quartile [62]. Independent predictors include: low BMD, history of prior fracture, smoking, multiple chronic illnesses, and non-use of hormone replacement therapy [35]. Risk stratification tools such as the FRAX algorithm combine femoral neck BMD with clinical risk factors like age, prior fracture, smoking, or glucocorticoid use to estimate the 10-year probability of a major osteoporotic fracture and guide decisions on screening and treatment [63]. Current guidelines recommend BMD screening for women younger than 65 with one or more risk factors, such as early menopause or low body weight. For women undergoing pharmacologic or hormonal treatments, repeat scans are advised every two to three years [64].

Advanced measures like TBS provide additional insight into bone microarchitecture, complementing BMD when fracture risk appears higher than density suggests [65]. Quantitative ultrasound and peripheral DXA may serve as preliminary tools but lack reliability for long-term monitoring [66]. Biomarkers of bone turnover can offer further predictive value in select cases. Early menopause, particularly before age 45, significantly elevates fracture risk (OR ~1.36 compared with menopause after age 45) [67], and population studies report an 8% incidence of fractures within three to four years among women aged 47–56, especially those with low BMD or prior fractures [68]. Interestingly, even women with relatively preserved BMD have reported stress fractures, suggesting that microarchitectural deterioration and biomechanical alterations also contribute [33]. Therefore, comprehensive screening using DXA, FRAX, and TBS, coupled

with periodic monitoring and preventive strategies such as resistance exercise, adequate calcium and vitamin D intake, and fall-risk reduction, is essential for mitigating both fragility and stress fractures during the menopausal transition.

Advancements and future directions in managing menopausal structural strain and overuse injuries

Future directions in the prevention and management of overuse injuries and stress fractures in menopausal and perimenopausal women must move beyond general screening toward integrated, biomarker-guided interventions [69]. Recent advances in skeletal imaging, particularly high-resolution pQCT, allows for detailed microarchitectural analysis capable of detecting trabecular thinning and cortical porosity that are undetected by standard DXA. This technology allows for earlier identification of women at imminent risk of fracture [70]. The clinical utility of biochemical markers of bone turnover (e.g., serum C-terminal telopeptide of type I collagen [CTX] and procollagen type I N-terminal propeptide [P1NP]) is gaining ground for dynamic monitoring of bone response to mechanical loading and pharmacologic therapy, especially in those undergoing antiresorptive or anabolic treatment. Additionally, machine learning models trained on large datasets of postmenopausal athletes have begun to predict injury risk with high specificity by integrating hormonal profiles, gait mechanics, previous loading patterns, and genetic predispositions (e.g., polymorphisms in collagen type I alpha 1 [*COL1A1*] and estrogen receptor 1 [*ESR1*]) [71].

Research is also shifting toward mitochondrial and inflammatory signatures as intermediate biomarkers linking estrogen decline with impaired skeletal adaptation and tendon resilience. These developments indicate a need for multi-modal, sex-specific prevention protocols. Exercise prescription is expected to evolve into algorithm-based, periodized models that cycle intensity, impact, and recovery in accordance with individual hormonal responsiveness rather than arbitrary age stratification. Crucially, future strategies must embed preventive interventions before the onset of menopause, during perimenopausal transition when bone loss accelerates (2%–5% annually), and neuromuscular control declines. As such, menopause should be reframed not as a risk state but as a predictable, modifiable window where early intervention is anchored in mechanobiology, which can prevent structural failure. This shift requires increased funding for large-scale, longitudinal studies to validate early diagnostic thresholds and stratify risk across diverse populations [72,73].

CONCLUSION

The current literature supports a clear associated between menopausal changes and increases musculoskeletal vulnerability, including elevated risk of overuse injuries and stress fractures. Estrogen deficiency contributes to reductions in bone density, alterations in tendon structure, as well as declines in muscle mass and neuromuscular function. However, injury risk appears to arise from the interaction between these biological changes and mechanical loading patterns rather than hormonal factors alone. Critical gaps persist, including limited sex-specific exercise guidelines, underrepresentation of diverse populations, and a need for more longitudinal interventional data. Although hormone therapy demonstrates benefits for bone health in selected populations, its use requires an individualized risk-benefit assessment and should be considered in conjunction with non-pharmacological strategies.

Future research should focus on integrated models that combine hormonal, biochemical, and lifestyle factors to better define injury risk and optimize prevention strategies. Early screening, progressive load programs, and targeted exercise and nutrition interventions represent practical clinical approaches that can be implemented in preserving musculoskeletal health during menopausal transition.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

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Enhancing Diagnostic Precision and Treatment Effectiveness Using Indocyanine Green Lymphography in Lymphedema

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Indocyanine green (ICG) lymphography has rapidly emerged as a key imaging modality for improving the diagnosis and management of lymphedema. ICG lymphography offers superior sensitivity and detailed assessment of dermal backflow patterns, functional lymphatic channels, and collateral drainage routes. Evidence also supports its role in guiding targeted rehabilitation, including ICG-guided lymphedema treatment. Clinicians can enhance diagnostic precision and potentially improve therapeutic effectiveness by integrating ICG lymphography into clinical practice. This review summarizes current evidence on its clinical utility, highlighting how real-time visualization of superficial lymphatic pathways and lymph nodes allows for detection of dysfunction, and improved treatment planning. Future work should focus on standardizing protocols and developing quantitative metrics to expand its values in comprehensive lymphedema care.

Keywords: Lymphedema, Indocyanine green, Lymphography, Manual lymphatic drainage

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INTRODUCTION

Lymphedema is a chronic and progressive disease that significantly impacts patients' quality of life and function [1]. Indocyanine green (ICG) lymphography enables highly sensitive visualization of superficial lymphatic drainage and allows clinicians to assess lymphatic flow before and after lymphedema treatment. Although ICG lymphography is not yet formalized as a fully validated primary outcome measure, it has emerged as a highly promising tool for quantifying lymphatic function. ICG lymphography also contributes to the early identification and timely management of lymphedema by detecting lymphatic flow impairment at subclinical stage [2,3].

ICG dye was first photographed using near-infrared (NIR) imaging at Kodak Research Laboratories. It has traditionally been used for hepatic function testing, cardiovascular assessments, and retinal blood flow evaluation [4]. Clinically, its earliest and most widespread application in lymphatic imaging has been in sentinel lymph node mapping and intraoperative navigation for breast cancer [5]. Following early reports on lymphatic imaging and dynamic parameters such as propulsion velocity and contraction rate in both healthy individuals and patients with lymphedema [6,7], a rapidly expanding evidence of ICG lymphography has emerged as a reliable assessment tool for lymphedema diagnosis and monitoring [8].

In South Korea, ICG lymphography has been formally recog-

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nized as a reimbursable diagnostic imaging modality for lymphedema since 2024, leading to rapid adoption across medical centers. In practice, its applications can be broadly categorized into three areas: diagnostic evaluation, assistive tool as image-guided treatment, and patient education. While diagnosis forms the foundation, the latter two are increasingly utilized in routine care. Given that lymphedema requires lifelong self-management, ICG lymphography serves as an effective educational tool by helping patients visually understand their condition, reinforcing motivation for self-care, and supporting more tailored management strategies. Although evidence on the role of ICG lymphography during lymphedema treatment is still evolving, personalized mapping of lymphatic pathways and real-time visualization of individual lymphatic dysfunction strongly suggest its potential benefit [9]. Furthermore, patients often gain clearer insight into their condition through imaging procedure, making ICG lymphography an invaluable adjunct for self-management guidance and clinical education.

In this review, we summarize the utility of ICG lymphography along with introducing our representative cases to illustrate how ICG lymphography can enhance diagnostic precision, support individualized lymphedema treatment and ultimately improve outcomes in patients with lymphedema.

THE BASICS OF ICG NIR FLUORESCENCE IMAGING

ICG is a tricarbocyanine dye having a molecular weight of 751.4 Da, soluble in water. It is classified as a relatively safe agent with no active metabolites, low toxicity and rapid biliary excretion [10]. Determining the optimal dose and concentration is essential for maximizing image quality. When the concentration is too low, visualization of the target region and fine lymphatic structures may be insufficient. Conversely, if the concentration is excessively high, the reduced molecular spacing can theoretically induce a quenching effect, whereby functional lymphatic channels lying beneath areas of segmental dermal backflow (DB) may become difficult to be identified [11]. When ICG dye is injected into the dermis, ICG rapidly binds to lipid-protein complexes, which facilitates its uptake to the lymphatic vascular compartment and drainage into superficial lymphatic vessels. When the excitement light illuminates with NIR light, the injected dye absorbs photons within NIR range and emits fluorescence that can be detected by NIR-sensitive imaging system (Fig. 1).

The quality of ICG lymphographic images depends largely on how efficiently photons emitted from activated fluorophores are collected after passing through biological tissues. ICG molecules function as fluorophores capable of repeated cycles of excitation and emission, theoretically producing thousands of photons per second. In addition, NIR excitation light induces minimal tissue autofluorescence, resulting in a high contrast-to-background ratio that facilitates visualization of superficial lymphatic vessels located just beneath the skin [12]. However, NIR photons possess relatively low energy and are highly susceptible to scattering within tissue. Consequently, despite the high theoretical photon count rate, the effective imaging depth remains limited, with reliable resolution generally restricted to approximately 3–4 cm below the skin surface. For this reason, ICG NIR fluorescence imaging is most widely used for applications involving superficial lymphatics [13].

Fig. 1. Near-infrared imaging system and representative indocyanine green lymphography visualization.

KEYNOTES FOR ICG GUIDED LYMPHATIC MAPPING

Improving patient experience with ICG lymphography

A major barrier to patient comfort during ICG lymphography is the pain caused by the low pH of the injected solution. Several alternative diluents have been explored to optimize both patient comfort and imaging reliability. Among them, ICG mixed with 5% dextrose has demonstrated a markedly improved pain, typically yielding Visual Analog Scale (VAS) of 0–1, while 5% albumin has also been investigated as a physiologically compatible option [14]. In our clinical practice, we adopted a hybrid approach administering a small amount of 2% lidocaine using a 30 gauge needle immediately before ICG injection, to minimized procedural discomfort while avoiding direct mixing of lidocaine with the ICG solution which have caused depressing effect of lymphatic contractility [15]. This strategy has effectively improved patient tolerance without compromising lymphatic imaging quality.

Protocols focusing on identification of an individual lymphatic drainage pathway

ICG-guided lymphatic mapping and manual lymphatic drainage (MLD) require careful attention to both anatomical visualization and functional assessment. Suami and colleagues demonstrated that the superficial lymphatic system is organized into distinct lymphosomes, territorial units by specific lymphatic collectors. Suami's cadaveric microdissection and dye-injection studies revealed that each lymphosome is separated by watershed lines and that lymphatic collectors run in consistent longitudinal patterns with limited cross-communication between territories [16]. Based on this principle, during ICG mapping, clinicians should assess which lymphosome the injection site belongs to, whether the expected collector pathway within that lymphosome remains intact, and whether drainage deviates into adjacent lymphosomes, indicating compensation or obstruction.

During the exam, initial observation should include monitoring the spontaneous movement of ICG to identify baseline propulsion patterns and potential stagnation zones. This was followed by MLD to facilitate the transit of ICG through functional superficial lymphatics, enabling clearer visualization of dynamic flow. Subsequently, detailed mapping and demarcation of superficial lymphatics can be performed (Fig. 2), real-time ICG visualization was then used to adjust MLD direction, pressure, and sequence for each patient, consistent with emerging evidence supporting personalized treatment strategies based on individual lymphatic drainage pathways rather than a stereotype anatomical approach [17].

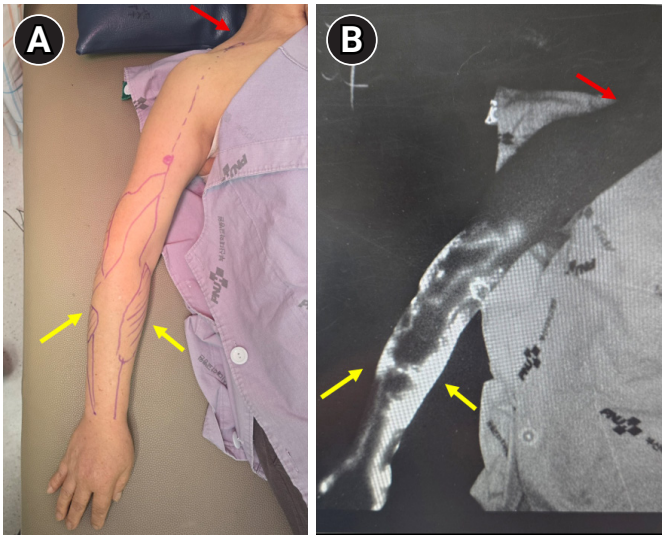

Fig. 2. Mapping superficial lymphatics and demarcation of dermal backflow (yellow arrows) in a breast cancer-related lymphedema patient (red arrow: final drainage pathway). (A) Surface mapping of superficial lymphatics and dermal backflow area projected onto the skin. (B) Corresponding indocyanine green lymphographic image of the patient.

INTERPRETING THE ICG LYMPHOGRAPHY FINDINGS

Interpreting ICG lymphography requires a systematic and anatomically informed approach. Precise mapping should document four key components: (1) preserved linear superficial lymphatic vessels; (2) presence of collateral or alternative pathway; (3) DB patterns with corresponding staging; and (4) subcutaneous pathways and fluid transport in advanced lymphedema. Real-time visualization allows the clinician to fine-tune the direction, sequence, and pressure of MLD based on each patient's unique lymphatic physiology rather than relying on conventional and uniform drainage patterns. Based on these principles, we propose the ICG-NIRS Image-Based Comprehensive Lymphedema Classification (Table 1), a structured framework consisting of three domains. First, patterns of ICG distribution are assessed by distinguishing functional and non-functional zones. Functional zones are defined by linear lymphatic flow with directional movement and are further characterized by

Table 1. ICG-NIRS Image-Based Comprehensive Lymphedema Classification

(1) Patterns of ICG distribution	
Functional zone	☐ Linear pattern with directional flow Velocity ☐ Rapid (<30 min) ☐ Delayed (30–60 min) ☐ Stagnant (>60 min) Visualized final drainage pathway ☐ Yes ☐ No
Non-functional zone	Proportion of dermal backflow areas relative to the total are _____ % ☐ Focal dermal backflow (e.g., elbow crease only) ☐ Segmental dermal backflow (e.g., forearm medial side) ☐ Regional dermal backflow (e.g., entire forearm) ☐ Extensive dermal backflow (e.g., forearm+arm) ☐ Diffuse dermal backflow (e.g., whole limb)
(2) Final drainage pathway analysis	
Original pathway	☐ Yes ☐ Partial ☐ No
Upper limb	☐ Ipsilateral clavicular ☐ Parasternal ☐ Intercostal ☐ Contralateral axilla ☐ Ipsilateral inguinal
Lower limb	☐ Popliteal ☐ Lower abdominal ☐ Upper lateral thigh ☐ Posterior thigh ☐ Gluteal ☐ Contralateral inguinal ☐ Axilla or parasternal
Breast	☐ Parasternal/internal mammary ☐ Intercostal/posterior scapular ☐ Clavicular ☐ Contralateral axilla ☐ Inferior/abdominal
(3) Severity grading system	
Grade 0 (Normal)	Normal linear lymphatic flow to axilla; no DB in breast
Grade 1 (Mild)	Localized DB in limb or peri-areolar region; >80% functional
Grade 2 (Moderate)	Regional DB or; delayed breast drainage
Grade 3 (Severe)	Diffuse DB involving limb or breast; <30% functional; alternative drainage dominant
Grade 4 (Very severe)	Whole-area DB with no detectable flow even after MLD

ICG, indocyanine green; DB, dermal backflow; MLD, manual lymphatic drainage.

flow velocity and the presence of a clearly visualized final drainage pathway. Non-functional zones are identified by DB, which is the proportion from the total limb area and categorized into focal, segmental, regional, extensive, or diffuse patterns based on anatomical distribution. Second, final drainage pathway analysis evaluates whether the original lymphatic pathway is preserved or identifies alternative drainage pathway. Their pathways are systemically classified according to anatomical regions, including upper limb (e.g., ipsilateral clavicular, parasternal, intercostal, contralateral axilla, ipsilateral inguinal), lower limb (e.g., popliteal, lower abdominal, upper lateral thigh, posterior thigh, gluteal, contralateral inguinal, or axillary/parasternal pathway), and breast (e.g., parasternal/internal mammary, intercostal/posterior scapular, clavicular contralateral axilla, or inferior/abdominal pathways). The identification of alternative drainage pathways is based on established anatomical lymphatic mapping concepts, including the lymphosome framework described by Hiroo Suami, which demonstrated that lymphatic flow follows distinct territories and can be rerouted through collateral pathways following disruption [17-19]. Finally, a severity grading system is applied based on the extent of DB, the proportion of functional lymphatic flow, and the dominance of alternative drainage pathways.

Preserved linear superficial lymphatic vessels

Preserved linear superficial lymphatic vessels indicate functional lymphatic channels with intact propulsion. These vessels often demonstrated rhythmic peristaltic contraction and direc-

tional flow, representing physiological drainage capacity. Mapping these linear structures helps determine whether the primary lymphosome-specific pathway remains patent and identifies potential targets for MLD to where lymph flow is directed. According to the MD Anderson Cancer Center (MDACC) ICG staging scale, the presence of continuous linear channels corresponds to stage 0–I, representing early or mild disease with preserved collecting lymphatics and minimal DB. As disease progresses beyond this stage, linear collectors become interrupted or completely absent, giving way to segmental or diffuse DB patterns (Fig. 3).

Despite the theoretical depth limitations of NIR fluorescence imaging, our anecdotal experience indicates that ICG lymphography can reliably visualize not only superficial lymphatic vessels but also lymph nodes located in the deep subcutaneous layers. As demonstrated in Fig. 4, drainage to the lateral humeral axillary lymph node was also well delineated in the upper arm. The epitrochlear lymph node within the antecubital fossa and along the medial aspect of the elbow was clearly identifiable, receiving lymphatic drainage from the ulnar side of the hand and forearm. Similarly, the popliteal lymph node, typically classified as a deep node in the posterior compartment, can be distinctly visualized in the lower limb. Even in the inguinal region, lymph nodes on the inferolateral aspect can be detected as they receive lymphatic drainage from the lower extremity. In such cases, where lymphatic function is relatively preserved, lymphatic flow remains functional, allowing clear visualization of lymphatic structures, including lymph nodes in the deep subcutaneous layer. However, as lymphedema progresses and lymphatic function deteriorates, visualization of these structures becomes less consistent and may be diminished. These observations support the expanding utility of ICG lymphography in mapping not only superficial lymphatics but also lymph nodes when they lie within the effective penetration depth of NIR light.

Presence of collateral or alternative drainage pathways

The identification of the lymphatic drainage pathway was an important parameter to determine treatment strategy, especially how to proceed MLD. ICG lymphography has capability to detect altered lymph drainage site in lymphedema (Fig. 5). Enhancement of ICG signal in the supraclavicular LN represented an alternative pathway at the same time as performing the MLD

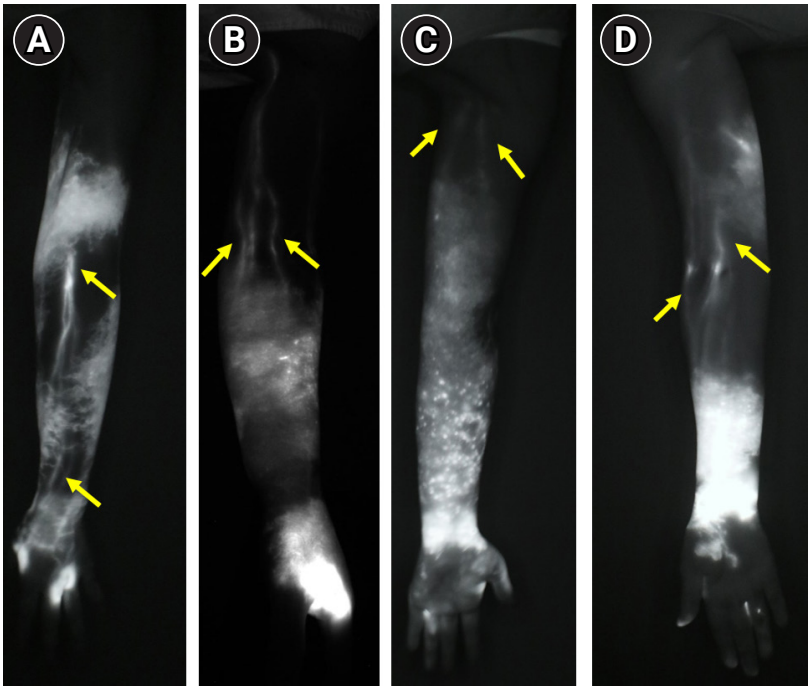

Fig. 3. Various dermal backflow patterns, expansion ranges, and the degree of functional lymphatic preservation patterns in the front upper limbs (arrows: preserved lymphatic vessels). (A) Extensive dermal backflow in the upper limb with preserved underlying functional lymphatic vessels. (B) Dermal backflow in the wrist and forearm with continuity to functional lymphatic in the proximal upper arm. (C) Extensive dermal back flow in the upper arm connected to the functional lymphatic vessel drainage toward axillary region. (D) Functional lymphatic vessel bridging dermal back flow in the proximal and distal upper limb.

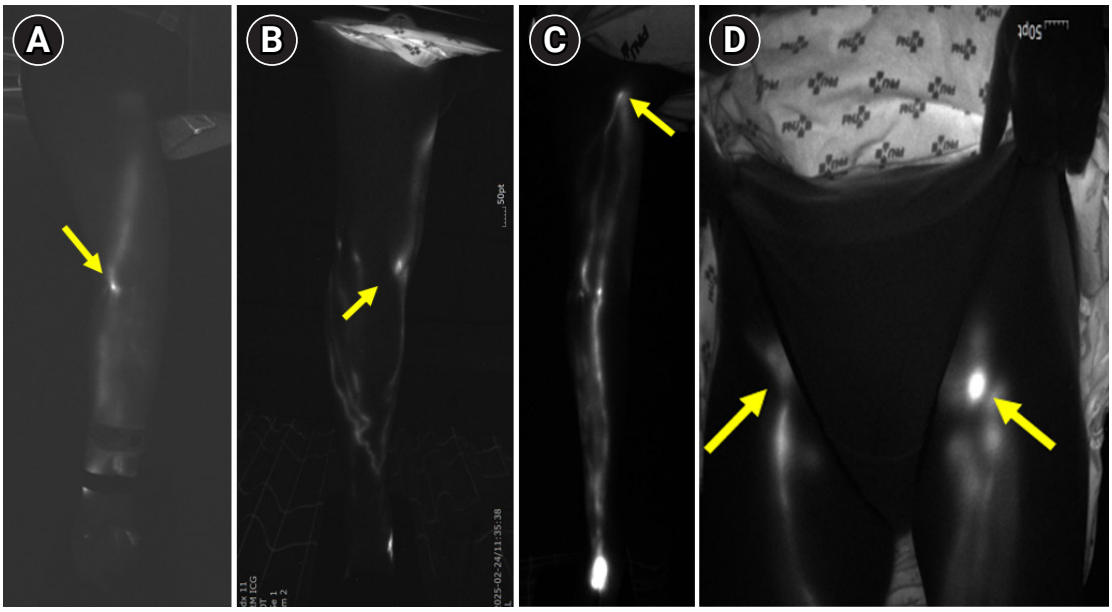

Fig. 4. Lymph node (LN) visibility (arrows) of indocyanine green lymphography of patients with early stage lymphedema. (A) Epitrochlear lymph node located in the antecubial fossa and medial aspect of elbow receiving lymphatic drainage from the ulnar-side-of the hand and forearm. (B) Popliteal LN located in the popliteal fossa and the efferent lymph vessels in the posterior thigh ascended upward and headed toward the inguinal LN. (C) Lymph fluid of upper limb drained to the lateral axillary LN. (D) Inguinal LN of inferolateral side with received lymph drain from lower limb.

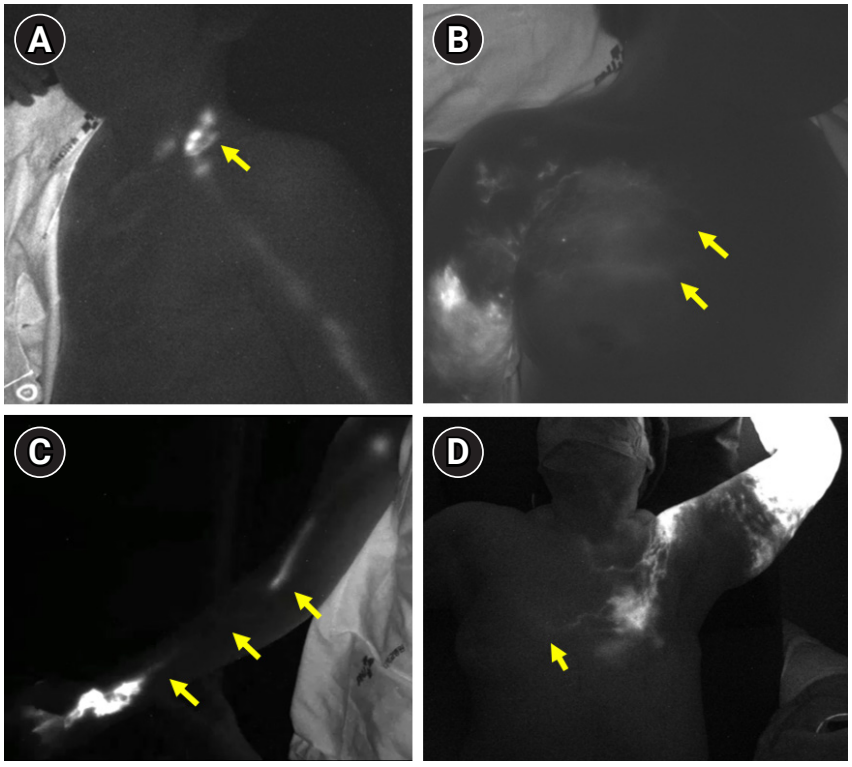

Fig. 5. Demonstration of alternative drainage pathways (arrows). (A) Enhancement of the supraclavicular lymph node at the same time as performing manual lymphatic drainage of the upper limb. (B) Alternative pathway draining to the parasternal site. (C) Connections between the superficial and deep lymphatic systems as a detour route. (D) Indocyanine green extended beyond the sagittal midline watershed and headed toward the contralateral axilla.

of the upper limb (Fig. 5A). In addition, alternative drainage can be observed to the parasternal site or extended beyond the sagittal midline watershed toward the contralateral axilla (Fig. 5B, 5D) In addition, alternative detour pathway may form between the superficial and deep lymphatic lymphatics. (Fig. 5C) Since identification of the alternative drainage site is important in determining the direction of MLD in addition to the diagnostic value, the imaging procedure should continue until confirmation of the final drainage pathway.

ICG lymphography is also useful to identify collateral routes in breast lymphedema cases after breast-conserving treatment. Several alternative lymphatic drainage pathways were identified when the primary axillary route was impaired, including parasternal, intercostal, clavicular and contralateral axilla [19]. In addition to these previously reported patterns, our observations identify an additional inferior/abdominal pathway, in which lymphatic flow diverges from the lateral or inferior breast and drains toward the abdominal or inguinal lymphatic territories (Fig. 6). This drainage pattern appears particularly when both axillary and parasternal drainage pathways were severely impaired, suggesting that the inferior/abdominal route functions as a dominant alternative pathway in severe breast lymphedema.

DB patterns with corresponding staging

DB has been specific image criterion for the diagnosis of lymphedema. DB represents a compensatory response of the body to redirect lymph fluid following lymphatic vessel injury. The pattern and distribution of DB correlate closely with the severity of lymphatic dysfunction, providing critical information for staging and clinical decision-making for treatment options [20]. DB forms a bridge between obstructed and patent lymphatic vessels, and also serves as a substitute route to transport lymph fluid following the obstruction of the superficial collecting vessels (Fig. 7) [21]. Lymphoscintigraphy and ICG lymphography have been taken on complementary roles to evaluate lymphatic function. Therefore, there was an essential need for the clinicians to determine the correlation of both examinations for obtaining comprehensive understanding. Yoon et al. [22,23] conducted two retrospective studies in lymphedema representing the DB severity stage on both examinations were very strongly correlated with substantial agreement. These studies confirmed that DB

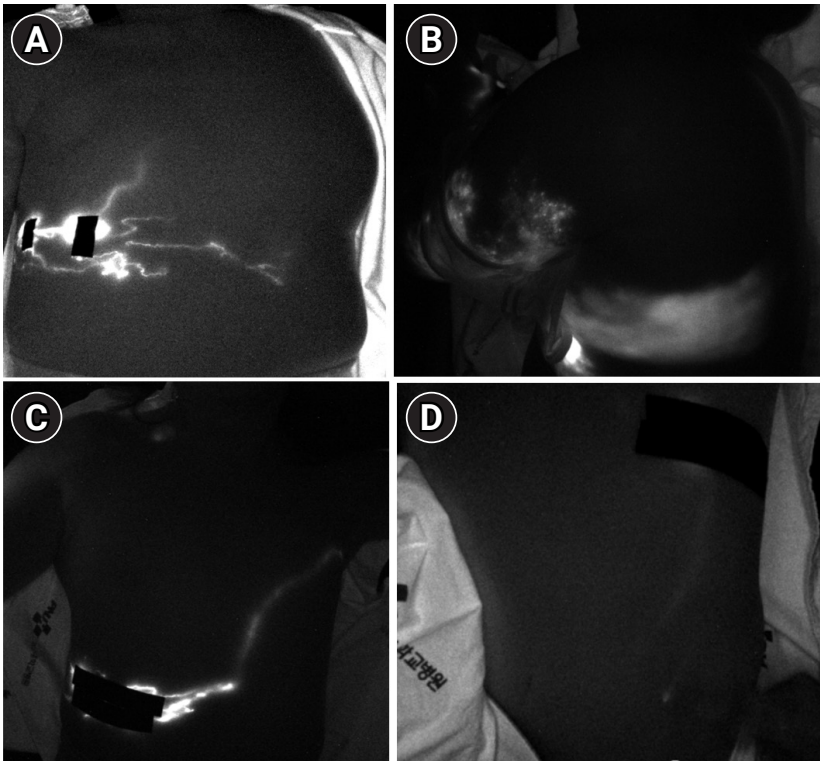

Fig. 6. Drainage pathway of breast lymphedema patients. (A) Ipsilateral axilla pathway. (B) Posterior/scapular pathway. (C) Contrallateral axilla pathway. (D) Parasternal/internal mammary pathway.

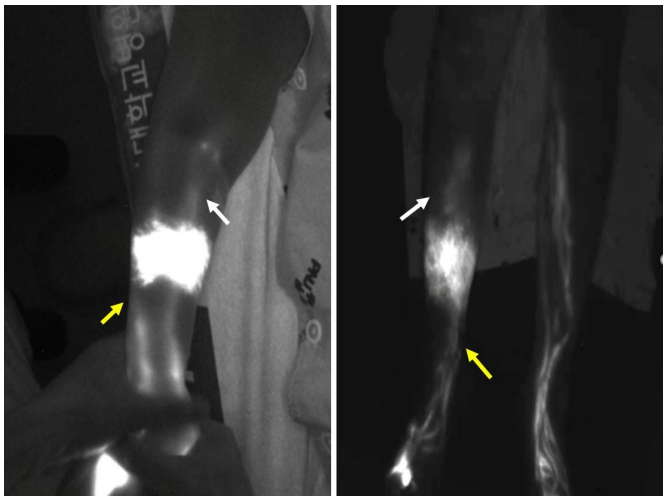

Fig. 7. Dermal backflow bridging the gap between the non-patent (yellow arrows) and patent vessels (white arrows).

corresponded to the lymph backflow from the collecting lymph vessels to the dermal lymphatics and thus both imaging modalities demonstrated the same information. The findings help to interpret the images of both tests in clinical practice.

Subcutaneous pathways and fluid transport in advanced lymphedema

In addition to the retrograde flow toward initial dermal lymphatics, diffusion of ICG exudates from the lymphatic vessels into the interstitial tissues can be seen simultaneously. In this condition, lymph drainage through the subcutaneous channel is considered as the main drainage route of lymph fluid. Therefore, MLD must be performed during ICG imaging to distinguish whether bridging DB from the obstructed lymphatic vessels to the adjacent patent lymphatic vessels or stagnant fluid in the subcutaneous channel. Identification of where the tissue fluid is located is useful for designing pneumatic devices for limb massage as well as for rational MLD in terms of dosage of external pressure [24]. The lymph fluid accumulated in the interstitial tissue mainly forms tissue channels within the subcutaneous tissue layer and along the fascia in patients with severe lymphedema. Since it is a stagnant fluid without a spontaneous propelling force, an increasing external force is essential to remove it [25].

IMAGE-GUIDED MLD

ICG lymphography enables clinicians to visualize superficial lymphatic structures in real time. Unlike traditional methods relying on anatomical assumptions or physical signs, ICG lymphography provides visualization of real-time motility and patency of superficial collectors, presence of DB, alternative drainage pathways, and functional response of lymphatic to various treatment modalities. This new image information allow to compose rehabilitation strategies, including MLD, compression, exercise, and patient self-management to be tailored according to each patient's unique lymphatic architecture in lymphedema rather than standardized, uniform protocol based on normal anatomy. Accordingly, image-guided approaches may offer a more physiologically informed basis for treatment planning.

MLD is a core component of lymphedema treatment and is known to promote lymph transport through enhanced superficial venous circulation, increasing uptake of interstitial fluid into functional lymphatic vessels, and reduction of skin fibrosis. Traditional MLD technique characterized by gentle and rhythmic strokes are usually applied along normal anatomical lymphatic routes [26]. However, recent systematic review has reported inconsistent evidence regarding treatment values of MLD, with some studies suggesting limited benefit beyond compression therapy in advanced lymphedema [27].

These discrepancies may be attributed to heterogeneity in MLD techniques, variability in disease severity, and the lack of individualized treatment planning based on objective lymphatic imaging. In this context, advances in lymphatic imaging have introduced the concept of image-guided MLD, in which real-time visualization of lymphatic function is incorporated into therapeutic decision-making. While direct evidence demonstrating superior clinical outcomes remains limited, preliminary studies suggest that ICG lymphography can enhance the understanding of patient-specific lymphatic flow patterns and may support more targeted and individualized interventions [28-30]. Most recent evidence suggest the ICG lymphography guided conservative management may lead to changes in treatment strategies and is associated with short-term improvement in objective measures [31]. However, these findings should be interpreted cautiously due to the lack of controlled comparisons. Therefore, further well-designed clinical studies are required to establish the long-term therapeutic effectiveness of this approach. Overall, image-guided MLD may be considered a physiologically informed and promising approach for individualized treatment planning but its clinical superiority over conventional methods has not yet been established.

CONCLUSION

The integration of ICG lymphography into routine lymphedema care represents an important advancement in both diagnostic precision and individualized rehabilitation. However, translating innovative technologies into clinical practice remains inherently complex. As ICG lymphography continues to demonstrate value in mapping patient-specific lymphatic architecture, guiding personalized treatment strategies, adequate training and organization readiness will be essential. Ultimately, embracing ICG lymphography within a structured implementation framework has the potential to improve diagnostic accuracy, optimize therapeutic approach, and enhance the overall quality of lymphedema care.

CONFLICTS OF INTEREST

Jin A Yoon is an Associate Editor of *Annals of Rehabilitation Medicine*. The author did not engage in any part of the review and decision-making process for this manuscript. Otherwise, no potential conflict of interest relevant to this article was reported.

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AUTHOR CONTRIBUTION

Conceptualization: Yoon JA, Suami H. Methodology: Yoon JA. Formal analysis: Yoon JA. Funding acquisition: Yoon JA. Project administration: Yoon JA, Suami H. Visualization: Yoon JA. Writing – original draft: Yoon JA. Writing – review and editing: Yoon JA, Suami H. Approval of final manuscript: all authors.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

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Identifying the Factors With Later Standing Acquisition in Patients With a Right-Hemisphere Stroke: A Cross-Sectional Study Using POSTIM Data

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Objective: To identify factors associated with later standing acquisition in subacute post-stroke patients with right-hemisphere stroke.

Methods: This cross-sectional study used baseline data from the POSTIM multicenter randomized controlled trial (ClinicalTrials.gov: NCT01677091), involving eight rehabilitation units in France. Included patients were patient aged 18–80 with a first right supratentorial stroke (within 9 months), who could stand unassisted for at least 30 seconds with eyes closed but had <40% body weight bearing on the paretic leg during posturography. Evaluations included motor weakness, spasticity (triceps surae, quadriceps, adductors), epicritic and arthrokinetic sensitivity, spatial neglect, body representation, and balance. Logistic regression identified factors associated with later standing acquisition (>3 months).

Results: Among 86 participants (mean age 59.7±10.3 years; 68.6% male), 49 (57%) acquired standing capacity within 3 months, while 37 (43%) did so later. Those with later standing acquisition showed greater spasticity in all muscle groups (p<0.02), more severe motor weakness (p=0.003), and impaired arthrokinetic sensitivity (p=0.02). Balance was significantly worse in this group (p<0.005). Multivariate analysis identified three independent factors of later standing acquisition: spatial neglect (odds ratio [OR]=3.22; 95% confidence interval [CI], 1.09–9.51; p=0.03), ischemic stroke (OR=3.27; 95% CI, 1.08–9.90; p=0.04), and quadriceps spasticity (OR=1.98; 95% CI, 1.17–3.35; p=0.01).

Conclusion: In right-hemisphere stroke, ischemic etiology, quadriceps spasticity, and spatial neglect are significantly associated with later standing acquisition. These factors may be useful for identifying patients at risk of later standing acquisition and for guiding future interventional research.

Keywords: Stroke, Perceptual disorders, Muscle spasticity, Standing position

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INTRODUCTION

Among the various consequences of stroke, the challenge of regaining the ability to stand is particularly significant, as it is essential for restoring independent mobility [1]. Difficulties in achieving this standing capacity can lead to several adverse consequences, including impaired transfers and walking ability, increased risk of falls, and reduced participation in daily activities [2]. Understanding how post-stroke deficits interact with later standing acquisition is essential for optimizing rehabilitation protocols and patient outcomes.

Several studies have investigated different factors influencing post-stroke standing capacity, i.e., ability to stand unassisted, at the acute stage or sub-acute, including lower limb motor weakness [1,3], spasticity [4], spatial neglect [5-7]. However, discrepancies exist in the literature regarding the relative impact of these factors, likely due to variations in outcome measures, sample sizes, and patient heterogeneity and stroke stage. Moreover, patients with right-hemisphere stroke (RHS) appear to face unique challenges. Notably, they require more time to achieve a stable standing position compared to those with left-hemisphere stroke (LHS) [8,9]. This delay can be attributed to the crucial role of the right hemisphere in multisensory integration and spatial perception [10-12]. Lesions in the right hemisphere are frequently associated with disturbances in spatial body representation, manifesting as both egocentric (subjective straight ahead [SSA], longitudinal body axis [LBA] [12,13]) and allocentric reference (subjective visual vertical [14]) distortions and spatial neglect impairments [6], which can affect standing and balance control [5,13], increasing the complexity of rehabilitation.

To date, no study has specifically focused on the factors affecting later standing acquisition in subacute patients with RHS. In this context, our study aims to identify key factors associated with later standing acquisition using data from the POSTIM database. A deeper understanding of these factors could optimize rehabilitation strategies and improve personalized care. Recognizing that the first three months post-stroke represent a critical period for motor neuroplasticity and recovery [15,16], our population was stratified into two groups: (1) those who regained standing capacity within three months, and (2) those who achieved it later. We hypothesized that persistent disturbances in spatial body representation and spatial neglect would be major factors of later standing acquisition.

METHODS

Design and ethics

This study is a secondary cross-sectional analysis of baseline data from the multicentric randomized controlled trial conducted in adult physical and rehabilitation medicine units across eight hospitals in France. The original trial (ClinicalTrials.gov: NCT01677091) evaluated the effects of prism adaptation and neck-muscle vibrations on weight-bearing asymmetry (WBA) in patients with RHS. This analysis used only pre-intervention data. The participants were stratified retrospectively based on the timing of standing capacity acquisition, and all independent variables were measured prior to this classification. The study adheres to the STROBE guidelines for cross-sectional studies and was approved by the Institutional Review Board of Poitiers-France III West (N°05/12/16) in accordance with the Declaration of Helsinki. Each participant received information about the protocol and signed a consent form before the study began in accordance with the Declaration of Helsinki.

Participants

Patients aged between 18 and 80 years who were admitted to one of the eight physical and rehabilitation medicine units with a first right unilateral supratentorial stroke within 9 months before study inclusion were eligible for inclusion. Patients were included in the original study as soon as they were to be able to stand upright unassisted for at least 30 seconds with their eyes closed and have less than 40% of their body weight supported by the paretic lower limb during a posturographic assessment. Patients with orthopedic, rheumatologic, or visual disorders affecting their postural balance were excluded. The original study's primary outcome was WBA.

Outcomes

The outcomes analyzed in this study were based solely on data collected at baseline, prior to the intervention, in the original trial. All assessments were performed as soon as the patients were eligible to be included, rather than at a fixed post-stroke time point.

Assessment of post-stroke deficiencies

Age (in years), gender (male/female), post-stroke delay (in days) and etiology of stroke lesion (ischemic/hemorrhagic) were reported. The Motricity Index ranging from 0 to 100 [17] with higher scores indicate better motor strength was used to

assess motor weakness of the paretic lower limb, and spasticity scores of the paretic triceps surae, quadriceps and adductor according to the Modified Ashworth Scale (MAS) [18]. The MAS was treated as a continuous variable in the logistic regression model, consistent with the analytical approach applied to all clinical variables in order to preserve the full range of variability and maintain a uniform statistical framework. Scores were coded numerically from 0 to 5, with grade 1+ assigned a value of 2, grade 2=3, grade 3=4, and grade 4=5. Two clinical examinations were performed to assess the patient's sensitivity. The examinations included epicritic and arthrokinetic sensitivity tests on the knee, ankle, and toes of the lower paretic limb. Each test was scored on a scale of 0 to 2, with 0 indicating anaesthesia, 1 indicating impairment and 2 normal sensitivity, after comparison with the non-paretic side. The total score for the lower paretic limb was calculated by summing the sub-scores.

Spatial neglect and body representation assessments

Four tests were conducted to assess spatial neglect: the Bell Cancellation Test [19], the 20-cm Line Bisection [20], the Fluff Test [21], and the Catherine Bergego Scale [22]. Spatial neglect was defined by the presence of at least three positives out of four tests. This conservative criterion was chosen to increase diagnostic specificity by requiring consistent impairment across multiple complementary assessments (paper-and-pencil, personal neglect, and functional evaluation), in line with recommendations advocating multimodal assessment of neglect rather than reliance on a single test [23,24]. Two tests were performed to assess spatial body representation: the SSA [25], and the LBA [13]. The SSA was conducted with patients in a seated position in front of a measuring table. Patients were blindfolded and instructed to indicate the direction of "straight ahead" with their right hand, dividing the space into two parts. This was done in six starting positions, sequenced in the following order: 30°, -20°, 10°, -30°, 20°, and -10°. LBA was performed with the patient lying supine in complete darkness. A light strip was placed in front of them, and their head, trunk, and lower limbs were aligned and supported by cushions. Patients were instructed to indicate when the strip was parallel to their body axis using the same sequence of starting positions. No visual reference other than the wand was available. For both the SSA and LBA, results were recorded in degrees. The Algebraic error (mean of signed deviations) was calculated.

Balance assessments

Balance was evaluated using the Postural Assessment Scale for Stroke (PASS) [26], the Timed Up and Go (TUG) [27], the Berg Balance Scale (BBS) [28], and WBA, which is defined as the percentage of body weight supported by the affected lower limb, was measured using posturography (Feetest6©; Techno Concept). The participants stood with both feet on the platform, looking straight ahead (or closing their eyes, depending on the instructions given). The eyes-closed condition was used to remove visual input in order to assess visual dependence and the ability to maintain postural control without visual information [29]. They had to remain as still as possible during the 30-second recording. The average of the two trials with eyes open and the two trials with eyes closed was used to calculate WBA [30].

Statistical analysis

Normality was assessed using the Shapiro–Wilk test. Quantitative variables were expressed as means±standard deviation or medians with interquartile ranges, and categorical variables as numbers and percentages. Group comparisons (standing acquired ≤3 months vs. >3 months) were performed using chi-square or Fisher's exact tests for categorical variables and t-tests or Mann–Whitney tests for continuous variables. Logistic regression identified factors associated with later standing acquisition. Balance assessments were not entered into the multivariate logistic regression model due to their conceptual proximity to the outcome (standing capacity), in order to avoid collinearity and to focus on independent underlying impairments associated with later standing acquisition. Variables with $p<0.20$ in univariate analysis were included in a multivariate model with stepwise backward selection. Missing data were handled using complete-case analysis. For each univariate analysis, all available data were used, leading to variable sample sizes across analyses. Analyses were performed using SAS v9.4 (SAS Institute).

RESULTS

Participants

Eighty-nine individuals were enrolled between May 2013 and May 2018. After excluding three patients due to missing data on post-stroke delay, 86 participants (68.6% male; mean age 59.7±10.3 years) were included. Ischemic stroke was observed in 56 (65.1%) of cases and hemorrhagic stroke in 30 (34.9%). Mean Motricity Index for the paretic lower limb was 55.3±21.1 and other assessments are detailed in Table 1. Out of the 86 partici-

pants, 49 patients (57%) achieved standing capacity within three months, while 37 (43%) did so after three months (Fig. 1).

Standing capacity acquisition

Univariate analysis

The later standing acquisition group exhibited significantly higher spasticity of the triceps surae (1.4/5±1.1 vs. 2.1/5±1.4; p=0.02), the quadriceps (0.6/5±0.8 vs. 1.2/5±1.2; p=0.01) and the adductor (0.7/5±1.1 vs. 1.5/5±1.4; p=0.003), greater motor weakness (61.0/100±17.5 vs. 47.4/100±23.3; p=0.003), and more impaired arthrokinetic sensitivity (4.9/6±1.6 vs. 3.9/6±2.0; p=0.02) compared to the early group. Additionally, balance assessments (BBS, PASS, TUG, WBA) were significantly worse in the later standing acquisition group (all p<0.005) (Table 1).

Multivariate analysis

The multivariate model included several variables such as age, stroke etiology, spasticity, motor weakness, epicritic and arthrokinetic sensitivity tests, spatial neglect assessment (Table 2). Three factors were independently associated with later standing acquisition group: the ischemic stroke etiology (odds ratio [OR]=3.27; 95% confidence interval [CI], 1.08–9.90; p=0.04), spasticity of the quadriceps (OR=1.98; 95% CI, 1.17–3.35; p=0.01), and spatial neglect (OR=3.22; 95% CI, 1.09–9.51; p=0.03) (Fig. 2). No other variables were independently associated with the delay of standing acquisition.

DISCUSSION

This study investigated factors associated with later standing acquisition in patients with RHS. Our first finding indicates that only fifty percent of our cohort achieved standing capacity within three months (Fig. 1), and 3 out of 4 did so by four months. This recovery period is notably longer than the one-month timeframe generally reported in the literature for cohorts similar to ours neurorehabilitation unit [31,32]. While the eyes closed condition during the assessment may partially explain this extended recovery time, it does not fully account for the delay. A more plausible explanation lies in our inclusion of RHS patients, who are known to demonstrate more pronounced

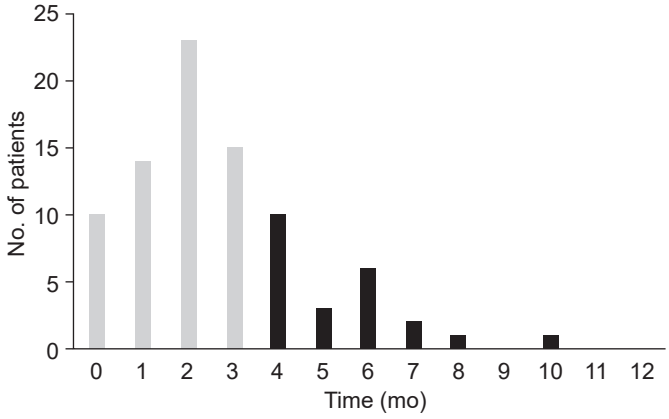

Fig. 1. Distribution of patients by time post-stroke (months) and standing acquisition (grey: ≤3 months; black: >3 months).

Table 1. Characteristics of participants and comparison on the standing capacities between before and after 3 months

Variable	Total (n=86)	Post-stroke delay		p-value
		≤3 months (n=49)	>3 months (n=37)	
Age (yr)	59.7±10.3	58.3±11.1	61.5±9.1	0.1
Male/Female	59/27	33/16	26/11	0.7
Ischemic/Hemorrhagic	56/30	35/14	21/16	0.1
Longitudinal body axis (°)	3.7±2.9	3.8±3.0	3.6±2.8	0.7
Subjective straight ahead (°)	6.8±5.2	6.7±4.0	6.9±6.5	0.3
Spasticity triceps surae (/5)	1 (1–3)	1 (1–2)	2 (1–3)	0.02
Spasticity quadriceps (/5)	0 (0–2)	0 (0–1)	1 (0–2)	0.01
Spasticity adductors (/5)	0 (0–2)	0 (0–1)	1 (0–3)	0.003
Epicritic sensitivity (/6)	3.7±2.2	4.0±2.3	3.3±2.1	0.1
Arthrokinetic sensitivity (/6)	4.5±1.9	4.9±1.6	3.9±2.0	0.02
Spatial neglect (positive/negative)	30/46	13/30	17/16	0.059
Motricity Index (/100)	55.3±21.1	61.0±17.5	47.4±23.3	0.003
Berg Balance Scale (/56)	35.6±11.1	39.9±9.6	29.4±10.2	<0.0001
Weight-bearing asymmetry (%)	32.2±9.9	35.1±9.1	28.5±9.9	0.002
Postural Assessment Scale Stroke (/36)	29.0±4.2	30.6±3.0	26.8±4.8	0.0001
Timed Up and Go (sec)	47.6±33.0	35.6±25.7	64.7±35.1	0.0001

Values are presented as mean±standard deviation, number only, or median (interquartile range).

Table 2. Univariate analysis of factors related to later standing acquisition

Variable	N total	N >3 months	OR (95% CI)	p-value
Age	86	37	1.03 (0.99, 1.08)	0.1
Male[a]/Female	86	37	0.87 (0.35, 2.20)	0.7
Ischemic[a]/Hemorrhagic	86	37	1.90 (0.78, 4.68)	0.1
Longitudinal body axis	81	34	0.98 (0.84, 1.15)	0.8
Subjective straight ahead	82	35	1.01 (0.93, 1.10)	0.8
Spasticity triceps surae	83	35	1.54 (1.07, 2.22)	0.01
Spasticity quadriceps	83	35	1.90 (1.19, 3.03)	0.006
Spasticity adductors	83	35	1.67 (1.16, 2.42)	0.006
Epicritic sensitivity	83	35	0.86 (0.70, 1.05)	0.1
Arthrokinetic sensitivity	83	35	0.76 (0.59, 0.97)	0.02
Spatial neglect	76	33	2.45 (0.95, 6.30)	0.06
Motricity Index	83	35	0.97 (0.94, 0.99)	0.005

The total sample included in the multivariate analysis was 76 patients, of whom 33 had a stroke onset more than 3 months.
OR, odds ratio; CI, confidence interval.
[a]Reference categories for categorical variables.

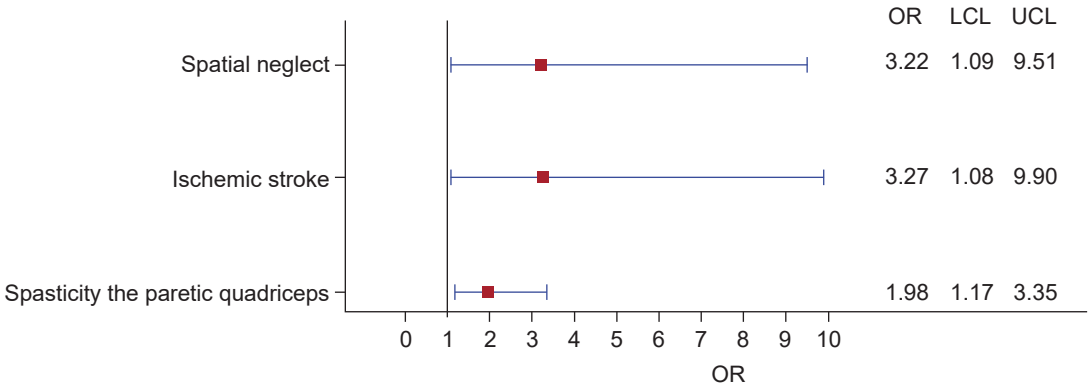

Fig. 2. Forest plot of multivariate analysis results. OR, odds ratio; LCL, lower control limit; UCL, upper control limit.

WBA and require more time to achieve postural stability then patients with LHSs [8,9].

Patients with ischemic stroke were three times more likely to experience later standing acquisition (OR=3.27). Moreover, a one-unit increase in spasticity of the quadriceps is significantly associated with a higher probability of prolonged recovery time (OR=1.98). Lastly, the presence of spatial neglect is linked to a threefold higher likelihood of later standing acquisition beyond three months post-stroke (OR=3.22).

Our results regarding stroke etiology diverge from previous studies [33,34], which reported more severe functional impairments in patients with hemorrhagic stroke compared to those with ischemic stroke. However, our sample appears to be representative of stroke etiology, with approximately two-thirds of participants having ischemic stroke and one-third hemorrhagic stroke [33]. Notably, in our sample, patients with ischemic stroke took longer to acquire an upright posture. This discrepancy is not entirely unexpected, as although hemorrhagic stroke often presents with more severe deficits at admission, these patients tend to have a greater recovery potential over time due to the resolution of edema [34]. Our assessment performed at the time patients attained the standing position, rather than at the onset of rehabilitation may have allowed the patients with hemorrhagic stroke to reach a similar level of performance as the ischemic stroke group. From a clinical perspective, although stroke etiology itself cannot be modified, these findings highlight the importance of careful monitoring of patients with ischemic stroke, who may be at higher risk of later standing acquisition.

Spasticity emerged as an unfavorable factor for later standing acquisition in our study, consistent with Singer et al. [4], who reported that lower-limb spasticity can impede the recovery of standing balance control over time. While our cohort with later standing acquisition exhibited increased spasticity across

triceps surae, quadriceps, and adductor muscle groups, multivariate analysis identified only the spasticity of the quadriceps as a statistically significant factor. This finding contrasts with Singer et al.'s [4] observation that ankle spasticity primarily compromised balance recovery. This discrepancy may stem from methodological differences, as Singer et al. [4] specifically included patients with ankle spasticity regardless of quadriceps involvement. Interestingly, although quadriceps hypertonicity may initially appear to promote upright stability by maintaining knee extension, it may paradoxically limit the controlled knee flexion required for weight transfer, resulting in abnormal joint mechanics during standing [35]. Spasticity fundamentally disrupts voluntary motor control and limits the generation of compensatory postural adjustments essential for maintaining upright posture [36]. While some heterogeneity exists in the literature, Genthon et al. [37] did not identify spasticity as a principal factor, potentially reflecting differences in study populations, assessment protocols, or evaluation timing, our findings emphasize the clinical relevance of early spasticity assessment as a factor associated with later standing acquisition and support further investigation of its role in postural control during subacute stroke rehabilitation.

Consistent with prior studies [6,7], our results indicate that spatial neglect is significantly associated with later standing acquisition in patients with RHS. Although our cross-sectional design cannot establish a direct causal relationship, this association underscores the need to systematically assess and address spatial neglect in rehabilitation programs for these patients. It is also important to note that only individuals who could eventually stand unassisted were included; therefore, patients who never achieved standing (potentially due to severe deficits in body representation or other factors) were not captured. In contrast, our measures of spatial body representation (SSA and LBA) were not associated with later standing acquisition, likely because they primarily evaluate egocentric space. In addition, these tests particularly the LBA have been reported to correlate with WBA [13]. They assess the perceived midline of the body, which may result in uneven weight distribution, however this does not appear to be a prognostic factor for the time required to acquire standing position, especially once the initial postural deficits are compensated for. By comparison, the visual vertical is crucial for postural control, requiring individuals to accurately perceive their environment and rely on verticality for balance [38]. Future research should therefore incorporate visual vertical assessments and consider a longitudinal design that captures patients throughout the recovery trajectory including those who do not attain standing to more definitively clarify how spatial perception deficits influence both the timing and overall potential for standing acquisition.

Study limitations

This study has certain limitations. First, the primary criterion for assessing standing acquisition required patients to maintain an upright posture unassisted for at least 30 seconds with their eyes closed. Consequently, our findings are specific to this subset of patients, which may not fully reflect the earlier stages of recovery. Future research should adopt a longitudinal design with repeated assessments, capturing the transition from sitting to independent standing and eventually walking, in order to provide a more comprehensive understanding of the recovery process. A second limitation is the inclusion of only patients with RHS, as the right hemisphere is strongly associated with spatial deficits. Although our cohort represents the largest population studied on this topic, we acknowledge that these findings may differ in a population with LHSs, and future studies should explore their applicability in such populations. However, it is also important to note that studying a homogeneous sample of patients with RHSs allows us to evaluate more precisely the specific factors influencing recovery of standing ability, making the findings more robust in this context. In addition, our sample included relatively young patients admitted to specialized rehabilitation units, which may limit the wider applicability of our results. Further studies are needed to determine whether these findings extend to older populations or those receiving less intensive rehabilitation services. Third, the relatively small number of patients in the later standing acquisition group may have increased the risk of overfitting in multivariate analyses, despite efforts to limit the number of included factors. Future studies with larger samples are warranted to confirm these findings and allow more robust multivariable modelling. Finally, spatial neglect was defined using a conservative multimodal criterion, which may have underestimated milder or task-dependent forms of neglect [39,40], future studies should consider more sensitive or continuous measures to capture the full spectrum of neglect severity. In addition, spatial neglect was assessed using standardized tools that, although valid, may not fully capture the complexity of this condition in real-world settings. Therefore, ecological assessments in dynamic environments should be considered to better understand spatial neglect and its impact on functional recovery [6].

Conclusion

Our study found that only fifty percent of patients with RHS, who were able to maintain an upright posture unassisted for at least 30 seconds with their eyes closed, achieved standing capacity within three months. It also confirms that persistent spatial neglect is associated with the time needed to regain standing capacity and further demonstrates that ischemic etiology and increased spasticity of the quadriceps are factors associated with later standing acquisition. These findings highlight clinically relevant factors associated with later standing acquisition which may help guide clinical assessment and identify targets for future hypothesis-driven rehabilitation research.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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AUTHOR CONTRIBUTION

Conceptualization: Jamal K, Bonan I. Investigation: Jamal K, Leplaideur S, Bonan I. Formal analysis: Jamal K, Leplaideur S, Viallard L, Painchaud S, Bonan I. Methodology: Jamal K, Leplaideur S, Foussat E, Painchaud S, Viallard L, Bonan I. Funding acquisition: Leplaideur S, Bonan I. Software: Rousseau C. Writing – original draft: Jamal K, Leplaideur S, Bonan I. Writing – review & editing: Foussat E, Rousseau C, Painchaud S, Viallard L. Approval of final manuscript: all authors.

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DATA AVAILABILITY STATEMENT

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Reconnecting Minds to the World: Patient Perspectives on Brain–Computer Interface After High Cervical Spinal Cord Injury

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Objective: To explore the perspectives of individuals with high cervical spinal cord injury (C-SCI) regarding expectations, concerns, and desired applications of brain–computer interface (BCI).

Methods: A structured focus group interview was conducted with four individuals with chronic high cervical spinal cord injury, all with neurological levels of C4 or above. Pre- and post-interview questionnaires were administered to assess expectations, concerns, and acceptance of BCI before and after discussion. The interview was facilitated by experts in rehabilitation medicine and biomedical engineering, and qualitative data were analyzed inductively to identify key themes.

Results: Five major themes emerged: digital accessibility, offline physical activity, social interactions and psychological health, usability, and acceptance. Participants expressed strong interest in using BCI to improve digital independence, particularly for messaging, online banking, internet use, and smart home control. They also viewed BCI as a potential tool to enhance autonomy in daily activities and reduce reliance on caregivers. Most participants were open to training and, in some cases, invasive procedures; however, concerns regarding surgical safety, device maintenance, reliability, and practical usability were frequently raised. Views on the emotional and social impact of BCI varied across individuals. Questionnaire responses showed increased willingness to undergo invasive procedures after the focus group interview, while expected functional outcomes became more realistic, suggesting that structured group discussion may have shaped participants' understanding of BCI.

Conclusion: BCI was perceived as a promising pathway to greater independence, participation, and autonomy among individuals with high C-SCI. These findings emphasize user-centered design and demonstrate how lived experience can guide assistive neurotechnology development in rehabilitation research.

Keywords: Spinal cord injuries, Quadriplegia, Brain-computer interfaces, Focus groups, Self-help devices

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INTRODUCTION

With rapidly advancing brain–computer interface (BCI) technologies pioneered by companies such as Neuralink, Synchrom, and Paradromics, restoring lost motor function in severe paralysis is becoming increasingly realistic [1]. Neurological injuries including spinal cord injury [2], stroke [3], and amyotrophic lateral sclerosis [4] substantially impair motor function and limit activities of daily living (ADL). Among these, cervical spinal cord injury (C-SCI) is one of the most severe conditions, resulting in tetraplegia due to impaired voluntary movement of all four limbs [5]. Higher neurological injury levels are associated with greater motor and sensory loss, leading to marked reductions in independence and quality of life [6,7].

Assistive technologies such as powered wheelchairs [8], smart home systems [9], and robotic exoskeletons [10] aim to enhance mobility, communication, and ADL performance in individuals with C-SCI. However, those with high-level C-SCI often face fundamental difficulties in controlling these technologies because of severe motor impairment [6,7]. BCI has therefore emerged as a promising approach to enable direct neural control of assistive devices and restore functional autonomy in individuals with tetraplegia [5,6].

BCI establishes a direct communication pathway between the brain and external devices, allowing control via neural signals [9]. These signals are translated into commands for devices such as robotic arms, wheelchairs, and digital interfaces including smartphones and computers [1]. BCIs are classified as invasive or non-invasive. Invasive BCIs use surgically implanted electrodes with high signal fidelity but involve surgical risks and long-term biocompatibility concerns [3,5]. Non-invasive BCIs, most commonly based on electroencephalography, offer greater safety but reduced precision due to signal attenuation [9].

Despite technological progress, BCIs remain largely unavailable for routine clinical or consumer use because of limitations in reliability, training requirements, and cost [1,9,11]. As BCI development remains largely experimental, incorporating user perspectives is critical to ensure alignment with real-world functional needs, particularly for individuals with C-SCI.

Accordingly, this study explores perceptions of BCI among individuals in the chronic phase of C-SCI using a structured focus group interview (FGI) approach. It addresses two key questions: how users envision integrating BCI into daily life, and which requirements and concerns are essential for effective implementation. By engaging individuals with limited prior BCI exposure, this study aims to inform user-centered development of accessible and functionally meaningful BCI systems for tetraplegia.

METHODS

Participants

Study participants were recruited from between the period of November 8, 2024 and November 14, 2024. The number of C-SCI patients who participated in this study was four, consistent with the recommended group size of four to eight participants for FGI in clinical and health research [12,13]. Clinical characteristics of the participants are described in Table 1. All participants had high C-SCI with ASIA Neurological Level of Injury C4 or above. All participants were individually informed about this study and gave written consent. This study was approved by the Seoul National University Hospital Institutional Review Board (IRB No. 2409-067-1570) and the National Traffic Injury Rehabilitation Hospital Institutional Review Board (IRB No. 2024-08-001).

FGI

The FGI method was employed to explore potential applications of BCI and to understand perceptions of prospective users. FGI facilitates direct discussion of participants' experiences and viewpoints, allowing collection of diverse qualitative insights within a relatively short period and offering greater efficiency

Table 1. Focus group interview participants

ID	Age (yr)	Sex	AIS classification	Etiology	Time since injury (mo)	Living situation	Primary caregiver	Prior BCI exposure
A	48	Male	SCI C5/C4 NLI C4 AIS A	Non-traumatic	6	Hospitalized	Professional caregiver	No
B	71	Male	SCI C4/T9 NLI C4 AIS C	Traumatic	7	Hospitalized	Professional caregiver	No
C	59	Male	SCI C3/C3 NLI C3 AIS C	Traumatic	12	Hospitalized	Professional caregiver	No
D	34	Male	SCI C6/C4 NLI C4 AIS C	Traumatic	17	Hospitalized	Professional caregiver	Aware of BCI concept

AIS, American Spinal Injury Association Impairment Scale; BCI, brain–computer interface; SCI, spinal cord injury; NLI, neurological level of injury.

than one-on-one interviews [12,13]. A semi-structured format was adopted to promote interactive communication and allow clarifying questions during discussion [14].

The interview development team consisted of five experts with multidisciplinary backgrounds in rehabilitation medicine, occupational therapy, and biomedical engineering, each with 7–26 years of experience. FGI items are presented in Supplementary Table S1. In addition, a 10-item pre-interview questionnaire and a 14-item post-interview questionnaire were developed to assess participants' understanding of and expectations regarding BCI. The pre-interview questionnaire was administered five days before the FGI, and the post-interview questionnaire one week after, both by a research professor with 10 years of experience in occupational therapy (GS). All interviews and questionnaires were conducted in Korean and translated into English for this article (Supplementary Table S2).

Five days prior to the FGI, participants were informed about the study and completed the pre-interview questionnaire. The FGI was moderated by two trained facilitators, one with 8 years of experience in rehabilitation medicine (YM) and the other with 7 years of experience in biomedical engineering. After a brief introduction and a short educational video on BCI, participants engaged in two 45-minute FGIs focusing on clinical and engineering perspectives, separated by a 15-minute break. Sessions were recorded using two video cameras and five audio recorders, with individual microphones to ensure clear communication without caregiver assistance. Audio recordings were transcribed using ClovaNote (Corps.), and transcripts were cross-checked by all authors.

Data analysis

A general inductive approach was applied to analyze the qualitative FGI data, enabling systematic condensation of raw interview transcripts into meaningful themes [15,16]. The analysis proceeded through the following steps.

First, audio recordings from both FGI sessions were transcribed verbatim using ClovaNote and subsequently cross-checked against the original recordings by all authors to ensure transcription accuracy. All transcripts were produced in Korean and translated into English by bilingual members of the research team prior to analysis.

Second, two researchers (YM and BMO) independently read the finalized transcripts in their entirety to achieve familiarity with the data. Each researcher then conducted open coding, generating initial codes by identifying segments of text that were relevant to the study objectives—specifically, participants' expectations, concerns, and desired applications of BCI.

Third, the independently generated codes were compared and discussed between the two researchers. Discrepancies in coding were resolved through consensus, with reference to the original transcript text. Where disagreement persisted, a third researcher was consulted to reach a final determination.

Fourth, codes were grouped into broader categories based on shared conceptual content. These categories were then reviewed in relation to the study objectives and progressively refined into overarching themes. Five major themes emerged from this process: (1) digital accessibility, (2) offline physical activity, (3) social interactions and psychological health, (4) usability, and (5) acceptance and concerns.

Fifth, the identified themes and their constituent codes were reviewed by the full research team to confirm that they accurately represented the range of participant perspectives and were grounded in the transcript data. Representative quotations were selected for each theme to illustrate the findings in the Results section, with additional supporting quotations provided in Supplementary Table S3.

Pre- and post-interview questionnaire responses were analyzed descriptively, with individual-level pre-post comparisons conducted to examine changes in participants' perspectives on BCI acceptance, expected functionality, and tolerable risk following the FGI. These results are presented in Table 2 and Fig. 1.

Digital accessibility

Digital accessibility refers to the use of BCI to operate electronic devices such as computers, smartphones, and smart home systems [17]. This theme focuses on BCI as a control interface for digital communication, internet use, and home automation, highlighting its potential to expand independence in work, education, and daily activities. Usability considerations, including adaptability, learning burden, and intuitive interface design, were also addressed, underscoring the importance of technology-enabled independence for individuals with severe physical impairments.

Offline physical activity

This theme examines the role of BCI in supporting daily living activities and promoting independence in essential functions [18,19]. The term "offline physical activity" was adopted to distinguish real-world, in-person functional tasks—encompassing ADL, instrumental ADL, health management, and leisure

Table 2. Summary of pre- and post-interview questionnaire responses by participant

Item	Response option	A	B	C	D
Willingness to undergo surgery	1=Definitely not · 2=Unwilling · 3=Unsure · 4=Willing · 5=Definitely willing	3→5	3→5	3→4	2→2
Expected functional level	1=Predefined · 2=Slight improvement · 3=Moderate · 4=Enhanced · 5=Non-disabled equivalent	4→4	4→2	4→3	4→4
Tolerable side effects (surgery)	1=None · 2=Mild · 3=Severe but recoverable · 4=Risk of hemorrhage · 5=Risk of death	2→2	5→2	2→3	2→2
Willingness to undergo minimally invasive procedure	1=Definitely not · 2=Unwilling · 3=Unsure · 4=Willing · 5=Definitely willing	3→5	3→4	4→4	2→3
Expected functional level	1=Predefined · 2=Slight improvement · 3=Moderate · 4=Enhanced · 5=Non-disabled equivalent	4→4	4→4	4→3	4→4
Tolerable side effects	1=None · 2=Mild · 3=Severe but recoverable · 4=Risk of hemorrhage · 5=Risk of death	2→2	2→2	2→3	2→2
Willingness to pay	1=None · 2=≤$7,500 · 3=≤$37,500 · 4=≤$75,000 · 5=>$75,000	2→2	2→2	3→3	2→2
Most useful BCI domain	1=Communication · 2=Mobility · 3=Daily living · 4=Electronics · 5=Environmental accessibility	5→3	3→3	3→4	4→5
Necessity of sensory BCI (post only)	1=Unnecessary · 2=somewhat unnecessary · 3=unsure · 4=somewhat necessary · 5=necessary	5	5	3	4
Min. accuracy improvement to accept sensory BCI (post only)	1=85% · 2=90% · 3=95% · 4=100% · 5=Would not accept	2	2	1	3
Min. speed improvement to accept sensory BCI (post only)	1=10 s · 2=20 s · 3=30 s · 4=40 s faster · 5=Would not accept	1	3	3	4

BCI, brain–computer interface; Min, minimum.

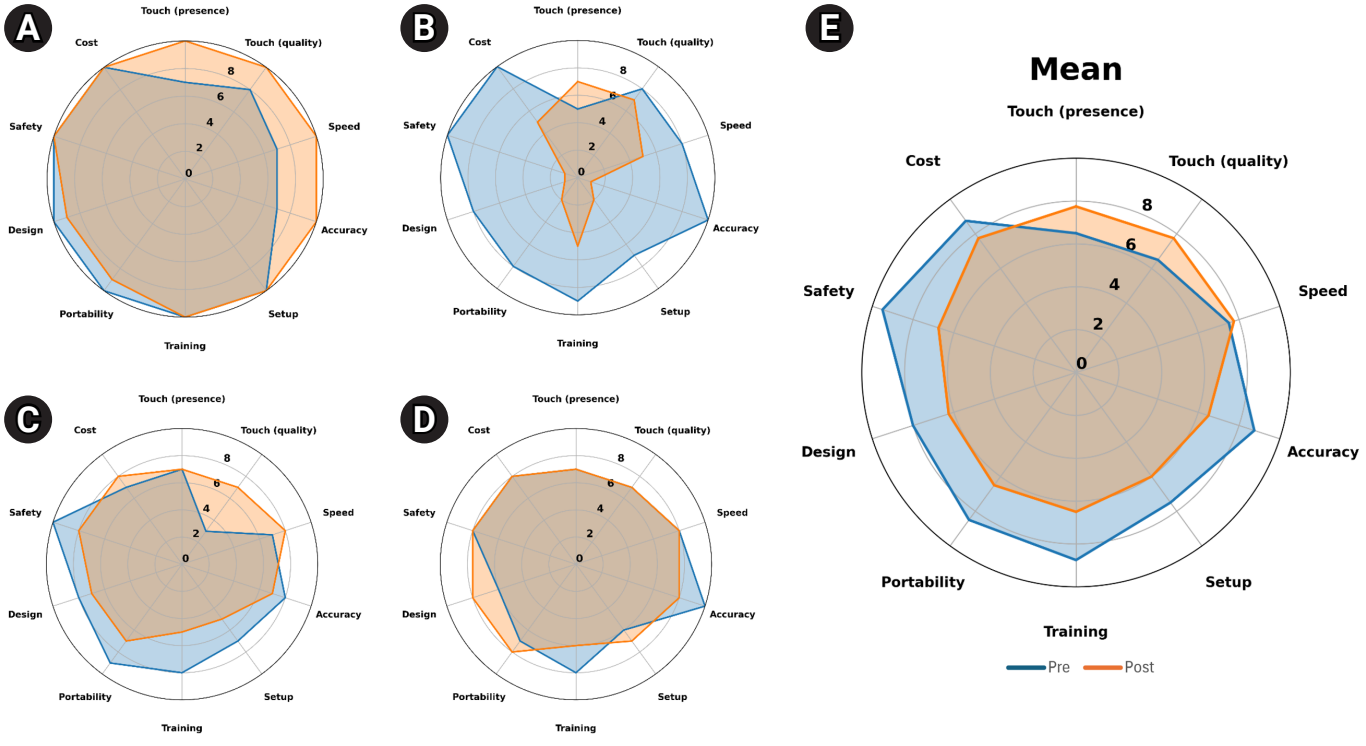

Fig. 1. Summary of pre- and post-interview questionnaire responses by participant. Radar plots illustrate changes in brain–computer interface (BCI)-related expectations and acceptance before and after the focus group interview. Panels (A-D) represent individual responses from participants A, B, C, and D, respectively, while panel (E) summarizes the average scores across all four participants. Blue lines indicate pre-interview responses, and orange lines indicate post-interview responses. Each axis represents a questionnaire domain related to BCI expectations or usability, including touch, speed, accuracy, setup, training, portability, design, safety, and cost. Higher scores indicate greater perceived importance, acceptance, or expectation for the corresponding domain.

participation—from the digitally mediated activities described in the preceding theme of digital accessibility. Participants' responses were categorized using two frameworks. First, activities were classified according to the Occupational Therapy Practice Framework: Domain and Process, Fourth Edition (OTPF-4) [20]. Second, the Generic Indicator Criteria (GIC) framework was applied to link activities with broader usability indicators [21]. This classification was performed by two board-certified physiatrists (YM and BMO) to systematically contextualize BCI-assisted activities within established functional domains.

Social interactions and psychological health

This theme addresses the potential impact of BCI on social participation, body image, and psychological well-being. Participants discussed how BCI could facilitate communication, environmental interaction, and engagement in social activities, potentially reducing barriers to social inclusion. The importance of seamless integration between BCI and communication technologies was emphasized to support meaningful interpersonal interactions.

Psychological considerations included changes in self-perception and body image following integration of neuroprosthetic devices. While some individuals anticipated improved confidence and independence, others expressed concerns about identity, emotional adjustment, and societal perceptions [22,23]. These findings highlight the need to address psychological adaptation alongside functional outcomes to support long-term BCI acceptance.

Usability

The usability theme focuses on factors influencing practical BCI adoption, including accuracy, response speed, setup complexity, and training demands [24,25]. Key parameters discussed included acceptable accuracy thresholds, response time expectations, training duration, device portability, maintenance requirements, and the level of caregiver assistance needed for daily use.

Acceptance and concerns

This theme explores participants' willingness to adopt BCI technology and concerns related to safety, invasiveness, and data privacy. Attitudes toward invasive versus non-invasive BCIs, perceived surgical risks, and ethical considerations associated with brain-controlled interfaces were examined [26,27]. Privacy and security issues regarding brain signal data collection and potential misuse were also discussed, providing insight into factors that may influence long-term adoption and societal integration of BCI technology.

RESULTS

Data analysis yielded five major themes reflecting participants' perspectives on BCI: (1) digital accessibility, (2) offline physical activity, (3) social interactions and psychological health, (4) usability, and (5) acceptance and concerns. For each theme, the most representative direct quotations are presented in the main text to illustrate key findings. Additional quotations supporting each theme are provided in Supplementary Table S3. Pre- and post-interview questionnaire responses are summarized in Table 2 and Fig. 1, which document changes in participants' perspectives on BCI acceptance, expected functionality, and tolerable risk following the FGI.

Digital accessibility

As communication and administrative or financial tasks increasingly rely on digital platforms, participants expressed a strong need for digital accessibility via BCI. Regardless of age, they emphasized the importance of accessing smartphone messaging applications such as KakaoTalk (Kakao Corp.), the primary messaging platform in Korea. In addition, the ability to write emails, make phone calls, and independently manage online banking was consistently identified as a priority.

> "It would be nice if BCI could let me send KakaoTalk messages, or make phone calls for me." (D)

> "I can't even enter my bank account password because I can't move my fingers. It would be better if BCI could help me do that." (A)

Offline physical activity

Participants remarked on the activities they want and need to perform the most from FGI questions 1–3. The responses categorized according to OTPF activity domains and GIC are shown in Table 3. Some of the responses made by the participants are as follows:

> "If I were discharged today, I wouldn't be able to manage essential daily activities like using the restroom or eating without full assistance. However, if BCI enables me to handle

Table 3. Activity classification according to OTPF-4 and GIC

Activity		Response	Generic indicator
ADL	Feeding	Having a meal, drinking water or juice	Self-care
	Personal hygiene	Using restroom, Showering, brushing teeth, washing hair, dressing/undressing	Self-care
	Home establishment and management	Turning on/off lights, locking/unlocking doors, using remote controllers for television	Home management activities
	Safety and emergency maintenance	Fastening safety belts on public transportation	Mobility
Instrumental	Functional mobility	Getting in/out of bed, getting on/off wheelchair	Mobility
	Driving and community mobility	Getting on/off public transportation, braking and controlling powered wheelchair, getting on/off curbside, driving a car	Mobility
Health	Physical activity	Assisting physical therapy and rehabilitation exercises, working out	Leisure activities
Leisure	Leisure participation	Hiking and jogging (ambulation assists)	Leisure activities

OTPF-4, Occupational Therapy Practice Framework: Domain and Process, Fourth Edition; GIC, Generic Indicator Criteria; ADL, activities of daily living.

these tasks independently, it could significantly improve my ability to live without relying on a caregiver." (C)

Social interactions and psychological health

Participants were strongly involved in discussing how BCI would affect their social interactions and psychological health. In general, participants responded favorably toward BCI on their social interactions and psychological health. Participants also expressed that not only will it be them who become independent via BCI, it will also be their caregivers (significant others and/or family) who will be freed from having to take care of them continuously. Participants described their needs and how BCI would benefit their lives.

"First of all, if the caregiver doesn't have to be constantly by my side and I can manage my daily life independently, it would create a more natural and harmonious environment for both of us. It would help maintain a comfortable relationship without feeling awkward. As for friendships, I can continue meeting my existing friends as usual, but making new friends might still be somewhat challenging." (A)

"I feel the same way. If I can manage daily activities at home independently without needing constant assistance from a caregiver, it would allow them to have more personal time and ease their burden. At the same time, I would feel more at ease within my home environment. This could improve the relationship between the patient and the caregiver, ultimately making both of us happier." (D)

Participants responded that if BCI could make them more independent, their self-image and emotional health would improve significantly.

"I think once I achieve a certain level of independence, my relationships and social connections would improve significantly. My self-esteem in daily life would also increase. Why? Because after the accident, my self-esteem took a hit. But if BCI allows me to regain some functional abilities, then regardless of how people look at me, the most important thing is that I can move and act on my own." (A)

One participant responded that, since he feels the same way about himself now compared to how he felt before, BCI would not impact his body image and emotional health.

"I don't think there would be a big difference. Ultimately, I'm just trying to live my life, and if someone were to use that against me or criticize me for it, that wouldn't be right. I don't see a need to tie this to self-esteem. My self-esteem hasn't changed much as it is, and whether I use BCI or not, I am still the same person. So, I don't think it would have much of an impact on my self-esteem." (B)

Usability

In the domain of usability assessment, we defined the key characteristics as follows: (1) motion speed, (2) accuracy, (3) setup, (4) training period for use, (5) usage time per single charge, and (6) cost. Table 4 shows the summary of usability perspectives from the participants.

Regarding motion speed, participants expressed that they are willing to endure some degree of latency and delay for im-

Table 4. Potential user perspectives on the usability of BCI system

Usability feature	Summarized description
Motion speed	Between 10 seconds to a minute per motion
Accuracy	Around 70% to 80% accuracy per task
Setup	Between 10 to 30 minutes
Training period for operation	Ranging from 3 months up to two years
Usage time per single charge	Between 3 and 8 hours
Cost	Ranging from USD 7,500 to USD 37,500

BCI, brain–computer interface.

proved accuracy. For accuracy, expectation was higher than motion speed.

"A delay of around 10 seconds when drinking water seems acceptable. I think it would be good if the accuracy were around 8 out of 10 times." (D)

"Of course, both accuracy and speed would be ideal, but accuracy should take priority over speed." (B)

When setting up the BCI, the participants expected to be helped by a caregiver, with minimum expected setup time of 10 minutes, to maximum 30 minutes.

"If the setup time is around 10 to 20 minutes, it seems manageable, but if it takes more than 30 minutes, relying on a caregiver would become a burden." (C)

Furthermore, the participants' expected usage time per single battery charge ranged between 3 to 8 hours.

"Ideally, it should last up to 3 hours on a single charge." (A)

"Five to six hours would be ideal." (D)

The expected training period to master the usage of BCI ranged widely, from 3 months to 2 years. However, the participants were in general willing to go through a rigorous training period for BCI use.

"If training takes three months, I'd accept it. Even if it's long, I could commit to about six months." (A)

"At a minimum, I think six months would be necessary." (B)

"One to two years would be fine for me." (D)

Lastly, three participants (A, B, and D) responded that they are willing to spend 10 million KRW (7,500 USD) or less on BCI, while one participant (C) was willing to spend 50 million KRW (37,500 USD) or less.

Acceptance and concerns

Even though most participants have never heard of BCI before and are rather aged, they were in general quite willing to use the technology, provided that BCI is safe and effective. Furthermore, they showed slightly favorable acceptance toward invasive BCI compared to noninvasive options primarily because they perceived it as offering greater reliability, higher accuracy, and a more seamless integration with their intended functions, reducing the need for external attachments or frequent recalibrations.

"If I'm going to do it, I might as well go for the best option. Since it's a significant decision, it should be done properly, even if it involves risks." (B)

"Even if there are risks, if the technology can significantly enhance functionality, then it's something worth considering." (C)

There were multifaceted concerns regarding the safety of the procedure.

"The biggest concern is death—undergoing surgery and not making it through. Also, I really don't want to end up in the ICU." (B)

Furthermore, safety during usage and maintenance issue were of large concern among the participants.

"If using an invasive BCI means that I would need another surgery if it malfunctions, then I wouldn't want to use it." (D)

"If I have to undergo another surgery due to side effects from the implant, I wouldn't be able to trust the device." (B)

DISCUSSION

Despite recent advancements in BCI technology [1], it has not yet achieved widespread clinical or consumer adoption [9,11,27], largely due to persistent challenges related to reliability, usability, and accessibility [26,27]. As BCI development

accelerates, incorporating user perspectives is increasingly important to ensure alignment with real-world functional needs rather than purely technological possibilities. In this study, we explored perceptions of BCI among individuals with high C-SCI using a structured, multidisciplinary focus group approach. Five key themes emerged—digital accessibility, offline physical activity, social interactions and psychological health, usability, and acceptance and concerns—revealing that while participants were generally receptive to BCI, they emphasized functional utility, safety, and reliability, alongside concerns regarding surgical risk, device longevity, and training burden.

The sample size of four participants warrants methodological consideration. FGI is a qualitative approach that does not follow power-based sample size calculations; rather, group sizes of four to eight participants are recommended in clinical and health research to balance diversity of perspectives with productive group dynamics [12,13]. In this study, recruitment was further constrained by the highly specific eligibility criteria—chronic-phase C-SCI with neurological level C4 or above—which represents a clinically rare population. Despite the small sample, considerable thematic convergence was observed across participants and across both FGI sessions, lending support to the adequacy of the sample for the exploratory aims of this study. Additionally, the wide age range of participants (34 to 71 years) may have introduced generational heterogeneity in baseline familiarity with digital technologies, potentially influencing perspectives on BCI-enabled digital accessibility. Notably, participant D, the youngest participant, was the only individual with prior awareness of BCI. Nonetheless, the core priorities identified across all participants—functional independence, safety, and caregiver burden reduction—were remarkably consistent, suggesting that the lived experience of high C-SCI may be a more dominant driver of BCI-related perspectives than generational background alone.

A central finding was participants' strong demand for improved digital accessibility through BCI. As communication, financial transactions, and administrative tasks increasingly rely on digital platforms, participants reported substantial limitations in independently using smartphones, messaging applications such as KakaoTalk, online banking, and internet services. BCI-enabled digital access was perceived as a critical means to enhance independence and participation across social, professional, and financial domains. Beyond personal convenience, digital accessibility was viewed as a way to reduce caregiver dependence and alleviate emotional and logistical burdens on families. Participants anticipated that greater independence in digital interactions would support more balanced caregiver relationships and help mitigate social isolation and stigma associated with severe physical disability.

The prominence of digital accessibility as a primary theme in this study warrants consideration in its sociocultural context. Korea's exceptionally high rates of smartphone penetration and digital platform dependency—with mobile banking, government services, and social communication mediated almost exclusively through applications such as KakaoTalk—mean that the inability to independently operate a smartphone represents a particularly acute form of social exclusion for individuals with high C-SCI in this setting. This may explain why digital accessibility emerged as a more salient priority in the present study than has been reported in comparable qualitative studies conducted in other populations [26,27], where physical mobility and communication restoration have tended to dominate user-defined BCI priorities. Future cross-cultural research should examine whether the relative weighting of digital versus physical BCI applications varies systematically across healthcare and technological contexts, as such differences would have direct implications for the design of culturally responsive BCI systems.

Participants also expressed interest in applying BCI to offline physical activities essential for daily living and mobility. While acknowledging the difficulty of fully restoring lost motor function, they envisioned BCI as a potential assistive tool for tasks such as eating, dressing, personal hygiene, home management, and wheelchair control. It should be noted, however, that current BCI technology remains largely experimental for such complex motor tasks, and the perspectives reported here reflect participant expectations and aspirational goals rather than established clinical capabilities. Nonetheless, these user-defined priorities offer valuable targets to guide future BCI development toward functionally meaningful applications. The identified activity domains align with prior studies documenting the potential of BCI to support functional independence in individuals with severe motor impairments [22,26], and integrating BCI across both digital and physical domains may ultimately reduce caregiver reliance and enhance personal autonomy.

Psychological and social implications of BCI use were also highlighted. Some participants anticipated improvements in self-esteem and emotional well-being through regained independence, whereas others expressed concerns related to body image, identity, and societal perceptions of neuroprosthetic use. One participant reported no expected change in self-image,

underscoring variability in psychological responses to assistive technologies and the importance of addressing psychosocial adaptation alongside functional outcomes.

Variability in psychological responses to BCI across participants highlights the heterogeneity of lived experience even within a clinically homogeneous population. While most participants anticipated meaningful improvements in self-esteem and social participation through BCI-enabled independence, participant B reported no expected change in self-image, framing his identity as stable and independent of functional capacity. This divergence may reflect differences in psychological adaptation to disability, coping style, or duration and mechanism of injury rather than age or technology familiarity per se. Prior qualitative work has identified self-concept stability and pre-injury identity as important moderators of assistive technology acceptance [26], and the present findings are consistent with this literature. Clinically, these individual differences underscore the importance of psychosocial assessment as a component of BCI candidacy evaluation, and suggest that standardized measures of disability adjustment and technology self-efficacy should be incorporated into future user-centered BCI research to enable more nuanced prediction of adoption outcomes.

Safety emerged as a dominant concern, particularly regarding invasive BCI procedures and unintended movements. Participants emphasized risks related to device malfunction, involuntary actions, and physical harm, underscoring the need for robust control accuracy and fail-safe mechanisms. Usability factors—including response speed, accuracy, portability, battery life, and setup complexity—were also emphasized, with most participants prioritizing accuracy over speed.

Training burden was another key factor influencing adoption. Although acceptable training duration varied, participants were generally willing to undergo prolonged training if meaningful functional benefits could be achieved, suggesting that adaptable training protocols and intuitive interfaces will be essential for broader BCI uptake.

The pre- and post-interview questionnaire data provide insight into how structured group discussion shaped participants' perspectives on BCI. Willingness to undergo brain surgery increased in three of four participants following the FGI, suggesting that expert-facilitated discussion and peer exchange may reduce ambivalence toward invasive procedures—an effect that has been observed in other contexts where deliberative group processes promote informed risk acceptance [26,27]. Notably, however, increased surgical willingness was accompanied by a downward recalibration of expected functional outcomes in two participants, with anticipated functional levels decreasing from "enhanced" to "moderate" or "slight improvement" after the FGI. This pattern suggests that the educational component of the FGI helped participants form more realistic expectations, tempering initial optimism with a clearer understanding of current technological limitations. Participant B showed the most pronounced shift, moving from willingness to accept even life-threatening surgical risk (score 5) to tolerance of only mild side effects (score 2) post-interview—a reversal that may reflect deeper engagement with the risk-benefit calculus prompted by group discussion. Taken together, these findings suggest that the FGI functioned not merely as a passive data collection instrument but as an active educational intervention that meaningfully restructured participants' understanding of BCI, underscoring the value of deliberative, multidisciplinary engagement in early-stage neurotechnology research.

The perspectives gathered in this study carry several implications for the future development and clinical translation of BCI technology. Participants consistently prioritized accuracy over speed, expressed tolerance for prolonged training periods, and demonstrated cautious but genuine openness to invasive procedures—provided that safety and long-term reliability could be assured. These user-defined benchmarks offer concrete targets for engineering development: an accuracy threshold of approximately 70%–80% per task was identified as the minimum for perceived usability, setup time should ideally remain within 30 minutes with caregiver assistance, and battery life should sustain at least four to eight hours of daily use. That participants were willing to undergo training periods of up to two years further suggests that the adoption barrier for BCI may be lower than previously assumed among motivated individuals with severe motor impairment, and that longitudinal training paradigms should be explored as a viable clinical pathway.

Beyond hardware and algorithmic improvements, the present findings highlight the need for systemic and policy-level interventions to support BCI adoption. All four participants in this study were hospitalized and reliant on professional caregivers, reflecting the broader reality that individuals with high C-SCI in Korea—and in many healthcare systems globally—remain institutionalized long after the acute phase of injury due to insufficient community support infrastructure. BCI technology, however sophisticated, will fail to deliver meaningful independence gains if the social and structural conditions for home-based use are not in place. Policymakers should therefore

consider BCI-enabling frameworks that include reimbursement pathways for device acquisition and maintenance, caregiver training programs, and home modification support, as parallel investments alongside device development. Furthermore, the participants' concerns regarding brain signal data privacy and the conditions under which continuous neural recording would be acceptable underscore the urgency of regulatory frameworks governing neurotechnology data, an area that remains largely unaddressed in existing biomedical device legislation in Korea and internationally. Future research should engage patients, caregivers, clinicians, engineers, ethicists, and policymakers in co-design processes to ensure that BCI systems are developed not only to be technically effective but also to be socially acceptable, economically accessible, and institutionally supported across the full continuum of rehabilitation care.

This study has several limitations. The small sample size and inclusion of only Korean male participants limit generalizability. Future research should include more diverse populations and individuals with other motor impairments, such as stroke, amyotrophic lateral sclerosis, and traumatic brain injury. As this study relied on qualitative FGI data, additional quantitative research is needed to establish standardized functional and usability benchmarks. Additionally, data on the level of social participation and daily activity prior to the interview were not systematically collected as part of the study protocol, which limits the extent to which individual contextual factors can be linked to the perspectives reported herein. Future studies should incorporate structured assessments of social participation and functional independence to enable more nuanced interpretation of user perspectives on BCI adoption. Finally, although this study focused on patient perspectives, successful clinical implementation of BCI will also require input from healthcare professionals. Integrating perspectives of physicians, therapists, and rehabilitation specialists will be essential to support shared decision-making and long-term clinical feasibility.

Conclusions

This study provides user-centered insights into perceptions of BCI among individuals with C-SCI, highlighting its potential to enhance independence, digital accessibility, and social participation, alongside challenges in safety, usability, and acceptance. Participants demonstrated cautious optimism toward BCI, emphasizing functional benefit, reliability, and user burden as key determinants of adoption. Future BCI development should prioritize user needs, safety, and accessibility to enable clinically meaningful and acceptable applications of neurotechnology in rehabilitation and assistive care.

CONFLICTS OF INTEREST

Byung-Mo Oh is the Editor-in-Chief of *Annals of Rehabilitation Medicine*. The author did not engage in any part of the review and decision-making process for this manuscript. Otherwise, no potential conflict of interest relevant to this article was reported.

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AUTHOR CONTRIBUTION

Conceptualization: Kim E, Shin G, Oh BM. Methodology: Myong Y, Kim E, Shin G; Data curation: Myong Y, Kim E, Shin G, Oh E. Funding acquisition: Oh BM. Supervision: Oh BM. Visualization: Myong Y. Writing – original draft: Myong Y, Oh BM. Writing – review & editing: all authors. Approval of final manuscript: all authors.

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DATA AVAILABILITY STATEMENT

The raw data (interview script) of this study can be retrieved upon reasonable request to the corresponding author.

SUPPLEMENTARY MATERIALS

Supplementary materials can be found via https://doi.org/10.5535/arm.260018.

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Adding Extracorporeal Shockwave Therapy to Conventional Treatment Improves Pain, Function, and Electrophysiological Function in Females With Carpal Tunnel Syndrome: A Randomized Controlled Trial

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Objective: To determine whether adding extracorporeal shockwave therapy (ESWT) to conventional treatment enhances pain, function, and electrophysiological functionality in females with carpal tunnel syndrome (CTS).
Methods: One hundred females (25–40 years) diagnosed with CTS were randomly allocated to a control group that received conventional therapy and an experimental group that received the same program augmented with ESWT. Outcome measures included the symptom severity scale (SSS), function severity scale (FSS), pain intensity assessed using the visual analog scale (VAS). In addition, distal sensory latency/distal motor latency (DSL/DML), and sensory nerve conduction velocity/motor nerve conduction velocity (SNCV/MNCV) were measured using a nerve conduction velocity study.
Results: The experimental group exhibited significantly greater improvements in SSS, VAS, DSL, DML, SNCV, compared to controls (all $p \leq 0.05$). However, changes in MNCV and FSS were non-significant ($p > 0.05$).
Conclusion: Integrating ESWT into rehabilitation enhances function, pain, and electrophysiological recovery in females with CTS.

Keywords: Extracorporeal shockwave therapy, Carpal tunnel syndrome, Taping, Electrophysiology

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INTRODUCTION

Carpal tunnel syndrome (CTS) is an entrapment neuropathy of median nerve in the carpal tunnel, manifesting as pain, tingling, and numbness in the thumb, index, middle, and radial half of the ring fingers, often accompanied by weakness of the thenar muscles and reduced hand function [1]. CTS risk factors include occupations involving repetitive wrist motions, fluid retention during pregnancy, and systemic diseases such as rheumatoid arthritis and diabetes mellitus [2].

Management of CTS encompasses both surgical and non-surgical approaches: physiotherapy, corticosteroid injections, orthotics, and pharmacological treatment [3]. Physical therapy modalities include laser therapy, therapeutic ultrasound, exercise therapy, manual therapy, Kinesio Taping (KT), and extracorporeal shockwave therapy (ESWT) [4-7].

ESWT has gained attention for its regenerative, anti-inflammatory, and analgesic properties. By delivering mechanical shock waves to affected tissues, ESWT increases blood flow, modulates nociceptor activity, and promotes tissue healing [1,8]. Clinical evidence supports its effectiveness in improving nerve conduction velocity (NCV) and functional performance in individuals having mild to moderate CTS [8,9].

KT is designed to relieve pain and enhance functional mobility by lifting the skin and decreasing pressure on underlying structures. KT has been demonstrated to improve circulation and lymphatic drainage, thereby reducing compression on the median nerve [10,11].

Therefore, we aimed to determine whether combining ESWT with conventional treatment enhances electrophysiological and functional outcomes more effectively than conventional treatment alone, as measured by pain, function, and electrophysiological parameters.

METHODS

Study design and participants

This randomized controlled trial was conducted between March and November 2024. The study followed the Declaration of Helsinki, approved by the Ethics Committee of the Faculty of Physical Therapy, Badr University in Cairo (IRB00014233-0), and was registered at ClinicalTrials.gov (ID: NCT06214286), with all participants providing informed consent. Eligible patients were initially referred for electrodiagnostic nerve conduction studies to confirm the diagnosis of CTS.

Sample size was calculated by G*Power software (v3.1.9; Heinrich-Heine-University) for a two-tailed test. Depending on F-tests (MANOVA: special effects and interactions), with α of 0.05, power of 0.80, an allocation ratio (N2/N1) of 1, and an effect size (d) of 0.585 derived from a pilot study, a minimum of 92 participants (47 per group) would be required, with a total sample size of 94. This calculation involved comparing two independent groups across five main dependent variable outcomes.

One hundred and twenty adult females aged 25–40 years diagnosed with CTS were screened. Participants were included if they were female, aged 25–40 years, had a diagnosis of mild to moderate CTS based on clinical diagnosis and NCV study, paresthesia in the median nerve distribution with nocturnal symptoms exacerbation, positive Phalen's and/or Tinel's sign, and symptom duration ≥3 months. Participants were excluded if they had a previous carpal tunnel release surgery, corticosteroid injection to the wrist within the preceding 3 months, traumatic wrist injury within the last 3 months, cervical radiculopathy, polyneuropathy, or pregnancy. Diabetic patients, patients with rheumatoid arthritis, or hypothyroidism were excluded from the study. One hundred participants met the inclusion and exclusion criteria and were randomized equally to the control or experimental group using a random number generator (https://randomizer.org). Thus, each group included 50 participants (Fig. 1).

Interventions

All participants in both groups received a combined 6-week program comprising median nerve gliding and tendon gliding exercises (3–5 sets per day, 10 repetitions per set). Participants were provided with a neutral-position wrist splint (0°–5° extension) to be worn during nighttime throughout the intervention period. All participants received education regarding ergonomic computer use and activity modification to avoid sustained wrist flexion or forceful gripping. KT was applied over the carpal tunnel region for all participants and reapplied every 3–5 days. The KT strip was cut into a Y-shape (approximately 15–20 cm), with the base anchored at the forearm proximal to the carpal tunnel. The two tails were applied around the wrist with mild tension (10%–20%), leaving the carpal tunnel area uncovered [1].

The experimental group additionally received radial ESWT (Fig. 2) applied directly over the carpal tunnel region. Participants received 6 sessions of shockwave therapy at a frequency of 1 Hz, energy of 60 mJ, and a total of 1,200 shocks per session.

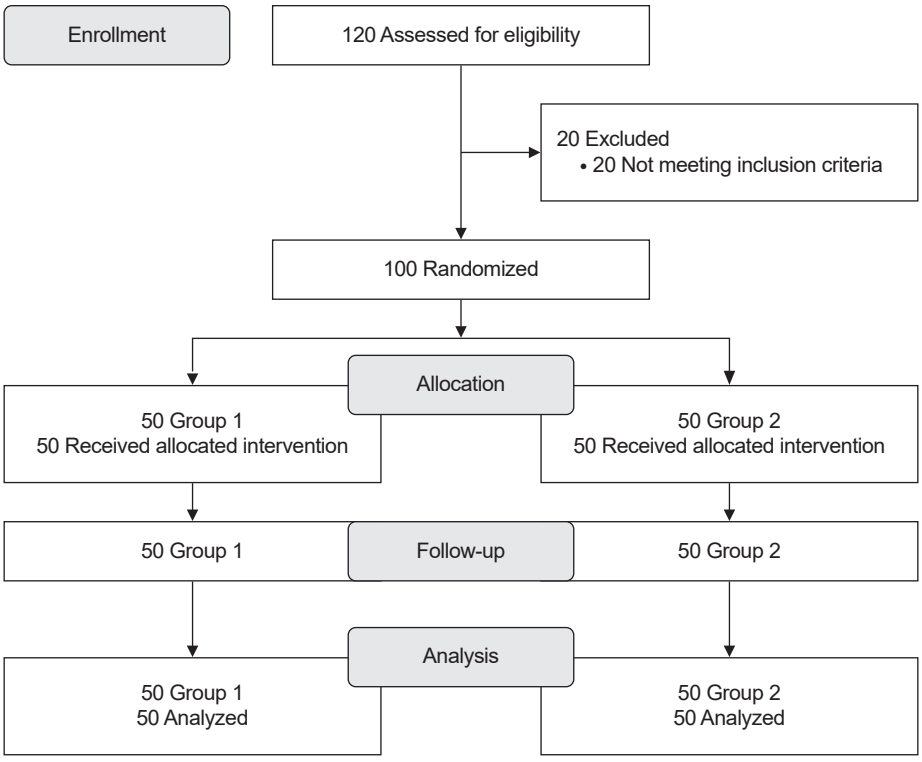

Fig. 1. Study flow diagram.

Fig. 2. Extracorporeal shockwave therapy application.

Sessions were administered once weekly for six weeks with participants in a sitting position [2].

All outcome measures were assessed by a blinded assessor unaware of the randomization or the interventions. Participants were assessed at baseline and after 6 weeks.

Outcome measures

Primary outcomes

(1) The Boston Carpal Tunnel Questionnaire

The Boston Carpal Tunnel Questionnaire is commonly used to assess symptom severity and functional status in patients with CTS and comprises a symptom severity scale (SSS) and a function severity scale (FSS). This 5-point Likert scale questionnaire includes an 11-item SSS assessing pain, numbness, tingling, and weakness, and an 8-item FSS evaluating difficulty performing daily tasks. Patients rated each item, and the instrument is valid and reliable for assessing symptom severity and function in patients with CTS, including validation in the Arabic language [3-7].

Secondary outcomes

(1) Pain intensity

Pain intensity evaluated using the visual analog scale (VAS). It

ranges from 0 to 10. VAS is a valid, reliable, and sensitive tool for pain assessment [8,9].

(2) Nerve conduction study

Nerve conduction study included measuring distal sensory latency/distal motor latency (DSL/DML), and sensory nerve conduction velocity/motor nerve conduction velocity (SNCV/MNCV) to confirm CTS diagnosis and severity. Active and reference ring electrodes were placed over the second proximal and distal inter-phalangeal joints. Afterward, Median nerve was stimulated at the wrist between the palmaris longus and flexor carpi radialis tendons at about 14 cm from the active electrode (Fig. 3) [10]. MNCV was measured using a fixed 8-cm distance between the surface recording electrode over the abductor pollicis brevis muscle belly and the reference electrode located just distal to the metacarpo-phalangeal joint. Afterward, Median nerve was stimulated at the wrist and elbow, conduction velocity was calculated by dividing the distance by the time difference between the two stimulation points (Fig. 4) [11].

Typical reference thresholds for sensory conduction (index finger to wrist, 14-cm distance) were DSL>3.5 ms or SNCV<50 m/s, indicating an abnormal response. For motor conduction (abductor pollicis brevis, stimulation at 8 cm), thresholds were DML>4.2 ms and MNCV<49 m/s [12,13].

Statistical analysis

Data were analyzed using IBM SPSS version 30 (IBM Corp.). Data normality was confirmed using the Shapiro–Wilk test. Data was summarized using mean and standard deviation. Unpaired t-test was used to compare basic demographic data between groups. Within-group comparisons between baseline and post-treatment were done using a paired t-test. To compare serial measurements across different time points, a repeated-measures ANOVA was used, with groups as the between-subjects factor and time points as the within-subjects factor. In addition, the interaction between group and time was also assessed. P-values less than 0.05 were considered statistically significant.

RESULTS

One hundred patients diagnosed with CTS completed this study. The mean age of participants in the experimental group was 34.12±3.12 years, while the mean age of participants in the control group was 34.64±3.02 years. There was no significant difference between the two groups regarding age (p=0.399). The

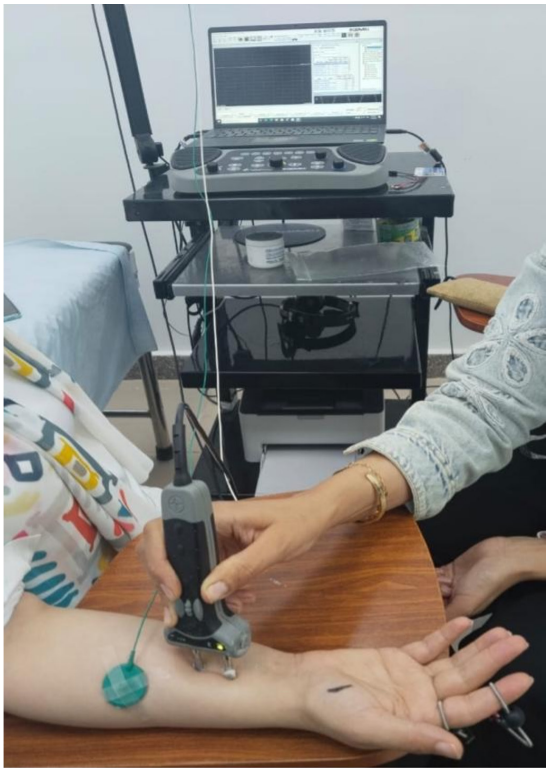

Fig. 3. Sensory nerve conduction velocity study.

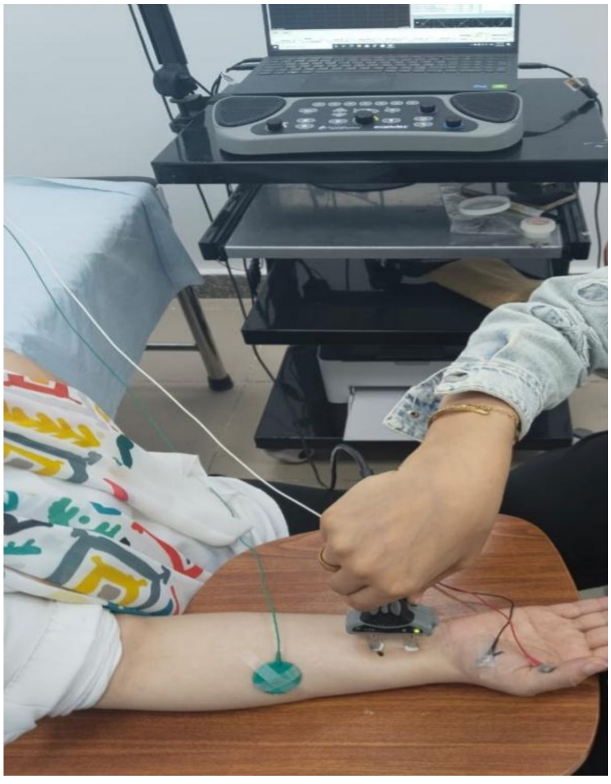

Fig. 4. Motor nerve conduction velocity study.

mean body mass index (BMI) of group 1 was 29.6±1.6 kg/m^2 while the mean BMI of group 2 was 29.5±1.7 kg/m^2. The mean disease duration of group 1 was 23.82±7.4 months, while the mean disease duration for group 2 was 24.02±7.7 months. There was no difference between the two groups in BMI or disease duration (p=0.724, 0.581, respectively).

SSS

There was no significant difference between the two groups in SSS at baseline (p=0.350). In addition, there was a significant difference between post-treatment and baseline in both groups (p=0.001). However, between-group comparison showed no significant difference when the averages across all time points were compared (p=0.307). Nevertheless, a significant interaction between groups and time was observed in favor of the treatment group (p=0.002) (Table 1).

FSS

There was no significant difference between both groups regarding FSS at baseline (p=0.195). Besides, there was a significant difference between post-treatment and baseline in both groups (p=0.001). Besides, between-group comparison showed a significant difference when the averages across all time points were compared (p=0.003). Nevertheless, no interaction between groups and time was observed (p=0.419) (Table 1).

Table 1. Comparison of mean pre-treatment and post-treatment scores of Boston-SSS, Boston-FSS, and VAS

Variable	Pre	Post	p-value
Boston-SSS			
Control group (A)	32.44±6.37	17.18±3.51	0.001*
Experimental group (B)	33.88±8.76	13.88±2.84	0.001*
Time (Pre vs. Post)			0.001*
Group			0.307
Time×Group			0.002*
Boston-FSS			
Control group (A)	27.64±3.83	10.80±1.70	0.001*
Experimental group (B)	26.58±4.29	9.06±1.74	0.001*
Time (Pre vs. Post)			0.001*
Group			0.003*
Time×Group			0.419
VAS			
Control group (A)	7.02±0.71	3.70±0.71	0.001*
Experimental group (B)	7.31±1.27	2.98±0.61	0.001*
Time (Pre vs. Post)			0.001*
Group			0.141
Time×Group			0.001*

Values are presented as mean±standard deviation.
SSS, symptom severity scale; FSS, function severity scale; VAS, visual analog scale.
*Significant at alpha level <0.05.

VAS

There was no significant difference between the two groups regarding VAS score at baseline (p=0.160). Besides, there was a significant difference between post-treatment and baseline in both groups (p=0.001). However, between-group comparison showed no significant difference when the averages across all time points were compared (p=0.141). Nevertheless, a significant interaction between groups and time was observed in favor of the treatment group (p=0.001) (Table 1).

DSL

There was no significant difference between the two groups regarding DSL at baseline (p=0.220). Besides, there was a significant difference between post-treatment and baseline in both groups (p=0.001). However, between-group comparison showed no significant difference when the averages across all time points were compared (p=0.743). Nevertheless, a significant interaction between groups and time was observed in favor of the treatment group (p=0.001) (Table 2).

SNCV

There was no significant difference between the two groups regarding SNVC at baseline (p=0.853). Besides, there was a significant difference between post-treatment and baseline in both groups (p=0.001). However, between-group comparison showed no significant difference when the averages across all time points were compared (p=0.116). Nevertheless, a significant interaction between groups and time was observed in favor of the treatment group (p=0.006) (Table 2).

DML

There was no significant difference between the two groups regarding DML at baseline (p=0.765). Besides, there was a significant difference between post-treatment and baseline in both groups (p=0.001). However, between-group comparison showed no significant difference when the averages across all time points were compared (p=0.349). Nevertheless, a significant interaction between groups and time was observed in favor of the treatment group (p=0.008) (Table 2).

MNCV

There was no significant difference between both groups re-

Table 2. Comparison of mean pre-treatment and post-treatment scores of the DSL, SNCV, DML, and MNCV

Variable	Pre	Post	p-value
DSL			
Control group (A)	4.52±0.59	3.86±0.53	0.001*
Experimental group (B)	4.66±0.54	3.56±0.25	0.001*
Time (Pre vs. Post)			0.001*
Group			0.743
Time×Group			0.001*
SNCV			
Control group (A)	44.24±3.03	47.21±2.56	0.001*
Experimental group (B)	44.36±3.54	48.76±2.46	0.001*
Time (Pre vs. Post)			0.001*
Group			0.116
Time×Group			0.006*
DML			
Control group (A)	5.01±0.54	4.50±0.47	0.001*
Experimental group (B)	5.04±0.54	4.65±0.49	0.001*
Time (Pre vs. Post)			0.001*
Group			0.349
Time×Group			0.008*
MNCV			
Control group (A)	48.92±0.31	49.11±0.23	0.001*
Experimental group (B)	49.03±0.32	49.33±0.36	0.001*
Time (Pre vs. Post)			0.001*
Group			0.002*
Time×Group			0.104

Values are presented as mean±standard deviation.
DSL, distal sensory latency; SNCV, sensory nerve conduction velocity; DML, distal motor latency; MNCV, motor nerve conduction velocity.
*Significant at alpha level <0.05.

garding MNVC at baseline (p=0.084), In addition, there was a significant difference between post-treatment and baseline in both groups (p=0.001). In addition, between groups comparison showed a significant difference when the averages across all time points were compared (p=0.002). Nevertheless, no interaction between groups and time was observed (p=0.104) (Table 2).

DISCUSSION

The current study examined the therapeutic impact of integrating ESWT into a conventional physiotherapy program for females with CTS. Both groups demonstrated significant improvements across all outcomes relative to baseline. Nonetheless, the experimental group showed significantly greater post-treatment improvements in SSS, SNCV, DSL, DML, and VAS score compared to the control group. However, there was no difference between groups regarding MNCV or FSS.

The current study demonstrated significant improvement in both groups, indicating the effectiveness of the physical therapy program in treating patients with CTS.

Night splinting in the current study was utilized to maintain the wrist in a neutral position during rest, thereby minimizing intracarpal pressure and mitigating nocturnal symptoms. A Cochrane systematic review reported modest short-term benefits of wrist splinting for pain relief and functional improvement compared to no treatment, although evidence supporting long-term efficacy remains limited [14]. More recent randomized trials suggest that combined daytime and nighttime splinting yields superior pain reduction and greater improvements in functional ability alongside quality of life relative to nighttime-only splinting or no splinting [15].

The conservative treatment in the current study also includes tendon and nerve gliding exercises, which are an essential component of conventional CTS rehabilitation and aim to enhance median nerve mobility and reduce perineural compression. Evidence indicates that incorporating these exercises into standard splinting protocols results in greater improvements in symptom severity and sensory function than splinting alone [16,17]. Proposed mechanisms include reduced intraneural adhesions, improved microcirculation, and support for median nerve recovery, with minimal adverse effects. Evidence suggests its efficacy when combined with other conservative treatments [18].

In addition, KT was applied to all participants in both groups. de Sire et al. [19] reported that KT significantly improved hand function in CTS, potentially through enhanced local circulation and reduced inflammatory compression on the median nerve.

Participants in the experimental group received ESWT along with conservative treatment. Participants in the experimental group showed greater improvements in symptom severity, pain intensity reduction, SDL, MDL, and SNCV than those in the control group. ESWT has been shown to induce biological effects, including neovascularization, nitric oxide–mediated anti-inflammatory activity, and neural regeneration [2]. These mechanisms may alleviate mechanical compression by minimizing perineural inflammation and edema in the carpal tunnel [20].

Our findings align with emerging evidence supporting the therapeutic role of ESWT in peripheral neuropathies, including CTS. ESWT has been reported to enhance nerve regeneration, reduce intraneural edema, and modulate inflammatory mediators, thereby improving sensory nerve conduction and symptom perception [20]. The superior clinical outcomes observed in the experimental group suggest a synergistic effect of

combining ESWT with conventional rehabilitation, potentially promoting biological recovery through improved vascularization, decreased inflammation, and accelerated median nerve regeneration [2,10].

Consistently, a meta-analysis by Zhang et al. [21] demonstrated that ESWT significantly improved pain, function, and electrodiagnostic parameters in mild-to-moderate CTS compared with control interventions. Similarly, Seok and Kim [13] reported superior medium-term outcomes with ESWT compared with corticosteroid injections. The positive effects observed in our study may reflect the cumulative impact of ESWT on vascular repair and axonal regeneration.

According to Chen et al. [1], the therapeutic effects of ESWT may be time-limited, with significant benefits observed at four weeks that attenuated thereafter. This suggests that the long-term effectiveness of ESWT may depend on treatment duration and combination with other therapeutic modalities.

The results also showed no difference between groups regarding MNCV or FSS. The reason behind this can be attributed to the difference in the regeneration velocity of sensory and motor nerves [22]. ESWT improves local blood flow and vascularization; thus, superficial sensory nerve improves faster than deeper motor nerves [23].

The results of the current study align with those of Habibzadeh et al. [24], who reported a significant difference between the ESWT group and the conventional treatment in SSS, SDL, and MDL. They also reported no difference in the FSS between groups. The current study also assessed the SNCV and MNCV. However, difference between the ESWT group and the conventional group was only detected in the SNCV in favor of the ESWT group.

The absence of a significant between-group difference in MNCV, related to the slower regeneration rate of motor fibers compared with sensory fibers, as well as the relatively short six-week intervention period, could explain the lack of difference between the two groups in FSS. Function improvement may require a longer time before it can be detected [25,26].

The difference between the results of the current study and those of Raissi et al. [27] may be due to differences in ESWT dosage and parameters as they applied only 3 sessions, whereas the current study applied 6 sessions. Their study reported only the difference between the ESWT and the conventional treatment group in terms of SDL. However, they couldn't detect a difference in either function, DML, pain intensity, or NCV. In the current study, there was a difference in favor of the ESWT group in SSS, SNCV, DSL, DML, and VAS score after 6 ESWT sessions.

Limitations and future directions

The study included only female participants, which may limit generalizability to males with CTS. Additionally, the six-week intervention period and lack of long-term follow-up preclude conclusions regarding sustained efficacy. Future studies should include both genders and incorporate extended follow-up durations.

Conclusion

Integrating ESWT with conventional conservative treatment yielded superior therapeutic outcomes in females with mild-to-moderate CTS. The combined intervention significantly improved function, reduced pain, and improved electrophysiological parameters compared with conservative treatment alone. These findings suggest a synergistic interaction between the biological effects of ESWT and the mechanical benefits of conventional rehabilitation. This combined approach represents a safe, non-invasive, and effective rehabilitation strategy that may serve as an optimal conservative option for CTS management before considering more invasive interventions.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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AUTHOR CONTRIBUTION

Conceptualization: Al-Afify DH, Saeed D, Wahba MM, Mohamed HS. Methodology: Al-Afify DH, Saeed D, Wahba MM, Sayed ENE, Mohamed HS. Formal analysis: Wahba MM, Ghoneim OSA. Project administration: Al-Afify DH, Saeed D, Wahba MM. Visualization: Wahba MM, Ghoneim OSA, Sayed ENE, Mohamed HS. Writing – original draft: Al-Afify DH, Saeed D, Ghoneim OSA, Sayed ENE, Mohamed HS. Writing – review and editing: Al-Afify DH, Saeed D, Zidan FS, Wahba MM, Ghoneim OSA, Sayed ENE, Mohamed HS. Approval of final manuscript: all authors.

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DATA AVAILABILITY STATEMENT

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Translation, Cross-Cultural Adaptation, and Validation of the Malay Version of the Roland-Morris Disability Questionnaire for Low Back Pain

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Objective: To translate, culturally adapt, and validate the Roland-Morris Disability Questionnaire (RMDQ) for Malay-speaking individuals with low back pain (LBP) in Malaysia.
Methods: A methodological study was conducted following established international guidelines for cross-cultural adaptation and psychometric validation. The process included forward–backward translation, expert review, content validation, face validation, and psychometric testing among individuals with LBP. Content and face validity indices were evaluated by rehabilitation professionals (n=8) and individuals with LBP (n=9). Psychometric testing was conducted with 102 participants to assess internal consistency, test-retest reliability (n=31), concurrent validity using the Malay Oswestry Disability Index, and known-groups validity.
Results: All items demonstrated excellent content and face validity (I-CVI, I-FVI, S-CVI/Ave, and S-FVI/Ave=1.00). The Malay RMDQ showed high internal consistency (Cronbach's α=0.932) and excellent test-retest reliability (ICC=0.996). Concurrent validity with the Malay Oswestry Disability Index was moderate (r=0.742, p<0.001). A preliminary known-groups comparison showed a statistically significant difference in the Malay RMDQ scores between participants with LBP and those without LBP (p=0.03).
Conclusion: The Malay RMDQ demonstrated preliminary psychometric support, including evidence of reliability, validity, and cultural appropriateness, for assessing disability in individuals with LBP. Future research should explore its responsiveness and utility in broader populations.

Keywords: Low back pain, Disability evaluation, Surveys and questionnaires, Reliability and validity, Cross-cultural comparison

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INTRODUCTION

Low back pain (LBP) is among the most common musculoskeletal disorders and is a major contributor to global disability and healthcare burden [1]. It is typically defined as pain or discomfort located between the lower costal margin and the superior gluteal line, with or without radiation to the lower limbs, and is classified as chronic when persisting for more than three months [2]. LBP can stem from various sources, including occupational strain, injury, degenerative changes, or systemic conditions, and affects individuals across all age groups.

Reflecting its global burden, LBP remains highly prevalent and impacts function, well-being, and productivity, especially among healthcare professionals [3]. In Malaysia, studies have reported prevalence rates between 12.4% and 84.6% across various occupational groups, including healthcare professionals, drivers, and office workers [4]. These figures highlight the multifactorial etiology of LBP, often linked to physical strain, prolonged sitting, poor posture, and degenerative changes.

Given the multidimensional burden of LBP, the use of reliable and valid instruments to detect and monitor disability is essential for clinical evaluation, intervention planning, and outcome monitoring. The Roland-Morris Disability Questionnaire (RMDQ), developed from the Sickness Impact Profile, is a widely used 24-item self-report tool designed to measure functional disability in individuals with mild to moderate LBP [5]. To date, the RMDQ has been translated into over 50 languages, enabling cross-cultural comparisons and global dissemination [6].

Despite its broad international usage, a validated Malay version of the RMDQ has not been available. Given that Malay is the national and most commonly spoken language in Malaysia, a linguistically and culturally adapted version is essential. Patients with limited English proficiency may misinterpret items or skip questions, resulting in inaccurate scores and compromised clinical utility [7]. Furthermore, ad hoc translation by clinicians can introduce inconsistencies, reducing measurement reliability. Cross-cultural adaptation ensures that translated instruments retain conceptual equivalence while being linguistically and culturally relevant for the target population [8]. Accordingly, this study aimed to cross-culturally translate and adapt the RMDQ into the Malay language and to evaluate its content validity, face validity, internal consistency, test-retest reliability, and construct validity among Malaysian adults with LBP.

METHODS

Study design

A methodological study of the translation, cultural adaptation, and psychometric validation was conducted in four sequential stages: (1) translation and cross-cultural adaptation; (2) content validity evaluation; (3) face validity evaluation; and (4) psychometric testing. The process adhered to internationally recognized guidelines for adapting health-related instruments across cultures [7,8]. This study was approved by the Research Ethics Committee of Universiti Teknologi MARA (Reference: FERC/FSK/MR/2024/00359). Written informed consent was obtained from all individual participants included in the study. The official RMDQ website states that the questionnaire and its translations are in the public domain and may be used without prior permission (https://www.rmdq.org/). Therefore, formal permission was not required for this translation, cross-cultural adaptation and validation study. The processes involved in this research are illustrated in Fig. 1.

Participants and sampling

A total of 102 participants were recruited using purposive sampling from three Malaysian states: Johor, Melaka, and Selangor. The sample comprised individuals with LBP and a comparison group without current LBP, which was included a priori to provide a preliminary test of known-groups validity. Participants in the LBP group were required to be adults aged 18 to 59 years experiencing mild to moderate LBP for a duration of 6 to 12 weeks. This criterion was selected because the RMDQ has been reported to demonstrate greater sensitivity in individuals with mild to moderate disability than in those with more severe disability [9]. Restricting the sample to this subgroup also helped to minimize floor and ceiling effects and reduce heterogeneity associated with severe or chronic LBP conditions, which often involve more complex clinical presentations. Exclusion criteria included (1) back pain due to specific pathological conditions (e.g., malignancy, infection, or fracture); (2) cognitive or psychiatric impairments affecting comprehension; and (3) a history of spinal surgery. Of the total sample, 31 participants from the LBP group participants completed the test-retest component after a two-week interval.

Stage 1: Translation and cross-cultural adaptation

Forward translation of the original English RMDQ into Malay was independently performed by two bilingual translators, one

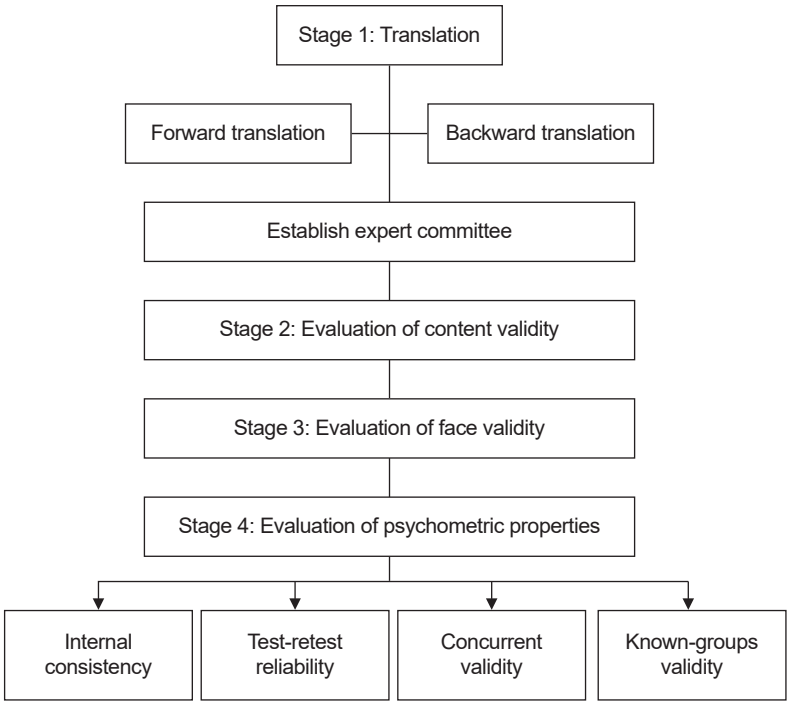

Fig. 1. Flowchart of the translation, cross-cultural adaptation, and validation process of the Malay Roland-Morris Disability Questionnaire.

with a clinical rehabilitation background and the other with linguistic expertise. The two versions were synthesized into a single reconciled draft. Backward translation was then conducted by another two independent translators, both blinded to the original version. An expert committee consisting of researchers and translators reviewed all versions to achieve semantic, idiomatic, experiential, and conceptual equivalence. The pre-final version Malay RMDQ was established following this process.

Stage 2: Content validity

Content Validity Index (CVI) was assessed by a panel of eight experts with clinical experience in rehabilitation, comprising three occupational therapists, three physiotherapists, and two rehabilitation doctors. Each item was evaluated for relevance, clarity, simplicity, and ambiguity using a 4-point Likert scale [10,11]. For the calculation of the CVI, ratings of 3 or 4 were considered indicative of agreement, while ratings of 1 or 2 were considered not acceptable. The Item-level Content Validity Index (I-CVI) was calculated as the proportion of experts who rated each item as acceptable. The Scale-level Content Validity Index was computed using two methods: the universal agreement approach (S-CVI/UA), defined as the proportion of items rated as acceptable by all experts, and the averaging approach (S-CVI/Ave), defined as the average of I-CVI values across all items [11]. An I-CVI value of ≥0.78 was considered acceptable for individual items, while S-CVI/UA ≥0.80 and S-CVI/Ave ≥0.90 indicated adequate content validity [11].

Stage 3: Face validity

Face validity was assessed by nine lay individuals with mild to moderate LBP. Each item was evaluated for clarity and comprehensibility using a 4-point scale [12]. For the calculation of the Face Validity Index (FVI), ratings of 3 or 4 were considered indicative of agreement (clear and understandable). The Item-level Face Validity Index (I-FVI) was calculated as the proportion of participants rating each item as clear and comprehensible, while the Scale-level Face Validity Index (S-FVI/Ave) was computed as the average of I-FVI values across all items [12]. Values ≥0.83 were considered acceptable for face validity. In addition, item impact scores were calculated to assess the perceived importance of each item. For each item, the impact score was obtained by multiplying the frequency of participants rating the item as important (score 4 or 5 on a 5-point scale) by the item's mean importance score. An item impact score of ≥1.5 was considered acceptable [10].

Stage 4: Psychometric evaluation

A target of 100–120 participants was established based on reliability study recommendations [13]. Internal consistency of the Malay RMDQ was assessed using Cronbach's α. Values between 0.70 and 0.95 were considered acceptable, and values between 0.80 and 0.90 were regarded as good [14]. To evaluate test-retest reliability, a minimum of 30 participants were targeted to complete the Malay RMDQ twice, with a two-week interval between administrations, consistent with recommended intervals for minimizing recall bias and clinical change [15]. The intraclass correlation coefficient (ICC) was calculated using a two-way mixed-effects model, absolute agreement, single measurement (ICC[3,1]), with values ≥0.75 indicating good reliability [16].

Concurrent validity was examined by correlating the Malay RMDQ scores with those from the validated Malay version of the Oswestry Disability Index (ODI) [17]. The ODI is another widely used questionnaire for assessing LBP-related disability, covering 10 functional domains such as pain intensity, lifting, walking, and social life. A validated Malay version of the ODI has shown acceptable reliability and construct validity among Malay-speaking individuals with LBP [17]. Preliminary known-groups validity was examined by comparing the Malay RMDQ scores between participants with LBP and those without LBP. A statistically significant difference ($p<0.05$) was interpreted as preliminary evidence of discriminative validity [18].

Outcome measures

The primary instrument used was the Malay version of the RMDQ, a 24-item self-report scale that assesses disability due to LBP. Each item is answered using a binary response format ("Yes"=1; "No"=0), with total scores ranging from 0 (no disability) to 24 (maximum disability). The Malay ODI was used to evaluate concurrent validity. A demographic questionnaire collected information on age, sex, occupation, and LBP characteristics. Structured rating forms were used for both expert and lay evaluations during the content and face validity phases.

Data analysis

All data were analysed using the IBM SPSS version 29 (IBM Corp.). Descriptive statistics were used to summarize participant characteristics. Content and face validity indices were computed using established formulas. Internal consistency was examined using Cronbach's α. Item-level analysis was also performed by calculating Cronbach's α if item deleted to assess the contribution of each item to the overall scale reliability. Test-retest reliability was evaluated using the ICC. Concurrent validity was assessed using Pearson's correlation coefficient, with correlation strengths interpreted as: poor (0.00–0.25), fair (0.26–0.50), moderate (0.50–0.75), and strong (0.76–1.00) [19]. Known-groups validity was analysed using independent samples t-tests. A significance level of $p<0.05$ was considered statistically significant for all inferential analyses.

RESULTS

Translation and cross-cultural adaptation

No major linguistic or conceptual difficulties were encountered during the forward or backward translation processes. The expert committee reached consensus on the linguistic, experiential, and conceptual equivalence of items. Specifically, extensive deliberations were undertaken for two Malay terms to ensure accurate semantic alignment with the original English version. The final version was clear and contextually appropriate for the Malaysian population (Supplementary Material S1).

Content validity

All 24 items demonstrated perfect agreement across relevance, clarity, simplicity, and ambiguity, with each item receiving an I-CVI score of 1.00. The overall S-CVI/UA and S-CVI/Ave values were both 1.00, indicating excellent content validity across all domains (Supplementary Material S2).

Face validity

Nine lay participants with varying degrees and types of LBP assessed the clarity and comprehensibility of the Malay RMDQ items. All items received an I-FVI score of 1.00. Similarly, both the S-FVI/UA and S-FVI/Ave reached a maximum score of 1.00, indicating complete agreement among participants that the items were clear and understandable. Additionally, impact scores were calculated, with the majority of items scoring 5.00 on a 5-point Likert scale. The lowest recorded mean score was 4.63, suggesting high perceived relevance and acceptability of the items (Supplementary Material S3).

Participant characteristics

A total of 102 participants completed the psychometric evaluation procedures. The majority were female (64.7%), and most were aged between 18 and 40 years (76.4%). More than half were employed (54.9%). Of the total sample, 60 participants (58.8%) were classified as having LBP of 6–12 weeks' duration,

while 42 participants (41.2%) were classified as without LBP (Table 1).

Internal consistency

The overall Cronbach's α was 0.932, indicating excellent reliability (Table 2). The standardized Cronbach's α was 0.936. Item-level analysis showed that removal of any item would not improve the overall α, with values ranging from 0.927 to 0.933 across all 24 items.

Test-retest reliability

A subset of 31 participants completed the RMDQ twice over a two-week interval. The overall ICC for the total score was 0.996 (95% confidence interval [CI]: 0.991–0.998), indicating excellent test-retest stability. Item-level ICCs ranged from 0.854 to 1.000, with most items demonstrating perfect agreement.

Table 1. Demographic characteristics of participants (N=102)

Demographic variable	Frequency
Age (yr)	
18–25	49 (48.0)
26–30	18 (17.6)
31–40	11 (10.8)
41–50	14 (13.7)
51–60	10 (9.8)
Sex	
Male	36 (35.3)
Female	66 (64.7)
Occupation	
Student	34 (33.3)
Worker	56 (54.9)
Unemployed	12 (11.8)
Working hours	
0–4	3 (3.0)
5–8	47 (46.0)
9–12	49 (48.1)
13–16	3 (2.9)
LBP	
Yes	60 (58.8)
Without LBP (other musculoskeletal pain)	23 (22.6)
Without LBP (no pain)	19 (18.6)

Values are presented as number (%).
LBP, low back pain.

Concurrent validity

The Malay RMDQ demonstrated moderate concurrent validity when compared with the Malay version of the ODI. All 102 participants completed both the RMDQ and the ODI, and the resulting Pearson correlation coefficient was r=0.742, p<0.001, indicating a statistically significant and moderate positive correlation between the two instruments.

Known-groups validity

As a preliminary assessment of discriminative validity, the Malay RMDQ scores were compared between participants with LBP (n=60) and those without LBP (n=42). A statistically significant difference in the Malay RMDQ scores was observed between the two groups, with a mean difference of 3.46 points (95% CI: 0.38–6.54, p=0.03). Table 2 summarizes the preliminary psychometric findings, including internal consistency, test-retest reliability, concurrent validity, and known-groups comparison.

DISCUSSION

This study aimed to culturally translate, adapt, and validate the RMDQ into the Malay language for use among individuals with LBP in Malaysia. Each stage of the translation and validation process followed rigorous guidelines, ensuring both linguistic and conceptual equivalence between the original and translated versions [8]. The absence of major linguistic challenges during the forward and backward translation processes, together with the strong consensus of the expert committee suggests that the final version likely preserved the original intent and meaning of the items and was culturally appropriate for the Malaysian context, as further supported by the subsequent psychometric findings.

Table 2. Summary of preliminary psychometric evaluation for the Malay RMDQ (N=102)

Type of analysis	Measure	Result
Internal consistency (n=102)	Cronbach's α (total scale)	0.932 (standardized=0.936)
Test-retest reliability (n=31)	ICC (total scale)	0.996 (95% CI: 0.991–0.998)
Concurrent validity (n=102)	Pearson correlation with ODI (Malay version)	r=0.742, p<0.001
Known-groups validity (n=102; LBP=60, without LBP=42)	Independent t-test (LBP vs. without LBP group)	t(100)=3.03, p=0.03
	Mean (LBP group, n=60)	7.26 (SD=5.39)
	Mean (without LBP group, n=42)	3.80 (SD=5.73)

RMDQ, Roland-Morris Disability Questionnaire; ICC, intraclass correlation coefficient; CI, confidence interval; ODI, Oswestry Disability Index; LBP, low back pain; SD, standard deviation.

The psychometric properties of the Malay RMDQ were consistent with those reported in previous RMDQ adaptations across various languages and populations, such as those in Hindi [20] Yoruba [21], Hausa [22], Arabic [23], Moroccan [24], Spanish (Argentinean) [25], and simplified Chinese [26]. These findings reinforce the robustness and transferability of the RMDQ as a cross-culturally applicable measure of LBP-related disability [5]. Expert panel evaluations demonstrated strong agreement on the relevance, clarity, and simplicity of the items, while feedback from lay individuals confirmed that the instrument was comprehensible and perceived as relevant. These outcomes are comparable to earlier studies that established good content and face validity in translated RMDQ versions [20-26].

The internal consistency results fell within acceptable ranges, with item-level values suggesting that the scale items work together to assess the intended construct. Similar internal consistency values have been documented in earlier translated versions [20-26]. Similarly, test-retest reliability was very high, demonstrating the scale's temporal stability and confirming its suitability for repeated use in both clinical monitoring and research contexts. In terms of construct validity, the Malay RMDQ showed moderate concurrent validity through its significant correlation with the Malay ODI, aligning with results from earlier studies [20,22,25,26].

A preliminary comparison between participants with and without LBP demonstrated significantly higher Malay RMDQ scores in the LBP group. However, this finding represents only preliminary discriminative evidence and should be interpreted cautiously, as the comparison was based on the presence or absence of LBP rather than clinically distinct severity subgroups. In addition, non-zero scores observed in the group without LBP may reflect nonspecific functional limitations or other musculoskeletal complaints. Future studies should therefore examine known-groups validity using clinically distinct LBP subgroups, such as categories based on pain severity, disability level, or clinical diagnosis.

From a practical perspective, the availability of a culturally adapted and tested Malay version of the RMDQ may assist healthcare professionals in evaluating LBP-related disability using a self-report format that reflects local language and context. It may be used not only for clinical screening and functional status monitoring but also as an outcome measure in rehabilitation research and workplace health surveillance programs, particularly given the high burden of LBP in Malaysia [4].

Nonetheless, this study is not without limitations. First, while the overall sample size of 102 participants met minimum recommendations for psychometric validation, a larger and more diverse sample would further strengthen the generalizability and robustness of the findings across both reliability and validity domains. Second, the sample was limited to selected regions and included predominantly younger adults, which may restrict the generalizability of findings to older populations. Furthermore, no formal assessment of clinical stability (e.g., global rating of change) was conducted during the two-week interval for test-retest reliability. As the sample included individuals with subacute LBP, some degree of clinical change may have occurred over time. Therefore, the very high test-retest reliability observed in this study should be interpreted with caution, as the absence of a formal stability assessment limits certainty that participants' clinical status remained unchanged during the interval.

The known-groups analysis was also based on comparison between participants with and without LBP rather than clinically distinct LBP subgroups, which limits the strength of the discriminative validity evidence. Lastly, responsiveness to change was not evaluated. Future research could address these gaps by including more diverse population groups, incorporating explicit stability measures for test-retest analysis, examining clinically relevant subgroup differences, and evaluating the tool's performance in longitudinal or intervention-based studies.

Conclusion

The Malay version of the RMDQ demonstrated preliminary evidence of reliability, validity, and cultural relevance for assessing functional disability in individuals with LBP. Through a rigorous translation and adaptation process, supported by expert and lay evaluations, the instrument showed promising psychometric properties, including high internal consistency, test-retest reliability, and construct validity. Its clarity and acceptability support its use in clinical and research settings within the Malay-speaking population. Future studies involving larger samples should examine floor and ceiling effects, measurement error, responsiveness, and applicability across broader and more diverse patient groups.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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AUTHOR CONTRIBUTION

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DATA AVAILABILITY STATEMENT

The datasets generated and/or analysed during the current study are available from the corresponding author on reasonable request, in accordance with data sharing policies and participant confidentiality agreements.

SUPPLEMENTARY MATERIALS

Supplementary materials can be found via https://doi.org/10.5535/arm.250173.

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Instructions for authors

Annals of Rehabilitation Medicine

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(10) Acknowledgments

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- For more on references, refer to the NLM Style Guide for Authors, Editors, and Publishers (http://www.nlm.nih.gov/citingmedicine).

Journals

1. Jeon JH, Jung YJ, Lee JY, Choi JS, Mun JH, Park WY, et al. The effect of extracorporeal shock wave therapy on myofascial pain syndrome. Ann Rehabil Med 2012;36:665-74.
2. Geraud G, Spierings EL, Keywood C. Tolerability and safety of frovatriptan with short- and long-term use for treatment of migraine and in comparison with sumatripan. Headache 2002;42 Suppl:S93-9.

Book & Chapter of book

3. Frontera W, Silver JK, Rizzo TD. Essentials of physical medicine and rehabilitation. 2nd ed. Saunders; 2008. p. 579-82.
4. Esquenazi A. Upper limb amputee rehabilitation and prosthetic restoration. In: Braddon RL, editor. Physical medicine and rehabilitation. 2nd ed. Saunders; 2000. p. 263-78.

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5. Harnden P, Joffe JK, Jones WG. Germ cell tumours V. Proceedings of the 5th Germ Cell Tumour Conference; 2001 Sep 13-15; Leeds, UK. New York: Springer; 2002.

Thesis (Dissertation)

6. Borkowski MM. Infant sleep and feeding: a telephone survey of Hispanic Americans [dissertation]. Mount Pleasant, MI: Central Michigan University; 2002.

(11) Tables

Tables should be submitted separately from the text, and each table should be created in MS Word on separate pages, using double space throughout. They should be simple, self-explanatory, and not redundant with the text or the figures. Limit 5 tables per manuscript. The title of the tables should be written in phrases, and capitalized the first letter of the first word. The title should be placed above the table, and abbreviations and footnotes should be placed under the table. Number the tables in order of appearance in the text (e.g., Table 1, Table 2). All abbreviations used in the table must be spelled-out in full under the table in the following order: abbreviation, comma, full word (e.g., RM, rehabilitation medicine;). Table footnotes should be indicated in superscripts in the following order: [a], [b], [c]… but p-values should be indicated by asterisk (e.g., *$p < 0.05$, **$p < 0.01$. ***$p < 0.001$).

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Annals of Rehabilitation Medicine

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☐ All pages are numbered in the following order: title page, structured or standard abstract, body of the text, conflict of interests, Funding information, Author contribution, Acknowledgments (when applicable), references, legends, and tables.

☐ The text is consecutively line numbered.

☐ The Submission Application & Copyright Transfer Form is signed by the guarantor at original submission.

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☐ A structured abstract with the headings of Objective, Methods, Results, and Conclusion (A nonstructured abstract for case reports) must succinctly describe the paper.

☐ At the end of the abstract, relevant keywords are listed.

References

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☐ There are less than 5 tables in the text of original articles.

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