Issue-2: ORTHOPEDICS

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Orthopedic conditions are diseases, or injuries of the muscle, ligaments, bones and joints. These disorders are debilitating and severely hamper the quality of life of the affected individual. Among varied orthopedic disorders, osteoarthritis and rheumatoid arthritis affect a large proportion of people worldwide. While osteoarthritis is a chronic disorder, rheumatoid arthritis is a systemic autoimmune illness. Both these conditions can affect any joint of the body and cause severe pain and discomfort. Clinical management protocols are frequently comprehensive, multimodal approaches that include pain control as one of the major requisites. This input is designed to include latest scientific coverage on major orthopedic disorders and aims to provide latest advancements and developments. We earnestly hope that this education initiative will serve as a useful resource for the readers.

Structural changes of bone and cartilage are the hallmarks of rheumatoid arthritis (RA) and psoriatic arthritis (PsA). Radiography can help in making diagnosis and in differentiating PsA and RA from other articular diseases. Radiography is still considered the preferred imaging method to assess disease progression, reflecting cumulative damage over time. This review discusses the use of conventional radiography for diagnosing and detecting early structural changes in RA and PsA and providing a historical overview of commonly used scoring methods.

RADIOGRAPHIC SCORING METHODS IN RHEUMATOID ARTHRITIS AND PSORIATIC ARTHRITIS

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Rheumatoid arthritis (RA) and psoriatic arthritis (PsA) are the most prevalent inflammatory arthritis leading to structural damage, affecting about 0.46% and 0.42%, respectively, of the population in Western countries [1, 2].

Since its introduction in clinical practice, radiographs of the hands and feet have been used to diagnose and to monitor the disease course of RA and PsA [3–5]. The presence of radiographic bone erosions is fundamental for RA classification, according also to the more recent classification criteria (American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) 2010 classification criteria) [6], while for PsA, in the Classification Criteria for Psoriatic Arthritis (CASPAR), radiography still remains one of the main criteria for classifying PsA [7].

Assessing radiographic abnormalities is one of the most powerful means available to the clinical investigator for determining the effects of RA and has been used as a relatively objective marker in clinical trials for evaluating treatment response [8]. The efficacy of disease-modifying antirheumatic drugs (DMARDs) traditionally has been registered as their ability to slow down radiographic damage [9]. These points are outlined in EULAR recommendations and models for management of early arthritis, and prognostic markers for persistent arthritis have been established [10]. Therefore, the current "gold standard" for radiological evaluation of disease progression in RA is the assessment of disease progression with plain radiographs.

Many researches have shown that in RA, joint damage occurs within the first 2 years after symptom appearance [11–14]. It has

been demonstrated that within 4 months of disease onset, 34.9% of patients have erosions evident on X-ray, and 54.9% were erosive at the 12th-month follow-up [15].

With the increasing use of DMARDs and biological DMARDs (bDMARDs), early diagnosis is now of paramount importance, and disease progression has to be assessed regularly to monitor efficacy of the treatment [16–18]. In addition, the identification of individual RA patients at high risk of rapid radiographic progression is critical to making appropriate treatment choices [19]. In these patients, effective therapy can reduce the odds of progression [20, 21], and both early and intensive treatment can alter the course of the disease by slowing the rate of radiographic progression [22, 23].

Regarding PsA, at the current state of the art, there is evidence supporting the concept of PsA being a distinct disease from RA clinically [24], radiologically, and pathologically [25]. PsA develops in about 30% of patients with psoriasis [26]. It is a heterogeneous disease, and there have been multiple attempts to subgroup patients according to their clinical presentation. As in RA, structural damage is the consequence of inflammation that can destroy cartilage and bone, leading to functional impairment and disability [27]. In PsA, the presence of radiological damage has been enhanced in 47% of patients within the first 2 years, and as in RA, the use of bDMARDs has been capable of inhibiting progression of structural damage in several randomized controlled trials [28].

Rheumatoid Arthritis and Psoriatic Arthritis Radiographic Comparison

As mentioned above, despite certain similarities, the two inflammatory joint diseases show considerably different features. Whereas RA primarily results in bone and cartilage resorption, PsA combines destructive elements with anabolic bone responses.

RA is the prototype of a destructive arthritis. In RA, usually, the metacarpophalangeal (MCP) joints, the proximal interphalangeal (PIP) joints, all wrist compartments, and the metatarsophalangeal (MTP) joints are the most commonly involved sites. In addition, joints in the midfoot and hindfoot, knees, glenohumeral joint at the shoulder, the elbow, and cervical spine can also be affected [29, 30].

In PsA, the distribution of affected joints is more often asymmetric and oligoarticular

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than in RA. The distal interphalangeal (DIP) joints are frequently and early involved, while in RA involvement of the DIP joints, in general, is rare and more often a feature of the late disease. In PsA, DIP joints, large joints of the lower extremities, the axial spine, and sacroiliac joints are commonly affected; the MCP and MTP joints and wrist can be involved as well.

The first radiographic changes observed in RA are soft tissue swelling and juxta-articular osteopenia as bone density is reduced adjacent to the joint as a result of local synovial inflammation [31]. The bone may appear less dense around the articular surfaces, although this is not necessarily a specific radiographic sign of RA [32]. Juxta-articular osteopenia is uncommon in PsA and, when present, is a sign of poor prognosis [33]. The lack of osteoporosis, even in patients with severe destructive arthritis, is a reliable sign in the differentiation of PsA from RA, although the presence of osteoporosis does not exclude PsA.

The erosions in RA tend to be periarticular and are often described as marginal erosions as they are close to the joint and reflect the direct mechanical action of the hypertrophied synovium and granulation tissue. The inflamed synovium slowly invades adjacent structures, causing damage and destruction to the cartilage and bone, leading to joint space narrowing (JSN) and bone erosion that can be seen on radiographs. The JSN in RA tends to be uniform and concentric, reflecting the generalized nature of the synovial inflammation within the joint.

In PsA, the early erosive changes predominate in the marginal articular areas, resembling “mouse ears.” Erosions progress over time and may affect the central area. Later, the bone appears as if it is being gnawed away, the bone surface becomes frequently irregular or jagged but still sharply delineated, whereas peripherally new bone formation may create an unclear ill-defined outline. The ends of the bones can become pointed, resulting in the image of “pencil in cup” or “cup-and-saucer” appearance. DIP involvement and the asymmetric distribution also can help differentiate PsA from RA. The uniform reduction of joint space is the radiographic expression of cartilage loss and could be seen at any involved joint, more typically at the DIP and PIP joints, and more infrequently at the MCP joints.

The proliferation of erosions may form irregular excrescences with a spiculated appearance. Along the shaft is possible to see periostitis, cottony cushion initially that may form solid new bone simulating enlargement of the phalangeal diaphysis. Periostitis in the metaphyses and diaphyses with periosteal bone neoapposition is a common phenomenon and may thicken an entire phalanx. It can occur early in the course of the disease before other features have developed. Condensation

Table 1: Radiological features that distinguish between rheumatoid arthritis and psoriatic arthritis.

Radiographic features	Rheumatoid arthritis	Psoriatic arthritis
Number of erosions	+++	+
Severity of erosions (size)	+++	++
Erosion distribution	Preponderance for radial sites	Evenly distributed
DIP erosions	–	+++
Number of osteophytes	+	+++
Severity of osteophytes (size)	+	+++
Bone proliferation	+	+++
Inflammatory changes		
Synovitis	+++	++
Tenosynovitis	+++	++
Enthesitis	+	+++
Dactylitis	–	+++
Mutilans (erosions on both sides of joints)	–	+

DIPs distal interphalangeal joints

of bone on the periosteal and endosteal surfaces accompanied by thickening of the trabeculae can cause radiodensity of an entire phalanx ("ivory phalanx"), another manifestation of bone proliferation. Intraarticular osseous fusion of joints predominantly affects DIP and PIP joints. Table 1 summarizes the main radiological differences between RA and PsA.

Radiographic Scoring Methods in Rheumatoid Arthritis

As discussed above, in RA all the synovial joints can be affected but only some joints in a scoring method can be included. Small joints are the most frequently affected, and Scott *et al.* [34] showed that they could give a good representation of the global progression of damage. Another advantage that is given from the use of hand and wrist X-rays is that erosions are easier detectable in small joints than in the large ones. X-rays of hands and wrists have been used for the creation of the previous scoring systems for RA. Several authors showed in inception cohort studies of patients with early RA that MTP are eroded earlier and show more damage [35, 36]. These studies indicate the importance to include feet in a scoring method assessing RA radiographic damage.

The scoring systems that have been designed to evaluate radiographic changes in RA can be divided into two main groups: global and detailed. Global scoring systems assign one score to the entire joint, taking into account all the abnormalities seen, whereas detailed systems assign scores on at least two separate variables for each joint evaluated [37, 38]. Radiographic scores, such as the Larsen and Sharp scores [39] and their modifications [40, 41], are the standard methods for determining joint damage and its progression [42, 43]. Table 2 summarizes the main RA features included in the different radiographic scoring methods described below.

Sharp Scoring Method (1971)

In 1971, Sharp and colleagues proposed a detailed scoring method for the hands and wrists that is divided into two scores, one for erosions and the other for JSN [44]. The number and selection of joints in the Sharp score evolved in the years, and a modification proposed in 1985 of the Sharp method [45] is now considered the standard for the method.

Larsen Scoring Method (1977)

The Larsen method was developed by Larsen *et al.* [39]. It has been modified several times by the authors [46]. It is a 6-point global scoring of joints, based primarily on erosive damage. However, grade 1 can be based on soft tissue joint swelling only, which is not a real sign of structural damage and is also difficult to assess reliably. The method can be applied to many joints but is primarily used for the hands and wrists and also for the feet. Larsen produced a set of standard reference films to compare the grading of the joints.

Modified Sharp Method (1985)

Sharp *et al.* [45] further defined which joints to score based on the frequency of RA involvement. They decreased the number of joints of each hand/wrist to 17 for erosions and 18 for JSN. Therefore, the final Sharp method includes two scores, one for erosions and the other for JSN. Erosions are counted when discrete, and surface erosions are scored according to the surface area involved [45].

Table 2: Features of rheumatoid arthritis included in the Sharp and in the Larsen scoring systems and further modifications.

Scoring method	Erosion	JSN	Osteoporosis	Soft tissue swelling	Alignment/ (sub)luxation	Ankylosis	Cyst
Sharp (1971)	+	+	–	–	–	+	+
Larsen (1977)	+	+	+	+	–	–	–
Modified Sharp (1985)	+	+	–	–	–	+	–
Kaye (1987)	+	+	–	–	+	+	+
Van der Heijde/Sharp (1989)	+	+	–	–	+	+	–
Modified Larsen (1995)	+	+	–	–	–	–	–
Genant (1998)	+	+	–	–	+	+	–
Ratingen score (1998)	+	+	–	–	–	–	–
SENS (1999)	+	+	–	–	+	+	–

JSN joint space narrowing, *SENS* simplified erosion narrowing score
+ = included in the scoring system; – = not included in the scoring system

Kaye Scoring Method (1987)

Kaye *et al.* [47] combined and modified the methods described by Genant [48] and Sharp *et al.* [45]. In this method, malalignment is scored in addition to erosions and JSN. Some of the joints that were evaluated in the Genant and Sharp methods were excluded and/or combined. Sites were considered inevaluable if they were missing from the radiograph or if they had flexion deformity. Inevaluable joints were not scored and were therefore excluded from analysis.

van der Heijde-Modified Sharp Scoring Method (1989)

The most noticeable difference in the van der Heijde modification is the addition of the joints of the forefoot. Another change was the decreased number of joints in each hand/wrist scored [49]. Some sites (triquetrum for erosions and lunate triquetrum, first IP joint and radioulnar joint for JSN) were difficult to assess in a reliable fashion, mainly due to superimposition, and often were difficult to score leading to interobserver disagreement. The Sharp/van der Heijde scoring system is currently the most widely used radiographic scoring system in clinical trials in RA including biological agents [16–20, 22, 23, 50, 51] (Fig. 1).

Modified Larsen Method (1995)

A modification of the original method [39] to evaluate radiographs in long-term studies was proposed later by Larsen *et al.* [46]. It incorporates several changes in the original method: scores for the thumbs and first MTP were deleted; the wrist was divided into four quadrants, and a distinction was made between erosions of different sizes (Fig. 2).

Genant-Modified Sharp Scoring Method (1998)

Similar to Sharp's method, Genant [48] scored erosions and JSN separately. The Genant modification of the Sharp method focuses on 14 sites for erosions and 13 sites for JSN. In Table 3 are shown the joints considered for erosions and JSN and the grading. Comparison of Genant–Sharp and van der

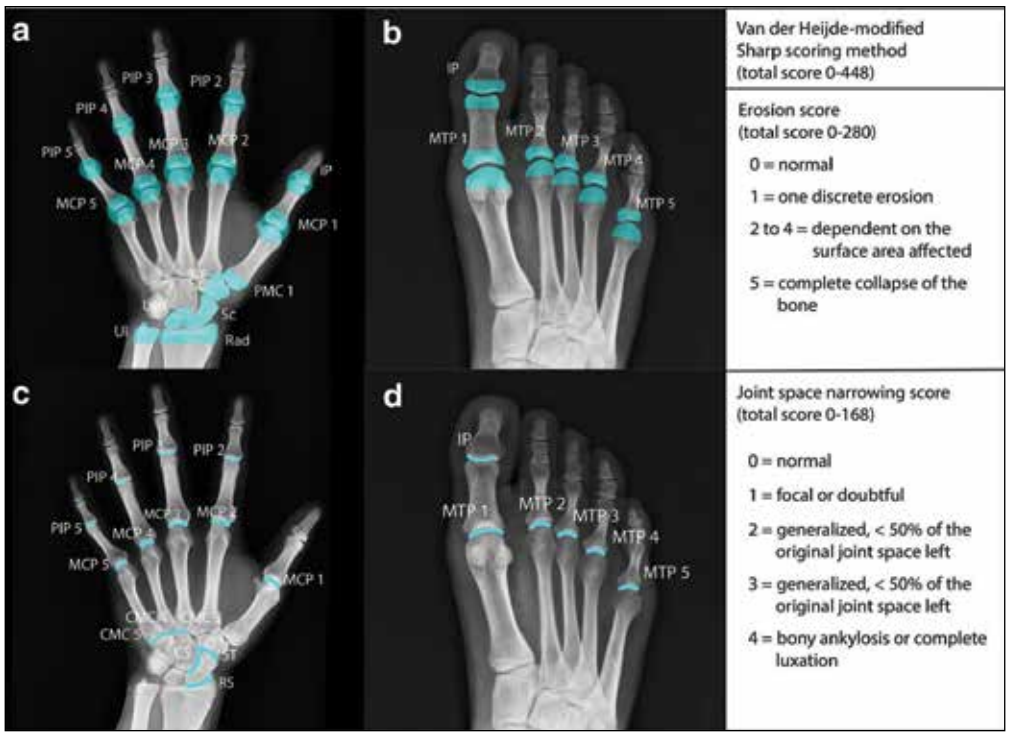
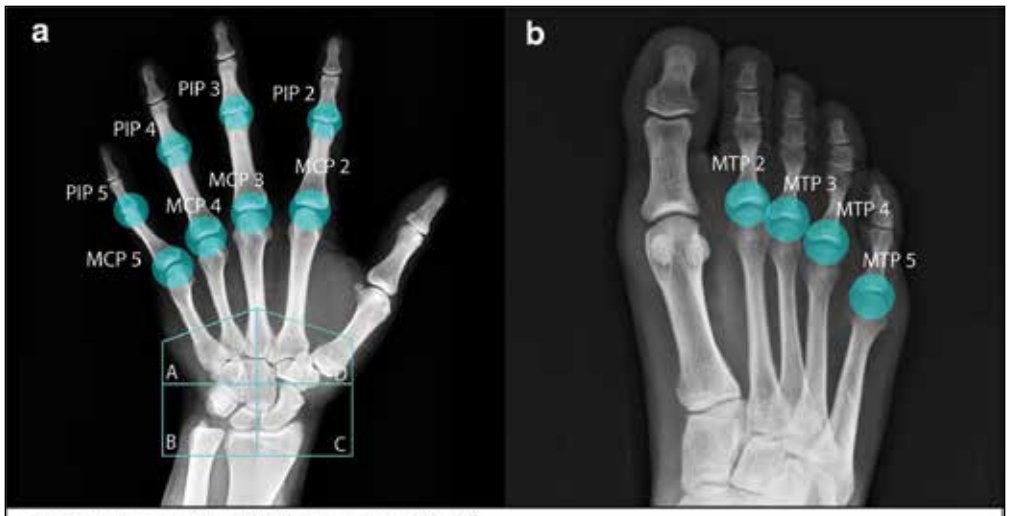


Fig. 1: van der Heijde-modified Sharp scoring method representation with figure and grading. **a** Joints selected in each hand for erosions: 4 PIP, 5 MCP, IP, scaphoid, lunate, distal ulna, distal radius, the two components of the CMC joints of the thumb are evaluated separately (PMC and trapezium–trapezoid). The maximum score for both hands is 160. **b** Joints selected in each foot for erosions: the proximal and distal articular components of the MTP and IP are evaluated separately resulting in a 0–10 score for each joint. The maximum score considering both feet is 120. **c** Joints selected in the hand: the CMC 3, CMC 4, CMC 5 are scored separately, the IP is not included, only the radio-scaphoid part of the radiocarpal joint is evaluated. The maximum score for both hands is 120. **d** Joints selected for JSN in each foot. The maximum score for both feet is 48. *CMC* carpometacarpal, *CS* capitate–scaphoid, *IP* interphalangeal joint, *Lun* lunate, *MCP* metacarpophalangeal joint, *MTP* metatarsophalangeal joint, *PIP* proximal interphalangeal joint, *PMC* proximal metacarpal, *Rad* radius, *RC* radio-scaphoid, *Sc* scaphoid, *ST* scaphoid–trapezium, *T–T* trapezium–trapezoid, *Ul* ulna



Modified Larsen Method (1995) (total score 0-160)

Grade 0	Intact bony outlines and normal joint space.
Grade 1	Erosions less than 1 mm in diameter or joint space narrowing
Grade 2	One or several small erosions (diameter more than 1 mm)
Grade 3	Marked erosions
Grade 4	Severe erosions. There is usually no joint space left: the original bony outlines are partly preserved.
Grade 5	Mutilating changes: the original bony outlines have been destroyed.

Fig. 2: Modified Larsen method represented with figure and grading. **a** Joints evaluated in each hand: 4 PIP, 4 MCP, the wrist is subdivided into four quadrants that are scored separately. The maximum score for both hands is 120. **b** Joints selected in each foot: in this method, the MTP and the IP of the big toe are not considered. The maximum score considering both feet is 40. *IP* interphalangeal joint, *MCP* metacarpophalangeal joint, *MTP* metatarsophalangeal joint, *PIP* proximal interphalangeal joint

Heijde/Sharp methods showed that both demonstrated a similar performance [52] (Fig. 3).

Ratingen Score (1998)

A new scoring method, derived from the Larsen score, was developed by Rau and Herborn. A notable difference is the inclusion of a quantitative appraisal of the percentage of loss of the joint surface. This method is known as a "Ratingen score" [53]. The amount of joint surface destruction is defined by the length of the clearly visible interruption of the cortical plate in relation to the total joint surface. In this method, the stages are described as a quantitative measure of the destroyed joint surface area and can, therefore, be applied more easily. These modifications also enhance sensitivity and increase reliability.

Simplified Erosion and Narrowing Score (SENS) (1999)

The SENS was developed by van der Heijde [54] and is a simplified method by summing the number of eroded and narrowed joints on selected joints on hand and foot radiographs. It exploits the same joints of hands and feet, but as opposed to applying a semiquantitative scale of 0–4 for JSN and 0–5 for erosions, the SENS simply dichotomizes (bimodal answer modality) whether an erosion is absent (score 0) or present (score 1) and whether JSN is absent (score 0) or present (score 1). The SENS showed a good intra- and inter-reader reliability and is sensitive to change [55]. Another important issue is the absence of a clear ceiling effect. Its decisive advantage is its feasibility in clinical practice [56]. It has been demonstrated that the carpal joints may be omitted from SENS without noticeable repercussion for its responsiveness and discriminant validity [57] (Fig. 4).

Feasibility of The Scoring Methods in Clinical Practice

An important disadvantage of the scoring methods for clinical trials is the fact that they require significant training and that scoring according to these methods is time-consuming, making these techniques unfeasible for routine clinical practice. Several authors calculated the time needed to score radiographs with different methods in RA. The time to score seven radiographs of hands and feet was

Table 3: Characteristics of the most used scoring methods for rheumatoid arthritis.

van der Heijde modification of the Sharp method (1989)	Genant modification of the Sharp method (1998)	Modified Larsen method (1995)
Type of scoring method		
Detailed	Detailed	Global
Description of scoring system		
Erosion is assessed in 16 joints for each hand and wrist, and six joints for each foot. One point is scored if erosions are discrete, rising to two, three, four, or five depending on the amount of surface area affected. JSN is scored as follows: 0 = normal; 1 = focal or doubtful; 2 = generalized, less than 50% of the original joint space; 3 = generalized, more than 50% of the original joint space or subluxation; 4 = bony ankylosis or complete luxation	Erosion is scored according to an eight-point scale with 0.5 increments, where 0 = normal; 0+ = questionable or subtle change; 1 = mild; 1+ = mild worse; 2 = moderate; 2+ = moderate worse; 3 = severe; and 3+ = severe worse. JSN is scored according to a nine-point scale with 0.5 increments, where 0 = normal; 0+ = questionable or subtle change; 1 = mild; 1+ = mild worse; 2 = moderate; 2+ = moderate worse; 3 = severe; 3+ = severe worse; and 4 = ankylosis or dislocation	It differentiates six stages from 0 (normal) to 5, reflecting progressive deterioration, and provides an overall measure of joint damage. The grading scale ranges from 0 to 5: 0 = intact bony outlines and normal joint space; 1 = erosion less than 1 mm in diameter or JSN; 2 = one or several small erosions (diameter more than 1 mm); 3 = marked erosions; 4 = severe erosions (usually no joint space left and the original bony outlines are only partly preserved); and 5 = mutilating changes (the original bony outlines have been destroyed)
Advantages and disadvantages		
Sensitive for detection of radiographic progression but requires training and is time-consuming to apply	Sensitive, but presents difficulties in assessing progression of structural damage. Requires training to apply efficiently	Semiquantitative global method, easier to learn and use, less sensitive to changes than the modified Sharp method

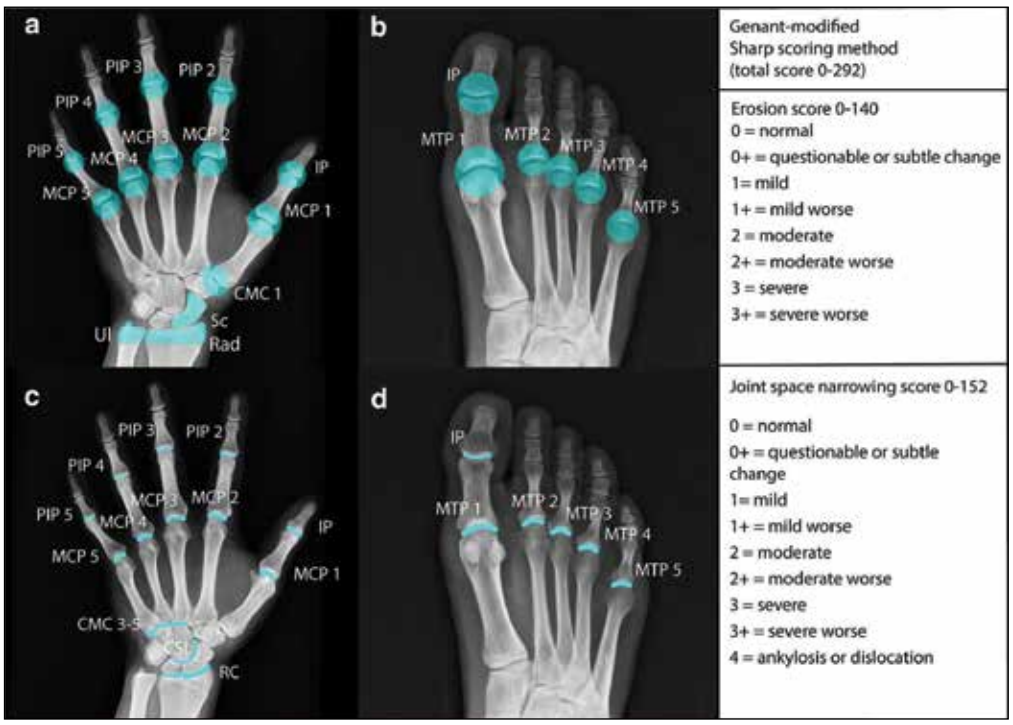


Fig. 3: Genant-modified Sharp scoring method illustrated with figure and grading. **a** Joints selected in each hand for erosions: 4 PIP, 5 MCP, the IP, the CMC of the thumb, scaphoid, distal ulna, distal radius. The maximum score for both hands is 98. **b** Joints selected in each foot for erosions: all the MTP joints and the IP joint of the big toe. The maximum score considering both feet is 42. **c** Joints selected in the hand in the Genant-modified Sharp: the CMC 3, CMC 4, CMC 5 are scored united. The lunate joint is considered for joint space narrowing in the capitate–lunate and radius–lunate joints, whereas the mSvdHS does not include it. The maximum score for both hands is 104. **d** Joints selected for JSN in each foot: all the MTP joints and the IP joint of the big toe. The maximum score for both feet is 48. *CMC* carpometacarpal, *CSL* capitate–scaphoid–lunate, *IP* interphalangeal joint, *Lun* lunate, *MCP* metacarpophalangeal joint, *MTP* metatarsophalangeal joint, *PIP* proximal interphalangeal joint, *PMC* proximal metacarpal, *Rad* radius, *RC* radiocarpal, *Sc* scaphoid *ST* scaphoid–trapezium, *UI* ulna. The "+" sign represents a 0.5 increment

found to be 3.9 min for Larsen, 19 min for Sharp, 25 min for the Sharp/van der Heijde method, and 9 min for the Ratingen method [58]. Other studies gave similar results for the Ratingen score method and the Sharp/van der Heijde method [53, 54]. The time needed to score seven radiographs of hands and feet was 7 min for SENS [54], appearing the most feasible in daily clinical practice. The time needed to score 12 radiographs of hands and feet with the Sharp/van der Heijde method for RA ranged from 11.1 to 20.5 min [59]. The time needed is one drawback of both the Sharp method and the Sharp/van der Heijde method; it is related to their higher degree of detail as compared with the Larsen and SENS methods.

Radiographic Scoring Methods in Psoriatic Arthritis

The measurement of radiographic joint damage in PsA is a core outcome measure in both randomized control trials for novel therapies [60] and longitudinal observational studies [61] and is included in the research agenda as a domain of interest by the Outcome Measures in Rheumatology (OMERACT) [62]. The development and validation of scoring methods for PsA have been less well worked out than those for RA. All of the currently used methods have their basis in scoring methods for RA. These instruments include the modified Steinbrocker global scoring method, the modified Sharp score (MSS), and the modified Sharp/van der Heijde score (mSvdHS) for PsA [36, 63]. Until now, the scoring system developed exclusively for PsA is the psoriatic arthritis Ratingen score (PARS) [64]. All these radiographic scores, based on semiquantitative assessment, are summarized in Table 4. As for scoring systems adopted in RA, their lowest common denominator is the large time to perform. Moreover, their scoring requires trained observers.

Modified Steinbrocker Global Scoring Method

This method was developed at the PsA clinic at the University of Toronto. This classification has been used not only for the mostly affected joint, but also for 40 joints in the hands and feet: all DIP, PIP, and MCP joints of the hands

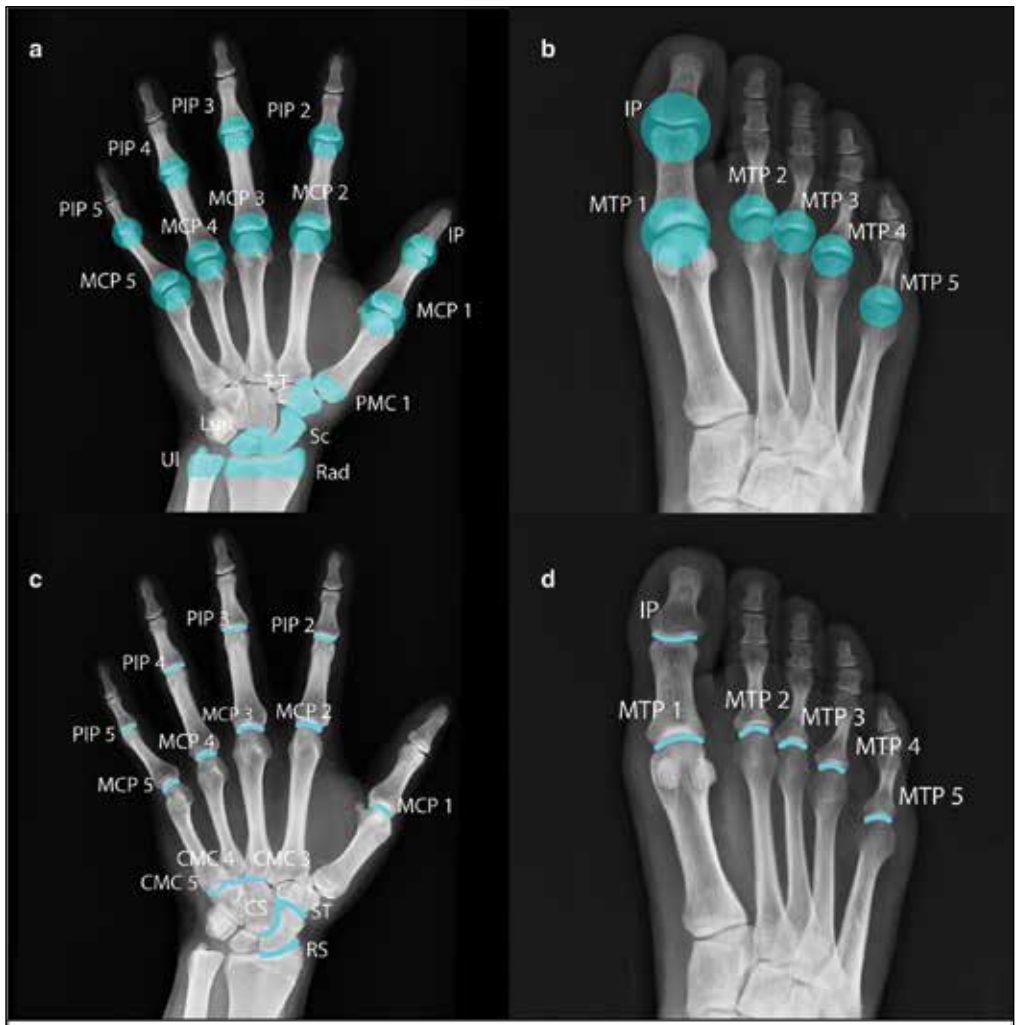


Fig. 4: Simplified erosion and narrowing score (SENS) representation with figure and grading. The grading in SENS is a dichotomic scale. **a** Joints selected in each hand for erosions: 4 PIP, 5 MCP, IP, scaphoid, lunate, distal ulna, distal radius, the two components of the CMC joints of the thumb are evaluated separately (PMC and trapezium–trapezoid). The maximum score for both hands is 32. **b** Joints selected in each foot for erosions. The maximum score considering both feet is 12. **c** Joints selected in the hand: the CMC 3, CMC 4, CMC 5 are scored separately, the IP is not included, only the radio-scaphoid part of the radiocarpal joint is evaluated. The maximum score for both hands is 30. **d** The joint selected for JSN in each foot. The maximum score for both feet is 12. *CMC* carpometacarpal, *CS* capitate–scaphoid, *IP* interphalangeal joint, *Lun* lunate, *MCP* metacarpophalangeal joint, *MTP* metatarsophalangeal joint, *PIP* proximal interphalangeal joint, *PMC* proximal metacarpal, *Rad* radius, *RC* radio-scaphoid, *Sc* scaphoid, *ST* scaphoid–trapezium, *T–T* trapezium–trapezoid, *Ul* ulna

Table 4: Features of psoriatic arthritis included in the five radiographic scoring systems for psoriatic arthritis.

Scoring method	Erosion	Joint space narrowing	Bony proliferation
Modified Steinbrocker global scoring method	+	–	–
Modified Sharp score (MSS)	+	+	–
Modified Sharp–van der Heijde method for psoriatic arthritis (mSvdHS)	+	+	–
Psoriatic arthritis Ratingen score (PARS)	+	–	+
Simplified psoriatic arthritis radiographic score (SPARS)	+	+	+

with the wrist as one joint, and all MTP and the IP of the big toe [65] (Fig. 5).

Psoriatic Arthritis Scoring Method Based on the Sharp Scoring Method for Rheumatoid Arthritis (MSS)

Radiographic evaluation was performed in the initial studies with biologic agents in PsA using a modification of the Sharp method for RA [66], which includes a separate evaluation of erosions and JSN. The same joints were scored as in the original method, with the addition of the DIP from 2 to 5 joints of hands [36, 63]. Other radiographically detectable changes in PsA, such as periostitis and tuft resorption are recorded and scored separately, but not included in the score value.

Sharp–van der Heijde-Modified Scoring Method for Psoriatic Arthritis (mSvdHS)

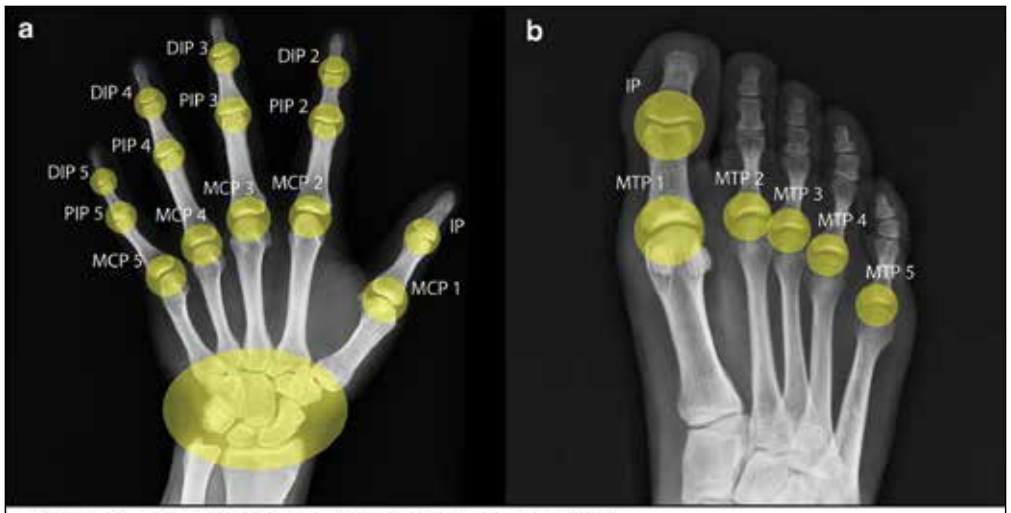
The modification based on the Sharp–van der Heijde method for RA scores the same joints and definitions as seen in RA [41], with the addition of the eight DIP joints for erosions and the eight DIP and two IP joints of the thumb for JSN. The presence of gross osteolysis and "pencil in cup" is scored separately; if one of these abnormalities is present, the joint gets the maximum score assigned for erosion and for JSN (Fig. 6).

Psoriatic Arthritis Ratingen Score (PARS)

This method was developed based on the Rau and Herborn modification of the Larsen Score [53]. This method includes 40 joints of the hands and feet (DIP 2–5 of the hands, 2 IP of the thumbs, 8 PIP of the hands, 10 MCP of both wrists, 2 IP of the great toes, and MTP 2–5). Destruction and proliferation of all joints are scored separately [53] (Fig. 7).

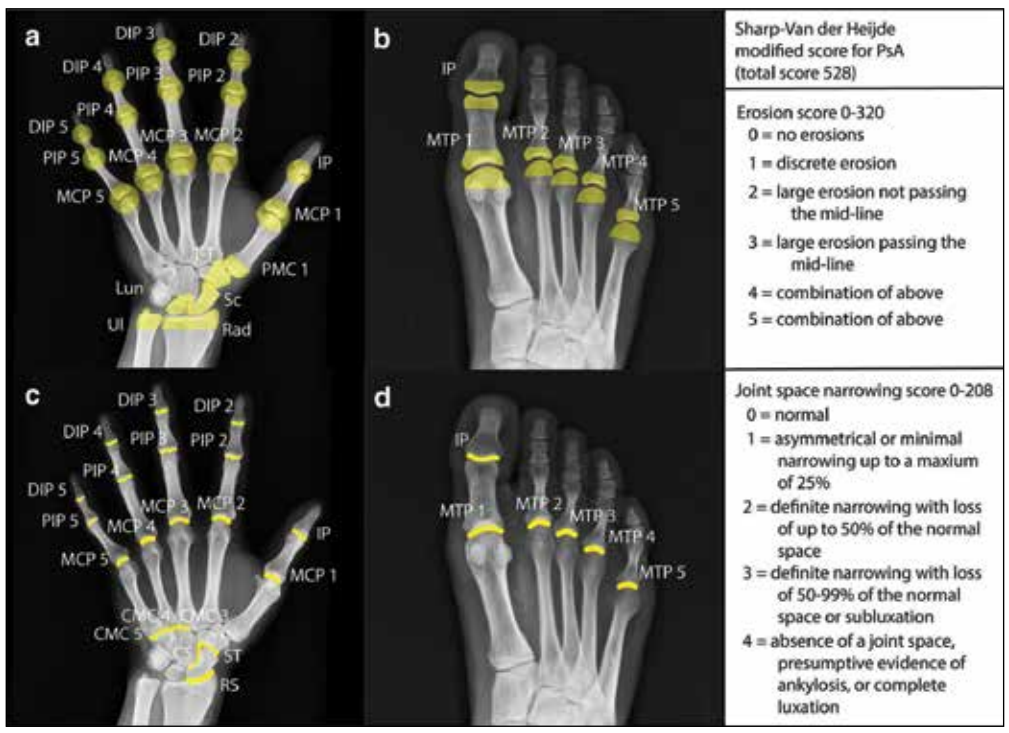
Simplified Psoriatic Arthritis Radiographic Score (SPARS)

Recently, our group has developed the SPARS, obtaining its definition through a consensus analysis, involving three radiologists skilled in musculoskeletal imaging and five rheumatologists with clinical experience on PsA and radiographic scoring systems [67]. SPARS assess the same joints of the PARS in a simpler manner: the grade of the combination of erosion and bony proliferation of the PARS is replaced by the sum of joints with erosion



Modified Steinbocker Global Scoring Method (Total score 0-168)	
Grade 0	Normal
Grade 1	Juxta-articular osteoporosis or soft tissue swelling
Grade 2	Erosions
Grade 3	Erosions and joint space narrowing or subluxation
Grade 4	Total joint destruction, either lysis or ankylosis

Fig. 5: Modified Steinbrocker global scoring method represented with figure and grading. **a** Joints evaluated in each hand: 4 DIP, 4 PIP, 5 MCP, the IP of the thumb, the wrist is evaluated as one joint. The maximum score for both hands is 120. **b** Joints selected in each foot: all the MTP joints and the IP joint of the big toe. The maximum score considering both feet is 48. *DIP* distal interphalangeal joint, *IP* interphalangeal joint, *MCP* metacarpophalangeal joint, *MTP* metatarsophalangeal joint, *PIP* proximal interphalangeal joint



Sharp-Van der Heijde modified score for PsA (total score 528)
Erosion score 0-320
0 = no erosions
1 = discrete erosion
2 = large erosion not passing the mid-line
3 = large erosion passing the mid-line
4 = combination of above
5 = combination of above
Joint space narrowing score 0-208
0 = normal
1 = asymmetrical or minimal narrowing up to a maxium of 25%
2 = definite narrowing with loss of up to 50% of the normal space
3 = definite narrowing with loss of 50-99% of the normal space or subluxation
4 = absence of a joint space, presumptive evidence of ankylosis, or complete luxation

Fig. 6: van der Heijde-modified Sharp scoring method (mSvdHS) representation with figure and grading. The presence of gross osteolysis and "pencil in cup" is scored separately; if one of these abnormalities is present, the joint gets the maximum score assigned for erosion (5 points) and for JSN (4 points). **a** Joints selected in each hand for erosions: 4 PIP, 5 MCP, IP, scaphoid, lunate, distal ulna, distal radius, the two components of the CMC joints of the thumb are evaluated separately (PMC and trapezium–trapezoid). The maximum score for both hands is 200. **b** Joints selected in each foot for erosions: the proximal and distal articular components of the MTP joints and IP are evaluated separately resulting in a 0–10 score for each joint. The maximum score considering both feet is 120. **c** Joints selected in the hand in the mSvdHS: the CMC 3, CMC 4, CMC 5 are scored separately, the IP is not included, only the radio-scaphoid part of the radiocarpal joint is evaluated. The maximum score for both hands is 160. **d** Joints selected for JSN in each foot. The maximum score for both feet is 48. *CMC* carpometacarpal, *CS* capitate–scaphoid, *DIP* distal interphalangeal, *IP* interphalangeal joint, *Lun* lunate, *MCP* metacarpophalangeal joint, *MTP* metatarsophalangeal joint, *PIP* proximal interphalangeal joint, *PMC* proximal metacarpal, *Rad* radius, *RS* radio-scaphoid, *Sc* scaphoid, *ST* scaphoid–trapezium, *T–T* trapezium–trapezoid, *Ul* ulna

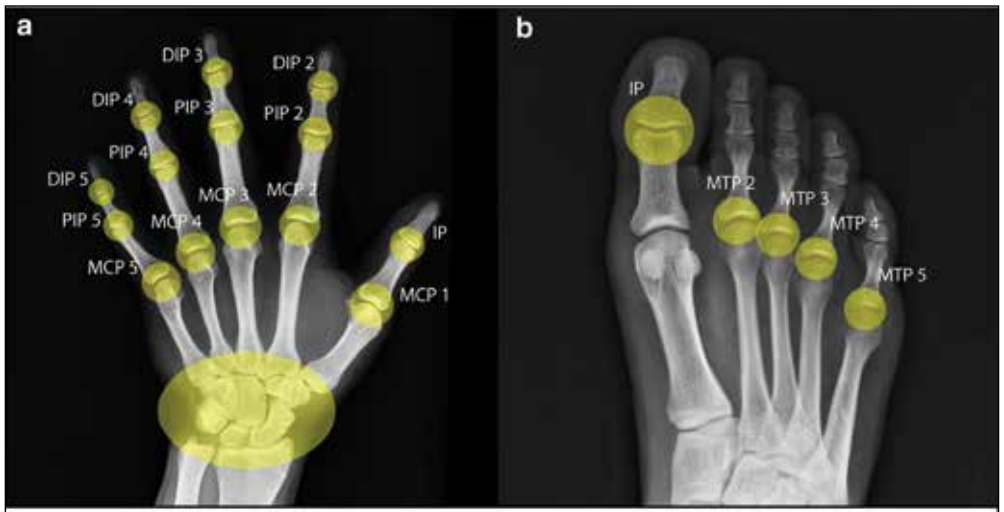
and the number of joints with bony proliferation. Similar simplifications have been already applied for the radiographic scoring systems in RA [54]. In SPARS, a joint is defined as eroded (score 1) if one or more erosions with an interruption of the cortical plate > 1 mm (PARS grade 1 of DS) can be observed (Fig. 8).

Comparison of The Scoring Methods in PsA

All radiographic scoring methods have been proven to capture radiographic change with reasonable precision in PsA. There was consensus that MSS and mSvdHS were the optimal tool to use in randomized controlled trials (where sensitivity to change is often the most important attribute of the outcome measure), but the most appropriate tool for use in longitudinal observational studies has yet to be established [62]. Tillett *et al.* [68] reported the first comparison of feasibility of four radiographic scoring methods for PsA in an observational cohort. The smallest detectable change (SDC) of the PARS is similar to that of the mSvdHS and MSS, but it can be scored faster. Furthermore, the PARS is the only one that focuses on bony proliferation. Proliferative lesions are pathognomonic for PsA and are considered the most specific PsA radiographic features [7]. The feasibility of each method was estimated based on the mean time taken to score each film as well. The method which took the least time to score was the Steinbrocker method followed by the PARS, the mSvdHS, and the MSS at 6.2 min, 10.5 min, 14.4 min, and 14.6 min, respectively. Recently, the SPARS, a new and faster method, has been developed. The SPARS has properties which are close to the ones of the mSvdHS and PARS allowing a quicker calculation [67].

Conclusion

Plain radiography remains the gold standard for the assessment of structural joint damage in RA and PsA. Characteristic radiographic findings are part of the ACR classification criteria for RA [69] and CASPAR criteria for PsA [7, 70]. Plain radiography can be helpful in the differentiation of RA from PsA and other joint conditions, including osteoarthritis, calcium pyrophosphate deposition disease, gout, and neoplasms [71]. Early bone erosions are correlated with poor long-term radiographic and functional outcome, and

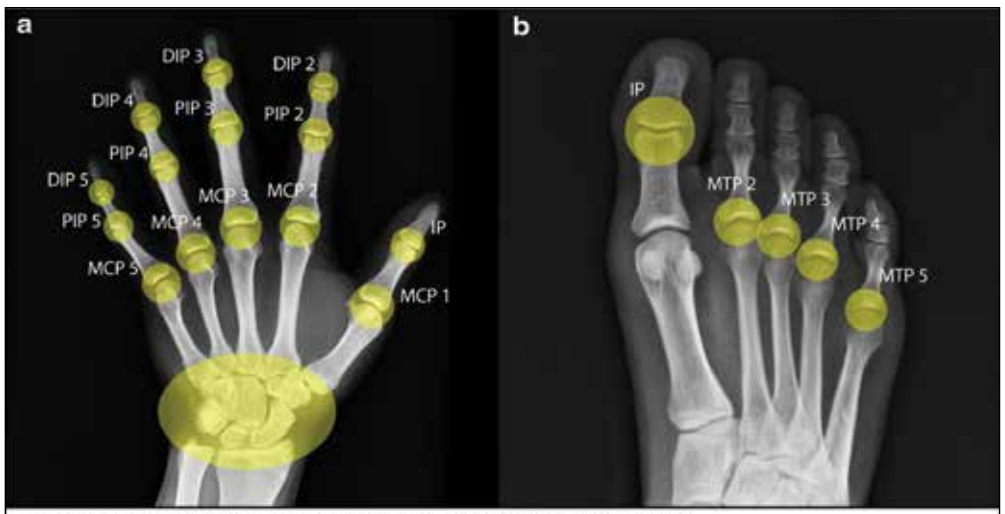


Psoriatic Arthritis Ratingen Score (PARS) (total score 0-360)

Destruction score 0-200
- 0 = normal
- 1 = one or more definite erosions with an interruption of the cortical plate of >1 mm but destruction of less than 10% of the total joint surface
- 2 = destruction of 11-25%
- 3 = destruction of 26-50%
- 4 = destruction of 51-75%
- 5 = destruction of more than 75%

Proliferation score 0-160
- 0 = normal
- 1 = bony proliferation measured from the originalbone surface of 1-2 mm, or, if the margins of the proliferation cannot be distinguished from the original bone surface, clearly identificable bone growth not exceeding 25% of the original diameter
- 2 = bony proliferation of 2-3 mm or bone growth between 25-50%
- 3 = bony proliferation > 3 mm or bone growth >50%
- 4 = bony ankylosis

Fig. 7: Psoriatic arthritis Ratingen score (PARS) representation with figure and grading. **a** Joints evaluated in each hand for destruction and proliferation: 4 DIP, 4 PIP, 5 MCP, the IP of the thumb and the wrist (evaluated as one joint). The maximum score for both hands is 270. **b** Joints selected in each foot for destruction and proliferation: the IP of the big toe and second to fifth MTP joints. The maximum score considering both feet is 90. *DIP* distal interphalangeal joint, *IP* interphalangeal joint, *MCP* metacarpophalangeal joint, *MTP* metatarsophalangeal joint, *PIP* proximal interphalangeal joint



Simplified Psoriatic Arthritis Radiographic Score (SPARS) (total score 0-120)

Erosion score
- 0 = normal
- 1 = one or more erosions with an interruption of cortical plate > 1 mm

Joint space narrowing (JSN)
- 0 = normal
- 1 = at least an asymemtrical or minimal narrowing up is detectable

Bone proliferation (BP)
- 0 = normal
- 1 = proliferation of 1-2 mm or bone growth < 25% of diameter are detectable

Fig. 8: Simplified psoriatic arthritis score (SPARS) representation with figure and grading. The grading in SPARS is a dichotomic scale. **a** Joints evaluated in each hand for erosion, joint space narrowing and bone proliferation: 4 DIP, 4 PIP, 5 MCP, the IP of the thumb, and wrist is evaluated as one joint. **b** Joints selected in each foot for erosion, joint space narrowing, and bone proliferation: the IP of the big toe and second to fifth MTP joints. The maximum score is considered. *DIP* distal interphalangeal joint, *IP* interphalangeal joint, *MCP* metacarpophalangeal joint, *MTP* metatarsophalangeal joint, *PIP* proximal interphalangeal joint

early progression in radiographic erosions is related to future impairment in physical function [72]. Radiographic measurement has been of major importance in the development of concepts concerning the severity of RA and PsA and the need for tight control to prevent anatomic damage. It will have, also, a crucial role in many aspects of treatment in the rheumatic diseases, including identifying patients who are suitable for use of disease-modifying antirheumatic drugs (DMARDs) and biological agents (bDMARDs), predicting patient response and relapse, and identifying true disease remission [17, 19, 71, 73, 74]. A deeper insight into the mechanism of structural changes triggered by these chronic joint diseases is essential for developing therapies that can arrest, prevent, and even reverse bone and cartilage changes.

Even though magnetic resonance imaging (MRI) and ultrasound (US) demonstrated to be more sensitive than radiographs in detecting early structural changes in joints and surrounding structures [75, 76], availability and costs may limit the use of these techniques in daily clinical practice.

Further research in the use of MRI and US will lead to their proper integration with conventional radiography. Therefore, it remains important for a rheumatologist to understand the scoring of plain radiographs and the history of the scoring methods. The introduction of easier scoring system in time allows the rheumatologist to use it in clinical trials but also in clinical practice.

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Rheumatoid arthritis (RA) tends to improve during pregnancy and flare postpartum. Several anti-rheumatic medication options during pregnancy and breastfeeding are now available including anti-tumor necrosis factor (anti-TNF) agents. Good disease control at all stages of reproduction is important to ensure best outcome for both mother and baby.

UPDATED PHARMACOLOGICAL MANAGEMENT OF RHEUMATOID ARTHRITIS FOR WOMEN BEFORE, DURING, AND AFTER PREGNANCY, REFLECTING RECENT GUIDELINES

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Rheumatoid arthritis (RA) is a chronic immune-mediated inflammatory disease which can cause significant disability, morbidity, and mortality. RA affects women three times more often than men, commonly in their childbearing years [1]. There are concerns about the teratogenic effects of many traditional disease-modifying anti-rheumatic drugs (DMARDs) and an ever-growing list of new therapeutic options with limited data in pregnancy and breastfeeding.

Active RA in pregnancy is associated with a number of negative outcomes for both mother and baby. These include increased incidence of low birth weight, pre-term delivery, cesarean section, and pre-eclampsia [2, 3]. But, thankfully, outcomes for women with well-controlled RA are comparable to the general population [4].

Before pregnancy, a key aim is to establish the RA patient in remission on medications that are relatively safe in pregnancy; this is usually achieved by the judicious use of synthetic and biological DMARDs. A specific withdrawal period is required for teratogenic medications such as methotrexate and leflunomide. Clinicians should be encouraged to enquire about family planning at the first consultation and each review thereafter, to allow all patients opportunity to discuss any concerns they may have.

Pre-conceptual risk assessment and counseling should be ideally performed in every woman with systemic autoimmune diseases before attempting pregnancy [5]. This is an opportune time to alter medication management if required and to refer for a pre-conceptual review with maternal medicine if available. This facilitates access to numerous specialities. Complex patients may benefit from a multidisciplinary approach from obstetrics, hematology, rheumatology, and respiratory or other specialties. This may be possible in a combined clinic.

Pregnancy itself may reduce the activity of RA [6]. In 1938, Hench suggested that remission rates during pregnancy were greater than 70% [7]. Later studies suggest that this rate is lower, with a recent prospective study giving a remission rate of 48% [3]. The exact mechanism of this improved disease control is unclear; one theory is downregulation of the maternal immune system with the presence of the fetus. It can be tempting to withdraw anti-rheumatic medications and treat symptomatically with steroids during pregnancy. Recent data would suggest that this may not be the best approach [8].

The postpartum period can be a difficult for the patient, the baby, and the treating healthcare providers. It is important to explain this to patients, their partners, and/or family. There is an increased rate of disease flare. A 2008 study showed a deterioration in RA control in 39% of patients postpartum [3]. One should also consider the additional strain of caring for an infant.

It may be difficult to differentiate what is normal postpartum from a disease flare, particularly for first time mothers. Breastfeeding and medication safety is another consideration. Postpartum complications such as wound infection may delay re-institution of RA medications.

Methods

Upon commencement of a multidisciplinary Rheumatology and Reproductive Health Service, a systematic approach to prescribing anti-rheumatic drugs in women of childbearing age was required. Thus, the published

data and guidelines were reviewed to develop a unified approach.

Methotrexate and leflunomide are completely contraindicated at conception and in pregnancy. They require specific washout periods of 3 months recommended for methotrexate and 2 years for leflunomide [9, 10]. An elimination protocol using cholestyramine or activated charcoal may also be used when circumstances warrant more rapid drug elimination of leflunomide such as with pregnancy [10]. Thus, we carefully consider whether to use these agents in women of childbearing age and always stress to women on these medications the importance of adequate contraception during any period of use and the withdrawal period.

Steroids are considered generally safe if required in pregnancy. Fetal risks with steroids include a slight increase risk of preterm delivery and a small risk of oral cleft with first trimester use. There is also of course the well-known side effect profile to the mother (including increased risk of infection). Thus, we aim to use the lowest effective dose for the shortest time possible in active disease. Non-fluorinated steroids, such as prednisolone or hydrocortisone, are generally preferred as they are metabolized by the placenta and have less fetal effects.

NSAIDs can contribute to the infertility and subfertility seen in RA due to anovulation [11]. Their use in early pregnancy can be associated with increased risk of miscarriage. In the third trimester, they may cause premature closure of ductus arteriosus.

Tumor necrosis factor (TNF) inhibitors may be safer than previously believed although we should not underestimate the risks. In 2010, a 4-month-old baby died from disseminated BCG [12]. His 28-year-old mother was treated with infliximab [TNF alpha inhibitor] throughout pregnancy for inflammatory bowel disease. The previously healthy infant received his BCG at 3 months of age.

Yet, there is now extensive experience and guidelines to support the use of biologics around and during pregnancy. Many rheumatologists would continue their use for at least the initial stages of pregnancy.

The updated BSR guidelines advise on timing of discontinuation of TNF inhibitors in pregnancy and breastfeeding. It is important to notice the differing timelines for the different biologic agents in these guidelines. Certolizumab pegol is compatible with all three trimesters of pregnancy and has reduced placental transfer compared with other TNF inhibitors. Infliximab may be continued until 16 weeks. Etanercept and adalimumab may be continued until the end of the second trimester. Golimumab is unlikely to be harmful in the first trimester. If these drugs are continued later in pregnancy to treat active disease, then live vaccines should be avoided in the infant until 7 months of age [9].

Compatible with breastfeeding	Inadequate data about lactation	Contraindicated while breastfeeding
Corticosteroids	TNF inhibitors	Methotrexate
NSAIDs	Abatacept	Leflunomide
Hydroxychloroquine	Anakinra	
Sulfasalazine[a]	Rituximab	
Azathioprine	Tocilizumab	
	Tofacitinib	

[a]Concerns with prematurity, glucose-6-phosphate deficiency, and hyperbilirubinemia

	DMARDs	Biologics	Steroids	Analgesics
Before pregnancy	Stop MTX 3 months prior to conception	Continue TNF inhibitors	None/as low as possible	Stop NSAIDs if difficulties in conceiving
	Wash out leflunomide (two years) Consider HCQ/SSZ	Stop other biologics before conception		Use paracetamol
During pregnancy	Continue HCQ/SSZ, may taper	Often stopped during trimester 2	None/as low as possible	Avoid NSAIDs
		Consider certolizumab throughout pregnancy		Use paracetamol
After pregnancy	Continue HCQ/SSZ Avoid leflunomide, MTX if breastfeeding	Aim to restart biologics within 2 weeks (consider wound healing, infection, and breastfeeding)	None/as low as possible	Consider restarting NSAIDs, ideally ibuprofen if breastfeeding Use paracetamol

DMARDs disease-modifying anti-rheumatic drugs, *MTX* methotrexate, with 5 mg folic acid weekly, *HCQ* hydroxychloroquine, *SSZ* sulfasalazine (with 5 mg folic acid daily), *TNF* tumor necrosis factor, *NSAIDs* non-steroidal anti-inflammatory drugs

There is little data available for the use of non-TNFi biologics in pregnancy or breastfeeding. BSR guidelines suggest stopping rituximab 6 months and tocilizumab 3 months prior to conception. Unintentional exposure to anakinra or abatacept in the first trimester is unlikely to be harmful. There are no data on the use of any of these agents in breastfeeding. EULAR guidelines suggest discontinuing tofacitinib 2 months prior to conception and to avoid breastfeeding while on the medication.

Lactation

Guidelines consider numerous anti-rheumatic drugs compatible with breastfeeding. Our approach is summarized in the chart.

Results

From reviewing previous studies and guidelines, we have created a joint Saint Vincent's University Hospital/National Maternity Hospital approach to medications for RA in women of childbearing age. The table summarizes our approach to managing RA in and around pregnancy.

Conclusions

Women with active RA might have increased subfertility and infertility. Patients should be encouraged to discuss their pregnancy plans with their healthcare providers at every consultation. Good disease control at all stages of reproduction ensures best outcomes for mother and baby. RA tends to improve during pregnancy and flare postpartum. Consideration should be given to the treatment of disease flares during pregnancy. There are now numerous anti-rheumatic drug options during pregnancy and breastfeeding with more widespread use of anti TNF agents in this group.

Compliance with ethical standards

Conflict of interest: The authors declare that they have no conflict of interest.

Ethical approval: This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent: Informed consent was not required as this study was a review of the relevant literature and guidelines on the topic.

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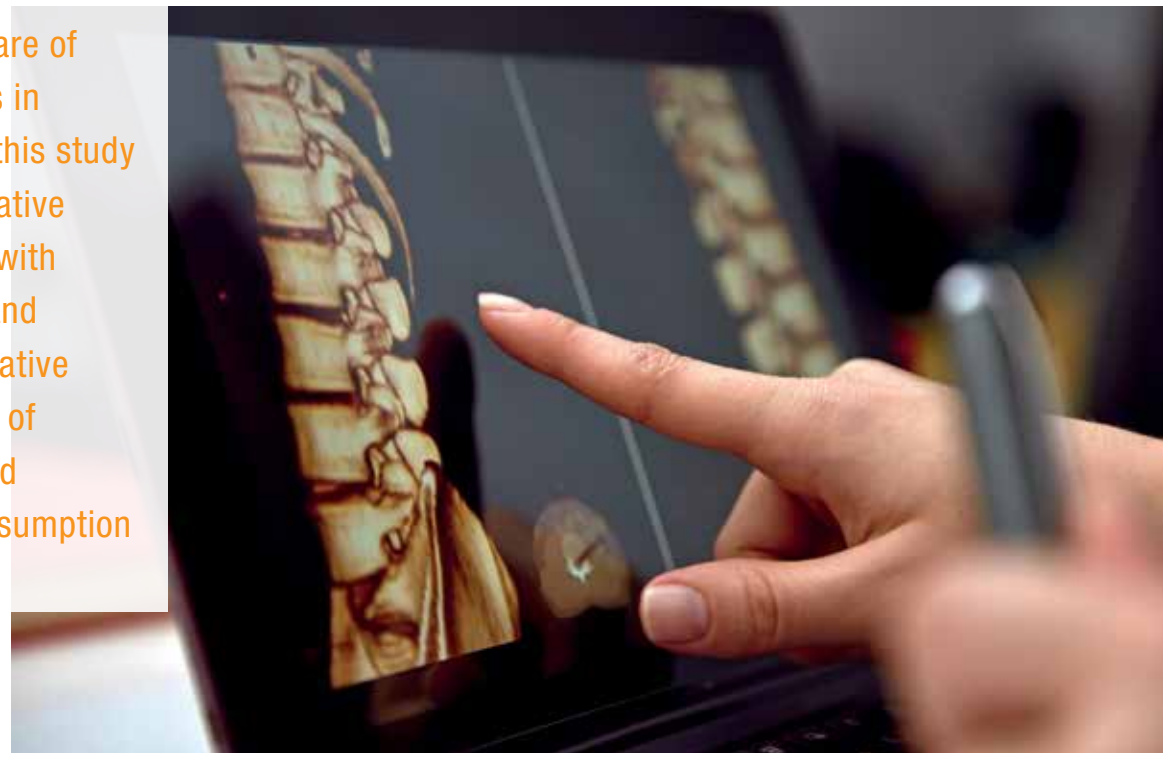
Duloxetine, Etoricoxib and opioid are of the commonly administered drugs in Lumbar laminectomy. The aim of this study is to assess the effect of perioperative use of Duloxetine in combination with Etoricoxib on postoperative pain and opioid requirements. The perioperative administration of the combination of etoricoxib and duloxetine improved analgesia and reduced opioid consumption without significant side effects.



PERIOPERATIVE DULOXETINE AND ETORICOXIB TO IMPROVE POSTOPERATIVE PAIN AFTER LUMBAR LAMINECTOMY: A RANDOMIZED, DOUBLE-BLIND, CONTROLLED STUDY

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Postoperative pain is mediated by different mechanisms at multiple neural sites. Thus, multimodal analgesics can reduce the postoperative pain [1]. Although Opioids are considered the analgesics of choice to treat moderate to severe pain, their use carries the risk of side effects and hyperalgesia [2]. Multimodal analgesia can be achieved by combining different analgesics and different methods of administration, to provide better analgesia synergistically compared with conventional analgesia [3]. Therefore, lower doses for each drug can be provided with fewer overall side-effects obtained from individual compounds [4].

Recently, antidepressants such as duloxetine, a selective serotonin and norepinephrine reuptake inhibitor (SSNRI), have accomplished pain relief in persistent and chronic pain as in fibromyalgia, postherpetic neuralgia, diabetic neuropathy [5], osteoarthritis and musculoskeletal pain [6]. The analgesic effect of duloxetine is attributed to its ability to enhance both serotonin and norepinephrine neurotransmission in descending inhibitory pain pathways. [7]. Moreover, some studies have promoted its use to improve the quality of recovery after surgery and reduce the acute postoperative pain after knee replacement surgery [8], mastectomy [9], hysterectomy [10], and after spine surgery [11]. In addition

it can improve postoperative quality of recovery through mood improvement that can be helpful in the postoperative period [12].

Another group of analgesics is the non-steroidal anti-inflammatory drugs (NSAIDs) which are used for acute pain management. It has pain-relieving, antipyretic, and anti-inflammatory properties [13]. It's thought that its analgesic effect is caused by suppression of cyclooxygenase (COX) thus it inhibits the synthesis of PGs [14]. However, being non-selective in inhibition of COX1 and COX2; several adverse effects can appear [15]. It is thought that the therapeutic activity of NSAIDs is due to the inhibition of COX-2, whereas the adverse effects results from inhibition of COX-1 [16]. Thus, many studies show that the selective COX-2 inhibitors have a great role in reducing the postoperative pain and reducing the dose of postoperative opioid consumption [17–19].

Etoricoxib is more highly selective of COX-2 over COX-1 than celecoxib [20], and characterized by longer duration of action ranging 22–24 h. In addition, it is absorbed rapidly after oral intake so the peak plasma concentrations are reached after 1 h [21]. It was examined preoperatively by different studies and revealed efficacy in providing postoperative analgesia after abdominal [17], laparoscopic [19], gynecological [22] and orthopedic procedures [18, 23]. However, additive or synergistic interactions can be detected when two analgesics are administered together at the same time [24]. In cases of synergistic interaction, we can use smaller doses of each drug to achieve good analgesia with fewer adverse effects derived from individual compounds [4].

The main objective of the present study was to examine perioperatively the analgesic efficacy with the combination of duloxetine and etoricoxib on postoperative pain and itsopioid-sparing properties when given as part of a multimodal pain strategy in patients undergoing surgery on the lumbar spine. In addition to evaluating the patient's satisfaction and the adverse effects related to the combination of both medications.

Methods

After institutional Ethics Committee approval, this prospective double-blind, randomized, controlled study was started in November 2015 at the department of anesthesia and intensive care unit; El-Minia University Hospital. The study involved 120 adult patients of both genders aging between 18 and 70 years of age with an ASA physical status of I, II and III,who were scheduled for single level lumbar spinal disc prolapse surgery. All patients gave written informed consent.

Exclusion criteria involved patients with history of allergic reaction to any of the study drugs, history of drug or alcohol abuse, and abnormal renal or liver function tests. Patients using antidepressants had to stop taking them 2 weeks before surgery. Also, Patients with previous cervical surgeries, psychiatric disorders and patients receiving opioid analgesic medications within 24 h preoperatively were excluded.

> *Selective COX-2 inhibitors have a great role in reducing the postoperative pain and reducing the dose of postoperative opioid consumption.*

We asked the patients to visit the outpatient clinic 1 day before surgery for assessment and performing laboratory investigations. We also explained to them the study protocols, including analgesic administration and the 11-point numeric rating scale (NRS) where 0 being 'no pain' and '10' being the maximal worst pain [25].

Study Design

The patients admitted to the hospital were randomized according to the computer-generated random numbers with closed-sealed envelopes into one of the four groups 30 patients each. The study medications were prepared by the pharmacy of the hospital and given to the patients by an investigator not involved in the study. They were duloxetine 60 mg capsules (Cymbalta; Eli Lilly & Company, Indiana, USA), etoricoxib 60 mg film coated tablets (Arcoxia; Merck Sharp & Dohme Limited, Hertford road, Hoddesdon, Hertfordshire, UK), and placebo capsules that matched the duloxetine capsules or etoricoxib tablet in color and size. All drugs were given 1 h before surgery and repeated after 24 h.

1. The Group P (Placebo) received placebo capsule + two placebo tablet
2. The Group E (etoricoxib) received placebo capsule + two etoricoxib tablet 60 mg
3. The Group D (duloxetine) received duloxetine capsule 60 mg + two placebo tablet
4. The Group DC (duloxetine + etoricoxib) received duloxetine 60 mg capsules + two etoricoxib tablets 90 mg

On arrival to the operating room, standard intraoperative monitoring included electrocardiogram (ECG), heart rate (HR), mean arterial blood pressure (MABP), oxygen saturation (SPO2) and end tidal CO2 were recorded and subsequent measurements were recorded every 5 min till the end of the operation using a multiparameter monitor (Mindray iMEC12, Hi-tech industrial Park, Nanshan, Shenzhen, china).

General anesthesia was induced by (1.5 μg/kg) fentanyl IV, (2 mg/kg) propofol IV, and endotracheal intubation was performed with (0.5 mg/kg) IV atracurium. Maintenance of anesthesia was done through inhalation of a mixture of oxygen (3 L/min) (1–2%) isoflurane and (0.05 mg/kg) atracurium as intermittent dose of muscle relaxant to ensure proper muscle relaxation during the procedure.

An anesthetist who was blinded to the groups took all the measurements. Their goal was to adjust the anesthetics concentration to keep the heart rate and blood pressure within 20% of the base line value throughout the anesthesia period.At the end of surgery, the first dose of paracetamol 1000 mg/100 ml intravenously (Medalgesic; ARABCOMED, Cairo, Egypt) was given to all patients before extubation. Then, reversal of neuromuscular blockade was performed with atropine (0.01 mg/kg) and neostigmine (0.05 mg/kg) given intravenously. After tracheal extubation, patients were transferred to the post-anesthetic care unit (PACU) where vital parameters were recorded every 1/2 h till complete recovery.

During the first 48 h, a standard analgesic regimen of paracetamol 1 g was given intravenously every 6 h to all patients. In addition, pain assessment in the ward was performed by nurses every 2 h and titrated doses of morphine (2 mg bolus at 10 min intervals) were given if patients reported pain (NRS was ≥3).

The postoperative data were collected by a senior resident (blinded to the study). The NRS pain scores was recorded at 30 min after the end of anesthesia (time = 0), all patients were able to answer questions and

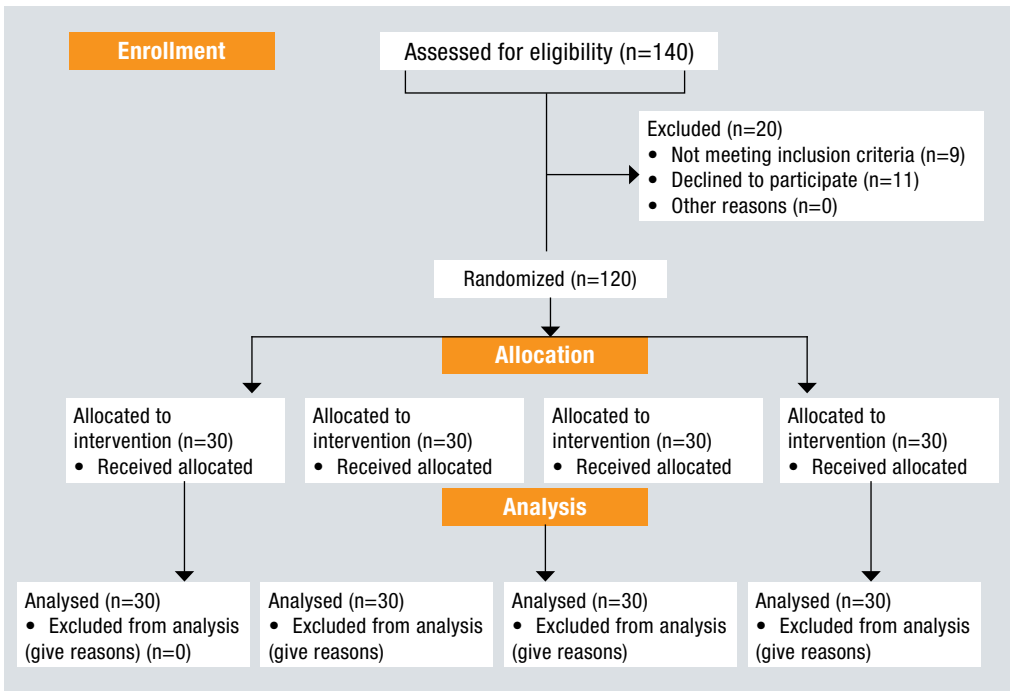

Fig. 1: Flow diagram for participant.

to rate their pain score at the end of 2, 4, 6, 12, 24 and 48 h postoperatively in the ward. Pain assessments were done at rest and with movement (after the patient completed a 90° logroll while in bed).

The time to first rescue analgesic, total morphine consumption at (24 h and 48 h) and the presence of side effects, such as headache, rash, nausea, vomiting, dizziness and drowsiness were recorded. The severity of postoperative nausea and vomiting (PONV) was graded on a four-point ordinal scale (I) not at all, (II) sometimes, (III) often or most of the time, and (IV) all of the time with vomiting [26]. Ondansetron, a rescue antiemetic, (4 mg) IV was given to all patients with PONV score more than II.

Patient satisfaction was measured at 24 h post-operatively using a numerical score of 1-4 (1 = poor, 2 = fair, 3 = good, 4 = very good).

After the study was completed, randomization and allocation were revealed for data analysis. Sample size estimation was made based on morphine consumption in a retrospective sample of 50 patients who was undergoing spinal surgery in our department. The sample size was calculated using power analysis ($\alpha = 0.05$, $\beta = 0.8$) to detect 50% difference in morphine consumption between groups at 48 h post-surgery and was found to require at least 24 patients per group. Thus, we decided to include 30 patients per group to allow for possible drop-out.

Statistical Analysis

Data were presented as median (with interquartile range) or mean ± standard deviation. While qualitative data were presented as number (frequency distribution). Data such as ASA grade, sex distribution, Patient's satisfaction, and Side effects were inferred by Chi-square test and fisher's exact test. Data such as age, weight, height, mean duration of surgery, time of first rescue analgesic and total morphine requirement were inferred by ANOVA and post hoc Bonferroni test was used for in intergroup comparison. Differences in NRS scores were analyzed using the Kruksal-Wallis test and the Mann–Whitney U-test was used for subsequent pair wise comparisons. The *p*-value of less than 0.05 was considered significance.

Results

From November 1, 2015 to March 1, 2017, 131 consecutive patients who met the inclusion criteria were allocated for the study (Fig. 1). Eleven patients refused to participate. Therefore, 120 patients were randomized and included in the study. Characteristics of patients and surgical procedures for each group (Table 1) showed no significant differences between the groups.

The Morphine Requirement

The time to first rescue analgesic was significantly prolonged in (D/E)when compared with group D, group E and group P. There was a significant prolongation when groups E and D were compared with group P respectively with no significant difference between group E and group D (Fig. 2).

The morphine requirement at 24 h was statistically different between the four groups.

There were significantly increased morphine requirements in the P group compared with E, D and D/E groups and significantly increased in E and D groups respectively

Table 1: Characteristics of patients and surgical procedures in the four groups.

Group Variable	Group (P) (*n* = 30)	Group (E) (*n* = 30)	Group (D) (*n* = 30)	Group (D/E) (*n* = 30)	*P* value
Age (years)	46.50 ± 8.74	45.26 ± 7.50	48.36 ± 9.80	47.50 ± 10.14	0.455
Male/Female (n)	15/15	17/13	18/12	16/14	0.471
Weight (kg)	81.23 ± 13.24	82.53 ± 12.90	80.60 ± 13.37	78.83 ± 16.78	0.794
Height (cm)	167.46 ± 8.50	165.53 ± 7.71	165.40 ± 8.21	165.00 ± 9.63	0.478
ASA (n)					
I	18	18	17	15	0.36
II	7	6	9	10	0.42
III	5	6	4	5	0.23
Duration of surgery (min)	109.9 ± 10.8	115.7 ± 9.8	113.2 ± 13.7	117.8 ± 9.7	0.65

Data are presented as Mean ± SD or number (n)
Placebo group (P), Etoricoxib group (E), Duloxetine group (D), Duloxetine/Etoricoxib group (D/E). Data were analyzed using ANOVA test with post hoc test (Bonferroni) and Chi-square test

when compared with D/E group with no significant difference between group E and group D (Fig. 3). At 48 h, total morphine requirement were still significantly increased in the P group compared with all groups with significant increases in both E and D groups when compared with D/E group with no significant difference between group E and group D (Fig. 4). But it was still significantly lower in the three groups at 48 h post-surgery when compared with those required at 24 h.

The Pain Score

With regard to pain scores at rest all time points, the duloxetine/etoricoxib (D/E) group had significantly lower pain scores when compared to placebo group P, while when it compared to etoricoxib group E, also when compared D/E with duloxetine group D (Table 2).

The pain score in group E was significantly decreased at most time periods when compared to group P at 0, 2 and 4 h at rest when compared with group D. The pain score in group D was significantly decrease at 24 and 48 h compared to group P (Table 2).

While on movement pain was significantly decreased in D/E at all times when compared to group P and when it compared to group E and when it compared to group D with no significant difference between other groups on movement (Table 3).

Patients' Satisfaction

The percentage of patients' satisfaction (excellent) shows significant differences between the four groups at 24 h (Table 4) with no significant differences between the three groups at 48 h.

The most common adverse effect expected by patients in the study was nausea and vomiting grades III and IV. There was a significant increase in percentage of patients in group P (43.3%) when compared with group D/E (16.6%) and who reported nausea and vomiting. All complained patients responded to i.v.ondansetron. No statistically significant differences were noted between groups with regard to adverse effects (Table 5).

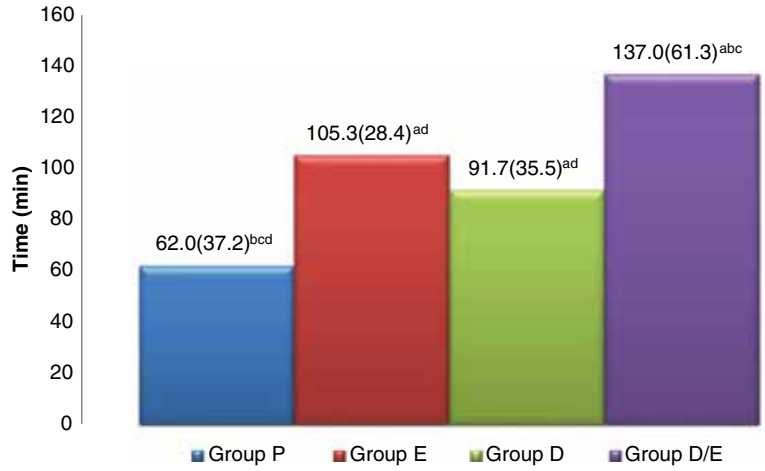

Fig. 2: Time to morphine administration after surgery in the four groups as Mean(SD). Placebo group (P), etoricoxib (E), duloxetine (D), duloxetine/etoricoxib (D/E). a: when compared with P group. b: when compared with E group. c: when compared with D group. d: when compared with E/D group.

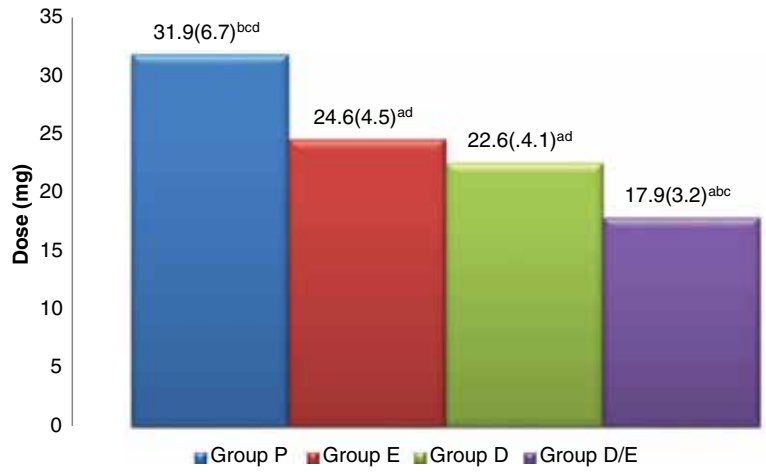

Fig. 3: Morphine requirements at 24 h in the four groups as mean (SD). Placebo group (P), etoricoxib (E), Duloxetine (D), duloxetine/etoricoxib (D/E). a: when compared with P group. b: when compared with E group. c: when compared with D group. d: when compared with E/D group.

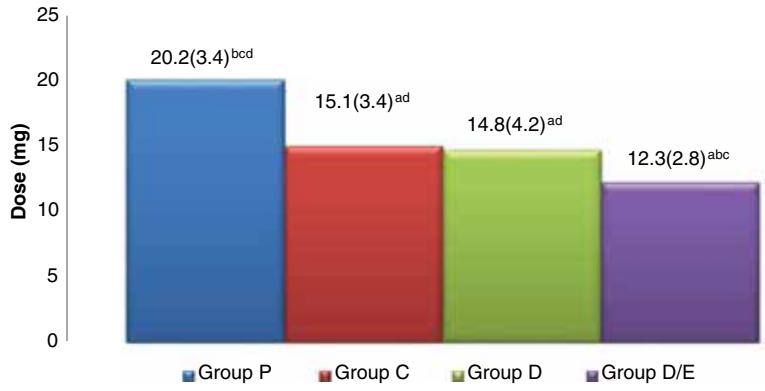

Fig. 4: Morphine requirements at 48 h in the four groups as mean (SD). Placebo group (P), etoricoxib (E), Duloxetine (D), Duloxetine/etoricoxib (D/E). a: when compared with P group. b: when compared with E group. c: when compared with D group. d: when compared with E/D group.

Discussion

To our knowledge, there have been no studies evaluating the combination of selective COX-2 inhibitors (etoricoxib) and a selective serotonin and norepinephrine reuptake inhibitor (SNRI) (duloxetine) after spine surgery. Therefore, we decided in this study to use this regimen based on the results of previous clinical trials. A number of reports have demonstrated success with either the use of etoricoxib [18–20, 23] or duloxetine [8–11] with less reported success about the efficacy of their combination in humans. Sun *et al.*, [24] reported that pretreatment with an intraperitoneal injection of duloxetine and celecoxib produced synergistic analgesia and could attenuate pain in mice 1 h after formalin injection.

Table 2: Pain scores (NRS) at rest in the four groups.

Group Variable	Group (P) ($n=30$)	Group (E) ($n=30$)	Group (D) ($n=30$)	Group (D/E) ($n=30$)	*P* value
At 0 h	5 (4-5.25) [bd]	4 (3-4) [acd]	4 (3-5) [bd]	3 (3-4) [abc]	0.0001
At 2 h	4 (3-5) [bd]	3 (3-4) [acd]	4 (3-5) [bd]	3 (3-3) [abc]	0.0001
At 4 h	4 (3-5) [bd]	3 (3-4) [acd]	3 (3-4) [bd]	2 (2-3) [abc]	0.0001
At 6 h	3 (3-4) [bd]	3 (2-4) [ad]	2.5 (2-3) [d]	2 (1-3) [abc]	0.0001
At 12 h	3 (3-3) [bd]	3 (2-3) [ad]	3 (2-3) [d]	2.5 (1-3) [abc]	0.0001
At 24 h	3 (2-3) [bcd]	2(2-3) [ad]	2.5 (2-3) [ad]	2 (1-2) [abc]	0.0001
At 48 h	3 (2-3) [bcd]	2 (2-3) [ad]	2 (2-3) [ad]	2 (0.75-2) [abc]	0.0001

Placebo group (P), Etoricoxib (E), Duloxetine (D), Duloxetine/Etoricoxib (D/E)
Data are presented as median (interquartile range). Data were analyzed by Mann–Whitney U-test and Kruksal-Wallis test and $P<0.05$ is considered significant.
a: when compared with P group
b: when compared with E group
c: when compared with D group
d: when compared with D/E group

Table 3: Pain scores (NRS) on movement in the four groups.

Group Variable	Group (P) ($n=30$)	Group (E) ($n=30$)	Group (D) ($n=30$)	Group (D/E) ($n=30$)	*P* value
0 h	5 (5-6.25) [d]	5 (5-6) [d]	5 (5-6) [d]	5 (4.5.25) [abc]	0.013
After 2 h	5 (5-6) [d]	5 (4-6) [d]	5 (5-6) [d]	5 (4-5) [abc]	0.002
After 4 h	4 (4-5) [d]	4 (4-5) [d]	4 (4-5) [d]	4 (3-4) [abc]	0.019
After 6 h	4 (3-5) [d]	4 (3-5) [d]	4 (4-5) [d]	4 (3-4) [abc]	0.007
After 12 h	4 (3-5) [d]	4 (3-4) [d]	4 (3-4.25) [d]	3 (3-4) [abc]	0.030
After 24 h	4 (3-5) [d]	4 (3-4.25) [d]	4 (3-4) [d]	3 (2.75-4) [abc]	0.059
After 48 h	3.5 (3-4) [d]	3 (3-4) [d]	3.5 (3-4) [d]	3 (2.75-4) [abc]	0.049

Placebo group (P), Etoricoxib (E), Duloxetine (D), Duloxetine/Etoricoxib (D/E)
Data are presented as median (interquartile range). Data were analyzed by Mann–Whitney U-test and Kruksal-Wallis test and $P<0.05$ is considered significant.
a: when compared with P group
b: when compared with E group
c: when compared with D group
d: when compared with D/E group

Table 4: Patient's satisfaction in the four groups at 24 h.

Group Patient satisfaction	Group (P) ($n=30$)	Group (E) ($n=30$)	Group (D) ($n=30$)	Group (D/E) ($n=30$)	*p*
Excellent	9 (30%)	12 (40%)	11 (36.7%)	21 (63.3%)*	0.004
Good	9 (30%)	10 (33.3%)	9 (30%)	5 (23.3%)	0.237
Fair	8 (26.7%)	5 (16.5%)	6 (20%)	2 (6.7%)	0.069
Poor	4 (13.3%)	3 (10%)	3 (10%)	2 (6.7%)	0.933

Data are presented as number (%). Data were analyzed using Chi square. Placebo group (P), Etoricoxib (E), Duloxetine (D), Duloxetine/Etoricoxib (D/E). $P<0.05$ is considered significant
*$P=0.016$ when compare with P

Table 5: Side effects in the four groups.

Group Side effect	Group (P) ($n=30$)	Group (E) ($n=30$)	Group (D) ($n=30$)	Group (D/E) ($n=30$)	*p*
PONV (%) IIII&IV	13 (43.3%)*	7 (23.3%)	7 (23.3%)	5 (16.6%)	0.027
Somnolence	1 (3.3%)	1 (3.3%)	2 (6.7%)	3 (10%)	0.225
Pruritus	5 (16.7%)	4 (13.3%)	3 (10%)	3 (10%)	0.390
Dizziness	1 (3.3%)	2 (6.7%)	4 (13.3%)	3 (10%)	0.239
Headache	6 (20%)	3 (10%)	5 (16.7%)	4 (13.3%)	0.907

Data are presented as number (%). Data were analyzed using Chi square test and Fisher's exact test. Placebo group (P), etoricoxib (E), duloxetine (D), duloxetine/etoricoxib (D/E). $P<0.05$ is considered significant. *$P=0.024$ when compare P and D/E

Duloxetine is a selective SNRI that is prescribed for treatment of depression and anxiety disorders [27]. It is also efficacious in treating pain in diabetic neuropathy and fibromyalgia [6]. The mechanism of its analgesic action could be explained by a combined central and peripheral pain modulating role [28] through the effect of serotonin and norepinephrine on descending inhibitory pain pathways in the brain and spinal cord [29] and activation of some cerebral prefrontal areas [5]. Also it has a antinociceptive effect through Na^+ channel blocks [30] with antihyperalgesic effects through the inhibition of the neuronal cell firing resulting from peripheral injury [31]. Therefore, duloxetine has a great role in management of neuropathic pain and reducing postoperative pain. In addition, it may improve the depression and anxiety that are common during the perioperative period [32].

In this randomized study, despite the fact that each of the two drugs separately could not produce analgesia during movement, their combination induced significant reduction in pain score at rest and on movement over the study time points and also improved patients satisfaction at 24 h postoperatively. Although, each of the drugs separately were able to prolong the duration of first rescue to analgesia and reduce postoperative morphine consumption, the combination also remained significantly effective when compared with them. Therefore, this may accelerate the rehabilitation and reduce postoperative morbidity [33].

The analgesic effect of antidepressants is typically seen after 7 to 14 days, therefore It's commonly used for chronic pain [34]. However, some investigators use duloxetine immediately preoperatively for acute pain management [8, 10]. In our study, we demonstrated that two doses of (60 mg) duloxetine 1 h before surgery and after 24 h could reduce opioid consumption with no significant effect on early postoperative pain score. Our result was comparable to Ho *et al.* [8] who assessed the use of two doses of duloxetine on pain scores postoperatively following knee arthroplasty. Also, Castro Alves *et al.* [10] examined the same regimen in patients undergoing abdominal hysterectomies and recently, Bedin *et al.* [11] performed the same assessment after spine surgery. On our study, the first dose of duloxetine was given 1 h before surgery.

In contrast, Nasr [9] gave the first dose of duloxetine 60 mg 2 days before surgery in patients undergoing mastectomy and recorded lower pain scores in the duloxetine group compared to a control group at the study period.

Although etoricoxib has been shown to have significant analgesic efficacy during pain at rest when compared to the control group in our results, there was no effect on pain score on movement. These results resembled those of Rawal *et al.* [35] where they evaluated the effect of etoricoxib (90 or 120 mg), versus ibuprofen (1800 mg) on postoperative pain following knee replacement and concluded that etoricoxib (90 and 120 mg) was significantly effective in reducing pain at rest and also reduced morphine consumption when compared to placebo with no significant effect on movement. Also Lierz *et al.* [23] used 120 mg of etoricoxib or placebo 1 h before induction of general anesthesia in knee arthroscopy surgery. They recorded similar results, showing reduction in pain only at rest and reduction in morphine consumption.

Opioids are considered the drug of choice for management of postoperative pain but it is difficult to induce an optimum analgesia without significant side effects [36]. Therefore, we suggest in our study that short-term duloxetine treatment in combination with etoricoxib may be a good adjuvant for decreasing the need for opioids in order to alleviate postoperative pain without significant adverse effects. In our results there were 13 patients complaining of nausea and vomiting in the placebo group with significant difference when compared to D/E group. There were no incidences of other adverse effects, such as sedation, dizziness, somnolence, pursuits or headache.

In this study we evaluate the acute postoperative pain not the chronic pain examined in previous studies [8, 9, 37] because our study was on a group of patients complaining from chronic back ache with high incidence of postoperative failed back pain syndrome with multifactorial conditions which may affect up to 10 to 40% of patients [38].

Conclusion

The present study demonstrates that the perioperative administration of the duloxetine/etoricoxib combination reduces postoperative pain, beside the need for morphine at 24 and 48 h after lumbar spine surgery, and the opioid-related side effects more effectively than either drug alone. Duloxetine/etoricoxib combination may thus be a useful adjuvant to be used along with opioid as part of a multimodal analgesia in the acute postsurgical setting.

Concerning limitations to our study, there are some to be applied. First it is not possible to prove that the combination of duloxetine and etoricoxib has more than just an additive effect because we did not make a full dose-response study nor associated ED50s. The second limitation of our study is that we evaluated a possible effect of duloxetine on acute postsurgical pain alone and not on the chronic one.

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Ethics approval and consent to participate: The study was approved by research ethics of Al- Minia University hospital, Faculty of medicine, Al- Minia University. The written informed consent was obtained from patients).

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References available on request
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Source: Attia, J.Z. & Mansour, H.S. *BMC Anesthesiol* (2017) 17: 162. https://doi.org/10.1186/s12871-017-0450-z.

The Gait Deviations of Ankylosing Spondylitis with Hip Involvement

Objective: The aim of the study was to investigate the gait deviations of ankylosing spondylitis (AS) patients with hip involvement.

Methods: Thirty-six subjects, including 18 AS patients with hip involvement (AS group) and 18 healthy people (control subjects, CS group), were enrolled in the study. Three-dimensional gait analysis of the AS group and CS group was performed. Kinematic parameters, kinetic parameters and surface electromyography (sEMG) during the gait cycle were measured.

Results: The AS patients with hip involvement had a lower gait velocity, shorter step length and shorter stride length. In the hip angles, there was significantly decreased flexion, excessive abduction and excessive external rotation; there was excessive flexion in the knee and reduction in plantar flexion of the ankle. AS patients had increased forward trunk flexion, excessive obliquity and restricted rotation of the trunk during the gait cycle. The hip moments of the AS group showed a significant reduction in flexion, abduction and external rotation during the gait cycle. The root mean square amplitude of the sEMG for the rectus femoris in the AS group was higher than that in the CS group.

Conclusion: The gait deviations in AS patients with hip involvement were described in this study. The gait analysis results demonstrated statistically significant alterations regarding the kinematic and kinetic gait parameters for the patients included in the sample. Coordination and balance were impaired by the disease. An efficient physical exercise plan can be formulated according to the results of gait analysis.

Source: Zhang, G., Li, J., Xia, Z. *et al.* Clin Rheumatol (2019) 38: 1163. https://doi.org/10.1007/s10067-018-4401-y.

Foot and ankle osteoarthritis (OA) is a common and disabling problem that adversely affects physical function and significantly reduces quality of life. Although the knee was considered to be the lower-limb site most often affected by OA, recent population data showed foot OA is as prevalent as knee OA, and rates increase with advancing years.

CLINICAL ASSESSMENT AND MANAGEMENT OF FOOT AND ANKLE OSTEOARTHRITIS: A REVIEW OF CURRENT EVIDENCE AND FOCUS ON PHARMACOLOGICAL TREATMENT

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Key Points

- Foot osteoarthritis (OA) is very common, particularly in older adults, and there is a growing body of evidence that it is highly disabling.
- There is little research on management strategies for foot and ankle OA; however, it is possible that pharmacological approaches recommended for knee and hip OA are effective, including acetaminophen (paracetamol) and/or topical non-steroidal anti-inflammatory drugs (NSAIDs) or capsaicin.
- Oral NSAIDs (including a cyclo-oxygenase-2 inhibitor) or intra-articular hyaluronic acid injections may be considered if initial pharmacological approaches are ineffective, especially for ankle OA, but further high-quality clinical trials are necessary.

Osteoarthritis (OA) is a major global public health problem, with a worldwide prevalence of 23.9% [1]. The condition causes significant pain and disability, and adversely affects quality of life. Disability associated with OA also results in a substantial economic burden. This economic burden is due to direct treatment-related costs, particularly joint replacement surgery, in addition to indirect costs such as lost productivity [2, 3]. Rates of OA are projected to rapidly increase over the coming decades as the population ages and rates of obesity rise [4]. As a consequence, it is anticipated that there will be a large increase in demand for health services for the symptoms and disability associated with OA in the coming years.

Foot OA has recently been found to be highly prevalent and disabling, yet in contrast to hand, knee and hip OA, there is little research in the field to guide clinical management. This paper provides a review of the assessment and non-surgical treatment of foot and ankle OA for clinical practice. Where evidence-based information specifically related to the foot, ankle or individual foot joints is lacking, relevant clinical research from other joints that may be generalised to the foot/ankle is provided.

Epidemiology and Impact of Foot and Ankle Osteoarthritis (OA)

Historically, the knee has been considered to be the most commonly affected weight bearing region, with a reported prevalence of 7.6–16.4% [1]. However, recent research revealed the population prevalence of symptomatic radiographic foot OA was 16.7% [5], suggesting it may be as common as knee OA. Within the foot, the first metatarsophalangeal joint (MTPJ) is the most commonly affected joint, with a prevalence rate slightly higher than hip OA at 7.8% [5]. Midfoot joints are also commonly affected, including the second cuneiform-metatarsal joint (6.8%), talo-navicular joint (5.8%), naviculo-cunieform joint (5.2%), and first cuneiform-metatarsal joint (3.9%) [5]. If these individual joints are considered as a single midfoot complex, as they typically are for clinical management [6], the prevalence of symptomatic radiographic midfoot OA is reported to be 12.0% [7]. The prevalence of symptomatic radiographic OA of the ankle has also been reported to be 3.4% [8], and it has been suggested that the majority of these are post-traumatic [9].

Foot and ankle OA are highly debilitating. An overwhelming 69% of people with symptomatic radiographic foot OA report experiencing disabling foot pain [5], and this pain has been shown to result in functional limitations and significant impairments in measures of balance, strength and locomotor ability [10]. Disabling foot pain is a significant and independent risk factor for falls [11], and foot OA, particularly of the first MTPJ, also leads to significant reductions in all domains of the foot health status questionnaire, and the physical and social function subscales of the Short Form 36 questionnaire [12]. It has also been shown to worsen symptoms at other joints, and to increase the risk of developing OA more proximally in people aged over 45 years. Specifically, a recent large cohort study found that the presence of foot/ankle pain significantly reduced health and physical function in people with knee OA [13]. Subsequent analyses from this cohort found that foot/ankle pain substantially increased the risk of developing symptomatic radiographic knee OA within the subsequent 4 years [14], and increased the risk of worsening knee pain in those with existing knee OA [15].

> *Foot OA has recently been found to be highly prevalent and disabling, yet in contrast to hand, knee and hip OA, there is little research in the field to guide clinical management.*

Foot and ankle problems are a common cause for consulting a general practitioner [16]. In fact, up to 32% of people with foot pain report consulting their general practitioner—more than those with musculoskeletal pain at any other site [17]. The adverse effects on health, physical function and quality of life from foot and ankle OA have also been shown to impact on working ability, with foot OA reported to be the only OA site significantly associated with employment reduction in males [18]. This is important given half of people with OA are of working age [19].

Foot and Ankle OA Phenotypes

The median number of foot joints affected by OA in people aged over 65 years is four [20], suggesting that the typical presentation of foot OA is as a multi-joint disease pattern. This was confirmed in a recent population-based study which used latent class analysis to investigate potential foot OA phenotypes. Outcomes showed two distinct foot OA phenotypes: a polyarticular form of foot OA that included a clustering of midfoot joints, and isolated OA of the first MTPJ [21]. Both subgroups were significantly older than people with no or minimal OA, whilst the polyarticular group were also more likely to be female, and to have more persistent and severe pain, greater functional limitation, a higher body mass index (BMI) and increased presence of nodal hand OA. The study also found that the disease was more prevalent in one foot only; however, when foot OA was bilateral, there was a strong association for a symmetrical distribution [21]. A high level of symmetry is also common in the polyarticular form of hand OA [22].

Assessment

Clinical Assessment

Evidence-based recommendations for the clinical diagnosis of OA currently exist for the knee [23], with a diagnosis made by three signs on examination (crepitus, restricted movement and bony enlargement) and symptoms (knee pain, short-lived morning stiffness and functional limitation). Despite the comparable prevalence, there are currently very few agreed guidelines for the clinical diagnosis of foot or ankle OA, which limits our ability to advance the development of interventions and provide targeted treatment.

A variety of foot and ankle assessment measures have been adopted by a number of OA-linked prospective cohort studies. The Johnston County Osteoarthritis Project and the Framingham Foot Study included a pictorial atlas of common foot disorders, foot structure (measured with the Arch Index), and assessment of hallux valgus and hallux rigidus [24, 25], whilst the Chingford 1000 Women Study used the International Musculoskeletal Foot and Ankle Assessment [26]. Although a number of measures have been validated against foot disorders [27], all have yet to be validated against OA-related outcomes.

CASF (Clinical Assessment Study of the Foot) derived a brief collection of static assessments from pre-study consensus work, including measures of foot posture, range of motion, observation and palpation [28]. None of these were able to discriminate between individuals with and without structural radiographic midfoot changes [29]. However, assessments including dorsal hallux and first MTPJ pain, hallux valgus, first interphalangeal joint hyperextension, keratotic lesions of the hallux and first MTPJ, decreased first MTPJ dorsiflexion, ankle/subtalar joint eversion, and ankle joint dorsiflexion range of motion were all significantly associated with radiographic

first MTPJ OA severity [30]. Findings from a smaller elderly population have shown that older people with radiographic OA of the talo-navicular joint and navicular-first cuneiform joint exhibit flatter feet represented by the Arch Index [31].

A diagnostic rule developed for first MTPJ OA suggests five clinical observations can accurately identify the presence or absence of radiographic first MTPJ OA in patients with first MTPJ pain [32]. These include pain duration longer than 25 months, the presence of a dorsal exostosis, hard-end feel, crepitus and less than 64 ° of first MTPJ dorsiflexion. More recently, a consensus study provided five recommended assessment components for first MTPJ OA, including pain on walking over the past week, first MTPJ and ankle joint range of motion, foot posture (foot posture index), resting calcaneal stance position and palpation to determine pain location [33].

Findings suggest that some of these physical examinations may be of limited use for discriminating the presence or absence of symptomatic midfoot OA, but a number may hold some value in diagnosing first MTPJ OA. Further work would be beneficial to determine if these and other clinical measures may be useful in discriminating between the presence and absence of symptomatic OA in all identifiable foot joints.

Imaging Assessment

The latest recommendation from the European League Against Rheumatism is that imaging is not required to make a diagnosis of OA in patients with a typical presentation of the disease [34]. Routine follow-up imaging to monitor disease progression or treatment response is also not recommended. The exceptions to these include cases where the patient's presentation is atypical and thus imaging may be needed to confirm a diagnosis of OA or make a differentiation diagnosis, or if there is a rapid and unexpected progression of symptoms, and imaging may be used to see if progression is related to symptoms or an additional diagnosis. In such cases, the guidelines recommend plain-film radiography in the first instance prior to other modalities. The vast majority of the recommendations were made based on studies from other sites given there is very little research available regarding imaging for foot and ankle OA. One exception was a small study that found that when ultrasound imaging was added to clinical assessment findings, the diagnostic confidence of rheumatologists in differentiating OA from inflammatory arthritis of the hands or feet was significantly increased [35].

> ***The latest recommendation from the European League Against Rheumatism is that imaging is not required to make a diagnosis of OA in patients with a typical presentation of the disease.***

Notwithstanding these recommendations, radiography is routinely used in the primary care setting [36], and in clinical research, to confirm diagnosis and/or OA severity grade. Regarding grading, a systematic review [37] of the radiographic prevalence of foot OA from 27 studies found that most (70%) used the Kellgren and Lawrence (KL) system [38]. This system classifies OA based on the presence or absence of osteophytes and joint space narrowing, using a scale of 1 (doubtful OA) to 4 (severe OA). The majority of studies (95%) in the review classified OA as being at least grade 2 (mild OA) [37].

Whilst the use of the KL system allows comparison between studies of radiographic OA at more proximal joints such as the knee, it has been argued that it places too much dependence on the presence of osteophytes, which are implied to precede joint space narrowing in a chronological progression of OA [39, 40]. Furthermore, another review reported large variation in the definition and grading of OA using the KL system [41]. In response to these limitations, Menz and colleagues [42] developed a foot-specific atlas which classifies radiographic OA of the first MTPJ, first cuneiform-metatarsal joint, second cuneiform-metatarsal joint, talo-navicular joint and naviculo-cunieform joint [42]. The atlas overcomes the major disadvantages highlighted in previous radiographic foot OA studies by (1) obtaining dorsoplantar and lateral views; (2) requiring x-rays to be taken while weight-bearing; and (3) grading both osteophytes and joint space narrowing separately on a scale of 0 (absent) to 3 (severe osteophyte or joint fusion). As an example, Fig. 1 is a dorsal view of the first MTPJ showing the grades for joint space narrowing. Radiographic OA is defined as present at any of the five foot joints if there is a score of 2 or greater for either osteophytes (indicating a moderate or severe osteophyte) or joint space narrowing (indicating severe joint space narrowing or joint fusion at at least one point) on either the dorsoplantar or lateral view [42]. The authors reported that the atlas had moderate to excellent within-rater reliability, and mostly fair to excellent between-rater reliability. The overall foot OA score was also found to possess moderate to excellent within- and between-rater reliability [42].

An additional atlas has recently been developed to grade radiographic OA at the ankle (tibiofibular and tibiotalar) and subtalar (talocalcaneal) joints [43]. The ankle and hindfoot atlas grades osteophytes and joint space narrowing from 0 (normal) to 3 (severe) from weight-bearing mortise and lateral views. Osteophytes are graded in the medial and lateral compartments from the

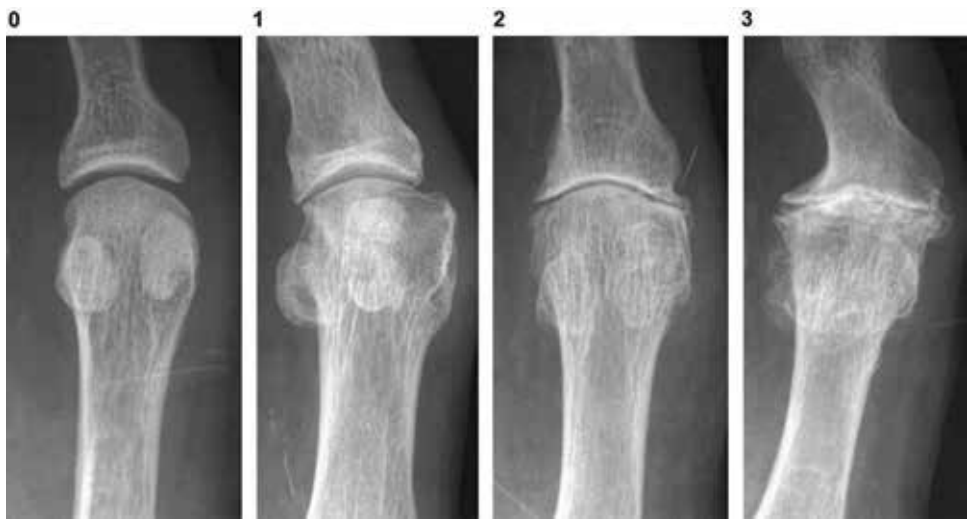

Fig. 1: Dorsal projection of the first metatarsophalangeal joint showing the grades for joint space narrowing based on the atlas developed by Menz *et al.* [42]. A grade of 0 indicates no joint space narrowing, 1 indicates definite joint space narrowing, 2 indicates severe joint space narrowing and 3 indicates joint fusion at at least one point. Reprinted from Menz *et al.* [42] with permission from Elsevier.

mortise view, and anterior and posterior from the lateral view, whilst joint space narrowing is graded in each joint in both views. The KL system is used to provide an overall OA grade as already described [38]. Using x-rays from 30 participants, the study found the atlas to possess good to excellent reliability for most radiographic features from most views.

Treatments

Although there are no clinical guidelines for the management of foot or ankle OA, it is reasonable to suggest that recommendations pertaining to the management of OA at other sites may be appropriately applied to the foot and ankle. The National Institute for Health and Care Excellence (NICE) guidelines for peripheral joint OA, developed largely from hip and knee OA trials, advise that core management strategies should include (1) advice and education regarding the disease and its prognosis; (2) strengthening and aerobic exercise; and (3) weight loss, where appropriate [44]. These recommendations are largely consistent with those from the Osteoarthritis Research Society International [45] and the most recent guidelines from the Royal Australian College of General Practitioners (RACGP) [46] and the European League Against Rheumatism [47]. It is probable, however, that many people with OA will experience symptoms that cannot be effectively managed by these non-pharmacological treatments. Sections 5.1 to 5.3 outline the use of pharmacological, injectable and conservative treatment strategies for foot and ankle OA.

Pharmacological Management

Acetaminophen (paracetamol) or topical non-steroidal anti-inflammatory drugs (NSAIDs) are generally recommended following first-line strategies. To date, there are no clinical trials of acetaminophen in foot or ankle OA. In knee OA, dosages from seven randomised controlled trials (RCTs) (n = 2491 participants) included in a systematic review and meta-analyses comparing acetaminophen with placebo ranged from around 1000 mg/day to nearly 4000 mg/day, with no clear benefit of one over the other [44]. The NICE guidelines advise clinicians to consider regular dosing of acetaminophen [44]; however, it should also be highlighted that the most recent RACGP guidelines were unable to recommend either for or against acetaminophen, and cautioned against regular dosing [46]. This was largely based on findings from a recent systematic review of eight observational studies on adverse events (AEs) from standard analgesic doses, which found that acetaminophen was associated with potential for some harms due to both short-term excess doses and longer-term regular dosing [48]. Furthermore, a large systematic review also showed that acetaminophen provided only minimal short-term OA-related pain reductions that were unlikely to be clinically relevant [49]. However, depending on the foot and/or ankle joint(s) affected, it is reasonable to suggest that lower doses in the order of 1000 mg/day may be trialled initially and gradually increased in case of ineffectiveness and the absence of AEs. Use should be discontinued if acetaminophen is not effective.

> *Although there are no clinical guidelines for the management of foot or ankle OA, it is reasonable to suggest that recommendations pertaining to the management of OA at other sites may be appropriately applied to the foot and ankle.*

Topical NSAIDs are both safe and effective and should be considered as an adjunct to non-pharmacological strategies. There are no clinical trials on the use of topical NSAIDs for the treatment of foot/ankle OA. The most recent systematic review and network meta-analysis of 36 RCTs in predominantly hip and knee OA found that topical NSAIDs were superior to placebo for OA-related pain relief and significantly improved physical function [50]. Diclofenac patches, followed by ibuprofen cream, were found to be the most effective for pain. Topical salicylate gel was the only topical NSAID to be associated with AEs, with users of all other topical NSAIDs not experiencing a higher rate of AEs than non-users or placebo [50].

Likewise, application of topical capsaicin should also be considered as adjunct to either core non-pharmacological treatments, or in place of topical NSAIDs [44]. A recent systematic review and network meta-analysis concluded that capsaicin prescribed at the recommended British National Formulary dosage (0.025% four times per day) is superior to placebo for pain relief [51]. Although no RCT has directly compared capsaicin to topical NSAIDs, the analysis showed capsaicin resulted in clinically meaningful improvements in pain that were similar to topical NSAIDs, suggesting the cream could be used in its place.

When acetaminophen and/or topical NSAIDs or capsaicin are ineffective for managing the symptoms of foot or ankle OA, clinicians should consider prescribing oral NSAIDs, including cyclo-oxygenase (COX)-2 inhibitors [44]. The clinical improvement in OA-related symptoms from NSAIDs is small, but greater than that of acetaminophen for most patients, and is clinically meaningful [46]. We recommend trialling an oral NSAID or COX-2 inhibitor at the lowest effective dose, such as 1000 mg/day of ibuprofen or naproxen or 100 mg/day of celecoxib, for the shortest possible period. This is consistent with the only published clinical trials of NSAIDs in foot OA. The first of these found similarly effective pain reductions with 800 mg of etodolac and 1000 mg of naproxen at 5 weeks [52], whilst the second found similar results at 8 weeks with 20 mg/day of piroxicam and 1000 mg/day of naproxen [53]. There is also good evidence that diclofenac 150 mg/day results in clinically meaningful improvements in pain for knee OA [54]; however, it may be prudent to trial doses of around 100 mg/day in the first instance for foot or ankle OA. Patients should be carefully monitored, and the dosage may be gradually and slightly increased in the absence of symptomatic improvements and lack of AEs. Indeed, the potential for harm with NSAIDs is well-recognised, particularly in older persons; thus, the co-prescription of a proton pump inhibitor may also be considered or, alternatively, clinicians may consider not prescribing oral NSAIDs in this population [45].

Evidence concerning opioid use is poor, and toxicity-related AEs (particularly in the elderly), in addition to dependence, remain serious concerns [44]. As such, the most recent guidelines recommend that both oral and transdermal opioids are not indicated for OA [46]. Additional pharmacological strategies that are either not recommended for peripheral joint OA or lack evidence include chondroitin, avocado soybean

unsaponfiables, vitamin D, turmeric, tricyclic agents, glucosamine and risedronate [44–46].

Intra-Articular Injections

Intra-articular (IA) injections have been investigated more than any other non-surgical approach for foot and ankle OA. Although ankle OA has a lower prevalence than first MTPJ or midfoot OA, the majority of studies used participants with ankle OA. A 2018 systematic review [55] found 22 studies that evaluated the effects of IA injections in people with ankle OA; however, only five of these were RCTs [56–60]. Of the five RCTs, three compared hyaluronic acid (HA) to saline [56, 57, 59], one compared HA to exercise therapy [58], and one compared HA and rehabilitation exercise to an injection of botulinum toxin type A. Pooled RCT results from the systematic review showed HA significantly improved ankle OA symptoms over saline at 6 months [55]. However, no trial blinded the administering physician, all were generally small (n = 20–75), and most had inadequate or unclear randomisation and/or allocation concealment. Case series on the effects of platelet-rich plasma, corticosteroids and mesenchymal stem cell injections also suggest symptomatic improvements; however, these trials are all small and lack a control group, which limits interpretation [55]. Larger studies with adequate randomisation, control and blinding are needed before firm conclusions regarding the efficacy of IA injections for ankle OA can be made.

> ***Evidence concerning opioid use is poor, and toxicity-related AEs (particularly in the elderly), in addition to dependence, remain serious concerns.***

In the first MTPJ, there has been one RCT comparing an IA injection of HA to saline [61] and one comparing HA to a corticosteroid injection [62]; however, only the former was adequately powered and reported randomisation and blinding information. Clinically meaningful reductions in first MTPJ pain were observed in both the HA and saline groups over 6 months [61] and in the HA and corticosteroid group over 3 months [62]. However, there were no statistically significant between-group differences in change in pain in either study. There have only been two uncontrolled studies comparing IA injections for midfoot OA, both of which used a corticosteroid [63, 64]. Results from both studies showed symptomatic improvements in the short term (3–4 months); however, these positive clinical responses were generally not maintained in the longer term (12 months).

Conservative Treatments

There is little research on conservative treatment options for OA of the foot and ankle. In fact, there are no RCTs investigating management strategies for multi-joint foot OA, and high-quality trials investigating single-joint foot or ankle OA are also lacking. To date, there have only been two non-pharmacological non-surgical RCTs published on OA of the first MTPJ [65, 66], three small pilot studies for midfoot OA [6, 67, 68] and no clinical trials for conservative treatment for ankle OA. Notably, no study has investigated the effects of core OA management strategies (derived from hip and knee OA trials) recommended by international OA clinical guidelines [44–46], with the exception of one small trial [65]. This study assessed the addition of a single foot-strengthening exercise, as well as sesamoid mobilisation and gait training, to a range of other physical interventions, and reported significant improvements in strength and function for the intervention group. However, the small sample size (n = 20), use of multiple interventions and lack of adequate control precludes an understanding of the effects of strength exercise on foot OA-related pain. Although no study has investigated the effects of aerobic exercise on foot or ankle OA symptoms, one cohort study of 221 participants aged between 40 and 91 years reported that regular exercise did not increase the risk for progression of foot OA [69]. The only other non-pharmacological non-surgical foot OA RCT compared the effects of rocker-soled footwear with prefabricated foot orthoses in 102 participants with OA of the first MTPJ [66]. The results showed that there were clinically meaningful symptomatic improvements in both groups; however, there were no between-group differences. It is worth noting that there were fewer AEs and greater adherence in the foot orthoses group.

Of the three small studies to assess a conservative intervention for midfoot OA, all used a foot orthosis/insert. The first investigated the effects of a full-length flat carbon graphite insert in 20 female patients with midfoot OA, and found symptomatic improvements with the intervention, albeit the study lacked adequate control [68]. Another non-randomised study compared the addition of a rigid carbon fibre footplate (insert) to custom semi-rigid foot orthoses in 57 participants with midfoot OA and found similar clinical improvements in pain, function and walking ability in both groups [67]. The final trial was a feasibility study in which 37 participants with symptomatic radiographic midfoot OA were randomised to receive a pair of semi-custom foot orthoses or a sham device [6]. Both groups reported improvements in pain, function and global impression of change over 12 weeks; however, benefits were greater in the intervention group.

Gaps in Our Knowledge and Key Areas for Clinical Focus

The burden of foot and ankle OA has not been well-understood until recently, and the condition has been neglected in clinical research. Consequently, there is a plethora of questions regarding the impact of foot and ankle OA in the community and its optimal management in the clinical setting. Perhaps most pressing is the urgent need for clinical trials investigating core management strategies recommended by international OA clinical guidelines, such as education and advice, exercise and weight loss where appropriate. The condition is a leading cause for consulting a general practitioner [70], and general practitioners largely manage the condition using medication, including for new presentations [36]. Thus, more clinical trials on the efficacy and safety of analgesic and anti-inflammatory medications for foot and ankle OA are also needed. Indeed, dosing is inferred based mainly on the larger knee and hip joints, and, while these may be appropriate, it would be useful for clinicians to be able to recommend evidence-based dosing specifically for foot and ankle OA. Likewise, given the strong association between foot and ankle OA and advancing age [5] and co-morbidities [7, 36] (as for most OA), clinical research on the short- and long-term benefits and harms of pharmacological treatments for older people (e.g. >70 years) and those with

Cont'd on page 28...

Although popliteal cysts are most frequently identified in patients with osteoarthritis (OA), they may occur in patients with rheumatoid arthritis (RA), in which serious complicated cases such as cyst rupture can be developed. The objective of this study was to report four patients with RA (six knees) in combination with OA with a brief review of literature of previous similar published cases.

SUCCESSFUL ARTHROSCOPIC TREATMENT OF REFRACTORY AND COMPLICATED POPLITEAL CYST ASSOCIATED WITH RHEUMATOID ARTHRITIS IN COMBINATION WITH OSTEOARTHRITIS: CASE SERIES AND LITERATURE REVIEW

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Rheumatoid arthritis (RA) is one of the most prevalent chronic inflammatory arthritis affecting approximately 1% of the population worldwide. It is characterized by inflammatory proliferation of the synovium of the joint, with subsequent destruction of the articular structure such as cartilage, bone, and adjacent ligaments and tendons [1–3].

Popliteal cysts are usually seen secondary to osteoarthritis (OA), RA, and less commonly trauma, infections, and other causes of inflammatory arthritis [4]. Several etiological mechanisms of popliteal cyst have been suggested: (1) enlargement of the gastrocnemius–semimembranosus bursa, which has communication with the joint, (2) rupture of the posterior articular capsule and its transformation to a cyst in a chronic course, and (3) herniation of the posterior articular capsule due to a chronic increase in the intra-articular pressure [5].

Fielding *et al.* [6], in their study using MRI, reported that popliteal cyst was seen in adult populations at a rate of 4%, with the rate being higher in the elderly population. Andonopoulos *et al.* [7] reported that popliteal cyst was detected in 47.5% of RA using ultrasonography, only 43.3% of which had been diagnosed clinically. Although cysts present as an asymptomatic

mass in most cases, they are also known to cause severe clinical problems such as pseudothrombophlebitis, thrombophlebitis, compartment syndrome, and neuropathy, most of which may need specific treatment such as surgical intervention [8–11].

A few previous reports have described the complicated popliteal cyst associated with RA [7, 12, 13]. However, since the underling pathophysiology of the disease itself and the particular pathology of popliteal cyst of RA might be quite different from that of OA, optimal surgical approaches and their technical aspect for good clinical outcome should be addressed. In this report, four patients with RA in combination with OA having refractory and complicated popliteal cysts who were successfully treated by means of arthroscopic treatment are described with a brief review of literatures of surgical management of popliteal cyst associated with RA.

Methods

This was a retrospective review of all cases with RA having refractory popliteal cysts that had been performed surgery during 2017–2018 at a single center in South Korea. We have reviewed the cases regarding demographic features, laboratory findings including autoantibodies such as rheumatoid factor (RF) and anti-citrullinated peptide antibody (ACPA), DAS 28-ESR (disease activity score 28-ESR), medications, radiographic findings including MRI, joint fluid analysis, number of intra-articular injection of glucocorticoid 6 months prior to surgery, and clinical outcomes after surgical treatment. The patients were informed that the data of the cases would be submitted for publication and provided their consent. This study was approved by the Institutional Ethics Review Board of Hanyang University Guri Hospital in South Korea.

Search Strategy

An electronic literature search was performed using the Medline, Embase, and Scopus databases. Articles written in English from 1960 to 2018 were searched. The following keywords were used along with the Boolean search function: “popliteal cyst” and “rheumatoid arthritis”. Because the scope of the literature review is limited to patients with RA who had been performed surgery for popliteal cyst, we carefully screened for appropriate studies. As a result, a total of nine reports (including one with only abstract available) were reviewed.

Results

A total of four patients were eligible for the current review. Table 1 summarizes details of the cases. The table includes initial clinical characteristics, autoantibodies such as RF and ACPA, DAS 28, medications, radiographic findings including MRI, and clinical outcomes after surgical treatment. All were females and seropositive (RF positive or ACPA positive). DAS28-ESR that are widely used for assessment of disease activity for RA was among 3.1–4.84, which means moderate disease activity except case 3 that showed low disease activity. All cases were combined with OA that represented by Kellgren–Lawrence grade (K–L grade) 2 or 3. Case 1 is described in detail below, which includes patient’s history and physical examination, radiography, MRI, surgical procedure, and arthroscopic and histologic findings. The remaining three cases are described briefly.

> *Popliteal cysts are usually seen secondary to osteoarthritis (OA), RA, and less commonly trauma, infections, and other causes of inflammatory arthritis.*

Case 1

A 62-year-old woman with 15 years of history of seropositive RA presented with left knee joint discomfort and lower leg swelling. She was taking sulfasalazine 2 g/day, prednisolone 5 mg/day, and subcutaneous golimumab (anti-tumor necrosis factor monoclonal antibody). Intra-articular glucocorticoid injection was performed three times in the affected knee joint over a year, but without improvement. Her lower leg swelling had been aggravated for over 12 weeks, and she had suffered from increased pain with motion and limited knee flexion despite conservative treatment. Physical examination revealed cutaneous erythema, swelling, and tenderness of the left calf. She showed moderate disease activity of DAS28-ESR 4.84, erythrocyte sedimentation rate 110 mm/h, and C-reactive protein of 5.99 mg/dl. Radiologic imaging showed mild joint space narrowing without a significant valgus or varus deformity (K–L grade 2) (Fig. 1). Ultrasonography revealed popliteal cyst with synovial hypertrophy and analysis of joint fluid revealed white blood cell 17,200 with polymorphonuclear (PMN) cell 74%. MRI (fat-suppressed fast spin-echo T2-weighted images) revealed 4.1-cm multiloculated ganglion cysts at the popliteal fossa and a complicated popliteal cyst with leakage to the distal limb through a subcutaneous extension (Fig. 2). The distal leakage extended down to the mid-calf area. The patient was hospitalized to further evaluate the status and prevent further swelling of the lower limb. Fortunately, the patient did not develop severe complications such as compartment syndrome. Arthroscopy-assisted cyst decompression was planned. The operative procedure was conducted using three arthroscopic portals: the standard anterolateral, anteromedial, and the posteromedial portals. Using the posteromedial portal, the opening of the cyst was identified by inferiorly displacing the overlying capsular fold located at the posteromedial side of the medial head of the gastrocnemius. Once the opening had been identified, the capsular fold was resected using basket forceps and an arthroscopic shaver. The valvular opening of the posterior capsule was enlarged to completely resect the capsular fold. The arthroscope was then switched to the posteromedial portal using a switching stick. The arthroscope was advanced further to the posterior and distal aspect which revealed the popliteal cyst consisted of debris and wall septa. The cystic wall was hypervascular and friable, which was different from the popliteal cyst wall in osteoarthritic knee joint (Fig. 3). Careful attention was given when debriding the lateral wall of the popliteal cyst to prevent damage to the adjacent neurovascular structures. Further debridement of the capsule was done down to the leakage area. A biopsy sample was taken from the cystic wall. Histopathological examination showed fibro-hyalinized tissue and plasma cells resulting from active chronic inflammation (Fig. 4). All procedures were performed with a standard 30° arthroscope. The water pump pressure was minimalized throughout the operation (not exceeding 50 mmHg) to prevent any further leakage through ruptured cyst which

Table 1: Summary of clinical characteristics of the presented four cases with rheumatoid arthritis combined with knee osteoarthritis.

	Case 1		Case 2	Case 3	Case 4	
Age at onset of symptom	62		75	54	66	
Disease duration (years)	16		11	18	7	
Sex	Female		Female	Female	Female	
Laboratory test						
Serology						
RF (IU/ml)	23		101	61	< 20	
ACPA (U/ml)	43		1740	3377	271	
ESR (mm/h)	110		31	85	42	
CRP (mg/dl)	5.99		0.1	2.55	0.1	
Disease activity at surgery						
Joint count						
TJC	3		0	1	0	
SJC	3		1	1	2	
DAS28-ESR	4.84		3.1	4.71	3.43	
Current medication						
DMARDs	Sulfasalazine 2 g/day		Leflunomide 20 mg/day	Methotrexate 15 mg/week	Methotrexate 15 mg/week, hydroxychloroquine 200 mg/day	
Glucocorticoid	Prednisolone 5 mg/day		Not used	Prednisolone 5 mg/day	Not used	
Biologics	Subcutaneous golimumab		Not used	Subcutaneous golimumab	Not used	
Location	Both		Left	Left	Both	
	Left	Right			Left	Right
X-ray						
K–L grade	2	2	2	3	3	3
MRI						
Size of cyst (cm)	4.1	5.4 × 3.0 × 1.6	2.4 × 1.3 × 6.7	3.0	2.0 × 3.7 × 2.1	4.1 × 3.0 × 5.3
Cyst septation	Yes	Yes	Yes	N/A	Yes	Yes
Cyst leakage	Yes	Yes	No	Yes	No	No
Meniscus tear	Yes	Yes	Yes	Yes	Yes	Yes
Ligament damage	No	No	Yes	Yes	No	No
Joint fluid analysis						
WBC count (1/mm^3)	17,200	NA	400	16,000	90	NA
PMN cell (%)	74	NA	45	73	28	NA
No. of glucocorticoid IAI within 6 months of surgery	2	1	1	1	1	1
Surgery	Arthroscopic cystectomy	Arthroscopic partial cystectomy	Arthroscopic cystectomy and debridement of medial meniscus	Arthroscopic cystectomy and synovectomy	Arthroscopic cystectomy with partial meniscectomy	
Follow-up duration after surgery	12	12	12	12	12	12
Recurrence	No	No	No	No	No	No

RF rheumatoid factor, *ACPA* anti-citrullinated peptide antibody, *ESR* erythrocyte sediment rate, *CRP* C-reactive protein, *TJC* tender joint count, *SJC* swollen joint count, *DAS28-ESR* disease activity score 28-ESR, *DMARDs* disease-modifying anti-rheumatic drugs, *K–L grade* Kellgren–Lawrence grade, *PMN* polymorphonuclear cell, *IAI* intra-articular injection, *NA* not applicable

might cause increased calf pressure (e.g., iatrogenic compartment syndrome of lower leg). The physical status of calf swelling was monitored continuously. In addition, radical synovectomy was performed intra-articularly, especially at the suprapatellar pouch and medial/lateral gutter area. A suction drainage was inserted at the cyst resection site and compressive dressing was applied. This drainage was removed the next day of operation and a full extension splint was applied for 7 days. Immediately after left knee operation, she complained of right knee pain and popliteal area discomfort due to the same complicated popliteal cyst, for which arthroscopic partial cystectomy was performed. Full weight bearing and active–passive motion were permitted from 1 week after surgery. Pain and swelling improved dramatically after surgery and further decreased after hospital discharge. Full range of motion of both knee joints was observed without recurrence of the popliteal cyst at the 12-month follow-up.

Case 2

A 75-year-old woman with 11 years of history of seropositive RA presented due to swelling of left popliteal fossa and discomfort when bending the knee. The patient had a low activity of RA (DAS28-ESR 3.1) without any other joint involvement except the left knee joint. She took leflunomide 20 mg daily. Simple X-ray of the knee showed OA change with K–L grade 2. MRI revealed the multiloculated cysts without leakage to the distal limb but combined with meniscal tear and ligament damage. Joint fluid analysis revealed white cell count 400 (PMN 45%). She was treated with the intra-articular glucocorticoid injection, but the symptoms recurred within a few days. Arthroscopic cyst excision and debridement of medial meniscus were performed 3 months after the onset of symptoms. After the operation, the patient is under observation for 12 months without recurrence.

Case 3

A 54-year-old-woman with 18 years of history of seropositive RA presented with newly developed swelling of left lower leg. On examination, swelling was observed from the left knee to the ankle and pain was not accompanied. The patient was taking methotrexate

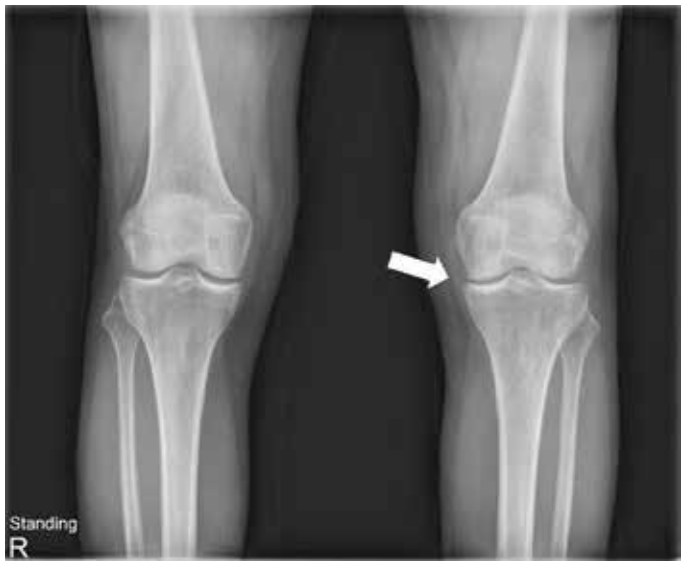
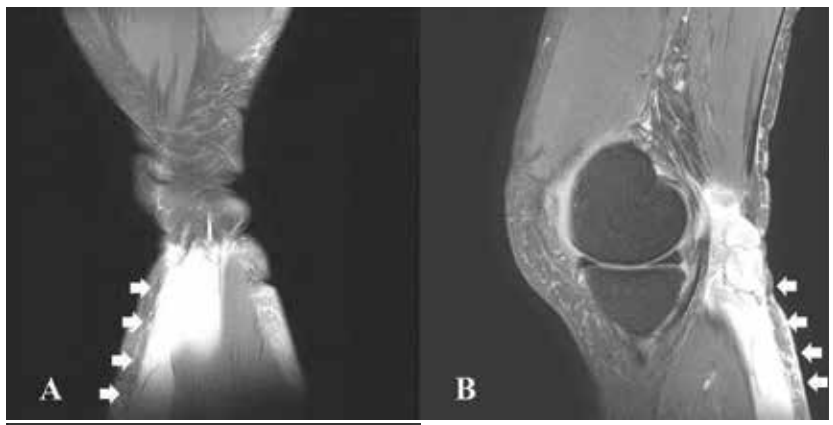


Fig. 1: Radiologic image showing mild joint space narrowing on left knee joint (*arrow*) without a significant valgus or varus deformity.



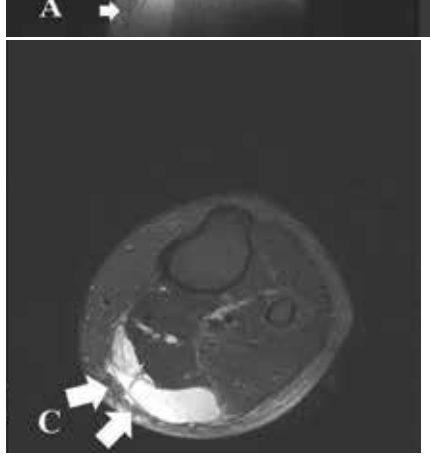


Fig. 2: Magnetic resonance images (fat-suppressed fast spin-echo T2-weighted images) showing 4.1-cm sized multiloculated ganglion cysts at the popliteal fossa and complicated popliteal cyst with leakage to the distal limb through a subcutaneous extension (*arrows*). **a** Coronal, **b** sagittal, and **c** axial images.

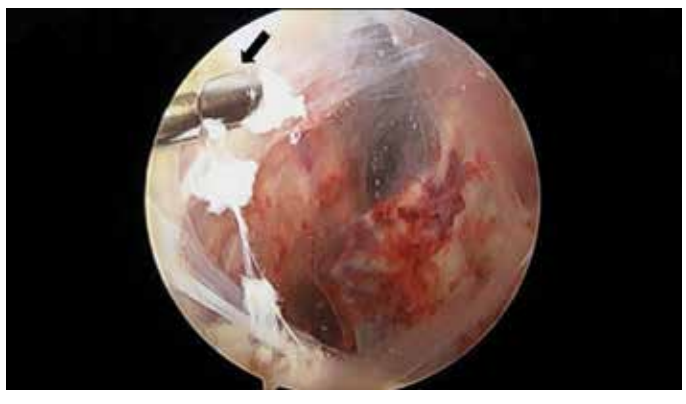


Fig. 3: Popliteal cystic wall consisting of debris and wall septa. The walls were hypervascular and friable, different from the popliteal cyst wall of an osteoarthritic knee joint. The scope was introduced via the posteromedial portal, whereas the arthroscopic shaver was introduced through the standard anterolateral portal (*arrow*).

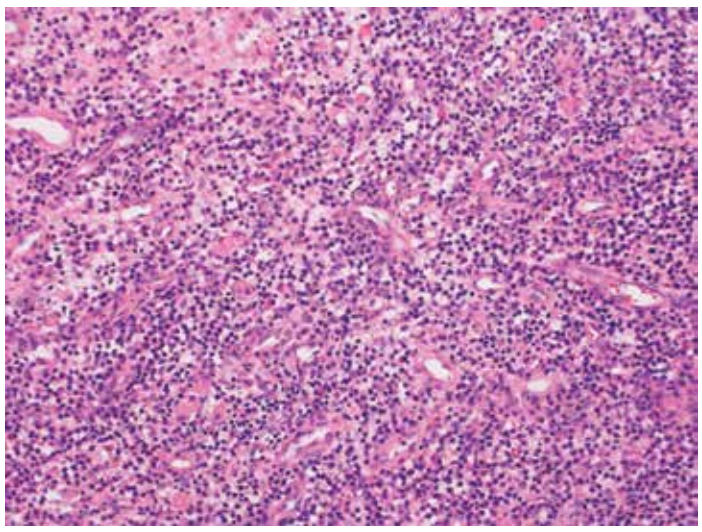


Fig. 4: Histopathological images showing fibro-hyalinized tissue and plasma cells resulting from active chronic inflammation (hematoxylin and eosin staining, original magnification × 200).

15 mg weekly, prednisolone 5 mg daily, and subcutaneous golimumab. She showed moderate disease activity (DAS28-ESR 4.71) and had no joint symptoms other than left knee. Simple knee X-ray showed OA change with K–L grade 3. MRI revealed popliteal cyst leakage with meniscal and ligament damage of left knee and laboratory investigation of aspirated fluid from cyst revealed white cell count 16,000 (PMN 73%). She underwent intra-articular glucocorticoid injection into the knee joint, but the symptoms recurred. Arthroscopic cystectomy and synovectomy was performed. During the follow-up period of 12 months after surgery, there was no recurrence of popliteal cyst.

Case 4

A 66-year-old woman with 7 years of history of seropositive RA presented with both knee pain. The disease activity of RA was well controlled and patient was taking methotrexate 15 mg weekly, hydroxychloroquine 200 mg daily. Simple knee X-ray revealed bilateral OA with K–L grade 3. MRI revealed septated popliteal cysts with meniscal tear in both knees and joint fluid analysis of left knee showed white cell count 90 (PMN 28%). Despite intra-articular glucocorticoid injection into both knee joints, symptoms persisted. Arthroscopic cyst excision and partial medial meniscectomy were performed on both knees. After the operation, the patient is under observation for 12 months without recurrence.

Discussion

In the present study, four RA patients (six knees) in combination with OA having refractory popliteal cysts have successfully been treated with arthroscopic operation including cystectomy, synovectomy, and/or correction of valvular communication of cysts. All cases have been actively treated with DMARDs and/or biologics such as golimumab for RA, by which disease activity of RA except knees was relatively well controlled.

Popliteal cysts are generated by the communication of the bursas around the knee joint. During knee flexion and extension, a pressure difference occurs between the intra-articular and intracyst regions, leading to fluid collection as a check-valve mechanism [14]. Popliteal cyst is usually asymptomatic;

Table 2: Review of all nine articles from literature search.

References, country	Number of case	RA activity	Symptoms	Diagnostic image	Rupture of cyst	Treatment	Outcome
Jayson *et al.* UK [15]	7	NA	Painful swelling	Arthrogram	No	Anterior synovectomy	Resolution
Kirkham *et al.* UK [16]	2	Active	Painful swollen left shin	US, arthrogram	Yes	Open surgical drainage + steroid injection	Resolution
Kanekasu *et al.* Japan [17][a]	5	NA	Pain and swelling in the popliteal region	MRI	No	Arthroscopic synovectomy (4 cases), open cyst excision (1 case)	No recurrence in arthroscopic treatment, recurred in open cystectomy patient
Tanaka *et al.* Japan [18]	31	NA	Swelling, pain, and discomfort	NA	No	Arthroscopic synovectomy plus pedicle graft capsuloplasty	74% resolution, 23% mild symptoms, 3% swelling and tenderness after normal activities
Lee *et al.* Korea [19]	1	NA	Knee pain, posterior tibial neuropathy	US, MRI	No	Open surgical cystectomy	Pain resolution, numbness remained
Ushiyama *et al.* Japan [20]	1	NA	Leg pain, drop foot, ant compartment syndrome	CT, arthrogram	Yes	Emergency fasciotomy	Palsy remained
Mikashima *et al.* Japan [21]	8	Active	Painful swelling	MRI	No	Direct view cyst resection and/or arthroscopic synovectomy	1 recurrence in cystectomy, only
Ravlic-Gulan *et al.* Croatia [22]	1	Inactive	Swelling in popliteal fossa	US, MRI	No	Arthroscopic synovectomy, open cyst excision	Re-cystectomy Anterior synovectomy
Adiyeke *et al.* India [23]	1	Maybe inactive	Swelling in popliteal fossa	MRI	No	Arthroscopic cystectomy	Resolution

RA rheumatic arthritis, *NA* not applicable, *US* ultrasound, *MRI* magnetic resonance imaging, *CT* computed tomography
[a]Article in Japanese with only abstract available

however, posterior knee pain, knee stiffness, swelling, palpable mass, and discomfort can occur with the cyst alone.

RA is a type of autoimmune disease that causes chronic inflammation in the whole body, in which the synovium is the primary target particularly. As the synovitis becomes more severe, the tissues become friable and may be easily torn in cases of popliteal cyst. If the extra-articular leakage is small and chronic, the patient may only present symptoms of swelling and/or edema of the lower extremity. However, if the leakage is acute and large in amount, this may result in serious complications such as compartment syndrome [8–11]. In cases of popliteal cyst rupture, extravasation of degraded blood products and inflammatory synovial fluid may cause irritation and inflammation of the surrounding fascia, muscles, and subcutaneous tissues. Liao *et al.* [4] have reported that RA was the second most common disease that were associated with popliteal cyst (20.6%) following OA (50.6%), which was investigated by ultrasonography. However, they have also emphasized that cases of ruptured popliteal cyst were more frequent in the inflammatory diseases (66.7%) such as RA than the degenerative one (33.3%).

Although various conservative treatments for popliteal cysts with RA could be successfully, surgical interventions may be required for refractory or/and complicated cysts as presented in this report. Optimal RA disease activity control is crucial to prevent recurrence.

One of the important implications of this report is that prompt evaluation should be conducted when lower leg swelling or edema develops in RA patients, as shown in case 1. All four cases in the present report were postmenopausal females and all six knees were combined with OA changes such as K–L grade 2 or 3, and meniscal/ligament damage on MRI. Therefore, underlying pathophysiology of popliteal cysts in the cases might result from that of OA. However, unlike the cystic wall of popliteal cyst in patients with only OA pathology, the popliteal cyst wall in RA patients tends to be hypervascular and inflammatory, which can possibly make the walls friable, leading to leakage and rupture. With extension of pain and swelling to the lower leg especially with acute development, popliteal cystic wall leakage and subsequent rupture should be considered in this subgroup of RA patients.

Since popliteal cyst is most frequently associated with OA, many reports regarding to treatment options have been focused on OA, with relatively few reports related to RA. In our literature review (Table 2) [15–23], which included nine reports, surgical interventions such as open synovectomy/cystectomy, arthroscopic synovectomy/cystectomy and biomechanical valve excision have been reported with overall successful outcomes. However, Ushiyama *et al.* [20] reported a case who had neurologic complication even after emergency fasciotomy, emphasizing the importance of early detection and intervention of such complicated popliteal cyst rupture for preventions of life-long neurologic impairments.

In conclusion, arthroscopic intervention which allows the surgeons to perform radical debridement, synovectomy, biomechanical valve excision, and/or cystectomy in a delicate nature should be considered in patients with refractory and complicated popliteal cysts associated with RA or RA in combination with OA.

Author contributions: JHY performed the surgery. JHY and HSL devised the project and the main conceptual ideas. HHK, JKL, and SYB aided in the interpreting the results and worked on the manuscript. JHY and HHK wrote the paper with input from all authors. JHY and HSL critically revised the manuscript at all stages of its production, final approval of manuscript, and review of literature. All authors discussed the outline and commented on the manuscript.

Compliance with ethical standards

Conflict of interest: Authors; Jae-Hyuk Yang, Hyuk-Hee Kwon, Jin Kyu Lee, So Young Bang, and Hye-Soon Lee declare that they have no conflict of interest.

References available on request
Healthcare.India@springer.com

Source: Yang, JH., Kwon, HH., Lee, J.K. *et al. Rheumatol Int* (2019). https://doi.org/10.1007/s00296-019-04278-9.

...Cont'd from page 22

concomitant chronic disease such as diabetes mellitus is needed. Finally, there are no adequately powered and controlled clinical trials of any intervention for midfoot OA, despite the region being the most commonly affected foot site [7], with a prevalence higher than hip OA [1]. Thus, research on management strategies for midfoot OA are also urgently needed.

Conclusion

Foot and ankle OA is highly prevalent, especially in older populations. Surprisingly, however, there has been very little clinical research in to the impact and treatment of foot and ankle OA, and much of the existing literature is based on small samples and has a number of methodological limitations such as a lack of blinding and/or controls. Knowledge of how to manage foot and ankle OA is extrapolated largely from OA studies at other lower-limb sites. Generally, OA guidelines advise advice and education, exercise and weight loss, where appropriate, as first-line strategies [44]. Low-dose acetaminophen, topical NSAIDs or topical capsaicin may also be considered as an adjunct to first-line treatments or in the case of inadequate pain relief. If these approaches remain insufficient, then either an oral NSAID or COX-2 inhibitor may be substituted or added. Patients should be carefully monitored for symptomatic response and for any AEs, particularly the elderly and those with co-morbidities. There is limited evidence to suggest that HA injections may be useful for up to 6 months in people with ankle OA; however, evidence for other IA injections and in other foot joints is limited. Overall, further well-designed large RCTs are needed to provide evidence-based management options for this common and painful problem.

Compliance with Ethical Standards

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Conflict of Interest: Kade Paterson and Lucy Gates declare they have no conflicts of interest relating to the content of this article.

References available on request
Healthcare.India@springer.com

Source: Paterson, K.L. & Gates, L. Drugs Aging (2019) 36: 203. https://doi.org/10.1007/s40266-019-00639-y.

Mild Depression in Low Back Pain: the Interaction of Thought Suppression and Stress Plays a Role, Especially in Female Patients

Purpose: Mild depression has been shown as a precursor and as a consequence of low back pain, even in early phases of acute or subacute pain. Chronic daily life stress as well as dysfunctional pain-related cognitions such as thought suppression (TS) seem to play a role in the pain-depression cycle; however, the mechanisms of these associations are less understood. Experimentally induced TS, conceived as the attempt to directly suppress sensations such as pain, has been shown to paradoxically cause a delayed and non-volitional return of the suppressed thoughts and sensations and to increase affective distress. These dysfunctional processes are supposed to increase under high cognitive load, such as high stress.

Method: In the present cross-sectional study, we for the first time sought to examine a possible interaction between habitual TS and

stress on depression in $N = 177$ patients with subacute low back pain (SLBP), using the following questionnaires: Subscale Thought Suppression from Avoidance-Endurance Questionnaire, Beck Depression Inventory, and Kiel Interview of Subjective Situation. A three-way ANOVA was conducted with two groups of TS (high/low), stress (high/low) and sex as independent factors and depression as dependent.

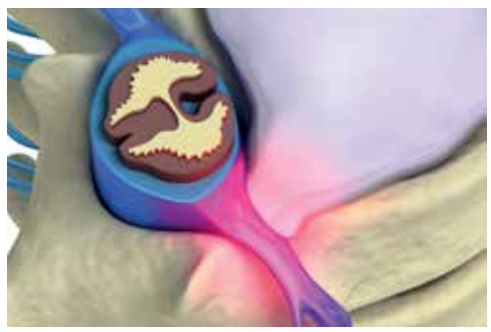
Results: Results indicated a significant three-way interaction with highest depression scores in female patients showing high TS and high stress. Overall main effects for sex and stress indicated higher depression in women and in highly stressed patients.

Conclusion: Our findings support the hypothesis that TS heightens depressive mood under conditions of high cognitive load especially in female patients with SLBP indicating a special vulnerability for depressive mood in women with SLBP.

Source: Konietzny, K., Chehadi, O., Streitlein-Böhme, I. *et al.* Int.J. Behav. Med. (2018) 25: 207. https://doi.org/10.1007/s12529-017-9657-0. © International Society of Behavioral Medicine 2017.

Post-Operative Nerve Injuries After Cervical Spine Surgery

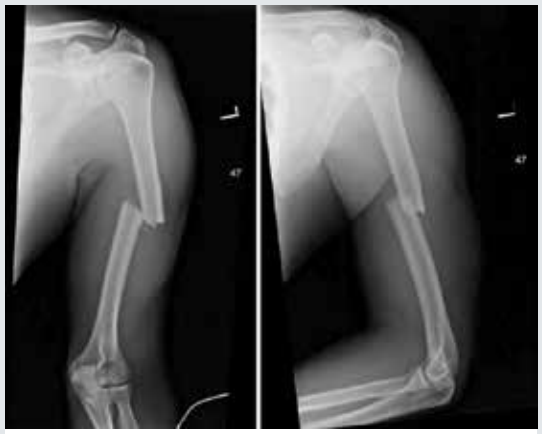
Although relatively rare, post-operative nerve injuries may occur after cervical spine procedures. The most common post-operative neural disorder is C5 nerve palsy. The risk factors for C5 nerve palsy are male gender, OPLL, and posterior cervical approaches. It generally presents with deltoid and/or biceps weakness, and may present immediately or several days after surgery. Treatment is generally conservative due to transient duration of symptoms, but evaluation of residual compression at C4–5 is essential. PTS (Parsonage-Turner syndrome) is an idiopathic plexopathy generally presenting with severe neuropathic pain in the shoulder, neck, and arms, followed by neurological deficits involving the upper brachial plexus. The deficits typically present in a delayed fashion after the onset of pain. Once residual nerve compression is ruled out, initial treatment is based on pain control and physical therapy. Post-operative C8-T1



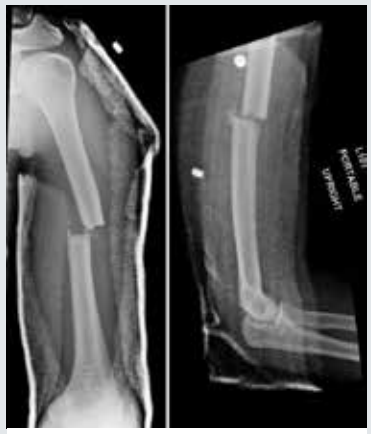
nerve palsies occur with weakness of the five intrinsic muscles of the hand innervated by the medial nerve, with sensory symptoms in the territory innervated by the ulnar nerve (ulnar two digits of the hand), and also the medial forearm. The risk factors for C8-T1 nerve injuries after surgery are C7 pedicle subtraction osteotomies and posterior fixation of the cervico-thoracic junction, especially in patients with preoperative C7-T1 stenosis. A wide foraminal decompression at C7-T1 region is necessary to minimize risk of this complication. Finally, Horner's syndrome can occur post-operatively, especially after anterolateral approaches to the middle and lower levels of the cervical spine. It is characterized by ipsilateral papillary miosis, facial anhydrosis, and ptosis secondary to injury of the cervical sympathetic nerves. Avoid using the cautery on the lateral border of the longus colli muscle, where the sympathetic chain lies and place the retractors properly underneath the muscle to decrease the chance of sympathetic injuries. It can also occur from iatrogenic compression or injury to the T1 nerve root, as the sympathetic chain gets some of its fibers from that level. Understanding the most common potential nerve injuries after cervical spine procedures is helpful in prevention, early diagnosis, and appropriate management.

Source: Joaquim, A.F., Makhni, M.C. & Riew, K.D. International Orthopaedics (SICOT) (2019) 43: 791. https://doi.org/10.1007/s00264-018-4257-4. © SICOT aisbl 2018.

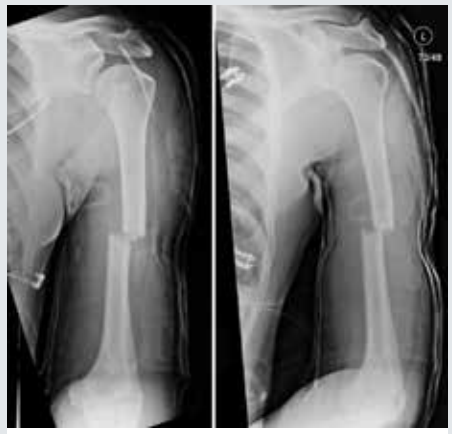
ISOLATED LEFT TRANSVERSE HUMERAL SHAFT FRACTURE



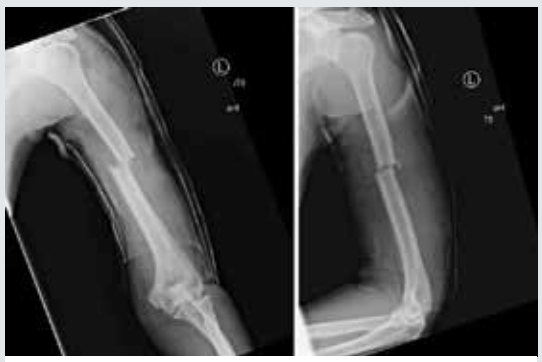
Injury radiographs of isolated left transverse humeral shaft fracture.



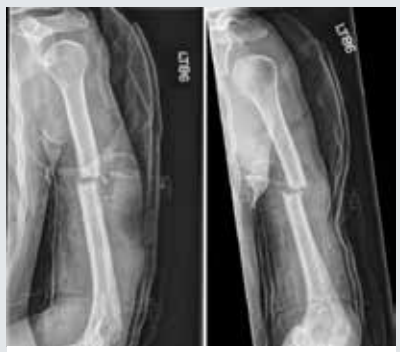
Splinting radiographs following reduction.



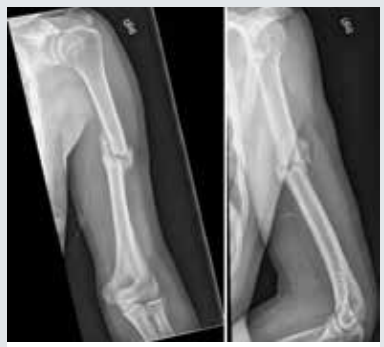
Radiographs following application of custom orthotic. Note mold at fracture site.



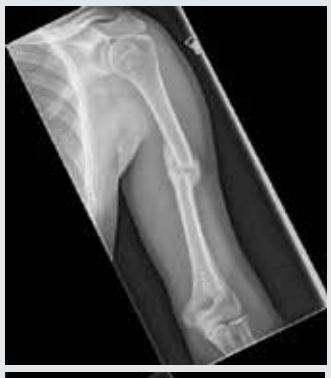
Follow-up radiographs 4 weeks from injury

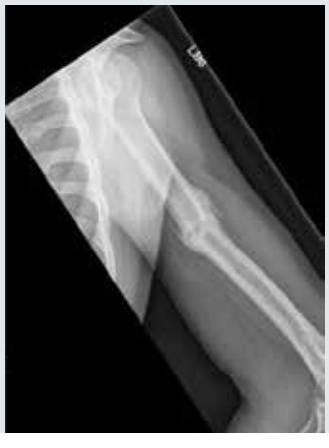


2-month follow-up radiographs. Note brace tendency to slip. Callus is present.



4 months from injury.

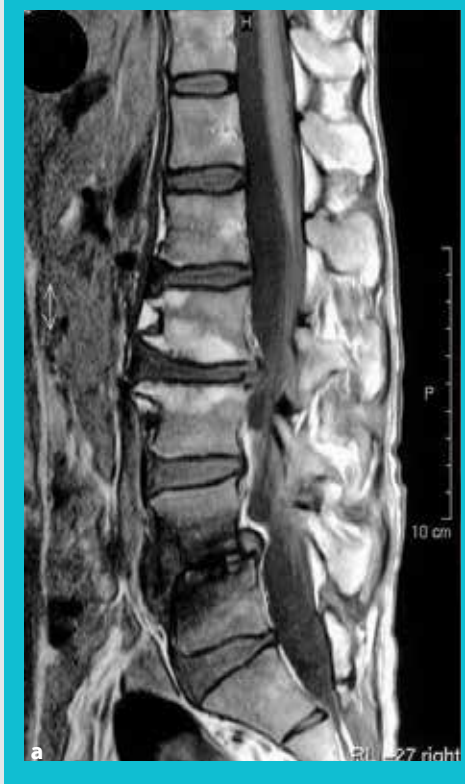


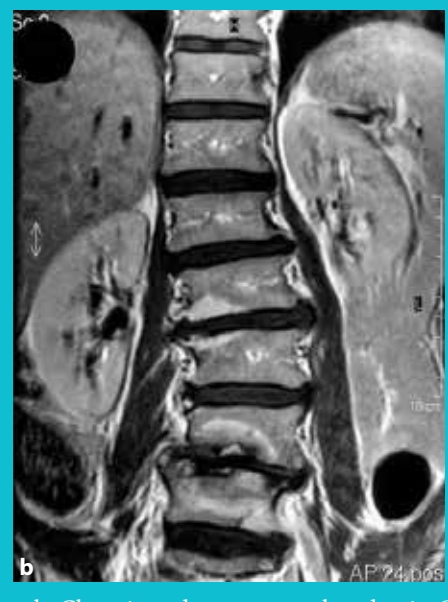


6 months from injury.

Source:Eglseder W.A. (2018) Humeral Fractures. In: Atlas of Upper Extremity Trauma. Springer, Cham. https://doi.org/10.1007/978-3-319-66857-4_10. © Springer International Publishing AG 2018.

CHRONIC AND ACUTE OSTEOCHONDROSIS

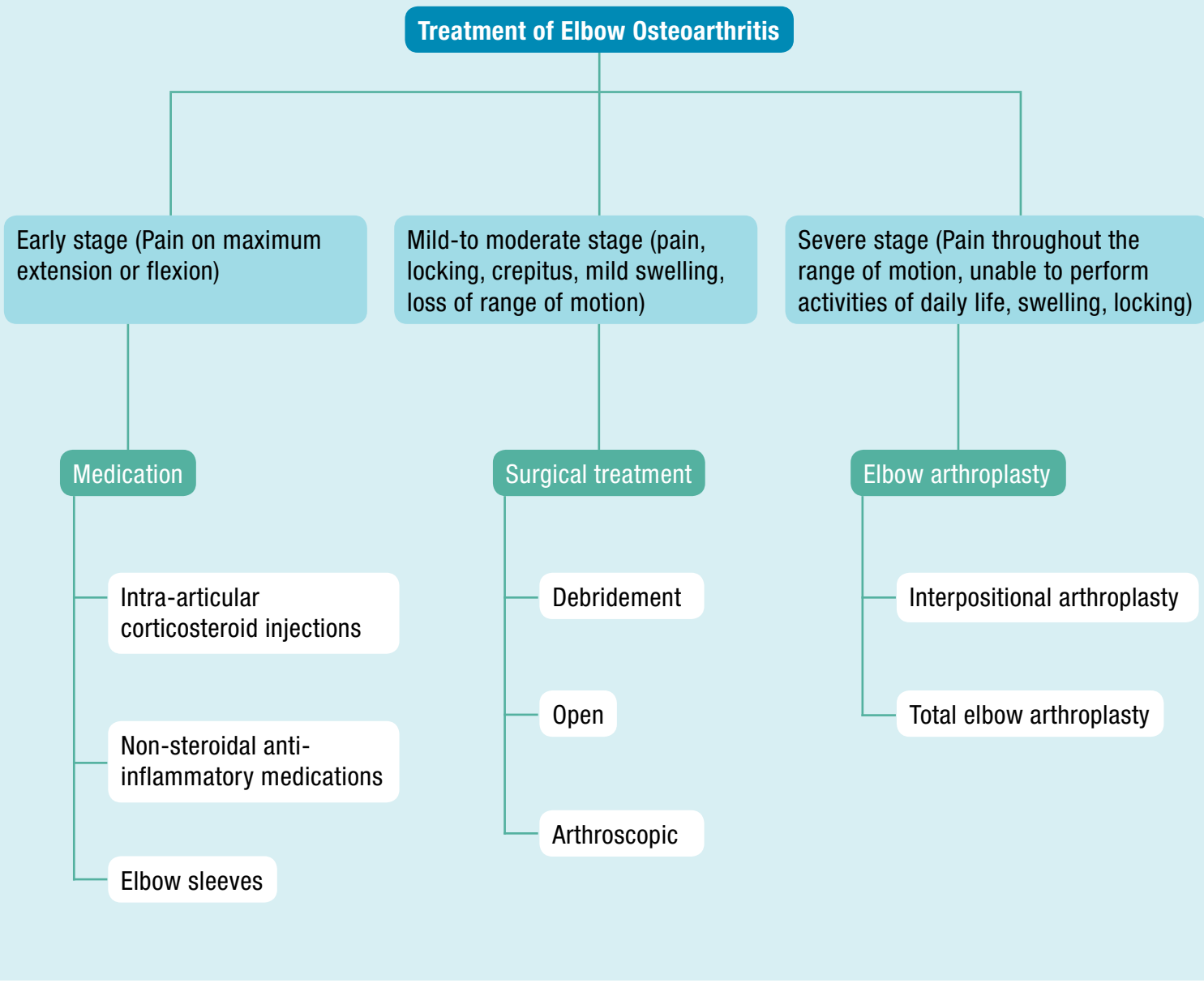




a, b. Chronic and acute osteochondrosis. Chronic osteochondrotic changes in the L2-3 segment are indicated by increased signal intensities in the anterior vertebral portion on T1-weighted image (**a**) and T2-weighted image (**b**). In contranst, acute osteochondrosis, seen here at the L4-5 level, is characterized by a decrease in signal intensity on T1 and an increase on T2.

Source: (2007) Degenerative Disorders. In: MRI Atlas Orthopedics and Neurosurgery The Spine. Springer, Berlin, Heidelberg. https://doi.org/10.1007/978-3-540-33534-4_4. © Springer-Verlag Berlin Heidelberg 2007.

TREATMENT OF ELBOW OSTEOARTHRITIS (DESCRIBING THE TREATMENT FOR EARLY, MILD, MODERATE AND SEVERE STAGE OF OSTEOARTHRITIS)



Source: Poonit, K., Zhou, X., Zhao, B. *et al. BMC Musculoskelet Disord* (2018) 19: 394. https://doi.org/10.1186/s12891-018-2318-x. © The Author(s). 2018.

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