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Difficulties in Defining a Clinical Score for Acute Flare-Ups in an Osteoarthritic Knee

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The basic idea of this editorial was to try to propose new techniques and laboratory measurements for future incorporation into a new score for identifying an acutely inflamed osteoarthritic knee joint. In the area of research, defining clinical status was always a hurdle to proper patient recruitment because working on quiet cases of OA with minimal to moderate pain is totally different from working on acute cases of OA with a lot of pain. Hence the problem of defining the clinical status at time of recruitment has become of an utmost importance. To achieve this goal we have navigated through all available methods and tests whether validated or still waiting for validation, to find the most suitable for a new sensitive score.

Osteoarthritis of the knee joint points to a clinical syndrome of joint pain associated with varying degrees of functional deterioration and lesser quality of life. It is the most prevalent form of arthritis, and one of the principal causes of pain and disability among the globe. A strong discrepancy has always been demonstrated between the level of radiological deterioration and clinical symptomatology. In other words minimal radiological changes can be associated with a lot of pain during flare-ups in contrast to a severe radiological deterioration with modest reduction in function and a modest level of pain [1].

Several scores and indexes have been created for OA serving many relevant points. A short description of the scores and indexes available will be done.

Lequesne's algo-functionnal index [2] has dealt with many points as nocturnal pain, walking ability, stiffness and some daily activities. The score gave special emphasis on the distance walked by the patients which is not accomplished by knee only as several body systems contribute to walking. The impression given to users was that the score deals with function more than it does with acuteness of symptoms. For example if the patient has severe nocturnal pain and stiffness but can walk, then the score gets down abrogating the element of pain, an important issue in acute flare-ups.

The American college of Rheumatology (ACR) radiologic and clinical criteria for knee osteoarthritis (OA) helped to diagnose a diseased degenerated joint, irrespective of the current level of inflammation, for this reason it did not help to define acute knee flare-ups [3].

As for Western Ontario and McMaster Universities (WOMAC) composite index, it incorporates the best detailing of pain among other scores and much more of the daily activities that we face every day. This score can be used more for following up patients in a longitudinal manner to detect ups and downs function wise rather than detecting a flare-up [4].

The first score dealing with knee flare-ups came when the KOFUS criteria was published six years ago. The score was constructed by assigning points to characteristics that were present, with a sway system based on the odds ratio for each characteristic for having a flare-up. Six features compose KOFUS score. Morning stiffness longer than 20 min: 0-1, nocturnal awakening: 0-2, effusion 0-2, limp 0-3, swelling 0-3 and warmth 0-3. Accordingly, the score could span from 0 to 14. The statistical receiver-operating characteristic curve demonstrated that 7 was the best cutoff for diagnosing a flare-up. However a patient may get more than 7 if having a joint swelling (3), effusion (2) and limping (3) and taking into consideration that those features may be present in a patient without or with minimal pain, the score can be of a limited value in picking up cases with acute flare-ups [5].

Updating criteria and scores is not an easy task but a rather mandatory one. The reason for that was the introduction of new methods for diagnosing joint diseases. Looking for such methods is not difficult however the easier the requirements' of the score, the more applicable it is. For this reason I will stay away from costly magnetic resonance imaging (MRI), and invasive methods such as biopsies and will try to discuss musculoskeletal ultrasonography (MSUS), simple blood tests and Phonoarthrography. The latter could have been used as a simple method needing only a microphone, software and a computer, calibrating sounds emerging from the knee joint on flexion and then extension. The problem is that the sounds emerging from the cartilage friction do not reflect the clinical status of the knee but rather the smoothness of degenerated surfaces [6].

In a useful work on using MSUS in acute osteoarthritis knees the authors concluded that MSUS remains the most useful tool for

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demonstrating synovial inflammation of the knee at the individual level [7] and in another work done on chronic OA knees the findings such as synovitis and effusion detected by MSUS, correlated positively with Kellgren-Lawrence grade and with clinical signs and symptoms suggestive of an inflammatory flare, such as joint effusion on clinical examination (OR=1.97 and 2.70 for synovitis and joint effusion, respectively) or sudden aggravation of knee pain (OR=1.77 for joint effusion). The authors stated clearly that MSUS can correlate positively with knee synovitis, effusion and clinical characteristics recommending an inflammatory flare [8], however we recommend another work also by MSUS to be carried on painful flared-up knees in order to validate the previous findings and maybe to define newer detections that may help in diagnosing a knee flare-up.

The cartilage and bone biochemical markers for cartilage degeneration, bone turnover or remodeling are not actually measured in the contemporary management of OA. Accordingly, no single marker is sufficient for predicting or monitoring OA in a single patient. In clinical trials and cohort studies, biomarkers are useful to clarify physiopathology of disease and to sustain a clinical state of the disease. Biomarkers can be related to different tissues forming the knee joint such as cartilage, bone and synovial membrane.

There is definitely an international urge to include a biomarker for the diagnosis of OA before any other typical change has occurred such as in radiology. There was an association between the quantitative level of CTX-II and scoring of MRI changes such as bone marrow lesions (BMLs) [9]. But again the idea of including MRI in a new score is still not welcomed due to cost and availability. The main limitation in including biomarkers in a new score is that we need to adjust to age, sex and body mass index, not to mention that they are not specific to a single joint. However they are very good predictors of progression as evidenced by the positive correlation of joint space narrowing with markers of degradation such as type I and II collagen [10]. Previously, Phonoarthrography was correlated to cartilage thickness measured by MSUS and biomarkers namely MMP-3 and TIMP. The results demonstrated that the lesser cartilage thickness, the higher phonoarthrographic values and higher MMP-3 values until grade 4, where it fell unexpectedly. This may be explained by the altered behavior of aging chondrocytes and synoviocytes responsible for the production of MMP-3 [11]. And because the previous work was done on chronic knees, another one was constructed by the same authors to measure biomarkers in acute knee flare-ups and found that IL-1 and mmp-3 were significantly higher (p 0.001) during flare-ups when compared to levels in remission [12] however these findings need further validation by other works.

In summary, all objectives used before in the different scores are still valid and logical and are used by many researchers to define their cohorts of patients. However, we must think of updating these scores by infusing new techniques and laboratory analysis to serve for the idea of evaluating an acutely inflamed osteoarthritic knee. The recommendation to use new technique such as MSUS and biomarkers are strongly suggestive to be incorporated into the body of a new score with the clinical exam.

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