

A pain in the knee – is it osteoarthritis?

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Old wisdom tells us that a careful history combined with an experienced clinical examination gives a correct diagnosis in the vast majority of cases. This needs to be remembered in this age of overuse of CT scans, MRI and other advanced technologies. This also applies to the diagnosis of knee joint osteoarthritis (KOA). But whereas it is easy to recognize advanced KOA, the diagnosis is not straight forward in incipient or early cases. And yet it is at this stage of development that intervention could be most helpful. An ambitious report in this issue (1), using only clinical and not laboratory or imaging methods, has explored a representative selection of the Spanish population to assess point prevalence of KOA. The investigators used validated questionnaires and interviews and clinical examination were performed by trained physicians. The simple design was chosen more for pragmatic than scientific reasons, since much of the work took place in rural health centres without access to radiology. The findings therefore must be considered with some caution, although on the whole confirming evidence from other population based studies. The main message is that KOA has a much higher prevalence in Spain than could have been extrapolated from the literature although this was largely due to elderly women suffering from overweight.

The authors rightly argue that symptoms are more representative of the burden of disease than objective findings. They use validated questionnaires, history taking and physical examination to identify probable cases of KOA. They also rely on the ACR clinical criteria published in 1986 (2). Can we trust their conclusions? One caveat which comes to mind is that several non-articular conditions are present in individuals complaining of knee pain. One study identifies some of them in no less than one third of old individuals (3). Widespread pain, referred pain from hip OA, bursitis, and low back pain with index leg referral were dominating causes. This evidence should be borne in mind when reading the Fernandez-Lopes paper.

The difficult early recognition of KOA

The last decades have witnessed a major breakthrough in the treatment of rheumatoid arthritis, pelvispondylitis and psoriatic arthropathy, based on more aggressive use of DMARDs such as methotrexate and the advent a number of targeted biological treatments. No similar development has been seen in the treatment of osteoarthritis (OA), although its prevalence is some 10 times higher. Better insight into its pathogenetic features have however been accomplished. Molecular mechanisms clarifying bone and cartilage biology and their dysfunction in OA have identified the importance of specific proteases, cytokines and transcription factors as well as putative roles of fragments from matrix components and crystals (4). A number of well recognised risk factors have been firmly defined, such as trauma, occupational overuse, sport injuries, joint laxity, overweight, and smoking. A minority of cases occur in families with monogenic defects. A growing number of minor susceptibility genes are being identified, one recent example is a polymorphism in the asporin gene (5). In population-based studies one therefore will encounter a mix of aetiologies, but the majority of cases will nevertheless be “primary”. The difficulty, as already mentioned, is to identify them in the very early stage of development and it is not surprising that only few such studies have been undertaken.

The Swedish Spenshult Cohort study, initiated some 15 years ago, identified knee pain lasting three or more months among 15% of individuals aged 35-45 in a community based on a questionnaire sent to a representative selection of the whole age groups. Two hundred and four of the identified 279 individuals accepted participation in a prospective still ongoing study. Initially, only some 10% had radiographic signs of OA according to the Lawrence-Kellgren definition (7). After 5 years this figure had risen to about 25%. At the ongoing 12-year follow-up, this figure is still only 56%. And yet knee pain had persisted in virtually all cases. Thus, chronic knee pain is very common

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even in not so old adults in a population in which the median BMI was 26, compared to 24 in the general population. This is evidence that chronic knee pain may often but not always signal KOA. In epidemiologic work it is thus important to distinguish KOA pain from other sources of pain

The distinguishing features of KOA signs and symptoms

The Spanish study based their diagnoses on the clinical criteria as defined by the American college of Rheumatology (9). These do not specify the quality or localisation of pain. Also these criteria include absence of inflammation, but it is now well recognised that low grade inflammation is present in the earliest phase of developing KOA (6, 10). Can a better analysis of the type of pain be more helpful? One study of 68 US patients found generalized knee pain in 35 and medially localized pain in 23 of these patients who all had well established disease (11). A more recent UK paper examined almost 700 elderly, 230 of which had KOA. In symptomatic patients with radiological OA the medial joint line and the infra-patellar region were the dominant sites affected in 70% of patients whereas the pes anserinus tenderness was present in 13%. All these signs however highly correlated with symptomatic KOA in contrast to peripatellar or lateral pain (12). Symptomatic KOA was distinctly more common in patients with medial and distally radiating pain. The mean BMI in the KOA patients was 31, only slightly higher than among the non-KOA individuals. Although no pathognomonic patterns were identified, this study to me illustrates that careful clinical examination is still a powerful diagnostic tool.

The source of KOA pain: the role of inflammation

Although cartilage pathology is a prominent feature of KOA this tissue does not contain nerves and cannot be the source of pain. A seminal paper published in 1991 (13) used MRI and scintigraphy and identified the presence of inflammation in several cases of KOA. Subchondral bone, joint capsule, tendon

insertions and synovialis all are possible sources of inflammation. Inflammation occurs early in the development as indicated *e.g.*, by elevated serum CRP in patients with knee pain who later develop full-blown KOA (6, 11). Histological examination confirms the presence of inflammation and angiogenesis in early KOA (14). Furthermore, *in vitro* studies show increased synthesis of inflammatory cytokines TNF- α and IL1 β and prostaglandin E2 in early disease stages (15). Episodes of joint effusion are not uncommon in KOA and intra-articular administration of glucocorticoids is effective in such patients although the effect is transient (16). Absence of inflammation as a diagnostic criterion for KOA as included by the ACR may therefore be misleading and actually exclude cases of KOA.

The differential diagnoses

The validation of the 1986 clinical criteria alone for a confirmed diagnosis of KOA rests on one single paper and this identified 6 patients in which arthroscopic evidence confirmed the diagnosis (17). This study involved patients with established KOA only and as the authors of the study point out a larger study is needed to assess the validity of the ACR clinical criteria. Most prevalence studies indicate that only about 50% of individuals with radiographic KOA suffer from chronic knee pain, but the relevant question addressed by the Spanish investigators is the prevalence of disabling knee pain. Among the 300 patients between 200 and 100 had any of the 6 clinical criteria. What one does not know is which combination of criteria and how many criteria individual patients exposed. Signs of inflammation and morning stiffness for more than 30 minutes in my opinion do not exclude KOA, neither does their absence necessarily support the diagnosis.

The Spanish study does not supply information on other causes of knee symptoms and these were excluded. In a recent UK study of knee pain in 745 patients over the age of 50, 273 or one third had non-articular conditions accounting for or accompanying knee pain. Widespread pain and low back pain were the most common occurring

in 159 and 102 patients respectively (3). Similar non-articular conditions could be present among the Spanish patients and be major contributors to the disability. Co-morbidity is common in elderly people and often makes it hard to ascribe disability to one single cause.

The impact of KOA – today and tomorrow

The impressive Spanish study suggests the presence of symptomatic KOA in one third of elderly women. This should correspond to perhaps two thirds of this population showing radiographic OA, and even if the figures may be exaggerated, the condition is definitely very common and often disabling. Demographic developments with increasing prevalence of elderly individuals with high BMI predict that the prevalence and impact on health care services of the community are growing. Total joint replacement remains the only truly effective therapy, but treatment, or better, prevention of obesity can be surprisingly helpful (18). Pending better understanding of the molecular pathogenesis of KOA and effective targeted pharmacotherapy, life style changes need to be implemented to reverse this trend of increasing prevalence of KOA.

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