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Review Article

When is the Osteoarthritis Label Inappropriate: Clarification of Diagnosis and Responsibility for Clinical Significance

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Abstract

Osteoarthritis is the name given not only to a common disease but also erroneously to other phenomena. While well-defined clinically, application of the term in the anthropologic literature is misleading because of use of speculative, actually erroneous criteria. The term erosive osteoarthritis is also problematic. It describes a disorder that is not responsive to standard treatments for osteoarthritis, but does respond to those utilized for calcium pyrophosphate deposition disease, suggesting that as the more appropriate diagnosis. Vertebral osteoarthritis (exclusive of the zygapophyseal joints) is also a misnomer. Not only do osteophytes on vertebral centra not represent an arthritis (as no diarthrodial joint is involved), but they are actually asymptomatic. Other misconceptions relate to association of osteoarthritis and weight, more likely related to joint instability and ambulation on artificial surfaces. Perhaps the best natural animal model for osteoarthritis is avian, a subject worthy of future attention.

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- Intraarticular corticosteroids

INTRODUCTION

Criteria for recognition of osteoarthritis

As the most common form of human arthritis, it might be thought that osteoarthritis would be quite amenable to epidemiologic study. While a popular subject of study, interpretation of the data and comparison of different study populations are often "mystifying." The name itself has been problematic. Previous names applied to osteoarthritis (with varying degrees of specificity) include arthritis deformans, degenerative joint disease, gonarthroses, hypertrophic arthritis, osteoarthritis deformans, and osteoarthroses [1]. The most common term had been degenerative joint disease, although the current term in vogue is osteoarthritis.

Any discussion of osteoarthritis is predicated upon its definition and that of the criteria utilized in its diagnosis [2-6]. Just as it takes a community to raise a child, it took a committee to identify and validate clinical criteria for recognition of osteoarthritis [2-4]. Criteria established for hands, knees and hips seem as applicable to other joints. While diarthrodial joint osteophytes are pathognomonic for osteoarthritis, equipment generally utilized for clinical radiology will not allow detection of osteophytes less than 1 mm in size. Thus, clinical recognition of osteoarthritis often requires dependence on additional criteria.

Santayana suggests that lack of familiarity with history results in repetition (of errors and erroneous thinking) [7]. Ergo, tracking osteoarthritis through human history has merit. The question is how? Similar to the developmental process for creating criteria applicable in the clinical setting, the anthropological community's approach also speculated as to criteria [8-10], but unfortunately left out a very important step [6,11,12]. They failed to validate the criteria they developed. Some of the criteria (e.g., porosity) have no clinical or medical correlate, and when actually critically reviewed [6,12,13], were falsified.

A major problem compromising anthropologic diagnosis seems to relate to establishment of criteria through circular reasoning. Waldron's [9] article on prevalence of osteoarthritis is exemplary of this genre. He quotes himself, from a postulated set of untested criteria, and then makes the claim that "presence of at least two"..."is required before the condition can be classified." His untested criteria are "eburnation, new bone formation around the joint margins or on the surface of the joint, pitting on the joint surface, scoring on the joint surface, and deformation of the normal contour of the joint." Pitting (porosity) has no

correlation in clinical practice. It is not visualized on x-ray. When critically examined in knees, there was no correlation of porosity (pitting) with the documented unequivocal sign of osteoarthritis (diarthrodial joint osteophytes). Since he states that certain joints met his criteria (while failing to provide original data), the results of the study seem totally uninterpretable. Further grouping osteophytes (vertebral and peripheral joint osteophytes) [9] does not appear to produce useful information. Bridges' [8] study, unfortunately also include porosity, but appropriately limit the other criteria to lipping (osteophytes) and eburnation. Reanalysis of that data set, deleting the data on porosity should prove useful in distinguishing patterns in hunger-gatherers and agriculturalists. One challenge in interpreting Bridges' study [8] is that she sampled the population. Given the vagaries of cemetery burial practices, biases cannot be excluded if examination is limited to portions of the population, rather than the entire population.

Observation of diarthrodial joint osteophytes is sufficient for making a diagnosis of osteoarthritis [11,14]. Severe damage destroys the cartilage, resulting in "bone rubbing on bone." The resulting "wear" effect is recognized as grooving and eburnation.

The latter reflects the polishing of osseous articular surfaces when total loss of intervening cartilage results in bone rubbing on bone. That criterion misses all but the most severe joint damage. More importantly, it is a non-diagnostic sign [5,6,14], the result of severe arthritis of any derivation (e.g., rheumatoid arthritis, spondyloarthropathy, calcium pyrophosphate deposition disease, neuropathic arthritis).

Derivation of osteoarthritis and its interpretation

Osteoarthritis, itself, can be divided into two varieties: primary, and secondary. Primary osteoarthritis is a disorder of bony enlargement of the distal two finger joints (as well as other areas of the peripheral skeleton) that tends to run in families. As hand involvement (first metacarpal trapezium excepted) is not significantly affected by treatment and may not be a significant source of patient disability, it is often ignored. Most osteoarthritis-related morbidity is related to secondary varieties. The term secondary identifies osteoarthritis complicating inflammatory, metabolic, and endocrine diseases and conditions causing mechanical disadvantage (to the joint). Malalignment, ligamentous abnormalities, and alterations or abuse related to overuse are typically responsible for the latter. Normal healthy joints are somewhat resistant to development of arthritis, in the absence of factors that overwhelm the normal protective mechanisms. This resistance is partially related to an alignment that is mechanically optimal. Any deviation from the normal alignment places the patient at risk for the development of arthritis. Alterations in the normal angle between the femoral shaft and the femoral neck (coxa vera or valgus, often secondary to slippage of the femoral epiphyses), produce alignment disorders, predisposing to osteoarthritis.

Anything that results in loss of normal joint constraints (e.g., ligamentous laxity), or use of a joint in a manner other than or to an extent greater than that for which it was designed, creates the opportunity for development of osteoarthritis. Altered perception of or response to pain often results in the development of osteoarthritis, whether the individual simply be stoic or fail to protect abnormal joints from abuse. Neuropathies predispose to development of arthritis by interfering with pain sensation and with normal protective mechanisms that limit excessive shear and compressive forces.

Any alteration in cartilage or bone that alters its ability to withstand shocks or handle loading predisposes to osteoarthritis. Growth hormone overproduction (acromegaly), hyperadrenalism, and Paget's disease are frequently associated with osteoarthritis.

The cartilage damage in osteoarthritis has sometimes been referred to as erosive, causing great semantic confusion. Destructive might be a better term, since the word "erosion" has caused so much confusion. There are no bone erosions in osteoarthritis [6,11,14,15], although subchondral cysts have at times mistakenly been called erosions. Presence of bone erosion infers an alternative diagnose.

Challenges to population comparisons

Study of joints at autopsy, study of clinically symptomatic joints and radiologic surveys reveal quite different information that is not directly comparable. Studies of clinic outpatients, hospitalized patients and general population surveys (with variable participation) reveal very different information [16-21].

Studies suggesting decreased osteoarthritis in Alaskan Eskimos are misleading [22], as only hand x-rays were examined. A critical factor affecting population comparisons is age. Osteoarthritis is a phenomenon of aging [6,11,14,23]. Thus the age determination is critical. Use of different aging techniques will result in very different ages and variance in patterns and frequencies across anthropologic populations [24].

One of the challenges to comparison of contemporary observations to those of antiquity is age-compression of data. Bridges [8], for example, groups individuals to thirty or over and to between ages 30 and 49, whereas most contemporary studies report older individuals. The proportion of individuals in each decade of course impacts the percentages. Thus it might perhaps be appropriate to provide specific age-related findings. Relationship of osteoarthritis to age was, however, independent of socioeconomic status in the United States and Great Britain [25].

Challenges to assessment of severity

The severity of osteoarthritis is determined by the amount of cartilage loss (recognized as joint space narrowing) and by degree of subchondral sclerosis (recognized on defleshed joint surfaces as grooving or eburnation). While the latter may be amenable to assessment in defleshed skeletons (by x-ray), the former is not. As eburnation appears to reflect the most severe osteoarthritis (and is relatively rare in humans) defining severity of joint involvement may not be an achievable goal in skeletal studies.

Impact is more difficult to assess. There is a disconnect between severity of bone damage and morbidity. While 2.3% of working British men and 1.3% of women retired because of osteoarthritis [26] and five percent of individuals 55-64 cannot

work for at least three months because of osteoarthritis, the issue is actually more complex, because only a fraction of radio logically-detectable osteoarthritis is symptomatic [27]. Only nine percent of men and 25% of women with moderate to severe osteoarthritis (by x-ray) of distal interphalangeal joints, had symptoms [27], contrasted with 56% and 80% of men and women (respectively) for the knee. Twenty-eight percent of moderate and 57% of severe (radiologically recognized) hip osteoarthritis was symptomatic [25]. There is also no linear relationship between structural changes and functional limitations [28]. It is unknown why some individuals with osteoarthritis have pain and others do not. Should asymptomatic individuals be considered as actually having a different disease? What is categorized as osteoarthritis may actually not be one disorder. It could be a variety of disorders with the observed form of joint damage representing the "final common pathway" [29].

Neuropathic arthropathy

Among the phenomena that can mimic osteoarthritis is neuropathic arthritis. The latter is critical to recognize as its implications and management are very different from those of osteoarthritis. Application of osteoarthritis therapeutic approaches to neuropathic arthritis actually increases morbidity [30]. Observation of exaggerated osteoarthritis-like changes should prompt workup for neuropathic disease and its causes. Accompaniment of osteoarthritis-like changes by other evidence of joint destruction suggests a diagnosis other than osteoarthritis: Neuropathic arthropathy or an unusual form of trauma or joint use. When the small joints of the fingers are affected, calcium pyrophosphate deposition disease must also be considered [6,31,32].

Inflammation in osteoarthritis?

Analysis of osteoarthritis in the anthropology literature is complicated by previous misconceptions, including lumping a variety of forms of joint pathology as osteoarthritis. The term itself, is somewhat of a misnomer. While a non-inflammatory disease of diarthrodial joints, the "itis" in osteoarthritis has long been a source of confusion. Inflammation does not appear to be a primary component of osteoarthritis [6,11,14,23], but appears to be a secondary phenomenon. Occurrence of inflammation in individuals with osteoarthritis appears to represent the complication of crystalline shedding. The latter releases hydroxyapatite and calcium pyrophosphate (pseudogout) crystals [33-36].

Osteoarthritis involvement of the proximal and distal interphalangeal joints of the hands appears to be a commonly inherited phenomenon, but how pathologic is it? Most afflicted individuals express concerns related to potential morbidity or cosmetic appearance. As interventions actually aggravate or create morbidity and don't alter the natural history, it is unclear if osteoarthritis of the fingers (in the absence of pain) requires any more intervention than patient reassurance. However a major caveat must be considered: Inflammatory disease of proximal and distal interphalangeal joints is not osteoarthritis. Presence of redness or warmth of those joints indicates an inflammatory process. Any disruption of articular surfaces (other than by osteophytes) falsifies a diagnosis of osteoarthritis. It is either another process or related to a complication – crystal-shedding producing pseudogout (calcium pyrophosphate deposition disease) [5,6,31,37].

Erosive osteoarthritis versus calcium pyrophosphate deposition disease

That brings us to the subject of the phenomenon referred to as "erosive osteoarthritis." Clinical signs of joint tenderness, swelling, redness, heat or warmth and angulation are typically associated with evidence of abnormal articular surfaces. The associated erosions (which stimulated the appellation erosive osteoarthritis) differ from those of rheumatoid arthritis and spondyloarthropathy [6,31,32]. Their edges have an ill-defined appearance, which has been referred to as crumbling [6,32]. There may be adjacent calcific flecks. This phenomena is characteristic of calcium pyrophosphate deposition disease [6,14,31,32]. This crystalline arthritis is very different from osteoarthritis and has unique therapeutic responsiveness to agents not effective in management of osteoarthritis [37]. Calcium pyrophosphate deposition disease can mimic osteoarthritis. It is also responsible for occurrence of "osteoarthritis" in atypical locations.

Vertebral osteophytes and spondylosis deformans

Among the many sources of myths associated with osteoarthritis are vertebral osteophytes, which have been mislabeled vertebral osteoarthritis [10,24]. These projections from the endplates of vertebral centra have the radiological appearance of osteophytic overgrowths perpendicular to the long axis of the vertebral column. Osteoarthritis is a disorder affecting diarthrodial joints. Diarthrodial defines a joint occurring at the juncture of two bones at which movement occurs (and lined by a synovial membrane). Thus the term arthritis is inappropriate, and the term osteoarthritis, doubly so. Osteophytic vertebral overgrowths must be distinguished from osseous overgrowths that bridge disk spaces through the anulus fibrosus, parallel to the long axis of the vertebral column. These paralleling bony overgrowths are referred to as syndesmophytes [6,14]. While such bridging has at times been erroneously referred to as stage IV osteoarthritis [10], they are the result of a totally unrelated process. Presence of such vertebral bridging (syndesmophytes) identifies the category of arthritis referred to as spondyloarthropathy (e.g., ankylosing spondylitis, the arthritis related to the skin disease, psoriasis) [6,14].

Spondyloarthropathy is an inflammatory arthritis with significant morbidity [6,14], in contrast to "vertebral osteoarthritis" which is actually asymptomatic and appears to predominantly be a manifesting of aging [38-42]. Recognition of its asymptomatic nature has led to its current appellation, spondylosis deformans [14,43].

Just as osteophytes in osteoarthritis are not a measure of severity of disease, but only a sign that allows its recognition, vertebral spurs only identify a clinically irrelevant finding. Two exceptions to that generalization must be remembered.

1. An osteophytes can rarely compress a nerve.

2. Disappearance of a vertebral osteophyte should stimulate for presence of an aneurysm, the pulsations of which have produced a pressure erosion of the bones.

How did the myth of vertebral osteophyte-derived back pain originate? Musculoskeletal education is quite limited in both undergraduate and graduate medical education [44,45]. If musculoskeletal complaints are responsible for 30% of visits to primary care physicians, it is astonishing that this subject has received so little curriculum time. The product of medical education (the physician) has little guidance as to developing a response to patient complains of back pain, so much so that Osler is reputed to have attributed back door requirements for physician's offices. That allowed the physician to escape having to deal with a problem for which he/she was unprepared. Conscientious physicians took the approach characteristic of those lacking sufficient clinical acumen to assess a set of symptoms and signs, relying on technology. They obtained x-rays of the vertebral column. Anything outside their perspective of normal or of normal variation was perceived as pathology, with attribution as the source of that patient's complaint. Thus the innocent vertebral osteophyte was blamed and patient was provided with a diagnosis, if not actually any information that resolved the back pain. When x-rays, obtained for workup unrelated to back pain, revealed the same osteophytes, suspicion arose that perhaps vertebral osteophytes were not the cause of back pain. Subsequent studies revealed that vertebral osteophytes were no more common among individuals with back pain than in healthy individuals not so affected [38-42].

Zygapophyseal joint arthritis

The above comments relate to osteophytes affecting vertebral centra. There is another variety of vertebral osteophyte, that affecting zygapophyseal (facet) joints. A pathogenic role for these has been suggested. Clinically, attribution of back pain to zygapophyseal joint osteoarthritis is suggested by augmentation of pain by back hyperextension. Relief of pain by injection of zygapophyseal joints with anesthetic and corticosteroids would appear to support that consideration among patients in whom the injections were effective. However, accepting that conclusion requires verification that the injection actually entered the zygapophyseal joint and that the injected corticosteroid effect was local, not a systemic response. Water-soluble steroids (e.g., dexamethasone) injected into joints quickly disseminate systemically. Only results from verified zygapophyseal joint injection of a depot steroid (e.g., the water-insoluble triamcinolone) would confirm the responsibility of zygapophyseal osteoarthritis for that patient's pain.

Joint stability

Preconceived notions of association or correlation have also compromised care of individuals with osteoarthritis. Radiological evidence of severity has been confused with clinical significance. Loss of cartilage is a significant pathology, and a measure of severity [14], but not necessarily a direct cause of clinical symptoms. Loss of cartilage results in closer apposition of articular osseous components, resulting in a laxity of normal ligamentous structures. As afflicted individuals ambulate, tissue is apparently caught between the articular surfaces, resulting in pain. Additionally, joint instability results with associated joint malposition, often producing chondromalacia patellae, also referred to as patello-femoral osteoarthritis. The latter term is unfortunate as it misdirects attention away from a simple intervention. A quadriceps muscle strengthening exercise program restores joint mechanics and usually relieves related symptoms. Recognition of joint instability only on the basis of testing for meniscal and cruciate ligament testing misses ligamentous laxity, a common cause of knee pain. The latter is very responsive to a simple quadriceps muscle strengthening exercise program, although lifetime compliance is required.

Osteoarthritis as a product of environmental exposure

Assumptions of relationship to activity may derive, but a great deal of osteoarthritis appears directly attributable to joint instability [6,11]. Thus osteoarthritis may possibly reflect function, but does not indicate activity limitation. The issue is even more complex, as only a fraction of radiologically detectable osteoarthritis is symptomatic.

Correlation is sometimes mistaken for causality. The relationship of obesity to osteoarthritis of weight-bearing joints is an example. If joint instability is a major component of the symptoms associated with osteoarthritis, obesity of course aggravates the mechanical disadvantage of instability (simple lever effect). Examination of the zoological record provides additional insights. Osteoarthritis is extremely rare in the wild, but is common in captive mammals, whether they be in zoos or preserves [46-48]. Removal of rhesus macaques from the wild to their own personal (and exclusive) island was associated with an increase in frequency of osteoarthritis from less than 1% to 18% [49]. The difference is attributed to island life, related to availability of only one level of canopy, rather than the two or three found in their natural environment. They spend more time on the ground, as hurricanes have eliminated the upper levels of canopy. Thus, exposure to "unnatural" environments seems responsible.

Misunderstanding relationship between osteoarthritis and weight

While obesity has been considered a contributing factor to development of osteoarthritis in humans [50-55] the effect may actually be indirect. Joint instability appears to be the actual culprit [56-60]. Examination of osteoarthritis in birds provides a unique perspective [61,62]. Contrary observations in mammals, osteoarthritis in birds occurred at equal frequency in captive birds as those found in the wild [61,62]. The knee is the prototype of osteoarthritis in humans; the ankle, in birds [63]. Seemingly dissimilar joints, examination of the anatomy reveals that the bird ankle is analogous in morphology to the human knee [63]. The bicondylar distal tibiotarsus (bird ankle) seems indistinguishable from the human distal femur, including asymmetry of condylar size, produce geocentric, rather than hinge joints. Osteoarthritis is common in some species of birds (up to 25% in some species (e.g., Cooper's hawk *Accipiter cooperii*)), but inversely related to weight [62]. The suggestion is that weight is not the primary factor. The role of joint instability is suspected.

Logically, the load that a joint must bear seems important. Normal gait concentrates the body weight on a small fulcrum. The force transmitted across any fulcrum is dependent not only

on the actual weight of the object on the balancing arm (lever) but also on the length of the balancing arm, and the angle from which it deviates from the vertical. During normal gait, the hip is subjected to forces equivalent to six times the body weight. The effect of excess weight is therefore magnified six fold in its impact on the hip. While portage of excessively heavy materials may adversely affect joints, the technique is probably more important. Poor technique in task performance predisposes to secondary osteoarthritis.

SUMMARY

Osteoarthritis has a long history of semantic confusion. Historical recognition has been compromised by use of speculative criteria, most of which have been falsified. Primary osteoarthritis is predominantly mechanical in origin, especially related to joint instability and malalignment and is a natural component of normal aging. There is a disconnect between extent of structural damage, pain and morbidity, with individuals with total loss of cartilage often asymptomatic. It is unclear if inflammation is an inherent component of osteoarthritis or actually occurs because of mechanical damage, as a complication of crystalline arthritis. So-called erosive osteoarthritis seems to be more a manifestation of calcium pyrophosphate deposition disease than actually of osteoarthritis and requires a specific treatment approach. Vertebral centra osteophytes are a separate manifestation, again a manifestation of aging and not of the disease known as osteoarthritis, in contrast to zygapophyseal disease which has a very specific clinical picture. Joint stability is the major function aggravated by excess weight in humans. It is unclear that osteoarthritis would develop in overweight individuals if joint stability were preserved. We are reminded to treat the patient and not the x-ray appearance and of the value of being perspicuity in diagnosing primary osteoarthritis and distinguishing it from other diseases and normal aging.

FUTURE OPTIONS

Future productive research on osteoarthritis will be facilitated by attention to definitions/classification. Animal models are interesting, but most mimic a surgical condition (e.g., cruciate ligament rupture). The effect of unnatural or artificial environments appears to be a fruitful area for future research on mammals. Birds seem an extraordinary model for deciphering the pathophysiology of the disease.

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