Relationship Between Symptoms and Structural Change in Osteoarthritis. What Are the Important Targets for Osteoarthritis Therapy?

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As Eric Radin observes elsewhere in these proceedings[1], osteoarthritis (OA) is a mechanical disease. If biomechanics drives this disease, why are we working on chondroprotective drugs, tissue engineering, cartilage transplantation, and things like that? If we do not correct the biomechanics are we not just going to bust up the whole thing a second time around? Brandt and others have reminded us repeatedly over the last few years that OA is not a disease of cartilage, but involves the whole joint. OA is about bone, synovium, and capsule as much as if not more than it is about cartilage. I belong to the camp of those who think the bone is "the real McCoy," but what Brandt and his colleagues have recently emphasized is that there are 2 other bits that may be even more important than cartilage, bones, synovium, and capsule — i.e., muscle and neuromuscular control[2].

In addition to the concept that OA is a disease defined by the radiograph, there is an illness that we generally regard as being characterized by pain, and there are rather different statistics for the population prevalence of these 2 things (Figure 1). You'll notice they don't overlap terribly well. This is highlighted in terms of epidemiology elsewhere in these proceedings by David Felson[3] and Mark Hochberg[4].

The problem is that because we have been brought up to believe in diseases, we try to shoehorn the illness of OA into our radiographic concept of a disease. That works quite well in some instances in medicine — it's been a surprisingly effective model for treatment of certain issues — but it does not work for musculoskeletal problems of older people, such as OA.

Data from Creamer, *et al*[5] (Figure 2) show that this approach doesn't work. There is a threshold effect between Kellgren and Lawrence (K-L) grade 0 and K-L grade something, with respect to an association with joint pain, but very little effect after that. Thus, a little bit of joint damage, as defined by the K-L radiographic grade, predisposes to an illness, but after that, more damage doesn't have very much additional effect.

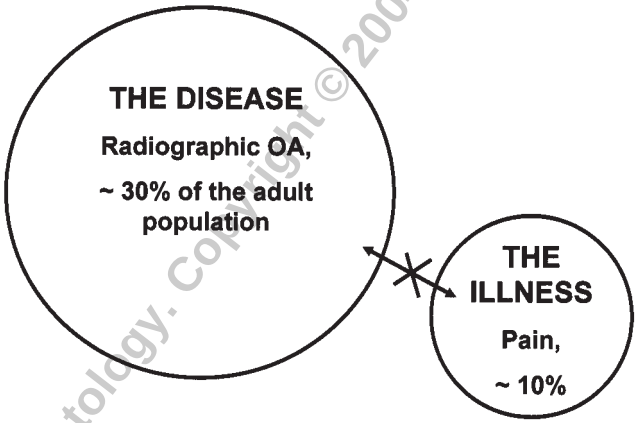

Figure 1. The disease called OA, defined by radiography, bears little relationship to the illness characterized by pain and functional impairment.

If this were any other sort of risk factor, we wouldn't take it very seriously. However, because we want to believe that the radiograph can give us a disease, we take it terribly seriously. I suggest we should not. It works equally badly longitudinally as it does cross-sectionally. Years ago we published data[6-8] on a cohort, the Bristol "OA 500," a group of 500 patients with peripheral joint OA whom we recruited for an observational study. Four hundred fifteen of those subjects were seen again at 3 years and 349 at 8 years. A significant number died because they were given arthritis medications and had fatal iatrogenic complications. We found absolutely no relationship between a change in structure, as seen in the radiographs, and changes in pain or disability. I suggest that the concept that we have a disease in which we can tie patient-related outcomes to a structural change in the joint is fatally flawed, and that until we get rid of that paradigm we are not going to progress in the field of OA.

Let us look at the illness, because that is what matters. Let's not assume it has anything to do with the radiograph. I suggest that if we do that, we have to go beyond pain. Leena Sharma[9] emphasizes elsewhere in these proceedings that there is disability as well as pain in OA, although she was still trying to shoehorn disability into the disease. There is disability as well as pain — she's right about that — and functional improvement is arguably more important than pain. Certainly our qualitative work with people suggests that disability is more important to them than pain[10].

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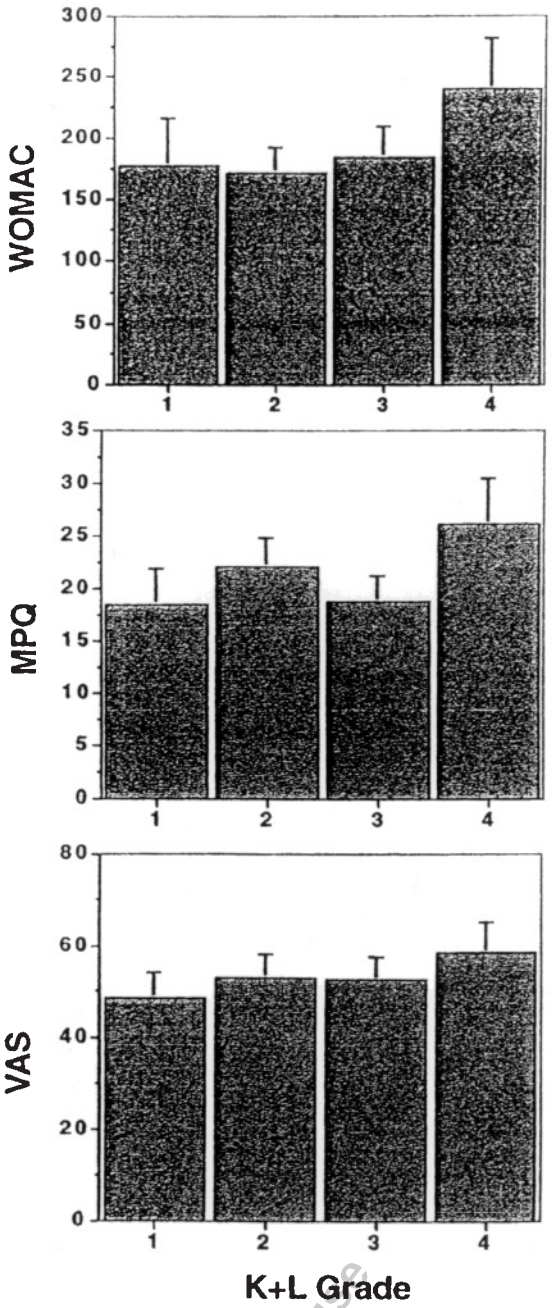

Figure 2. Poor correlation between structural severity of OA, based on the Kellgren-Lawrence (K-L) grade of radiographic severity and pain scores of patients with knee OA. WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index; MPQ: McGill Pain Questionnaire; VAS: visual analog scale. A relatively small amount of structural damage, as indicated by the K-L grade, may predispose to an illness but beyond that, more damage is not associated with more joint pain. From Creamer *et al*. J Rheumatol 1999;26:1785-92.

There are 2 types of OA outcomes: the effects on the individual, such as pain and locomotor problems, and things such as the utilization of services, which also must be taken seriously. The model we work in now is the new World Health Organization (WHO) International Classification of Function[11] (Figure 3). This model, which does not use words such as disability, handicap, and impairment, talks about structure and function. In *oldspeak*, "activities" was about disability and "participation" about handicap. One of the important aspects of the new model is that the arrows (Figure 3) now go in both directions, in recognition of the fact that these are not necessarily straight-line relationships. This model recognizes that health conditions may be important; if you want to take your radiograph and chuck it into the model, you can do so. However, you must recognize that other factors, such as environmental and personal factors, are as important, if not more so, with respect to the musculoskeletal problems of older people. The potential complexity of the interactions within the WHO model is obvious. We have recently begun to study the problem of limitations of activities and of participation among older people in relation to the musculoskeletal system.

In neither cross-sectional nor longitudinal studies of OA can the variations in patient outcomes be explained by radiographic changes or by any other classical OA disease variables that you might put into the model[7,8,10]. If we can't explain OA outcomes that way, we obviously need to examine other types of variables.

In this context, we have explored the concept of the disability paradox — a concept with which any clinician is familiar. It exists in relation to all sorts of problems, including problems with the musculoskeletal system. It is illustrated by the person with OA in whom limitation is not a problem. Mrs. X, our patient, can walk for miles — she doesn't have much of an activity problem. However, she doesn't participate in life. In contrast, other people whose functional limitations are severe — whom you'd regard as being severely disabled – participate fully in life. This paradox is a very important way of looking at the type of problems we're trying to address in OA. If we are trying to do anything, it is to deal with the types of problems created by not participating in life. We have begun to look at this discordance using both standard quantitative epidemiologic approaches and qualitative approaches, within a research

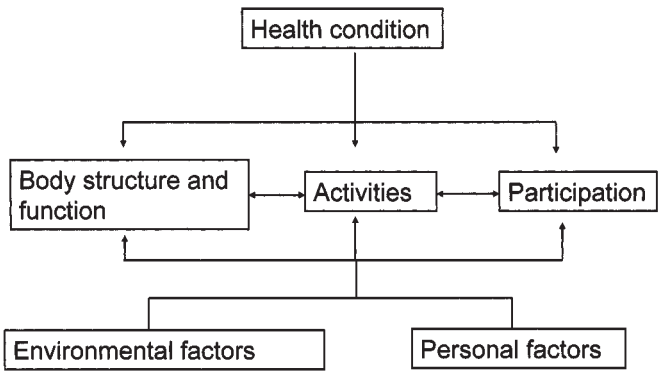

Figure 3. World Health Organization (WHO) International Classification of Function, 1999.

program that has the pretentious title of "locomotor activities limitation."

The first finding to come out of this work is that comorbidity is a key issue. If you want to go on thinking about OA as a condition, remember that, in fact, on its own, OA does not matter very much to the majority of people who have it, most of whom are pretty fit and well. But if they then get something else, they are in trouble. If you have a little bit of OA and then get a bit of Parkinson's disease or become depressed, or become socially isolated for some other reason, you're in deep trouble. That's something we need to emphasize to people who are thinking about trying to help other people in their lives. I suspect the right thing to do in many of those situations is to treat the depression or the Parkinson's, rather than trying to treat the OA.

Some additional data that address this point are derived from a survey by the United Kingdom Office of National Statistics. We found that musculoskeletal problems (e.g., OA) were the main disease-related determinant of limiting, long-standing illness in older people (OR = 3.2). Significant additional associations the model identified as independent risk factors were feelings of vulnerability (OR = 1.8) and having relatives living nearby (OR = 1.5)[12]. Psychosocial factors and the presence of other diseases, acting in consort in an older person with a bit of a problem with joint pain or limitation of movement, add up to a major problem in activities or participation.

The other type of outcome relating to the development of musculoskeletal problems in older people pertains to the utilization of health services. We're doing a lot of *doublespeak* here, insofar as we encourage people to utilize traditional health services. Many of them have much more sense than that, however, and perceive doctors as being dangerous. In the United Kingdom, interesting things are happening — the customers are voting with their feet. There is now much, much greater usage of complementary and alternative medicine than of allopathic medicine by people with musculoskeletal problems. I suspect the trend is similar in the United States. It shows that the customers are a lot more sensible about it than we are.

The other point I wanted to make about utilization of services is that, like joint pain and function, I don't think activities limitation and participation limitation depend upon things like radiographic readings or other disease measures. Nor do I believe that utilization of services depends upon that.

We haven't gotten very far with this yet, but we have begun to look at why people get joint replacements. Some people have joint replacement surgery when there is absolutely no evidence there is anything wrong with them. Based upon our qualitative work, pressure from family members and friends — which can go in either direction — is probably the biggest determinant of whether a person with OA undergoes joint replacement surgery. If the family and friends say, "It's a great thing, you must have it done," most will give in and have it done. If family and friends say, "It's absolutely awful, it always goes wrong," they never have it done. We believe the major determinant in this decision is related to the experiences of people the patient knows[13,14].

Another issue about which we have not taken much notice in the past is people's perceptions of illness, i.e., the concept a person has of herself and of what's wrong with her. Many older people with OA do not consider they have anything wrong with themselves even if they have a lot of pain and can't walk very far. And who's to say that's wrong? Or that we should force them into believing they have something wrong and need to do something about it? They don't see it that way and that's why they don't have anything done. This concept of illness perception seems to be exceedingly important.

Finally, at least in systems in which healthcare is rationed, as it is in the United Kingdom, whether you shout very loudly or not at all has a huge effect on whether you receive a joint replacement[14].

In conclusion, I think we must separate the illness from the disease, at least until we are a lot further along with the characterization of OA and know whether it is one disease or many. We must continue the type of work that tries to decide that but, in the meantime, let's not pretend we know the answer and shoehorn things together, as we've been doing up to now in OA.

We have yet another problem: A lot of OA is very mild, causing pretty minimal discomfort and limitation of activities. Whether we should medicalize it at all, as an issue for healthcare, is highly debatable. I think we probably should not and rather approve of the recent approach recommended by Moynihan and Smith[15], which rekindles a discussion of the issues Ivan Illich raised in the 1970s[16], when he suggested that much too much medicine is being dished out and that this is, in general, a force for bad in a society. I think if we start to do too much medicine for people with very mild problems in the community we will perform a serious disservice to mankind. What, then, should we do for an illness that affects over 10% of the older people in our community?

I think we have 3 options: The first is to assume that OA is a normal part of the human condition and ignore it. I believe that is a viable position. Second, we could assume that OA is a disease and that it can be cured by some high tech expensive interventions. In fact, that's what we are doing as a community. I think it is the wrong way to go. It might mean that a very small percentage of the world's population will be able to buy their expensive way out of OA. We will then have exactly the same situation we now have with AIDS, i.e., if you live in the rich Western world, you are in not too much trouble, but Africa and Asia are being wiped off the map. With OA, it would obviously be a good deal less dramatic than that, but if we insist that the

approach to OA is cartilage transplantation or the like I think we will go the same direction. I think there is a third option, which I believe is the option we should be going for: We should be looking for low tech, inexpensive, simple ways of reducing the burden of illness with respect to pain, limitation of activities, and participation in life by older people. If we're going to progress in this field, I believe we must make these paradigm shifts.

REFERENCES

1. Radin EL. Who gets OA and why? J Rheumatol 2004;31 Suppl 70: 10-15.
2. Brandt KD, Heilman DK, Slemenda C, et al. Quadriceps strength in women with radiographically progressive osteoarthritis of the knee and those with stable radiographic changes. J Rheumatol 1999;26:2431-7.
3. Felson DT. Obesity, vocational and avocational overload of the joint as risk factors for osteoarthritis. J Rheumatol 2004;31 Suppl 70:2-5.
4. Hochberg MC. Do risk factors for incident hip OA differ from those for progression of hip OA? J Rheumatol 2004;31 Suppl 70:6-9.
5. Creamer P, Lethbridge-Cejku M, Hochberg MC. Determinant of pain severity in knee osteoarthritis: effect of demographic and psychosocial variables using 3 pain measures. J Rheumatol 1999;26:1785-92.
6. McAlindon TE, Cooper C, Kirwan JR, Dieppe PA. Determinants of disability in osteoarthritis of the knee. Ann Rheum Dis 1993;52:258-62.
7. Dieppe PA, Cushnaghan J, Shepstone L. The Bristol 'OA500' study: progression of osteoarthritis (OA) over 3 years and the relationship between clinical and radiographic changes at the knee joint. Osteoarthritis Cartilage 1997;5:87-97.
8. Dieppe P, Cushnaghan J, Tucker M, Browning S, Shepstone L. The Bristol 'OA500 study': progression and impact of the disease after 8 years. Osteoarthritis Cartilage 2000;8:63-8.
9. Sharma L. The role of proprioceptive deficits, ligamentous laxity, and malalignment in development and progression of knee osteoarthritis. J Rheumatol 2004;31 Suppl 70:87-92
10. Tallon D, Chard JA, Dieppe PA. Exploring the priorities of patients with osteoarthritis of the knee. Arthritis Care Res 2000;13:312-9.
11. World Health Organization. International classification of functioning, disability, and health [Internet]. Cited Dec. 15, 2003. Available from: http://www.who.int/classification/icf
12. Ayis S, Gooberman-Hill R, Ebrahim S. Long-standing and limiting long-standing illness in older people: associations with chronic diseases, psychosocial and environmental factors. Age Ageing 2003;32:265-72.
13. Sanders C, Donovan J, Dieppe P. The significance and consequences of having painful and disabled joints in older age: co-existing accounts of normal and disrupted biographies. Sociology Health Illness 2002;24:227-53.
14. Woolhead GM, Donovan JL, Chard JA, Dieppe PA. Who should have priority for a knee joint replacement? Rheumatology 2002;41:390-4.
15. Moynihan R, Smith R. Too much medicine? Almost certainly [editorial]. BMJ 2002;324:859-60.
16. Illich I. Limits to medicine. London: Penguin Books; 1977.