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Musculoskeletal diseases — a continuing challenge for epidemiologic research

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In this paper some quality issues of epidemiologic studies on work-related musculoskeletal diseases are discussed. The advantages and disadvantages of different types of epidemiologic studies are described, among them the rarely applied case-crossover design. Problems in the ascertainment of disease, as well as the assessment of exposure to physical load, are also brought up. The importance of understanding the pathomechanisms of the diseases under study is stressed.

Key terms ascertainment of disease, exposure assessment, physical load, study design.

Recently 3 overviews, based on systematic and critical scrutiny of the literature, have appeared on work-related risk factors of musculoskeletal disorders (1—3). In all of them only a small proportion of the eligible articles that had addressed the question of the work-relatedness of musculoskeletal disorders fulfilled the scientific quality criteria and had therefore been considered to provide evidence. The exclusion of the majority of the studies from the reviews actually means that much research effort is wasted in this field because of the suboptimal scientific quality of the studies. It is easy to share the opinion presented by Sven Hernberg (4) in his editorial of this journal that "'Sample size zero' is surprisingly often the best study size" [p 163].

The epidemiology of musculoskeletal disorders shares many validity issues with other areas of epidemiologic research, but in this domain there are some special issues which derive their origin from the characteristics of both the disorders and their work-related risk factors. This feature should, however, not be used as an excuse; instead researchers should continuously strive to improve the quality of work in this field. Some of the challenges are discussed in this paper.

Type of study

The objectives of a study, but also some feasibility issues, determine the optimal study design. A thorough description of the advantages and disadvantages of design options can be found in textbooks of epidemiology, such as that by Rothman & Greenland (5). In my presentation only a short description of the applicability of different study types in the domain of epidemiology of musculoskeletal disorders is given.

Most epidemiologic studies of musculoskeletal disorders have been cross-sectional. Cross-sectional studies are easy and quick to perform and also relatively inexpensive. They are particularly suitable for descriptive surveys, but less so for etiologic research due to the great susceptibility to bias. Among prevalent cases of disease, those with a long duration are overrepresented, and the study is vulnerable also to other types of selection bias (eg, the healthy worker effect). Current exposure may not be etiologically relevant to the current disease, and the temporal sequence of the cause and effect is often impossible to discern. Information bias is also a problem, especially when the data on exposure and disorder are

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based on a questionnaire; people with a current musculoskeletal disorder may recall better than others or overestimate their past exposure, and, likewise, people with certain exposures may be more prone to report their symptoms. This situation may lead to spurious associations between exposures and disorders. Especially in low-back pain research, the exploratory phase based on simple cross-sectional studies should be considered complete, and more ambitious studies should be planned in the future.

The classic structure of a cohort study is depicted in figure 1. From the source population existing or prevalent cases of the disease under study are removed, and then the incidence of the disease is followed from time T_0 to time T_1 in the exposed and unexposed cohorts. In fact, in many studies there is a single cohort that is heterogeneous with regard to many exposures. The incidence of disease is then compared across subgroups with different exposures. In a prospective cohort study the relevant exposure period can be defined, given the onset of disease can be determined unambiguously. A cohort study is considered as the least susceptible to bias, and it is the only feasible design with which to study the effects of rare exposures. Prospective cohort studies are time consuming and, for that reason, also expensive to carry out. A cohort design is applicable only for diseases that are common in the source population. Severe problems are encountered in cohort studies on musculoskeletal disorders. For many of them the definition of a prevalent case of disease, as well as the onset of an incident case, is ambiguous and therefore leads to difficulties in determining the relevant time period for exposure.

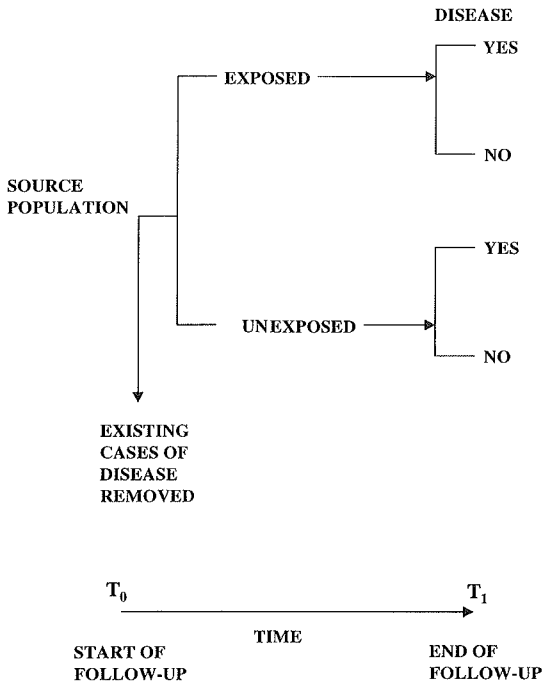

Figure 1. The cohort study design.

In a case-referent study a case can be defined in any feasible but preferably clinically reasonable way. The case definition defines the source population of the cases, from which the referents should be drawn. Both the cases and referents can be randomly sampled from the source population for inclusion, as long as sampling is independent of the exposure under study. In studies on the work-relatedness of musculoskeletal disorders, this condition may not be satisfied, if case ascertainment is based on patient records, because seeking treatment may be related to exposure (eg, physical load at work). For rare diseases the case-referent design is the only feasible option. Many exposures can be studied, and often a case-referent study is faster and less expensive to carry out than a cohort study. In general, a case-referent study is, however, more susceptible to bias than a cohort study is. The exposure assessment must often be done retrospectively, and it therefore renders the study susceptible to information bias. For musculoskeletal disorders the ascertainment of incident cases is often next to impossible and therefore leaves the use of prevalent cases as the only option. It may then be difficult to distinguish between the effect of exposure on the incidence and duration (prognosis) of the disease.

A special type of case-referent study is the case-crossover study, in which, for each case, one or more earlier time periods preceding the disease onset are selected as matched reference periods (5, 6). The exposure status of the case at the time of the disease onset is compared with the distribution of exposure status for that same individual in earlier periods. This type of study is easy and quick to carry out, but until now this approach has been applied infrequently. With this design, only exposures varying for the individual person can be studied, and the design is suitable only if the induction time of the disease is short (eg, triggering effects) and the effect of exposure is transient. Such is the case for many musculoskeletal injuries, and thus case-crossover studies could provide a useful approach to learn about the acute effects of work-related exposures on the musculoskeletal system.

Ascertainment of disease

The classification of musculoskeletal disorders and the setting of diagnostic criteria are continuing challenges in clinical practice and, accordingly, in epidemiologic studies. For some disorders, such as carpal tunnel syndrome and epicondylitis, the diagnostic criteria are fairly well

established (7, 8), whereas for tendon disorders (tenosynovitis, peritendinitis) the diagnostic criteria are more difficult to define. Perhaps most problems are encountered with back and neck disorders, for the majority of which the classification relies mainly on symptom reporting. Another challenge is the definition of the onset of a musculoskeletal disorder. This definition is of utmost importance in epidemiologic studies because the time of onset defines the time period for relevant exposure in etiologic considerations on one hand and for prognostic considerations on the other (figure 2). For disorders with a short induction period [period of time from causal action until disease initiation (5)], this definition is easy to make. For disorders with long induction periods and insidious progress, such as degenerative disorders of the spine and the joints, defining the onset may not even be possible, and some approximation, like the first occurrence of symptoms, must be used. A typical characteristic of both back and neck symptoms is their episodic and intermittent occurrence. Some of the spells may be independent of any of the previous ones, but it is also possible that the acute episode is part of a continuing disease process. A muscle sprain is a good example of the former, while a spell of discogenic pain represents the latter. Currently we do not have reliable means to differentiate between the 2 types of back or neck symptoms, but in epidemiologic studies we should formulate hypotheses of the underlying pathomechanisms and of induction times for the exposure effects. These hypotheses should then guide the design of the studies.

The most common practice in epidemiologic studies on back disorders has been to use self-reported low-back pain during a specified period of time (mostly the past 12 months) as the disease outcome. No additional information is usually available about the previous history of low-back pain. In a study among the employees of a large Finnish enterprise in the forest industry a questionnaire survey of low-back symptoms was repeated 4 times with 1-year time intervals (9). Complete data were obtained from 2321 employees. In the last survey in 1995, 30% of the subjects reported no experience of low-back pain during the past 12 months. Of these subjects 42% had reported no low-back pain in any of the 1992—1995 surveys, whereas 58% had reported low-back pain and 22% sciatic pain (low-back pain radiating to the leg below the knee) in at least 1 of the 1992—1994 surveys. Likewise, of the subjects who reported having experienced low-back pain during the past 12 months in 1995, 10% had their first known episode already 1 year earlier. For 14% the occurrence had been 2 years earlier, and for 66% it had been 3 years earlier. Even without any knowledge of the history of low-back pain before 1992, these figures make one wonder about the time of onset of the underlying disorder and also about how to define the "healthy" subpopulation in 1995.

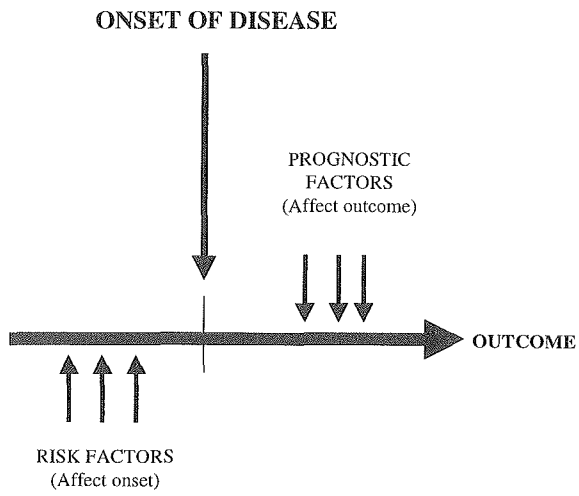

Figure 2. Differentiation between the risk factors and prognostic factors of a disease.

An obvious reason for the popularity of a questionnaire survey as a means to ascertain the disease outcome lies in the fact that other sources of information are not readily available or they involve validity concerns. This situation also explains why only a few case-referent studies on musculoskeletal disease have been performed. One of the important validity issues in epidemiologic studies is that the sampling of both the cases and referents should be done independently of exposure. This requirement makes the use of most register data questionable; register data on occupational diseases or injuries, and pensions due to musculoskeletal disorders, as well as data from health care records, are probably not free of selection in this respect. The registers of arthroplasties in some Nordic countries can be mentioned as exceptions, because the health care systems in these countries provide people with equal opportunity for such treatment. Another aspect that hampers the use of the records of health care providers (such as hospital discharge registers) is the nonuniformity of diagnostic practices of clinicians.

A great challenge for the future epidemiology of musculoskeletal disorders is to develop standardized classification criteria for the disease outcomes. This should be an area of research interest by itself, especially for the disease outcomes for which only symptom-based definitions may be feasible. For example, ascertainment of the current episode of low-back pain may be sufficient if short-term (acute or triggering) effects of current exposures are the focus of the research, but it is not sufficient for studying long-term effects of cumulative exposures. In the classification, symptoms (type, localization, intensity, duration) and the duration of the current episode, as well as past history, should be taken into account. For the current episode, physical signs and function can also be useful. In 1982 Nachemson & Andersson (10)

presented a classification system for low-back disorders that included the aforementioned elements, but unfortunately their proposal never gained general acceptance.

Recent studies confirm that about 90% of acute cases of low-back pain are resolved within 3 months (11, 12). In longer follow-ups, a large proportion of the cases of low-back pain has a chronic or recurrent course (13, 14). In the earlier mentioned study in the Finnish forest industry (9), 45% of those who reported both local low-back pain and sciatic pain in the first survey reported the same symptoms in the 3 consecutive surveys. Another reason to reconsider the time of onset of low-back disorders is the increasing number of studies among adolescents. As an example, in a case-referent study by Salminen et al (15), 42% of the 15-year-old schoolchildren with recurrent or continuous low-back pain had signs of disc degeneration of the lumbar spine in magnetic resonance imaging as compared with 19% of the healthy age- and gender-matched referents. During the 3-year follow-up, the prevalence of disc degeneration increased to 58% in the index group and to 26% in the reference group. These results indicate that disc degeneration is prevalent among adolescents, and low-back pain is related to disc degeneration. To learn more about the etiology of low-back disorders, the focus should be directed towards young populations.

Assessment of exposure to physical load

Be it a challenge to improve the disease outcome ascertainment in epidemiologic studies on musculoskeletal disorders, it is at least as great a challenge to assess exposure to physical load in a relevant and feasible way.

Physical load is composed of the exertion of force, motion, and postures, something that everyone has been continuously "exposed" to since birth. However, not all exertions of force, motion, and posture are hazardous to the musculoskeletal system. Often the exposure-response relationship between physical load and musculoskeletal disease is described as a U-shaped curve — little and much load increasing the risk. On one hand this notion is based on knowledge of the detrimental effect of immobilization on the musculoskeletal tissues, which however differs from the deconditioning effect of low-level physical activity. On the other hand, some early epidemiologic studies have suggested that sitting is associated with an increased risk of low-back pain (16). Later studies and available evidence from the literature do not confirm such an association (1, 2). A low level of physical activity as such does not injure musculoskeletal tissues.

A plausible underlying pathomechanism of musculoskeletal disease, caused by physical load, is major or minor tissue damage due to overload that exceeds physiological tissue endurance or tolerance. Accordingly, it seems feasible to conceptualize exposure to physical load as overload. Overload can be due to sudden overexertion (causes injury), sustained exertion (causes fatigue or injury), or repetitive exertion (causes fatigue or injury). Operationally different parameters (amplitude, frequency, and duration) are relevant measures for different types of physical load (force exertion, posture, and motion). The parameters to be estimated are average and peak exposures. Stochastically occurring high peak loads are rare and, as such, difficult to measure by any means.

A reasonable goal for exposure assessment in epidemiologic studies would be to classify physical load (average and peak load) reliably into the 4 categories of no exposure, low exposure, medium exposure, and high exposure to overload. In epidemiologic studies mechanical exposure can be assessed using self-reports, observation methods, or direct measurements. Winkel & Mathiassen (17) have described the feasibility of different assessment methods. Capacity, versatility, and generality decrease, whereas exactness and cost increase from self-reports to observations to direct measurements. With modern sophisticated measuring technology it is possible to get accurate measures for current exposure to various dimensions of physical load at work. Direct measurements are usually not feasible for large studies and the accuracy of measurements is of value only if current exposure is relevant with regard to the study objective. In addition, if current exposure can be considered a valid proxy for past exposure, direct measurements are warranted. However, often this may not be the case, and other means of past exposure assessment, such as interviews or expert assessment based on occupational history, must be utilized.

One matter of concern with direct measurement data is the huge amount of raw data that must be reduced to some meaningful indices. Even then one can wonder if the essence of exposure to the hazard in question can be extracted from the data and if the accuracy of the measurement data is only illusory. Direct measurements are an excellent means with which to validate other methods of exposure assessment that are more suitable for large field studies, and thus the measurement techniques should be developed and their application for this purpose encouraged. Also, in laboratory experiments, the classification criteria for exposure to overload could be studied based on direct measurements of the physical load and physiological responses of the subjects.

Exposure assessment strategy should be founded on either knowledge or hypotheses of the pathomechanism of the disease of interest. A crucial factor is the hypothesized induction time for the exposure that determines the relevant time period or time window for the exposure. The determination of the relevant parameters of exposure assessment should also be based on the pathomech-

anism of the disease. The relevant parameter could be a common metric of force acting, for instance, on a certain joint of the spine (18), the force being calculated, for example, from biomechanical models or as a life-time cumulative exposure index for average exposure or for peak exposures or as a time-weighted average of different measures. Particularly for musculoskeletal disorders with long induction times, such as degenerative disease, the law of incompatibility presented by Lotfi Zadeh [as referred to by McNeill & Freiberger (19)], one of the great names in fuzzy logic, seems to hold true for exposure assessment: as complexity rises, precise statements lose meaning and meaningful statements lose precision.

Naturally there are many other validity aspects of epidemiologic studies on musculoskeletal diseases than those dealt with in this paper, but, particularly, the ascertainment of disease outcome and exposure assessment are the crucial challenges. As to the other validity aspects, the reader is referred to textbooks on epidemiology (5, 20). Despite the encouraging progress in the epidemiology of musculoskeletal disorders, this field continues to be very demanding and a great challenge to researchers. For future progress in epidemiology we need support from many disciplines, such as basic science, physiology, psychology, biomechanics, clinical science, and sociology.

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