Dear Patient: Association Is Not Synonymous with Causality

It has become quite common for patients to bring me newspaper or magazine clippings, or, more recently, print-outs from a Web site. These media pronouncements usually describe the results of new clinical trials or observational epidemiologic studies. The patients inquire whether any of these latest findings concerning a new “miracle” drug, surgical procedure, or diagnostic study would be “just the thing” for them. Alternatively, patients want to know if the results of the latest epidemiological study should cause them to make important changes in their diet or lifestyle practices because of a reported association between components of their daily lives and occurrence of one or more diseases. Usually, the associations involve a relationship between diet and various serious illnesses such as cancer, diabetes, heart disease, and dementia.

In an earlier editorial, I commented on the problems involved when patients obtain medical information from Web sites of dubious validity. Patients want to know if changes in their diet or lifestyle will decrease their risk for developing a specific disease, particularly when they have considerable dread about a relatively common chronic disease such as cancer or coronary artery disease. These inquiries lead to some of the most difficult conversations that I have with patients. Especially challenging are patient discussions that extend to differences in the meaning of absolute versus relative risk reductions or increases noted in these observational epidemiologic investigations. Equally difficult are discussions involving disease prevalence/incidence in the patient of a specific age and sex who is sitting before me in either the ambulatory care or hospital setting.

The problem in responding to these questions is that the answer often involves a discussion of the difference between an “association” and “causality” presented in layperson’s language. It is important for the patient to understand that epidemiologic studies by their very nature produce a number of statistically significant associations that are not necessarily directly related to the development of a particular disease. For example, women in Western society who regularly took hormone replacement therapy (HRT) were noted in observational epidemiologic investigations to have a decreased likelihood of developing atherosclerotic cardiovascular disease or dementia. Carefully executed, randomized, double-blinded trials have demonstrated that HRT does not reduce the risk of heart disease or dementia in comparison to non-users of HRT. The previously demonstrated association of HRT with lessened disease risk seen in non-randomized epidemiologic investigations was shown in these carefully controlled and blinded therapeutic trials to be unrelated to clinical illness in a way that could be manipulated therapeutically, at least with current pharmacologic agents.

This recent example underscores the problem that arises when patients confuse epidemiologic associations with etiology or cause of a specific disease. Thus, it is likely that the association of lessened disease risk observed with HRT in previously conducted observational epidemiologic studies was the result of confounding by one or more factors, such as greater health concerns on the part of patients taking HRT. This greater awareness of health risks in individuals taking HRT could well have led to preventive lifestyle behaviors that were the reason for a lower risk of heart disease and dementia. This recent example demonstrates the dangers inherent in the commonly held belief that an epidemiological association is equivalent to causality.

The concept of absolute versus relative risk also may need to be explained to patients. For example, the latest Cable News Network (CNN) news report might suggest that persons who consume large quantities of pine nuts may be at considerably increased risk for developing pancreatic cancer as compared with pine nut abstainers; however, the absolute risk of developing pancreatic cancer is extremely low for both pine nut lovers as well as abstainers. Let us consider a hypothetical epidemiologic study involving many tens of thousands of adults. This investigation demonstrated that consumption of large quantities of pine nuts on a regular basis was associated with a 2% risk of developing pancreatic cancer over a 10-year period of follow-up. The pine nut abstainers had a 1% risk of developing pancreatic cancer over the same time period. This might be reported by the media as “Eating pine nuts doubles an adult’s risk of developing pancreatic cancer.” The actual interpretation of this study should be as follows: There is a small increased risk of developing pancreatic cancer associated with eating large quantities of pine nuts; however,
over a 10-year period, among both pine nut lovers and pine nut abstainers, the real risk of developing pancreatic cancer is very, very small. Even though the 1% absolute difference in risk may be highly statistically significant because thousands of individuals were followed over an extended period of time in the study, the biological reality is that the actual risk of developing pancreatic cancer in both groups is very small indeed. Unfortunately, thorough explanations of research studies don’t fit into 30-second sound bites and are generally reserved for popular news outlets such as The New York Times, the Discovery Health Channel, and public television and radio.

Given the shortcomings of popular news coverage, it is up to practicing physicians to help patients understand the potential relevance of medical research to their health. As noted earlier in this essay, the difference between association and causality can be difficult for patients to understand and requires a careful explanation in terms that can be easily understood by a layperson. This is an important concept for patients to comprehend. Only then can they make intelligent choices about changes in their lifestyles that are initiated because of the latest CNN health report.

The practicing physician needs to be cognizant of common misconceptions in the interpretation of observational epidemiologic investigations and even randomized controlled trials based on small select patient populations. We understand that the results cannot be generalized to the general population. By educating patients and their families, the physician can better assist patients in making intelligent preventive health choices. Patients can then adopt the most effective primary and secondary actions to avoid the risks of serious illness.

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References