Risk Factors that Patients Should Avoid

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A risk factor increases a person's susceptibility to developing a disease. This can be a particular patient characteristic (e.g., obesity for heart disease), patient behavior (e.g., cigarette smoking for lung cancer), or a specific drug intervention (e.g., steroid intake for myopathy). Observational studies like case-control or cohort study designs are commonly used when evaluating the harmful effect of an exposure. Family and community medicine practitioners should always take the opportunity to advice patients regarding these risk factors to promote wellness and enhance primary care.

Appraisal

Relevance

1. Is the objective of the article on risk factor addressing the clinical dilemma?

Validity

1. Were there clearly identified comparison groups?
2. Were the exposures and outcomes measured in the same way in the groups compared?
3. Was there a temporal relationship and follow-up sufficiently long and complete?

Results

1. What is the magnitude of the association between risk factor and outcome?
2. Was the estimate statistically significant and dose response gradient present?

Applicability

1. Are the study patients similar to my own?
2. Should I attempt to stop the exposure?

Key words: Evidence-based family practice, risk factor, cohort study, case-control study

Introduction

A risk factor increases a person's susceptibility to developing a disease. This can be a particular patient characteristic (e.g., obesity for heart disease), patient behavior (e.g., cigarette smoking for lung cancer), or a specific drug intervention (e.g., steroid intake for myopathy).[1] Family and community medicine practitioners should always take the opportunity to advice patients regarding these risk factors to promote wellness and enhance primary care.

Observational studies like case-control or cohort study designs are commonly used when evaluating the harmful effect of an exposure. Both designs have a control group for comparison, in the former, controls are chosen by absence of the outcome or disease and in the latter by absence of an exposure. In a case-control study, patients with the outcome are gathered. Then a group of patients without the outcome matched for certain characteristics other than the exposure is also gathered. The presence or absence of the risk factor in both groups is then ascertained. The advantage of this study design is that it can establish the effect of multiple risk factors. But the temporal relationship of the exposure should have occurred before the outcome. In a cohort study, a group of patients are observed. They are divided into those with the risk factor and those without. Then the outcome is observed forward in time.[2] A cohort study can only establish one or a limited number of risk factors. The STROBE statement is the standard for writing the report of these study designs.[3]

Scenario

Family physicians are often consulted for uncomfortable premenopausal symptoms. Hormonal replacement therapy (HRT) is the recommended treatment to relieve these symptoms, but there are some patients who worry about the risk of breast cancer that comes with HRT.

A family practitioner may face this choice of balancing symptom relief vs. risk of breast cancer when considering HRT.

A focused clinical question from such a scenario may be stated as "Among women with premenopausal symptoms (P-population), what is the association of hormone replacement therapy (E-exposure) with the risk of developing breast cancer (O-outcome)?" To look for an evidence-based answer to this clinical dilemma, a literature search using the keywords from the clinical question arising from the scenario shall be conducted. Searching PubMed using the terms "menopause," "hormone replacement," "risk factor," and "breast cancer" yielded the study Tan MM, et al. A case-control study of breast cancer risk factors in 7,663 women in Malaysia. PLoS One 2018 Sep 14; 13(9):e0203469.4

Appraisal

Relevance

1. Is the objective of the article on risk factor addressing the clinical dilemma?

In appraising the relevance of the study, the PEO of the searched literature should correspond well with those of the focused clinical question. In the scenario presented, the dilemma was about the association of HRT with the risk of developing breast cancer among premenopausal women.

The chosen article written by Tan, et al., reported the association of hormonal treatment with breast cancer from a hospital-based case-control study of 7,663 women, making it relevant in responding to the dilemma raised in the clinical scenario.

Validity

1. Were there clearly identified comparison groups?

Similar to studies of treatment effectiveness, risk factor or harm studies require that a control group for comparison should be present. The groups are readily identified in a cohort study by the presence or absence of exposure. In a case-control study, the comparison groups are identified by the presence or absence of the undesirable outcome or disease, but the more important point of comparison for the purpose of appraising a study on harm, is the presence or absence of the risk factor of interest, while making sure that this risk factor preceded the outcome (temporal relation). Once the comparison groups have been identified, it must be ensured that both groups are similar in terms of all the important prognostic factors. This is easily done in an RCT, but difficult to achieve in a cohort or case-control. If there is imbalance in the prognostic factors between comparison groups, statistical adjustments should have been made.[5]

The study by Tan, et al. is a case-control study which classified 3,683 patients with breast cancer diagnosis as cases, and 3,980 patients aged 40 to 74 with no history of breast cancer but with recorded history of attending mammography screening as controls. With regards to the use of hormone replacement therapy, the authors defined it as "ever used oral contraceptives for at least one month," and the group who is positive for this exposure was compared with those who did not fit the definition and thus were deemed unexposed. The authors also performed statistical adjustments during the analysis of results to account for the imbalance in prognostic factors between groups.

2. Were the exposures and outcomes measured in the same way in the groups compared?

The measurement of exposures and outcomes must be similar in both groups. In an RCT and cohort study, the investigators must show that diligent observation for the outcome was done in the group with the exposure (high risk) as well as the group without the exposure (low risk). If the patients with the exposure were observed more diligently, there will be a higher detection rate of the outcome leading to an increased incidence of the disease in the exposed group. This is called surveillance bias, and this is best avoided by ensuring blinding of outcome assessors.[5]

Bias may also occur in case-control studies, when the detection of exposure is more diligent in the group with the disease or outcome, which could happen either through a recall bias (i.e., when exposed patients have more motivation to remember their exposures) or an interviewer bias (i.e., when interviewers are more motivated to probe on risk factors among the exposed group).[5]

In the study of Tan, et al., all subjects in the cases and controls were interviewed by trained interviewers. The subjects completed a questionnaire that included items related to demographics, personal and family history of cancers, history of breast surgery, menstrual and reproductive history, use of oral contraceptive and hormone replacement therapy (HRT), breast cancer diagnosis (cases only), and history of and motivation of attending mammography screening (controls).

3. Was there a temporal relationship and follow-up sufficiently long and complete?

For an exposure to cause an effect, the exposure must be present before the outcome. This parameter is readily established in a cohort and RCT, but it has to be ensured in a case-control study, and oftentimes, doing so could be difficult. Cross-sectional studies usually cannot establish a temporal relationship, making them less appropriate for studying risk factors, but cross-sectional studies can establish a dose response gradient and a comparison between groups. The length of follow-up must also be sufficiently long enough to detect the outcome. This criterion is particularly important for RCTs and cohort studies. If follow-up is short, the chance of underestimating the effect of the exposure is high.

The temporal relationship between the HRT and breast cancer was not clarified in the study of Tan et al., as it stated "ever used contraceptive or HRT" as one of the exposures investigated. It is reasonable to assume, however, that HRT exposure happened in the past based on how the question was asked (i.e., "ever used").

Results

1. What is the magnitude of the association between risk factor and outcome?

Cohort studies and RCTs will report the association between exposures and outcomes using the relative risk (RR), which is the incidence of the adverse effect in the exposed group divided by the incidence of adverse effect in the unexposed group. A value of greater than 1 for the RR indicates an increased risk of the outcome associated with the exposure, while a value of less than 1 implies a reduced risk.[5] In case-control studies, odds ratios (OR) are reported. The odds ratio is the odds that the outcome will happen if the exposure is present divided by the odds that the outcome will not happen if the same exposure is present. If the OR is more than 1, then the exposure is causing harm, and if less than 1, the exposure reduces harm.

In the study of Tan, et al., the odds ratio of breast cancer among those having ever used HRT was 0.52 (less than 1). This means that HRT does not increase the risk of breast cancer.

2. Was the estimate statistically significant and dose response gradient present?

For the relative risk or the odds ratio to be statistically significant, the values of 95% confidence interval should be greater than 1 to say that the exposure really causes harm. If one value of the 95% confidence interval is less than 1 and the other is more than 1, then the effect of the exposure is uncertain.[5]

In the study of Tan, et al., the 95% confidence interval of the odds ratio is 0.44-0.61. Both values are lower than 1, which means that it is statistically significant that HRT does not increase the risk of breast cancer. The presence of a dose-response gradient cannot be ascertained, because the variable measured for HRT use was simply its presence or absence.

Applicability

1. Are the study patients similar to my own?

Similar to an article about a beneficial intervention, a decision must be made if the harmful effect may be extrapolated to the patient whose case inspired the formulation of the clinical dilemma. The characteristics of the patient should be similar to the study's inclusion criteria, with respect to morbidity, age, race, or other potentially important prognostic factors.[5]

Tan, et al., included women between ages 40 and 74 years, majority of whom are in the 45-54 years old range. These women are the ones commonly suffering from menopausal symptoms who might benefit from HRT.

2. Should I attempt to stop the exposure?

In answering this criterion, consider the following guide questions. First, how large and precise is the risk of harm? If both the magnitude and likelihood for harm are great, it would be reasonable to stop the exposure. Second, what are the consequences if the exposure is withdrawn? If the adverse consequences to reducing or eliminating the exposure is more than when the exposure is continued, the patient would have a net benefit from proceeding with the factor being considered. In case of exposure to essential drugs and there is a safe, inexpensive, and well-tolerated alternative available, it is reasonable to discontinue the exposure even if the magnitude and likelihood of harm is low. Decision is simple when the answers to these questions are clear. The family physician, armed with the information that HRT does not increase the risk of breast cancer, can now consider giving advice to the patient to balance the benefit of symptom relief and the fear of breast cancer — which may not be real based on the study of Tan et al. The alternatives may be less effective treatment for the management of menopausal symptoms.

Patient-centered Communication

The use of EBFP through conducting critical appraisal of publications like a risk factor study has an advantage of learning on other factors that might influence the development of the disease. While Tan et al. (2018) showed that HRT is not associated with breast cancer, it was also able to show that soy in the diet, increased physical activity, and prior breastfeeding also decrease the probability of breast cancer. All these information can be given as advice to the patient when making a shared decision about HRT.

Communicating information about risk modification to patients can be a difficult task. Aside from effective communication, we need skills to support patients and their families with making lifestyle changes. Counseling skills will be very helpful for a family practitioner. Working through effective interdisciplinary team-based care that includes nurse educators, pharmacists and psychologists have been proven to be effective.[6] Another useful tool that a family physician can use is digital technology. Technology solutions have the potential to both promote health and wellness by improving health literacy. New and emerging technologies such as remote patient monitoring, wearables, and health apps are available and have been shown to promote healthy behavior.[7]

Shared Clinical Decision

Shared decision making (SDM) is a process by which a healthcare choice is made jointly by the family physician and the patient. This is the basis of the patient-centered care. Policy makers also perceive SDM as desirable because of its potential to reduce overuse of options not clearly associated with benefits, enhance the use of options clearly associated with benefits, and promote the right of patients to be involved in decisions concerning their health. SDM has been recommended in some guidelines to enhance adherence to the recommendations by individual patients. Like guidelines, SDM improve quality of care by promoting decisions that reflect what is best for an individual patient based on their risks, as well as their comorbid conditions and socio-personal context. Brief, evidence-based, and patient-oriented tools can support thoughtful, patient-centered decision-making and improve the rates of appropriate lifestyle adherence.[8]

Despite this potential, SDM has not yet been widely adopted in family and community practice. Development and distribution of educational material, educational meeting and audit and feedback to patients and physicians may promote the uptake of SDM. Examining

and addressing the barriers may also be another strategy. These things need to be further examined in terms of their effectiveness to promote adoption.[9]

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