ORIGINAL ARTICLE

Five-year malignancy incidence in patients with chronic pruritus: A population-based cohort study aimed at limiting unnecessary screening practices

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Background: The incidence of malignancy in patients with chronic pruritus and nondiseased skin is unknown.

Objective: We sought to assess the hazard ratio (HR) of incident overall malignancy and incident malignancy by subtype in patients with chronic pruritus during the 5 years after diagnosis.

Methods: A population-based cohort study was performed in the Health Improvement Network. In all, 8744 patients with chronic pruritus were matched with 31,580 patients without chronic pruritus based on sex, age, and practice. Primary outcomes were HR of incident malignancy and HR of malignancy subtypes.

Results: The fully adjusted HR for incident malignancy in patients with chronic pruritus was 1.14 (95% confidence interval 0.98-1.33). The fully adjusted HR for incident hematologic malignancy and incident bile duct malignancy in patients with chronic pruritus was 2.02 (95% confidence interval 1.48-2.75) and 3.73 (95% confidence interval 1.55-8.97), respectively. The incidence of hematologic malignancy and cholangiocarcinoma in patients with chronic pruritus was 0.0016 and 0.0003 per person-year, respectively.

Limitations: Potential for misclassification and detection biases is a limitation.

Conclusions: Chronic pruritus without concomitant skin changes is a risk factor for having undiagnosed hematologic and bile duct malignancies, but not other malignancies. The overall incidence of these malignancies in patients with chronic pruritus is very low. (J Am Acad Dermatol http://dx.doi.org/10.1016/j.jaad.2013.11.045.)

Key words: chronic pruritus; generalized pruritus; itch; paraneoplastic signs; pruritus; skin signs of systemic disease.

Chronic pruritus, defined as itch lasting for equal to or greater than 6 weeks, affects 8.4% to 22.6% of the population.[1-3] Patients with chronic pruritus are divided into clinical and etiologic groups by the International Forum on the Study of Itch.[4] Clinical classifications are based on the presence or absence of skin disease.[4] Clinical classification group 1 includes patients with cutaneous diseases, such as eczema or psoriasis, as the cause of their pruritus; group 2 includes patients with normal-appearing skin and pruritus; and group 3

Abbreviations used:

CI:	confidence interval
HR:	hazard ratio
THIN:	the Health Improvement Network

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includes patients with chronic scratch lesions and pruritus.[4] Recommendations by expert groups for additional laboratory tests and imaging to determine the cause of a patient's pruritus are based on their clinical classification (ie, group 1, 2, or 3).[4,5] The patients who make up group 2, patients with normal-appearing skin and pruritus, are thought to have systemic, neurologic, or psychogenic causes of their itch and first-line recommended workup includes a thorough history and examination, basic laboratory tests, and chest x-ray.[4-6] Malignancy is frequently feared as the lurking cause of chronic pruritus and therefore recommended second-line workups often include computed tomography imaging.[4-20] However, computed tomography imaging for malignancy screening is expensive, exposes patients to significant amounts of radiation, leads to additional testing to work up incidental findings, and has not been shown to decrease morbidity or mortality from malignancy other than in patients with high risk of lung cancer.[21-31]

CAPSULE SUMMARY

- Patients with chronic pruritus and normal-appearing skin have systemic, neurologic, or psychogenic causes of itch.
- Five-year risk of diagnosis of hematologic or bile duct malignancy is elevated in these patients, without an increased risk of other malignancies.
- Screening practices should be limited to evaluation for bile duct and hematologic malignancies.

Given the costs and risks of computed tomography screening for malignancy in low-risk populations, our study set out to define the 5-year incidence of overall malignancy and malignancy subtypes in patients with chronic pruritus without concomitant skin findings (group 2 patients) to help physicians make informed decisions about the use of screening these patients for malignancy.

We conducted a large, population-based cohort study to assess the risk of incident malignancy, incidence of subtypes of malignancies, and incidence of death within 5 years of diagnosis in a cohort of patients with chronic pruritus and normal-appearing skin, as compared with their age-, sex-, and practice-matched control subjects.

METHODS

Study design

Methods conformed to the Strengthening the Reporting of Observational Studies in Epidemiology statement.[32] The Health Improvement Network (THIN) is a population-based longitudinal electronic medical records database that is anonymized for research purposes. THIN contains reliable and valid information on approximately 11 million patients in the United Kingdom across over 550 medical practices, followed up for an average of 9 years, making it an ideal data source for a cohort study.[33,34] General practitioners enter patient demographics, medical diagnoses (in READ codes), laboratory results, and prescriptions as part of routine medical care. Data quality assessments are routinely carried out and general practitioners are incentivized to improve data quality.[33] THIN data from 1995 to 2012 were used in this study.

Using the THIN database, we conducted a population-based cohort study of adults greater than 18 years of age with chronic pruritus and without concomitant skin findings (the exposed cohort) versus patients without chronic pruritus (the unexposed cohort).

This study was approved by the University of Pennsylvania Institutional Review Board and the THIN Scientific Review Committee.

Study population, exposure, and outcome definition

Chronic pruritus was defined as having at least 2 READ codes for generalized pruritus separated by at least 6 weeks. The enrollment date was the date on which a READ code for generalized pruritus that was separated by 6 weeks or more from a prior READ code for generalized pruritus was coded. To ensure that the exposed patients had chronic pruritus with normal-appearing skin (ie, group 2 patients), patients were excluded if they had any READ codes for dermatologic disorders associated with pruritus (eg, rash, psoriasis, eczema, xerosis) or secondary scratch lesions (eg, prurigo) before the enrollment date. Exposed patients (patients with chronic pruritus without concomitant skin changes) were eligible for the cohort if they were 18 years of age or older at the enrollment date, and had participated in THIN for 6 months or more at the time of enrollment.

As this study was focused on incident malignancy, patients were also excluded if they had any READ codes for malignancy (with the exception of non-melanoma skin cancers) before the enrollment date.

To construct an unexposed comparison group, each exposed patient was randomly matched to up to 4 patients without chronic pruritus and without prior READ codes for malignancy who were of the same sex and age (±3 years), and treated in the same practice for a minimum of 6 months before the enrollment date. The unexposed