CLINICAL RESEARCH STUDY

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The Risk of Cancer in Patients with Benign Anal Lesions: A Nationwide Population-based Study

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ABSTRACT

OBJECTIVE: To evaluate the risk of cancer among patients diagnosed with hemorrhoids and benign anal inflammatory lesions.

METHODS: A population-based, retrospective cohort study was conducted that included patients diagnosed with hemorrhoids or benign inflammatory anal lesions (eg, anal fissure, fistula, and perianal abscesses) that were registered in the National Health Insurance Research Database in Taiwan between January 1, 2000 and December 31, 2010. Standardized incidence ratios (SIRs) were calculated to compare the cancer incidence of these patients to the general population.

RESULTS: During a median observation period of 6.23 years, 3080 cancers developed among 70,513 hemorrhoid patients, with a follow-up period of 438,425.6 person-years, entailing the SIR of 1.52 (95% confidence interval [CI], 1.47-1.58). Increased cancer risk (SIR 1.16; 95% CI, 1.11-1.21) was still noted even after excluding the first year of observation. Significant long-term risk for colorectal cancer (SIR 1.50; 95% CI, 1.35-1.66) and prostate cancer (SIR 1.40; 95% CI, 1.17-1.66) was observed after corrections were made for multiple comparisons. In contrast, there was no remarkable increase in cancer risk for patients with inflammatory anal lesions when cancers detected within the first year of diagnosis were excluded.

CONCLUSION: The presence of hemorrhoids is associated significantly with a long-term risk of developing colorectal cancer or prostate cancer. In contrast, benign inflammatory anal lesions do not appear to increase the risk of malignancy.

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KEYWORDS: benign anal lesions; hemorrhoids; cancer risk

Hemorrhoids are a common, noninflammatory disease that can be frequently observed in clinical practice. They are normal vascular structures in the anal canal that arise from a channel of arteriovenous connective tissues and drain into the superior and inferior hemorrhoidal veins. In contrast, anal fissure, anal fistula, and perianal abscesses represent inflammatory diseases.

There are few studies that have evaluated the relationship between benign anal lesions, including hemorrhoids, and anal cancer or other cancers.[1-5] An increased incidence of

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anal squamous cell carcinoma has been observed in patients with inflammatory anal lesions.[4] It is hypothesized that chronic inflammation with cytokine expression might account for such carcinogenesis.[6,7] However, this result was controversial in other studies.[2,3,5] Moreover, to our knowledge, a study of hemorrhoids in an Asian population has not been published.

In this study, the relative risk of malignancies, including specific cancer types, among patients with hemorrhoids or other benign inflammatory anal lesions were evaluated using the National Health Insurance Research Dataset (NHIRD).

CLINICAL SIGNIFICANCE

- Hemorrhoids and inflammatory anal diseases are very common in clinical practice.
- Previous studies had demonstrated the inconsistent association between benign anal diseases and anal cancer or colorectal cancer.
- Although hemorrhoids are benign noninflammatory diseases, they are noted to be associated with an increased long-term risk of colorectal cancer and prostate cancer.

MATERIALS AND METHODS

Data Sources

Beginning in 1995, the National Health Insurance (NHI) program was established as a mandatory universal health insurance program in Taiwan. It offers comprehensive medical care coverage to all residents, with a coverage rate up to 98%.[8] It includes coverage for outpatient, inpatient, emergency, dental, and traditional Chinese medicine services, as well as prescription drugs. The Longitudinal Health Insurance Database, a subset of the NHIRD, is a representative database composed of 1,000,000 patients randomly sampled from the registry of all enrollees. The Registry for Catastrophic Illness, another subset of NHIRD, was used to identify subjects who were diagnosed with cancer (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM]: 140-208). The database provides comprehensive enrollment information for all patients with severe diseases. Application for a Catastrophic Illness Certificate requires histological confirmation.

The confidentiality of the data abides by the data regulations of the Bureau of National Health Insurance and the National Health Research Institute. Because the NHI dataset consists of de-identified secondary data for research purposes, the study was exempt from full review by the institutional review board.

Study Population

A retrospective cohort study was conducted from January 1, 2000 to December 31, 2010 using the Longitudinal Health Insurance Database. Patients who were diagnosed with hemorrhoids (ICD-9-CM: 455) on 2 or more occasions between January 1, 2000 and December 31, 2008, and did not have any antecedent malignancies, were enrolled in this study. As a separate group, patients with benign inflammatory anal lesions (ICD-9-CM: anal fissure/fistula 565, perianal abscess 566) also were identified. Patients who fulfilled the criteria for participating in both cohorts were excluded from the hemorrhoids cohort and enrolled in the other one for its inflammatory reactions.

Statistical Analyses

The main dependent variable was occurrence of cancer. The cohorts were followed until cancer developed, death occurred, the patient dropped out of the NHI program, or until the end of 2010. The risk of cancer among the cohorts was determined using calculations of the standardized incidence ratio (SIR), which is defined as the observed number of cancer occurrences divided by the expected number. The latter was calculated by multiplying the national incidence rate of cancers stratified by sex, calendar year, and age in 5-year intervals by the corresponding stratum-specific person-time accrued in the cohort. The incidence rates of cancers among the general population were obtained from the Taiwan National Cancer Registry. The 95% confidence intervals (CIs) for the SIRs were estimated based on the assumption that the observed number of cancers followed a Poisson probability distribution. SIRs for subgroups according to sex, age group, and duration of follow-up also were calculated. In addition, SIRs were estimated for 22 cancer types, and Bonferroni correction was used to counteract the problem of multiple comparisons (P-value $\leq$.05 divided by 22, approximately 0.002, was considered significant).[9]

RESULTS

Characteristics of the Study Population

Based on patient data available from the NHIRD, a total of 70,513 patients with hemorrhoids were identified. Of this cohort, 49% were male, the median age at diagnosis was 42.79, and 75% of the patients were diagnosed between the ages of 20 and 59 years. In addition, the median follow-up period was 6.23 years and the cohort was observed for 438,425.6 person-years (**Table 1**). For the second cohort, a total of 16,214 patients with benign inflammatory anal lesions were identified. Of these patients, 63.85% were male and the median age at diagnosis was 39.16 years. In addition, the median follow-up period was 5.88 years (interquartile range 3.59-8.36) and the cohort was observed for 96,600.2 person-years (**Table 2**).

All Cancers

Hemorrhoids Cohort. During the follow-up period, 3080 cancers occurred. These patients had a significantly increased cancer risk, with a SIR estimate of 1.52 (95% CI,