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Appendectomy increased the risk of ischemic heart disease



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ARTICLE INFO

Article history:

Received 7 May 2015

Received in revised form

2 June 2015

Accepted 19 June 2015

Available online 25 June 2015

Keywords:

Appendix

Appendectomy

Ischemic heart disease

ABSTRACT

Background: Although the appendix may not be considered vital, recent studies have noted adverse health consequences after appendectomy. This study aimed to use a population-based data set to explore whether appendectomy increases the risk for subsequent ischemic heart disease (IHD) in a 3-y follow-up period.

Materials and methods: This study used data from the Longitudinal Health Insurance Database 2000 in Taiwan. The study cohort included 5413 patients who underwent appendectomies. The comparison cohort was selected by randomly recruiting 16,239 enrollees matched with the study group in terms of sex, age, hypertension, hyperlipidemia, and diabetes. Each individual was tracked for 3 y to identify whether he and/or she developed IHD during the follow-up period. Cox proportional hazard regressions were performed for analysis.

Results: During a 3-y follow-up, 196 (3.62%) and 375 (2.31%) IHD incidents developed in the study and the comparison cohorts, respectively. For adults aged ≥ 18 y, experiencing an appendectomy was independently associated with a 1.54-fold increased risk of IHD during the 3 y of follow-up (95% CI = 1.29–1.84). The association persisted in further analyses stratified by age.

Conclusions: There is an increased risk of subsequent IHD within 3 y after appendectomy, and this underscores the need for more serious clinical decision-making in removing the appendix. Regular monitoring for IHDs is also recommended for patients who have undergone an appendectomy.

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M.-C.T. and S.-D.C. have equal contributions to this study.

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<http://dx.doi.org/10.1016/j.jss.2015.06.049>

1. Introduction

Acute appendicitis is inflammation of the appendix and a common cause of acute abdominal pain. It may happen at any age but is relatively uncommon at extremes of age [1]. Prompt clinical diagnosis for possible surgical intervention is required to avoid appendiceal perforation and peritonitis [2]. Based on a life table model using the national registry data from 2005 through 2007, the lifetime risk of appendicitis is 16.33% for males and 16.34% for females, whereas the lifetime risk of appendectomy is 9.89% for males and 9.61% for females [1].

The real function of the appendix remains unclear. Although it may not be considered vital to the body, recent studies note an association between appendectomy and other diseases, including increased risk for Crohn disease and reduced risk for ulcerative colitis [3–6]. Aside from chronic inflammatory disorders of the gastrointestinal tract close to the appendix, long-term health effects have also been investigated for other inflammation-related diseases, including ischemic heart disease (IHD) [7]. Because the cecal appendix is a secondary lymphoid organ and an important constituent of the mucosa-associated lymphoid tissue system, surgical removal of mucosa-associated lymphoid tissue may alter immune function. The link between appendectomy and inflammation with IHD is biologically plausible [8].

In a population-based cohort study in Sweden with a mean follow-up of about 23 y, Janszky *et al.* [7] report that appendectomy performed before 20 y of age is associated with an elevated risk of acute myocardial infarction (AMI) for both males and females. However, no significant finding is observed for appendectomy performed ≥ 20 y of age, as well as the subsequent risk of AMI. Nevertheless, in the same report, childhood exposure to appendectomy is mainly examined, and the study population remained relatively young even at the end of follow-up. Only a smaller subset of individuals aged ≥ 20 y at the time of appendectomy has been included for analysis. This is an important limitation to consider because myocardial infarction or IHD grows dramatically more common with increasing age [9]. Moreover, in terms of the longer-term effects of appendectomy on IHD, the higher risk among those with appendectomy is not evident until 15–20 y after the surgery [7].

To date, no study has specifically examined the risk of IHD shortly after appendectomy in an adult population. Using a nationwide population-based data set, this study aimed to explore whether appendectomy increases the risk of subsequent IHD during a 3-y follow-up period.

2. Materials and methods

2.1. Database

Data for this retrospective cohort study were retrieved from the “Longitudinal Health Insurance Database (LHID2000)”. Taiwan initiated a National Health Insurance (NHI) program in 1995 and the LHID2000 was composed of registration files and original medical claims for 1,000,000 enrollees. These 1,000,000 enrollees were randomly retrieved from all enrollees

listed in the 2000 Registry of Beneficiaries under the NHI program ($n = 23.72$ million) by the Taiwan National Health Research Institute. The LHID2000 allowed researchers to longitudinally trace the utilization of medical services for 1,000,000 enrollees and provides an excellent opportunity to explore the relationship between appendectomy and the subsequent risk of IHD.

This study was exempt from full review by the Institutional Review Board of Taipei Medical University (TMU-JIRB 201412035) because the LHID2000 consisted of deidentified secondary data released to the public for research purposes.

2.2. Study sample

This study cohort included 7119 patients who underwent an appendectomy (*International classification of Diseases (ICD)-9-CM procedure code 470, 470.1, or 470.9*) between January 1, 2002 and December 31, 2009. The date of the appendectomy procedure was defined as the index date. Acute appendicitis is the main indications for appendectomy. Patients aged < 18 y ($n = 1386$) were excluded, as well as all patients who had a diagnosis of IHD (ICD-9-CM codes 410–414 or 429.2) before their index date ($n = 320$) since the inauguration of the NHI program in 1995. The study cohort included 5413 patients who underwent appendectomies.

For the comparison cohort, 16,239 subjects (three for every patient who underwent an appendectomy) matched to the study cohort in terms of sex, age group (< 40 , 40–49, 50–59, 60–69, and > 69), hypertension, hyperlipidemia, diabetes, and year of index date were randomly retrieved. In this study, the matched comorbidities were only included if the condition occurred in an inpatient setting or appeared in two or more ambulatory care claims coded before the index date. The year of the index date for the comparison cohort was simply a matched year in which they used medical care.

The first health care use occurring in the index year was defined as their index date. However, patients would be excluded if their first episode of medical care in the relevant year of diagnosis was IHD. Patients in the comparison cohort aged < 18 y or those diagnosed with IHD before index date since the inauguration of the NHI program in 1995 were excluded. Furthermore, none of the selected comparison patients had ever undergone an appendectomy between the beginning of the NHI program in 1995 and the end of the 3-y follow-up period.

Each sampled patient ($n = 21,652$) was individually tracked for a 3-y period from their index date to identify those who had subsequently received an IHD diagnosis (ICD-9-CM codes 410–411, 413–414, or 429.2) during the follow-up period. In this study, IHD cases were only counted if this condition occurred in an inpatient setting or appeared in two or more ambulatory care claims coded during the follow-up period in both cohorts of patients with and without appendectomy.

2.3. Statistical analysis

The SAS system was used for all statistical analyses. Pearson χ^2 tests were performed to examine differences between patients who underwent appendectomies and comparison

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