Association between Nonalcoholic Fatty Liver Disease and Colon Polyps: A Case-Control Study in Taiwan

Kuan-Fu Liao,1,2 Pei-Ying Chung,3 Yu-Hung Kuo,4 and Shih-Wei Lai5,6

1College of Medicine, Tzu Chi University, Hualien, Taiwan
2Division of Hepatogastroenterology, Department of Internal Medicine, Taichung Tzu Chi Hospital, Taichung, Taiwan
3Department of Obstetrics and Gynecology, Taichung Tzu Chi Hospital, Taichung, Taiwan
4Department of Research, Taichung Tzu Chi Hospital, Taichung, Taiwan
5Department of Medicine, College of Medicine, China Medical University, Taichung, Taiwan
6Department of Family Medicine, China Medical University Hospital, Taichung, Taiwan

Correspondence should be addressed to Shih-Wei Lai; wei@mail.cmuh.org.tw

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Objective. To investigate the potential association between nonalcoholic fatty liver disease (NAFLD) and colon polyps in Taiwan.

Methods. We utilized 2006–2015 claims data of the Taiwan National Health Insurance Program as a data source. A case-control study was conducted, involving individuals 20 years or older with and without colon polyps. Cases comprised individuals diagnosed with colon polyps, identified through diagnosis codes. Controls were selected from individuals without colon polyps, matched to cases based on sex, age, and comorbidities. NAFLD was identified based on diagnosis codes. The logistic regression model with odds ratio (OR) and 95% confidence interval (CI) was employed to assess the association between NAFLD and colon polyps.

Results. The study included 16,890 cases with colon polyps and 67,560 matched controls without colon polyps. The mean age was 57 years old and about 61% of study subjects were males. Among cases with colon polyps, 1.0% had a diagnosis of NAFLD, whereas only 0.4% exhibited NAFLD in the control group. After adjustment for confounding variables, a multivariable logistic regression model revealed a statistically significant association between NAFLD and colon polyps, with an odds ratio of 2.32 (95% CI = 1.91–2.82).

Conclusion. This case-control study suggests a positive association between NAFLD and colon polyps. These results contribute to our understanding of the potential links between NAFLD and gastrointestinal health.

1. Introduction

Nonalcoholic fatty liver disease (NAFLD) is known as the accumulation of fat in the liver, typically defined as hepatic fat accumulation of 5% or greater, in the absence of significant alcohol consumption [1, 2]. NAFLD increasingly emerges as a global health concern and its prevalence continues to escalate, now affecting approximately 25% of the global population [3]. Currently, the impact of NAFLD extends beyond hepatology, with growing evidence suggesting potential associations with extrahepatic conditions, including metabolic and gastrointestinal disorders [4–6].
NAFLD, [12–15] but one study found no significant association between NAFLD and colon polyps [16]. This discrepancy emphasizes the complexity of the relationship between NAFLD and colon polyps, highlighting the need for additional research to resolve conflicting findings and elucidate the underlying mechanisms.

Therefore, our study aimed to contribute to this evolving field by conducting a case-control investigation into the association between NAFLD and colon polyps specifically within the population of Taiwan. Through rigorous methodology and careful adjustment for potential confounders, we seek to provide clarity on the extent of the association and its implications for clinical practice.

2. Methods

2.1. Data Source. We utilized data from the Taiwan National Health Insurance Program spanning from 2006 to 2015 as our primary data source. This comprehensive dataset encompasses the medical records of 2 million beneficiaries, capturing information on outpatient visits, inpatient admissions, emergency department visits, and medication usage.

2.2. Study Subjects and Study Design. The case group included subjects aged 20 years or older who were newly diagnosed colon polyps (based on International Classification of Diseases, Ninth Revision, Clinical Modification, ICD-9 codes 211.3 and 211.4). The date on which a subject was diagnosed with colon polyps was designated as the index date. In order to increase statistical power, for every one case with colon polyps, 4 controls were selected. The control group comprised randomly selected individuals aged 20 years or older who did not have a diagnosis of colon polyps. Cases and controls were matched with sex, age, and comorbidities (Figure 1). We performed a population-based case-control study to assess the association between NAFLD and colon polyps (Figure 2). The diagnosis of NAFLD was based on ICD-9 codes 571.8.

2.3. Comorbidities. Comorbidities before the index date were included as follows: cerebrovascular disease, chronic kidney disease, chronic obstructive pulmonary disease, coronary artery disease, diabetes mellitus, hyperlipidemia, and hypertension. All comorbidities were diagnosed based on ICD-9 codes.

2.4. Statistical Analysis. The statistical analysis involved the application of the chi-square test to evaluate differences in categorical variables between cases and controls. In addition, the t-test was employed to evaluate differences in continuous variables between cases and control. The logistic regression model with odds ratio (OR) and 95% confidence interval (CI) was employed to evaluate the association between NAFLD and colon polyps. Variables that exhibited statistical significance in the crude model were subsequently included in the multivariable logistic regression model. In this study, results with a P value less than 0.05 are considered statistically significant. The SAS (statistical analysis system) software was utilized in all analyses (version 9.4 for Windows; SAS Institute Inc., Cary, NC, USA).

3. Results

3.1. Basic Characteristics of Study Subjects. The study comprised 16,890 cases diagnosed with colon polyps and 67,560 matched controls without colon polyps (Table 1). The mean age was 57 years old, and about 61% of study subjects were males. Among cases with colon polyps, 1.0% had a diagnosis of NAFLD, whereas only 0.4% exhibited NAFLD in the control group. This discrepancy suggests a higher prevalence of NAFLD among cases with colon polyps compared to controls, with statistical significance observed (chi-square test, \( P < 0.001 \)). The proportion of chronic kidney disease was higher in the case group compared to the control group, with statistical significance observed (chi-square test, \( P = 0.004 \)).

3.2. Association between Colon Polyps, NAFLD, and Other Covariables. After adjustment for confounding variables, a multivariable logistic regression model revealed a statistically significant association between NAFLD and colon polyps, with an odds ratio of 2.32 (95% CI = 1.91–2.82, Table 2). Furthermore, chronic kidney disease was found to be associated with colon polyps (OR = 1.12, 95% CI = 1.03–1.22).

4. Discussion

In this case-control study, the prevalence of NAFLD was 1.0% among cases with colon polyps, signifying a higher prevalence compared to the control group, which was 0.4%. After adjusting for relevant confounding variables, there remains a substantial and independent association between NAFLD and colon polyps. The magnitude of the odds ratio (2.32) indicates a strong association. The existing literature reveals that most studies were consistent with our observations [12–15], but only one study showed no association between NAFLD and colon polyps [16]. Previous systematic review and meta-analysis also demonstrated a significant positive correlation between NAFLD and colorectal adenomas [17, 18]. These consistent observations support the hypothesis that hepatic metabolic conditions may influence colorectal health. The identification of NAFLD as a potential link to colon polyps has implications for clinical practice and public health. Clinicians should consider assessing colorectal health in individuals with NAFLD and vice versa. This integrated approach may lead to more effective preventive strategies, including lifestyle modification, early colorectal cancer screening, and targeted interventions for high-risk individuals.

The biological mechanisms underlying the association between NAFLD and colon polyps warrant consideration. Shared risk factors, such as insulin resistance, chronic inflammation, and alterations in gut microbiota, may contribute to the development of both conditions [19–22]. That
People enrolled in the Taiwan National Health Insurance Program, N=2,000,000
Excluding ages < 20 or ≥100 N=481,765
Colon polyp N=16,890
No colon polyp N=1,501,345
1:4 matched with sex, age, and comorbidities
Colon polyp N=16,890
No colon polyp N=67,560

Figure 1: Flow chart for selection of study subjects.

Colon polyp
No
colon polyp

NAFLD
No
NAFLD

NAFLD
No
NAFLD

Past
Onset of study
Time

Figure 2: Time frame for a case-control study. Nonalcoholic fatty liver disease (NAFLD).

Table 1: Characteristics between cases with colon polyps and control subjects.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cases with colon polyps</th>
<th>Control subjects</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N = 16,890</td>
<td>N = 67,560</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td>0.772</td>
</tr>
<tr>
<td>Male</td>
<td>10282 60.9</td>
<td>41046 60.8</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>6608 39.1</td>
<td>26514 39.2</td>
<td></td>
</tr>
<tr>
<td>Age group (years)</td>
<td></td>
<td></td>
<td>0.581</td>
</tr>
<tr>
<td>20–39</td>
<td>1684 10.0</td>
<td>6725 10.0</td>
<td></td>
</tr>
<tr>
<td>40–64</td>
<td>10254 60.7</td>
<td>40796 60.4</td>
<td></td>
</tr>
<tr>
<td>65–84</td>
<td>4669 27.6</td>
<td>18811 27.8</td>
<td></td>
</tr>
<tr>
<td>≥85</td>
<td>283 1.7</td>
<td>1228 1.8</td>
<td></td>
</tr>
<tr>
<td>Age (years), mean ± standard deviation†</td>
<td>57.4 ± 13.3</td>
<td>57.5 ± 13.4</td>
<td>0.356</td>
</tr>
<tr>
<td>Nonalcoholic fatty liver disease</td>
<td>161 1.0</td>
<td>278 0.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Comorbidities before index date</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>1035 6.1</td>
<td>4059 6.0</td>
<td>0.558</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>775 4.6</td>
<td>2769 4.1</td>
<td>0.004</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>1481 8.8</td>
<td>5787 8.6</td>
<td>0.401</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>2004 11.9</td>
<td>7888 11.7</td>
<td>0.493</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>2686 15.9</td>
<td>10763 15.9</td>
<td>0.929</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>3810 22.6</td>
<td>15111 22.4</td>
<td>0.594</td>
</tr>
<tr>
<td>Hypertension</td>
<td>6010 35.6</td>
<td>24050 35.6</td>
<td>0.971</td>
</tr>
</tbody>
</table>

*Chi-square test. †t-test comparing cases with colon polyps and control subjects.
is, hepatic inflammation and metabolic dysfunction associated with NAFLD could potentially influence the colonic environment and could further promote the formation of colon polyps. However, more studies combining the biomarker analysis and molecular pathways are needed to prompt a comprehensive exploration of potential mechanisms and clinical implications.

Some limitations of our study are discussed. First, the case-control design does not allow us to establish causality definitively. In addition, because NAFLD and colon polyps often have no symptoms or signs, we cannot determine which appears first. While we observed a strong association between NAFLD and colon polyps, it is essential to interpret these findings as evidence of an association rather than a causal relationship. Second, despite cases and controls were matched with sex, age, and comorbidities, unmeasured confounding variables, such as obesity, alcohol consumption, smoking, dietary factors, and family history of colon polyps/colon cancer, might affect the results. Third, due to the constraints of the database utilized, the definition of NAFLD and colon polyps was based solely on the ICD-9 codes, lacking detailed clinical criteria or confirmed diagnoses through specific diagnostic procedures such as liver biopsy or colonoscopy. It may introduce misclassification bias. For example, it is currently estimated that 32.4% of the adult population has NAFLD worldwide [23], but in our study, only 1.0% of cases with colon polyps and 0.4% of controls were found to have NAFLD. The prevalence of NAFLD seems to be underestimated in our study. In addition, we cannot quantify steatosis and fibrosis of NAFLD because ICD-9 codes do not address the pathological findings. Similarly, the subtypes of colon polyps, such as adenomatous polyps, serrated polyps, and hyperplastic polyps, as well as variations in the number and size of polyps, cannot be distinguished solely based on ICD-9 codes. However, differentiating the subtypes of colon polyps and assessing the number and size of polyps are crucial due to their distinct clinical implications. Prospective studies with more rigorous diagnostic criteria and long-term follow-up are necessary to validate and extend our observations. Despite the aforementioned limitations, a notable strength of our study lies in the utilization of a large dataset. This enabled robust statistical analysis and provided sufficient power to detect meaningful association between NAFLD and colon polyps. In addition, the findings of the study have potential implications in clinical practice, including risk assessment, screening strategies, and targeted interventions for individuals at a higher risk of developing colon polyps due to the presence of NAFLD.

5. Conclusions
In conclusion, this case-control study suggests a significant association between NAFLD and colon polyps. While our findings contribute to the understanding of the potential link between NAFLD and gastrointestinal health, further research is imperative to validate and extend these observations. Given the widespread use of noninvasive abdominal ultrasound as a health screening tool in the general population, our study has the potential to inform the development of colonoscopic strategies for individuals who undergo such screenings. By elucidating the association between NAFLD and colon polyps, physicians may consider heightened vigilance for colon polyps in individuals diagnosed with NAFLD.

Data Availability
Insurance reimbursement claims data used in the study were available for public access.

Ethical Approval
All methods were performed in accordance with relevant guidelines and regulations. Patient identification numbers had been scrambled to ensure confidentiality.

Consent
The informed consent was waived.

Conflicts of Interest
The authors declare that they have no conflicts of interest.

Table 2: Odds ratio and 95% confidence interval for the association between colon polyps, nonalcoholic fatty liver disease, and other covariables by the logistical regression model.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Crude OR (95% CI)</th>
<th>Adjusted† OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (male vs. female)</td>
<td>1.01 (0.97–1.04)</td>
<td></td>
</tr>
<tr>
<td>Age (per one year)</td>
<td>1.00 (1.00–1.00)</td>
<td></td>
</tr>
<tr>
<td>Nonalcoholic fatty liver disease (yes vs. no)</td>
<td>2.33 (1.92–2.83)</td>
<td>2.32 (1.91–2.82)</td>
</tr>
<tr>
<td>Comorbidities before index date (yes vs. no)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>1.02 (0.95–1.10)</td>
<td></td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>1.13 (1.04–1.22)</td>
<td>1.12 (1.03–1.22)</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>1.03 (0.97–1.09)</td>
<td></td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>1.02 (0.97–1.07)</td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1.00 (0.95–1.05)</td>
<td></td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>1.01 (0.97–1.05)</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.00 (0.97–1.04)</td>
<td></td>
</tr>
</tbody>
</table>

†Variables that exhibited statistical significance in the crude model were subsequently included in the multivariable logistic regression model.
Authors’ Contributions
Kuan-Fu Liao and Pei-Ying Chung initiated the conception of the article and contributed equally to the article. Shih-Wei Lai initiated the draft of the article and approved the final draft. Yu-Hung Kuo conducted data analysis.

References
[14] K. W. Huang, H. B. Leu, Y. J. Wang et al., “Patients with nonalcoholic fatty liver disease have higher risk of colorectal adenoma after negative baseline colonoscopy,” Colorectal Disease, vol. 15, no. 7, pp. 830–835, 2013.