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Research Article

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

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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]. The association between NAFLD and colon polyps has garnered attention, raising interesting questions about the interaction between liver and gastrointestinal health.

Colon polyps, particularly adenomatous polyps, are recognized as precursors to colorectal cancer, a leading cause of morbidity and mortality globally [7, 8]. While lifestyle factors and genetic predispositions have been extensively explored in the context of colon polyp development, the potential involvement of metabolic conditions remains an area of active investigation [9–11]. To date, several studies have demonstrated a positive association, suggesting an increased risk of colon polyps among individuals with

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 statistic 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

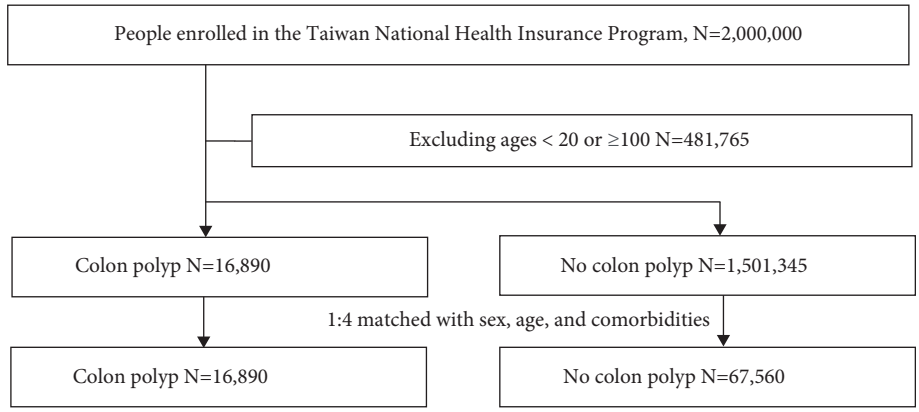

Figure 1: Flow chart for selection of study subjects.

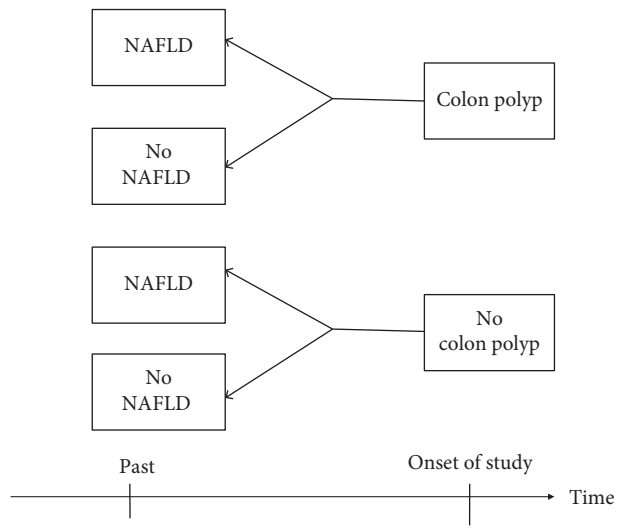

Figure 2: Time frame for a case-control study. Nonalcoholic fatty liver disease (NAFLD).

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

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

*Chi-square test. †*t*-test comparing cases with colon polyps and control subjects.

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.

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

[†]Variables that exhibited statistical significance in the crude model were subsequently included in the multivariable logistic regression model.

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.

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.

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