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CE - RESEARCH LETTER TO THE EDITOR

Patients with appendectomy are at increased risk of herpes zoster: real-world data in Taiwan

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Some case reports showed that despite being rare, acute appendicitis could be caused by primary varicella-zoster virus infection [1]. Epidemiologic studies have shown that appendectomy is associated with increased risk of various infections including pyogenic liver abscess and biliary tract infection [2, 3], but the relationship between appendectomy and herpes zoster has not yet been explored. To explore this relationship, a cohort study was conducted using the database of the Taiwan National Health Insurance Program with 23 million citizens living in an independent country of Taiwan [4].

Subjects aged 20–84 years with newly diagnosed appendectomy from 2000 to 2012 were identified as the appendectomy group. To increase a statistic power, for each subject with appendectomy, four sex-matched and age-matched subjects without appendectomy were identified as the non-appendectomy group. Both appendectomy and non-appendectomy groups were followed until herpes zoster was newly diagnosed or until the end of 2013.

The study population consisted of 9485 subjects in the appendectomy group (mean age ± standard deviation 43.0 ± 16.1 years) and 37,940 subjects in the non-appendectomy group (mean age ± standard deviation 42.8 ± 16.4 years). Table 1 presented that at the end of follow-up, the appendectomy group had a higher incidence of herpes zoster than the non-appendectomy group (4.35 versus 3.31 per 1000 person-years, incidence rate ratio 1.31, 95% confidence interval 1.23–1.40). As stratified by sex and age, the incidence of herpes zoster was all statistically higher in the appendectomy group than the non-appendectomy group. Female subjects, no matter in appendectomy group or non-appendectomy group, had a higher incidence of herpes zoster than male subjects. The incidences of herpes zoster increased with age in both appendectomy and non-appendectomy groups, with the highest in the appendectomy group aged 65–84 years (12.0 per 1000 person-years). The Kaplan–Meier model showed that the appendectomy group had a higher cumulative incidence of herpes zoster than the non-appendectomy group at the end of follow-up (5.06% vs. 4.13%; $P < 0.001$, Fig. 1).

In the present study, we found that subjects with appendectomy were at increased risk of herpes zoster compared with non-appendectomy subjects. The risk of herpes zoster remained high with time. Because no other relevant study was reported for comparison, we suggest that other real-world evidence is needed to confirm our findings. We reviewed the relevant literature to make a rational explanation. The human appendix is recognized as a part of the immune system because many immune-related cells can be found in the normal appendix [5]. Appendectomy might alter the immune functions. It partially explains that subjects with appendectomy are at increased risk of various infections including pyogenic liver abscess and biliary tract infection [2, 3]. Similarly, appendectomy might be potentially associated with reactivation of latent varicella-zoster virus infection and subsequent development of herpes zoster. Because post-herpetic neuralgia is frustrating, from a concept of primary prevention, vaccination for herpes zoster is suggested in patients with appendectomy.

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Table 1 Incidences of herpes zoster in appendectomy group and non-appendectomy group stratified by sex and age

Variable	Non-appendectomy				Appendectomy				Incidence rate ratio (95% CI)[a]
	N	Event	Person-years	Incidence	*N*	Event	Person-years	Incidence	
All	37,940	926	279,431	3.31	9485	294	67,577	4.35	1.31 (1.23–1.40)
Sex									
Female	18,208	497	135,513	3.59	4552	164	32,858	4.99	1.39 (1.27–1.52)
Male	19,732	439	143,918	3.05	4933	130	34,719	3.74	1.23 (1.12–1.34)
Age group (years)									
20–39	26,408	359	204,110	1.76	6602	106	50,163	2.11	1.20 (1.11–1.30)
40–64	6784	284	45,945	6.18	1696	109	10,810	10.1	1.63 (1.43–1.86)
65–84	4748	283	29,376	9.63	1187	79	6603	12.0	1.24 (1.05–1.46)

Incidence: per 1000 person-years

[a]Incidence rate ratio: appendectomy versus non-appendectomy (95% confidence interval)

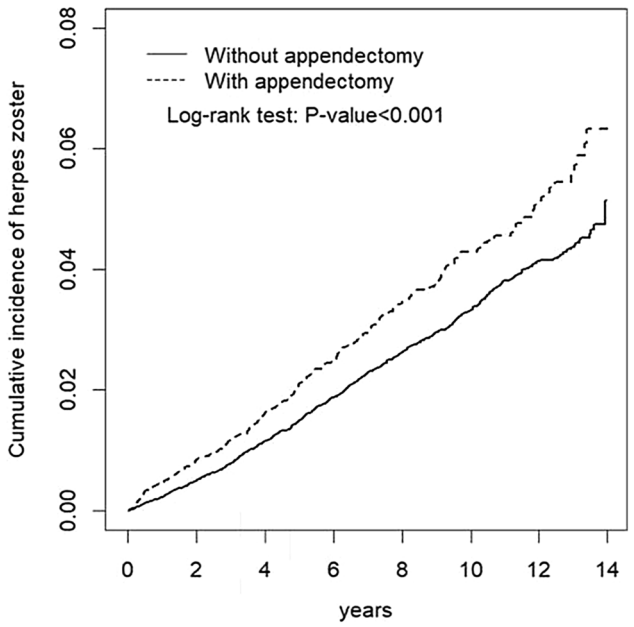

Fig. 1 Kaplan–Meier model showed that the cumulative incidence of herpes zoster for the appendectomy group and the non-appendectomy group (5.06% vs. 4.13%; $P < 0.001$)

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Author contributions S-WL contributed to the conception of the article, initiated the draft of the article, and revised the article. C-LL conducted data analysis.

Compliance with ethical standards

Conflict of interest The authors disclose no conflicts of interest.

Statement of human and animal rights Insurance reimbursement claims data used in this study were available for public access. Patient identification numbers were scrambled to ensure confidentiality. This study was approved by the Research Ethics Committee of China Medical University and Hospital in Taiwan (CMUH-104-REC2-115).

Informed consent Patient informed consent was not required.

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