Herpes Zoster and Subsequent Cancer Risk

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Dear Editor,

Epidemiological studies have shown that patients with cancer are at risk of developing herpes zoster [1, 2], but no consistent association has been shown between herpes zoster and subsequent cancer risk. Recently, a nationwide retrospective cohort study in the Republic of Korea conducted by Kim et al. [3] published in *Dermatology* reported that the overall incidence rate of subsequent cancer was similar between patients with and without herpes zoster (7.62 vs. 7.66 per 1,000 person-years), which was compatible with previous research [4]. The study by Kim et al. [3] added marked value to the current literature and indicates future research direction.

In order to test this issue in a different population, a preliminary nationwide cohort study was conducted using the 2003–2012 database of the Taiwan National Health Insurance Program with 23 million residents living in Taiwan [5, 6]. There were 17,624 subjects aged 20–84 years with newly diagnosed herpes zoster in the herpes zoster group and 35,248 randomly selected sex-matched and age-matched subjects without herpes zoster in the non-herpes zoster group. Subjects with a history of any cancers before the index date were excluded from the study. Table 1 demonstrates that the overall incidence

rate of subsequent cancer was 1.16-fold higher in the herpes zoster group than in the non-herpes zoster group (1.07 vs. 0.92 per 100 person-years, 95% confidence interval [CI] 1.07–1.27; $p = 0.001$). As stratified by sex and age, the incidence rates of subsequent cancer were all higher in the herpes zoster group than in the non-herpes zoster group. The incidence rates of subsequent cancer increased with age in both groups, the highest being in the herpes zoster group aged 65–84 years (1.98 per 100 person-years). Although the incidence rate of subsequent cancer was higher within 1 year of herpes zoster diagnosis when compared with the non-herpes zoster group (14.09 vs. 12.47 per 100 person-years), it did not reach statistical significance (95% CI 0.92–1.39; $p = 0.24$). The incidence rate of subsequent cancer appeared to be statistically higher after 1 year of herpes zoster diagnosis, compared with the non-herpes zoster group (0.89 vs. 0.77 per 100 person-years, 95% CI 1.06–1.27; $p = 0.002$).

Our study demonstrates that the relative risk for subsequent cancer was modestly higher in the herpes zoster group (incidence rate ratio 1.16), which is compatible with a meta-analysis showing that the relative risk for subsequent cancer was 1.42 (95% CI 1.18–1.71) among herpes zoster patients [7]. We noted that the risk of sub-

Table 1. Incidence rate of subsequent cancer between adults with and without herpes zoster

Variable	Herpes zoster				Non-herpes zoster				IRR (95% CI) ^a	p value
	n	events	person-years	incidence	n	events	person-years	incidence		
All	17,624	833	77,948	1.07	35,248	1,442	156,962	0.92	1.16 (1.07–1.27)	0.001
Sex										
Men	8,092	434	35,831	1.21	16,184	773	72,144	1.07	1.13 (1.01–1.27)	0.041
Women	9,532	399	42,117	0.95	19,064	669	84,818	0.79	1.20 (1.06–1.36)	0.004
Age group										
20–39 years	3,195	32	14,221	0.23	6,390	41	28,553	0.14	1.57 (0.99–2.49)	0.057
40–64 years	9,273	360	41,471	0.87	18,546	605	83,457	0.72	1.20 (1.05–1.36)	0.007
65–84 years	5,156	441	22,256	1.98	10,312	796	44,952	1.77	1.12 (1.00–1.26)	0.058
Follow-up period										
<12 months	2,244	146	1,036	14.09	4,451	248	1,989	12.47	1.13 (0.92–1.39)	0.240
≥12 months	15,380	687	76,912	0.89	30,797	1,194	154,973	0.77	1.16 (1.06–1.27)	0.002

Incidence rate: per 100 person-years. IRR, incidence rate ratio; CI, confidence interval. ^a IRR: herpes zoster versus non-herpes zoster.

sequent cancer was statistically higher among those with a diagnosis of herpes zoster for 1 year or longer. Due to the good quality of the Taiwan medical system, it did not need to take 1 year to make a diagnosis of cancer since the onset of cancer-related symptoms. Therefore, spending 1 year or longer to make a diagnosis of cancer seemed to be a long time since the presentation of herpes zoster. It is not a reasonable assumption that herpes zoster is associated with an increased risk of developing cancer, but whether herpes zoster could be a marker of occult cancer needs confirmation from other real-world data. Currently, there is no definite evidence to support screening all cancers among those with a new diagnosis of herpes zoster.

Key Message

Currently there is no definite evidence to support screening all cancers among those with a new diagnosis of herpes zoster.

Disclosure Statement

The authors have no conflicts of interest to declare.

Author Contributions

Shih-Wei Lai contributed to the conception of the article, initiated the draft of the article, and approved the final draft submitted. Yu-Hung Kuo and Kuan-Fu Liao conducted the data analysis.

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