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Risk of Psoriasis in Postgastrectomy Gastric Cancer Survivors: A Nationwide Population-Based Cohort Study

Bo Ri Kim*, Dong Ho Lee[1,*], Hyun Ik Shim[1], Jee Woo Kim, Sanghyun Park[2], Cheol Min Shin[1], Kyungdo Han[3], Sang Woong Youn

Departments of Dermatology and [1]Internal Medicine, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam, [2]Department of Biostatistics, The Catholic University of Korea, [3]Department of Statistics and Actuarial Science, Soongsil University, Seoul, Korea

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Corresponding Author
Kyungdo Han
Department of Statistics and Actuarial Science, Soongsil University, 369 Sangdo-ro, Dongjak-gu, Seoul 06978, Korea
Tel: +82-2-820-7025
Fax: +82-2-823-1746
E-mail: hkd917@naver.com
https://orcid.org/0000-0002-6096-1263

Sang Woong Youn
Department of Dermatology, Seoul National University Bundang Hospital, 82 Gumi-ro 173beon-gil, Bundang-gu, Seongnam 13620, Korea
Tel: +82-31-787-7312
Fax: +82-31-787-4058
E-mail: swyoun@snu.ac.kr
https://orcid.org/0000-0002-5602-3530

*These authors have equally contributed to the article.

Background: Although patients with psoriasis have an increased risk of cancers, little is known about the risk of psoriasis in cancer patients.
Objective: We aimed to comparatively analyze the incidence and risk factors of psoriasis in gastric cancer patients who underwent gastrectomy and in the general population.
Methods: A nationwide retrospective cohort of 52,608 gastric cancer survivors (2007~2015) was compared to 123,438 matched controls from the general population to estimate the incidence and hazard ratio (HR) of new-onset psoriasis. We also calculated the HRs for psoriasis according to adjuvant cancer treatment, obesity, and vitamin B_{12} supplementation in gastric cancer survivors.
Results: During a mean follow-up of 6.85 years, 645 of the 52,608 gastric cancer patients developed psoriasis, while 1,806 in the 123,438 matched control group developed psoriasis. Gastric cancer patients had a decreased risk of psoriasis (HR, 0.86; 95% confidence interval, 0.79~0.94), especially those who underwent subtotal gastrectomy. We found that vitamin B_{12} supplementation for more than 3 years had an additive effect on decreasing the risk of psoriasis in gastric cancer patients who underwent subtotal gastrectomy. Total gastrectomy, radio/chemotherapy, and obesity did not affect the risk of psoriasis in gastric cancer survivors.
Conclusion: The incidence of psoriasis is slightly lower in gastric cancer survivors than in the general population. Our results suggest that the development of psoriasis may be reduced by removing the source of systemic inflammation caused by *Helicobacter pylori* infection through subtotal gastrectomy in gastric cancer survivors.

Keywords: Epidemiology, Gastrectomy, Psoriasis, Stomach diseases, Stomach neoplasms

INTRODUCTION

Cancer is a major disease, with 18.1 million new cases and 9.6 million cancer deaths reported worldwide in 2018[1]. The number of cancer survivors continues to increase due to improvements in early detection and treatment, and in 2018, there were 43.8 million people who were alive within 5 years of their cancer diagnosis[1,2]. In Korea, gastric cancer is the most frequently diagnosed cancer, and the 5-year survival rate of gastric cancer in 2010~2014 (68.9%) was the highest in Korea among 71 countries[3,4]. The increased survival of patients with gastric cancer in Korea is the result of early diagnosis and treatment through its nationwide screening program; consequently, the 5-year survival rate of patients with gastric cancer who had undergone curative gastrectomy exceeded 80%[5,6]. As the number of gastric cancer survivors increases, the interest in their long-term outcomes and management is increasing substantially[7-10].

Psoriasis is a common chronic inflammatory disease affecting 1%~3% of the general population[11]. Although psoriasis

primarily affects the skin, it is considered a systemic disease characterized by immune system dysfunction and the production of pro-inflammatory cytokines[12-15]. Psoriasis is associated with multiple comorbidities related to systemic inflammation, including cardiovascular disease, obesity, metabolic syndrome, and diabetes[16]. Furthermore, the risk of malignancy is of special concern among patients with psoriasis because the chronic systemic inflammation of psoriasis itself and immunosuppressive treatments may be associated with an increased risk of cancer. Recent meta-analyses and large cohort studies have reported increased risk of overall malignancy in patients with psoriasis[17-21], and a study in Korea highlighted the increased risk of gastric cancer in such cases[22]. However, on the contrary, estimates of the incidence and relative risk of psoriasis for patients with cancer as compared to those for the general population are extremely limited. Although a Swedish population-based cohort study reported a 17% higher risk of psoriasis in patients with breast cancer than in the general population[23], no study has focused on the risk of psoriasis in other cancer patients. The risk of psoriasis in cancer survivors may be different from that in the general population because cancer cells and immunosuppressive cancer treatments such as chemotherapy can affect the immune system of cancer patients and change the immunopathogenesis of psoriasis.

In this study, we aimed to investigate the relative risk and incidence rates of psoriasis among gastric cancer patients who underwent gastrectomy and among the general population using a nationally representative sample. In addition, we evaluated the risk factors of psoriasis in gastric cancer survivors.

MATERIALS AND METHODS

Data source

Our retrospective cohort was obtained from the Korean National Health Insurance Services (NHIS) database. The NHIS is Korea's mandatory universal single-payer national healthcare system for approximately 97% of the Korean population. People in the lowest income bracket are covered by Medicaid, which is funded by general taxes.

The NHIS database contains data on the beneficiaries, such as age, sex, place of residence, monthly insurance premium, disability, medical claims information, such as disease codes (based on the International Classification of Diseases, 10th Revision; ICD-10), procedures, prescriptions, and costs incurred. It also contains the results of health screening examinations because the NHIS provides biennial National Health Screening Program to all beneficiaries who are 40 years and older and all employees regardless of age[24].

The study protocol was approved by the institutional review board (IRB number: X-2005/613-904). The requirement for informed consent was waived because we used only de-identified data.

Study population

We included 150,790 patients who underwent total or subtotal gastrectomy for gastric cancer (C16) between January 1, 2007 and December 31, 2015. Patients were excluded if they had no health check-up data or had a history of another cancer (C00 to C97 except C16) or psoriasis before their gastric cancer diagnosis. In addition, we excluded patients who died or developed psoriasis within 3 years after gastrectomy because the effect of gastrectomy would not be immediate[10]. Finally, we

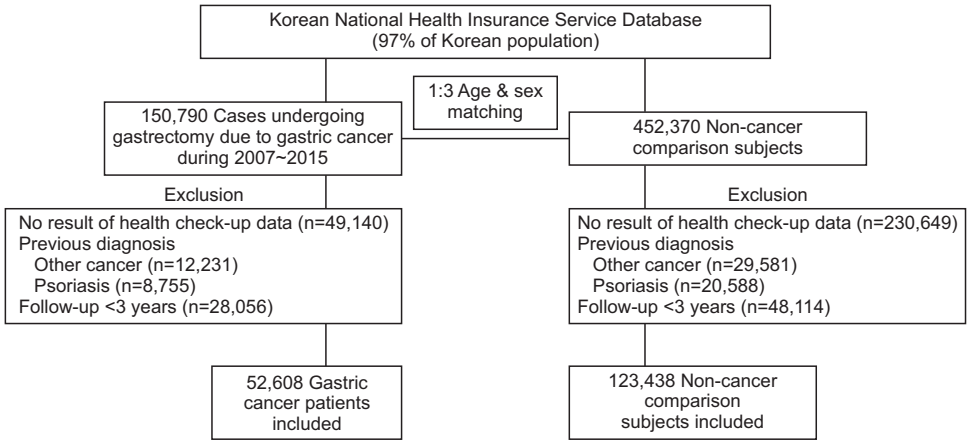

Fig. 1. Flowchart of study participants.

included 52,608 patients with gastric cancer in this study.

The control group consisted of 452,370 subjects without cancer were selected as a 1:3 age- and sex-matched control group for the 150,790 gastric cancer patients. Matching was performed on a year-by-year basis such that incident gastric cancer cases were matched to control cases based on information from the year of cancer diagnosis. The baseline characteristics used for matching were derived from the previous year. We applied the same exclusion criteria to the control group as we did to the gastric cancer group. Matched control subjects (n=123,438) were assigned an index date corresponding to the date of gastrectomy of their matched gastric cancer patients. The flow chart of the study participants is shown in Fig. 1.

Outcome measures

The primary outcome was the incidence of psoriasis. Psoriasis was defined as the presence of L40 code and antipsoriatic drug codes (including topicals, systemics, and biologics). Participants were followed from the index date until the development of psoriasis, death for censored date, or the end of the study on December 31, 2015.

Statistical analyses

The baseline characteristics of the study population are presented using descriptive statistics. A Cox regression analysis was performed to evaluate the risk of psoriasis according to gastrectomy status and was adjusted for age, sex, income, place of residence, diabetes, hypertension, dyslipidemia, smoking, alcohol, and body mass index (BMI). To study the effects of radiotherapy and chemotherapy on the risk of psoriasis, the hazard ratios (HRs) of psoriasis according to adjuvant cancer treatment in gastric cancer survivors were analyzed. In addition, we performed stratified analyses according to BMI or duration of vitamin B_{12} supplementation to evaluate whether obesity or vitamin B_{12} supplementation affected the development of psoriasis among gastric cancer patients. We used the prescribed drug claims records at 3 years after gastrectomy to classify the patients who received vitamin B_{12} supplementation for more than 3 years and those who received vitamin B_{12} supplementation for less than 3 years. Data were analyzed using the SAS software version 9.4 (SAS Institute, Cary, NC, USA). *p*-values less than 0.05 were considered statistically significant. The detailed codes used for analysis are described in the online supplementary content (Supplementary Table 1).

RESULTS

Characteristics of the study population

Table 1 shows the demographics and clinical characteristics of the patients with gastric cancer and matched controls. Their mean age was 58.60±11.17 years, and female accounted for 33.76% of the study population. The gastric cancer patients were more likely than the matched controls to have diabetes and hypertension, to be current smokers, to drink

Table 1. Baseline characteristics of study participants

Characteristic	Matched control (n=123,438)	Gastric cancer survivors (n=52,608)
Age (yr)	58.27±11.11	58.92±11.23
Sex		
Male	82,312 (66.68)	34,621 (65.81)
Female	41,126 (33.32)	17,987 (34.19)
Income		
Highest quartile	30,265 (24.52)	12,301 (23.38)
2nd quartile	27,459 (22.25)	12,058 (22.92)
3rd quartile	30,445 (24.66)	13,451 (25.57)
Lowest quartile and medicaid	35,269 (28.57)	14,798 (28.13)
Place of residence		
Metropolitan	74,152 (60.07)	31,065 (59.05)
City	34,402 (27.87)	14,996 (28.51)
Rural	14,884 (12.06)	6,547 (12.44)
Diabetes	18,584 (15.06)	9,452 (17.97)
Hypertension	51,808 (41.97)	22,716 (43.18)
Dyslipidemia	31,803 (25.76)	12,282 (23.35)
Smoking		
Non	72,008 (58.34)	27,832 (52.9)
Ex	22,778 (18.45)	9,458 (17.98)
Current	28,652 (23.21)	15,318 (29.12)
Alcohol		
Non	67,148 (54.76)	28,048 (53.62)
Moderate (<30 g/day)	34,561 (28.19)	14,922 (28.53)
Heavy (≥30 g/day)	20,904 (17.05)	9,336 (17.85)
BMI (kg/m^2)	24.03±3.00	23.84±3.06
Radiotherapy	0 (0)	865 (1.64)
Chemotherapy	0 (0)	8,743 (16.62)

Values are presented as mean±standard deviation or number (%).
BMI: body mass index.

alcohol and to have low BMI. The matched group was more likely to have dyslipidemia than the gastric cancer group. Among the gastric cancer survivors, 1.64% and 16.62% received radiotherapy and chemotherapy, respectively.

Psoriasis incidence in gastric cancer survivors

For the total study population, the mean follow-up period after the 3-year time lag was 3.85 years (3.78 years for the gastric cancer survivors and 3.87 years for the matched controls). During the follow-up period, 645 of the 52,608 gastric cancer patients developed psoriasis (incidence rate, 3.24 per 1,000 person-years), while 1,806 in the 123,438 matched controls developed psoriasis (incidence rate, 3.78 per 1,000 person-years) (Table 2). The crude and multivariable-adjusted hazard ratios (aHRs) for the incidence of psoriasis in those with and without gastric cancer were 0.86 (95% confidence interval [CI], 0.79~0.94) and 0.85 (95% CI, 0.78~0.94), respectively. When psoriasis risk was evaluated by type of surgery, only gastric cancer patients who underwent subtotal gastrectomy showed a decreased risk of psoriasis as compared with the matched non-cancer control group (aHR, 0.85; 95% CI, 0.77~0.94). Analyses by adjuvant cancer treatment showed no effect of radiotherapy and chemotherapy on psoriasis risk (Table 3).

Effect of BMI on the development of psoriasis

To investigate the effect of BMI on psoriasis development, the incidence of psoriasis was compared by categorizing the study participants according their status as obese (BMI ≥25 kg/m^2) or not obese (BMI <25 kg/m^2). Regardless of the obesity status, the risk of psoriasis in gastric cancer patients, especially those who underwent subtotal gastrectomy, was significantly lower than that in the controls (Table 4).

Effect of vitamin B_{12} supplementation on the development of psoriasis

In order to investigate the effect of vitamin B_{12} supplementation on the development of psoriasis, we further dividing the groups according to the duration of vitamin B_{12} supplementation (Table 5). The risk of psoriasis was significantly low (aHR, 0.85; 95% CI, 0.75~0.96) in gastric cancer patients who did not receive vitamin B_{12} supplementation and in those

Table 2. Event count and incidence rates of psoriasis in gastric cancer survivors and matched controls

Group	Number	Event*	Person-years (p-y)	Incidence rate (per 1,000 p-y)	HR (95% CI)	aHR (95% CI)
Matched controls	123,438	1,806	477,943.4	3.77869	1 (Reference)	1 (Reference)
Gastric cancer survivors	52,608	645	199,012.5	3.241	0.86 (0.79~0.94)	0.85 (0.78~0.94)
Surgery type						
Subtotal gastrectomy	42,624	524	162,693.51	3.22078	0.85 (0.77~0.94)	0.85 (0.77~0.94)
Total gastrectomy	9,984	121	36,318.99	3.33159	0.88 (0.74~1.06)	0.88 (0.73~1.05)

The multivariate model was adjusted for age, sex, income, place of residence, diabetes, hypertension, dyslipidemia, smoking, alcohol, and body mass index. HR: hazard ratio, CI: confidence interval, aHR: adjusted hazard ratio. *Participants who developed psoriasis.

Table 3. Hazard ratios (HRs) (95% CIs) for psoriasis in gastric cancer survivors stratified by adjuvant cancer treatment

Group	Number	Event*	Person-years (p-y)	Rate (per 1,000 p-y)	HR (95% CI)	aHR (95% CI)
Radiotherapy						
No	51,743	636	195,484.98	3.25345	1 (Reference)	1 (Reference)
Yes	865	9	3,527.52	2.55137	0.781 (0.40~1.51)	0.86 (0.45~1.66)
Chemotherapy						
No	43,865	540	169,976.72	3.17691	1 (Reference)	1 (Reference)
Yes	8,743	105	29,035.78	3.61623	1.142 (0.93~1.41)	1.125 (0.91~1.39)

The multivariate model was adjusted for age, sex, income, place of residence, diabetes, hypertension, dyslipidemia, smoking, alcohol consumption, and body mass index. CI: confidence interval, aHR: adjusted hazard ratio. *Participants who developed psoriasis.

Table 4. Incidence of psoriasis in gastric cancer patients and matched controls according to obesity

Group	Number	Event*	Person-years (p-y)	Rate (per 1,000 p-y)	HR (95% CI)	aHR (95% CI)
BMI <25 kg/m^2						
Matched controls	79,703	1,118	308,458.44	3.62448	1 (Reference)	1 (Reference)
Gastric cancer survivors	34,978	418	132,252.81	3.16061	0.87 (0.78~0.98)	0.86 (0.77~0.97)
Subtotal gastrectomy	28,120	339	107,407.78	3.1562	0.87 (0.77~0.98)	0.86 (0.76~0.97)
Total gastrectomy	6,858	79	24,845.03	3.17971	0.88 (0.70~1.10)	0.87 (0.69~1.10)
BMI ≥25 kg/m^2						
Matched controls	43,735	688	169,484.96	4.05936	1 (Reference)	1 (Reference)
Gastric cancer survivors	17,630	227	66,759.69	3.40026	0.84 (0.72~0.98)	0.84 (0.72~0.98)
Subtotal gastrectomy	14,504	185	55,285.73	3.34625	0.83 (0.70~0.97)	0.83 (0.71~0.98)
Total gastrectomy	3,126	42	11,473.96	3.66046	0.90 (0.66~1.24)	0.88 (0.64~1.21)

The multivariate model was adjusted for age, sex, income, place of residence, diabetes, hypertension, dyslipidemia, smoking, and alcohol consumption. BMI: body mass index, HR: hazard ratio, CI: confidence interval, aHR: adjusted hazard ratio. *Participants who developed psoriasis.

Table 5. Incidence of psoriasis in gastric cancer patients and matched controls according to vitamin B_{12} supplementation

Group	Number	Event*	Person-years (p-y)	Rate (per 1,000 p-y)	HR (95% CI)	aHR (95% CI)
No supplements						
Matched controls	49,636	651	171,279.57	3.8008	1 (Reference)	1 (Reference)
Gastric cancer survivors	38,644	467	143,326.52	3.25829	0.85 (0.76~0.96)	0.85 (0.75~0.96)
Subtotal gastrectomy	35,503	425	133,392.64	3.18608	0.84 (0.74~0.94)	0.83 (0.74~0.94)
Total gastrectomy	3,141	42	9,933.88	4.22795	1.11 (0.81~1.52)	1.08 (0.79~1.47)
Started supplementation but quit within 3 years						
Matched controls	5,384	60	16,497.09	3.637	1 (Reference)	1 (Reference)
Gastric cancer survivors	4,401	58	12,828.39	4.52122	1.25 (0.87~1.80)	1.26 (0.87~1.82)
Subtotal gastrectomy	2,756	44	9,290.96	4.73579	1.31 (0.89~1.93)	1.33 (0.90~1.98)
Total gastrectomy	1,645	14	3,537.43	3.95768	1.10 (0.62~1.98)	1.07 (0.60~1.93)
Started supplementation more than 3 years after surgery						
Matched controls	12,505	187	50,512.03	3.70209	1 (Reference)	1 (Reference)
Gastric cancer survivors	9,563	120	42,857.59	2.79997	0.74 (0.59~0.94)	0.76 (0.60~0.96)
Subtotal gastrectomy	4,365	55	20,009.91	2.74864	0.73 (0.54~0.98)	0.72 (0.53~0.98)
Total gastrectomy	5,198	65	22,847.68	2.84493	0.76 (0.57~1.01)	0.79 (0.59~1.05)

The multivariate model was adjusted for age, sex, income, place of residence, diabetes, hypertension, dyslipidemia, smoking, alcohol, and body mass index. CI: confidence interval, HR: hazard ratio, aHR: adjusted hazard ratio. *Participants who developed psoriasis.

who were supplemented with vitamin B_{12} for more than 3 years after surgery (aHR, 0.76; 95% CI, 0.60~0.96). However, the reduction in psoriasis risk in gastric cancer patients who underwent total gastrectomy was not associated with vitamin B_{12} supplementation.

DISCUSSION

In this large national cohort, the incidence of psoriasis was 15% lower in gastric cancer patients than in matched reference individuals. We found that subtotal gastrectomy and vitamin

B_{12} supplementation for more than 3 years were clinical factors associated with decreased risk of psoriasis in gastric cancer survivors, while total gastrectomy, radio/chemotherapy, and obesity did not affect the risk of psoriasis in gastric cancer survivors.

To the best of our knowledge, our study is the first to comparatively analyze the relative risk and incidence rates of psoriasis in gastric cancer patients who underwent gastrectomy and in the general population. We demonstrated that gastric cancer survivors who underwent subtotal gastrectomy had a 0.85-fold lower risk of psoriasis than the controls, whereas the risk of psoriasis was similar between those who underwent total gastrectomy and the controls. In contrast, a previous study reported a higher risk of psoriasis in patients with breast cancer than in the general population, explaining that radiotherapy or mastectomy for breast cancer treatment may lead to skin trauma and trigger the onset of psoriasis[23]. To date, gastrectomy and chemotherapy are the only therapeutic options for gastric cancer patients, and surgical resection to treat gastric cancer is different from mastectomy, which directly causes extensive skin wounds. Additionally, we found that radiotherapy or chemotherapy, used as neoadjuvant or adjuvant treatment approaches for resectable gastric cancer, did not affect the risk of psoriasis in gastric cancer survivors.

In our study, a decreased risk of psoriasis in gastric cancer patients was also not associated with obesity. Obesity is a significant risk factor for the onset and severity of psoriasis[25], and several case reports have shown that psoriasis rapidly improved after gastrectomy as a bariatric procedure for obese patients with psoriasis[26-28]. However, our results showed that even in the non-obesity group (BMI <25 kg/m^2), the risk of psoriasis significantly decreased in gastric cancer survivors, and the risk of psoriasis was consistently reduced only in gastric cancer patients who underwent subtotal gastrectomy, not total gastrectomy. Although the baseline obese group (BMI ≥25 kg/m^2) tended to low incidence of psoriasis after subtotal gastrectomy more than the non-obese group (BMI <25 kg/m^2), considering that the surgical procedure and metabolic beneficial changes of gastrectomy for gastric cancer patients are similar to those of bariatric surgery[29-31], the effects of gastrectomy itself or weight loss due to gastrectomy do not seem to be major factors reducing the risk of psoriasis in gastric cancer patients.

The decreased risk of psoriasis in gastric cancer patients who underwent subtotal gastrectomy may be related to the characteristic pathogenic mechanism of distal gastric cancer. Gastric cancer can be classified as per two topographic subsites: proximal gastric cancer, also known as cardia gastric cancer, and distal gastric cancer (noncardia cancer). The risk factors for proximal gastric cancer include Caucasian race, male sex, obesity, gastro-esophageal reflux, tobacco-alcohol abuse, high socioeconomic status, and low fruit and vegetable intake, while the risk factor for distal gastric cancer is well-known as chronic inflammation associated with *Helicobacter pylori* infection[32-34]. Recently, many studies have been performed concerning the potential role of *H. pylori* in different extra-gastric diseases such as ischemic heart diseases, obesity, insulin resistance, non-alcoholic fatty liver diseases, Alzheimer' disease and autoimmune diseases[35-37]. Because *H. pylori* infection is persistent and stimulates both a local and a systemic immune response that could cause significant changes in the markers of inflammation like C-reactive protein, tumor necrosis factor-α, interleukin (IL)-6, IL-12, and interferon (IFN)-γ, these pro-inflammatory factors also may be involved in the development of psoriasis[12,38-41]. From that point of view, subtotal gastrectomy, a treatment of choice for distal gastric cancer, could reduce the incidence of psoriasis by eliminating the distal part of the stomach (gastric antrum), which is a source of *H. pylori* colonization with inflammatory potential.

Two recent meta-analyses concluded that patients with psoriasis had increased *H. pylori* infection rate, and psoriasis patients with *H. pylori* infection were more severe[42,43]. These meta-analyses proved a significant association between psoriasis and *H. pylori* infection, which suggest that *H. pylori* infection could play a role in the pathogenesis of psoriasis by inducing the abnormal immunological cascade. Our study also supports a significant relationship between *H. pylori* infection and psoriasis. In contrast, Cho et al.[44] did not find a significant relationship between *H. pylori* infection and psoriasis, but their conclusion has a limitation in that they were based on a 1-year cross-sectional study.

Interestingly, vitamin B_{12} supplementation for more than 3 years further reduced the incidence of psoriasis in gastric cancer patients by about 10%. Although several studies have shown that vitamin B_{12} deficiency is associated with psoriasis[45,46], some studies have shown inconsistencies in this regard[47,48], and thus there is currently insufficient evidence supporting the role of vitamin B_{12} in psoriasis[49]. However, our

study suggests that vitamin B_{12} supplementation for at least 3 years or more had an additive effect on lowering the incidence of psoriasis in gastric cancer patients who underwent subtotal gastrectomy, and therefore, vitamin B_{12} deficiency could play a contributory role in the development of psoriasis. Potential mechanisms linking vitamin B_{12} deficiency and psoriasis include increased serum homocysteine level, which is a well-known risk factor for atherosclerosis[50]. Homocysteine metabolism is dependent in part on folate and vitamin B_{12}, such that deficiency of these vitamins may lead to elevated homocysteine levels, which in turn impair endothelial function and increase the risk of cardiovascular disease[51]. Psoriasis and cardiovascular disease share the same inflammatory pathophysiology[52,53], and hyperhomocysteinemia due to vitamin B_{12} deficiency may also be a risk factor for psoriasis associated with metabolic syndrome and cardiovascular disease.

Our study has several limitations. First, our study is an observational study that only demonstrates associations and not causation. Although we suggested risk factors that were statistically related to psoriasis development in patients with gastric cancer, prospective cohort studies and laboratory data are needed to confirm these associations and to elucidate the biological mechanisms. Second, the study was conducted in Korea, a country with a single-payer national health insurance system. Our findings may not be generalizable to other race/ethnicity groups or to other health care settings. In particular, gastric cancer is well known for its geographic variations, indicated by its higher incidence in East Asian countries than in Western countries; hence, there may be differences in the incidence and risk factors of psoriasis when studying gastric cancer patients of other races.

In conclusion, the gastric cancer survivors who underwent gastrectomy had a lower risk of psoriasis than the matched controls. Subtotal gastrectomy and vitamin B_{12} supplementation for more than 3 years were associated with a decreased risk of psoriasis in the gastric cancer patients. Our results suggest that chronic systemic inflammation induced by *H. pylori* as a critical pathogenesis of gastric cancer may contribute to the development of psoriasis, and inflammation due to atherogenic conditions induced by vitamin B_{12} deficiency may have synergic effects in the development of psoriasis. Further research is needed to evaluate the effects of subtotal gastrectomy and vitamin B_{12} deficiency on the onset of psoriasis in gastric cancer patients and to identify the biological mechanisms underlying this process.

SUPPLEMENTARY MATERIALS

Supplementary data can be found via http://anndermatol.org/src/sm/ad-34-191-s001.pdf.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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DATA SHARING STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Bo Ri Kim, https://orcid.org/0000-0002-2223-1606
Dong Ho Lee, https://orcid.org/0000-0002-6376-410X
Hyun Ik Shim, https://orcid.org/0000-0001-5551-1180
Jee Woo Kim, https://orcid.org/0000-0003-1618-7327
Sanghyun Park, https://orcid.org/0000-0003-0612-2562
Cheol Min Shin, https://orcid.org/0000-0003-2265-9845
Kyungdo Han, https://orcid.org/0000-0002-6096-1263
Sang Woong Youn, https://orcid.org/0000-0002-5602-3530

REFERENCES

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018;68:394-424. Erratum in: CA Cancer J Clin 2020;70:313.
2. DeSantis CE, Lin CC, Mariotto AB, Siegel RL, Stein KD, Kramer JL, et al. Cancer treatment and survivorship statistics, 2014. CA Cancer J Clin 2014;64:252-271.
3. Jung KW, Won YJ, Kong HJ, Lee ES. Cancer statistics in Korea: incidence, mortality, survival, and prevalence in 2016. Cancer Res Treat 2019;51:417-430.
4. Allemani C, Matsuda T, Di Carlo V, Harewood R, Matz M, Nikšić M, et al. Global surveillance of trends in cancer survival 2000-14 (CONCORD-3): analysis of individual records for 37 513 025 pa-

tients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries. Lancet 2018;391:1023-1075.
5. Jung KW, Won YJ, Kong HJ, Oh CM, Shin A, Lee JS. Survival of Korean adult cancer patients by stage at diagnosis, 2006-2010: national cancer registry study. Cancer Res Treat 2013;45:162-171.
6. Lee JW, Ali B, Yoo HM, Park CH, Song KY. Conditional survival analysis in Korean patients with gastric cancer undergoing curative gastrectomy. BMC Cancer 2015;15:1005.
7. Shin DW, Yoo SH, Sunwoo S, Yoo MW. Management of long-term gastric cancer survivors in Korea. J Korean Med Assoc 2016;59:256-265.
8. Shin DW, Ahn E, Kim H, Park S, Kim YA, Yun YH. Non-cancer mortality among long-term survivors of adult cancer in Korea: national cancer registry study. Cancer Causes Control 2010;21:919-929.
9. Shin DW, Suh B, Lim H, Suh YS, Choi YJ, Jeong SM, et al. Increased risk of osteoporotic fracture in postgastrectomy gastric cancer survivors compared with matched controls: a nationwide cohort study in Korea. Am J Gastroenterol 2019;114:1735-1743. Erratum in: Am J Gastroenterol 2020;115:150.
10. Choi YJ, Shin DW, Jang W, Lee DH, Jeong SM, Park S, et al. Risk of dementia in gastric cancer survivors who underwent gastrectomy: a nationwide study in Korea. Ann Surg Oncol 2019;26:4229-4237.
11. Christophers E. Psoriasis--epidemiology and clinical spectrum. Clin Exp Dermatol 2001;26:314-320.
12. Davidovici BB, Sattar N, Prinz J, Puig L, Emery P, Barker JN, et al. Psoriasis and systemic inflammatory diseases: potential mechanistic links between skin disease and co-morbid conditions. J Invest Dermatol 2010;130:1785-1796. Erratum in: J Invest Dermatol 2010;130:2517.
13. Boyman O, Conrad C, Tonel G, Gilliet M, Nestle FO. The pathogenic role of tissue-resident immune cells in psoriasis. Trends Immunol 2007;28:51-57.
14. Gaspari AA. Innate and adaptive immunity and the pathophysiology of psoriasis. J Am Acad Dermatol 2006;54(3 Suppl 2):S67-S80.
15. Bos JD, de Rie MA, Teunissen MB, Piskin G. Psoriasis: dysregulation of innate immunity. Br J Dermatol 2005;152:1098-1107.
16. Takeshita J, Grewal S, Langan SM, Mehta NN, Ogdie A, Van Voorhees AS, et al. Psoriasis and comorbid diseases: epidemiology. J Am Acad Dermatol 2017;76:377-390.
17. Pouplard C, Brenaut E, Horreau C, Barnetche T, Misery L, Richard MA, et al. Risk of cancer in psoriasis: a systematic review and meta-analysis of epidemiological studies. J Eur Acad Dermatol Venereol 2013;27 Suppl 3:36-46.
18. Kimball AB, Schenfeld J, Accortt NA, Anthony MS, Rothman KJ, Pariser D. Cohort study of malignancies and hospitalized infectious events in treated and untreated patients with psoriasis and a general population in the United States. Br J Dermatol 2015;173:1183-1190.
19. Chiesa Fuxench ZC, Shin DB, Ogdie Beatty A, Gelfand JM. The risk of cancer in patients with psoriasis: a population-based cohort study in the health improvement network. JAMA Dermatol 2016;152:282-290.
20. Reddy SP, Martires K, Wu JJ. The risk of melanoma and hematologic cancers in patients with psoriasis. J Am Acad Dermatol 2017;76:639-647.e2.
21. Jensen P, Egeberg A, Gislason G, Thyssen JP, Skov L. Risk of uncommon cancers in patients with psoriasis: a Danish nationwide cohort study. J Eur Acad Dermatol Venereol 2018;32:601-605.
22. Lee JW, Jung KJ, Kim TG, Lee M, Oh J, Jee SH, et al. Risk of malignancy in patients with psoriasis: a 15-year nationwide population-based prospective cohort study in Korea. J Eur Acad Dermatol Venereol 2019;33:2296-2304.
23. Yang H, Brand JS, Li J, Ludvigsson JF, Ugalde-Morales E, Chiesa F, et al. Risk and predictors of psoriasis in patients with breast cancer: a Swedish population-based cohort study. BMC Med 2017;15:154.
24. Lee H, Cho J, Shin DW, Lee SP, Hwang SS, Oh J, et al. Association of cardiovascular health screening with mortality, clinical outcomes, and health care cost: a nationwide cohort study. Prev Med 2015;70:19-25.
25. Bardazzi F, Balestri R, Baldi E, Antonucci A, De Tommaso S, Patrizi A. Correlation between BMI and PASI in patients affected by moderate to severe psoriasis undergoing biological therapy. Dermatol Ther 2010;23 Suppl 1:S14-S19.
26. Farias MM, Achurra P, Boza C, Vega A, de la Cruz C. Psoriasis following bariatric surgery: clinical evolution and impact on quality of life on 10 patients. Obes Surg 2012;22:877-880.
27. Yildiz BD. Rapid remission of psoriasis after sleeve gastrectomy. Indian J Surg 2016;78:60-62.
28. Babino G, Giunta A, Bianchi L, Esposito M. Morbid obesity and psoriasis: disease remission after laparoscopic sleeve gastrectomy. Obes Res Clin Pract 2017;11:370-372.
29. Lee EK, Kim SY, Lee YJ, Kwak MH, Kim HJ, Choi IJ, et al. Improvement of diabetes and hypertension after gastrectomy: a nationwide cohort study. World J Gastroenterol 2015;21:1173-1181.
30. Lee YH, Han SJ, Kim HC, Hyung WJ, Lim JS, Lee K, et al. Gastrectomy for early gastric cancer is associated with decreased cardiovascular mortality in association with postsurgical metabolic changes. Ann Surg Oncol 2013;20:1250-1257.
31. Tanaka K, Miyashiro I, Yano M, Kishi K, Motoori M, Shingai T, et al. Visceral fat changes after distal gastrectomy according to type of reconstruction procedure for gastric cancer. World J Surg Oncol

2013;11:146.
32. González CA, Agudo A. Carcinogenesis, prevention and early detection of gastric cancer: where we are and where we should go. Int J Cancer 2012;130:745-753.
33. González CA, Megraud F, Buissonniere A, Lujan Barroso L, Agudo A, Duell EJ, et al. Helicobacter pylori infection assessed by ELISA and by immunoblot and noncardia gastric cancer risk in a prospective study: the Eurgast-EPIC project. Ann Oncol 2012;23:1320-1324.
34. Huang Q. Unique clinicopathology of proximal gastric carcinoma: a critical review. Gastrointest Tumors 2014;1:115-122.
35. Bravo D, Hoare A, Soto C, Valenzuela MA, Quest AF. Helicobacter pylori in human health and disease: mechanisms for local gastric and systemic effects. World J Gastroenterol 2018;24:3071-3089.
36. Youssefi M, Tafaghodi M, Farsiani H, Ghazvini K, Keikha M. Helicobacter pylori infection and autoimmune diseases; Is there an association with systemic lupus erythematosus, rheumatoid arthritis, autoimmune atrophy gastritis and autoimmune pancreatitis? A systematic review and meta-analysis study. J Microbiol Immunol Infect 2021;54:359-369. Erratum in: J Microbiol Immunol Infect 2021;54:540.
37. Alvarez-Arellano L, Maldonado-Bernal C. Helicobacter pylori and neurological diseases: married by the laws of inflammation. World J Gastrointest Pathophysiol 2014;5:400-404.
38. Jackson L, Britton J, Lewis SA, McKeever TM, Atherton J, Fullerton D, et al. A population-based epidemiologic study of Helicobacter pylori infection and its association with systemic inflammation. Helicobacter 2009;14:108-113.
39. UstUn Y, Engin-UstUn Y, Ozkaplan E, Otlu B, Sait TekerekoGlu M. Association of Helicobacter pylori infection with systemic inflammation in preeclampsia. J Matern Fetal Neonatal Med 2010;23:311-314.
40. Tsai S, Clemente-Casares X, Revelo XS, Winer S, Winer DA. Are obesity-related insulin resistance and type 2 diabetes autoimmune diseases? Diabetes 2015;64:1886-1897.
41. Yildirim Z, Bozkurt B, Ozol D, Armutcu F, Akgedik R, Karamanli H, et al. Increased exhaled 8-isoprostane and interleukin-6 in patients with helicobacter pylori infection. Helicobacter 2016;21:389-394.
42. Yu M, Zhang R, Ni P, Chen S, Duan G. Helicobacter pylori infection and psoriasis: a systematic review and meta-analysis. Medicina (Kaunas) 2019;55:645.
43. Yong WC, Upala S, Sanguankeo A. Association between psoriasis and Helicobacter pylori infection: a systematic review and meta-analysis. Indian J Dermatol 2018;63:193-200.
44. Cho SI, Lee H, Yang MS, Cho SJ, Lee DH. Inverse association between Helicobacter pylori infection and atopic, skin, and autoimmune diseases: a nationwide population-based study in South Korea. Allergy 2021;76:3824-3826.
45. Brazzelli V, Grasso V, Fornara L, Moggio E, Gamba G, Villani S, et al. Homocysteine, vitamin B12 and folic acid levels in psoriatic patients and correlation with disease severity. Int J Immunopathol Pharmacol 2010;23:911-916.
46. Segal R, Baumoehl Y, Elkayam O, Levartovsky D, Litinsky I, Paran D, et al. Anemia, serum vitamin B12, and folic acid in patients with rheumatoid arthritis, psoriatic arthritis, and systemic lupus erythematosus. Rheumatol Int 2004;24:14-19.
47. Abedini R, Goodarzi A, Saeidi V, Hosseini SH, Jadidnuri A, Salehi Taleghani M, et al. Serum homocysteine level, vitamin B12 levels, and erythrocyte folate in psoriasis: a case-control study. Int J Womens Dermatol 2019;5:171-174.
48. Tsai TY, Yen H, Huang YC. Serum homocysteine, folate and vitamin B12 levels in patients with psoriasis: a systematic review and meta-analysis. Br J Dermatol 2019;180:382-389.
49. Millsop JW, Bhatia BK, Debbaneh M, Koo J, Liao W. Diet and psoriasis, part III: role of nutritional supplements. J Am Acad Dermatol 2014;71:561-569.
50. Thambyrajah J, Townend JN. Homocysteine and atherothrombosis--mechanisms for injury. Eur Heart J 2000;21:967-974.
51. Debreceni B, Debreceni L. The role of homocysteine-lowering B-vitamins in the primary prevention of cardiovascular disease. Cardiovasc Ther 2014;32:130-138.
52. Lockshin B, Balagula Y, Merola JF. Interleukin 17, inflammation, and cardiovascular risk in patients with psoriasis. J Am Acad Dermatol 2018;79:345-352.
53. Boehncke WH, Boehncke S, Tobin AM, Kirby B. The 'psoriatic march': a concept of how severe psoriasis may drive cardiovascular comorbidity. Exp Dermatol 2011;20:303-307.