Original articles

Full Title: Risk of Myocardial Infarction in Patients with Psoriasis: A cross-sectional patient-population study in a Japanese hospital

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Abstract

Background: Some epidemiological studies have demonstrated the association between psoriasis vulgaris and coronary artery disease (CAD). However, there is a lack of specific data regarding the association between psoriasis vulgaris and myocardial infarction (MI), the more severe and critical presentation of CAD, in the Japanese population.

Methods and results: We retrospectively analyzed 113,065 patients of all ages at our hospital from January 1, 2011 to January 1, 2013. We extracted the data of patients with psoriasis vulgaris, diabetes mellitus, dyslipidemia, or MI (acute, sub-acute, or old), including sex and age from the electronic medical record database. The prevalence of MI in patients with hypertension, dyslipidemia, diabetes mellitus, and psoriasis vulgaris were 4.8% (794/16,476), 5.0% (459/9,236), 4.6% (531/11,555), and 2.7% (32/1197), respectively. Multivariate analysis showed that psoriasis vulgaris was significantly associated with MI (adjusted odds ratio [OR]: 1.87; 95% confidence interval [CI]: 1.26–2.68; p=0.0022). In a subgroup analysis of 24,069 patients who had one or more comorbidities including diabetes mellitus, dyslipidemia, and hypertension, psoriasis vulgaris was still independently associated with MI after adjusting for sex and age (adjusted OR; 1.49; 95% CI: 1.02–2.18; p=0.0358) in adults.

Conclusion: Psoriasis vulgaris was significantly associated with MI in a Japanese hospital-based population.

Introduction

Psoriasis vulgaris is regarded as an immune-mediated chronic low-level inflammatory skin disorder associated with metabolic and cardiovascular comorbidities [1-3]. Some epidemiological studies have shown that, although there was a racial difference in the prevalence of psoriasis [4-8], there was a clear association between psoriasis vulgaris and coronary artery disease (CAD) regardless of race [9-12], as we previously reported in hospital-based Japanese population [13]. In addition, the association with the risk of myocardial infarction (MI), a more severe and clinically significant condition of CAD, and psoriasis was reported in US, Europe, central China, and Taiwan [14-22]. However, there is a lack of data regarding the association between MI and psoriasis vulgaris in the Japanese population. In the present study, we tested the hypothesis that psoriasis vulgaris is independently associated with MI in a Japanese hospital-based population.

Methods

Patients and data collection

From the medical accounting system we retrospectively researched all clinic and in-hospital 113,065 patients of all ages from January 1, 2011 to January 1, 2013 in this cross-sectional observational study. First, we identified the total number of patients from the medical accounting system. Second, we extracted the data of patients with psoriasis, metabolic comorbidities, or myocardial infarction regarding sex, age, and diagnoses including psoriasis vulgaris (International Classification of Diseases [ICD]-10 code L40.0), hypertension (ICD-10 codes I10, I11, I12, I13, I14, and I15), dyslipidemia (ICD-10 code E78), diabetes mellitus (ICD-10 codes E10, E11, E12, E13, and E14), and acute, sub-acute, or old myocardial infarction (ICD-10 codes I21, I22, and I25.2, respectively) from the medical record database. Hypertension, dyslipdemia, and diabetes mellitus are the typical risk factor for MI and regarded as potential confounders. If the diagnoses of each disease were recorded in the medical charts, we considered each disease as present. Patients were automatically and without intension extracted from the medical accounting system. We evaluated the risk of MI in patients with psoriasis vulgaris. The present study was approved by the institutional review board of Kitano Hospital (P15-06-005) in concordance with the Declaration of Helsinki.

Patient consent was not obtained because of the retrospective study. We disclosed the detail of the present study to the public as an opt-out method and the notice clearly informed patients of their right to refuse enrollment. Identifiable patient data were anonymized before analysis.

Statistics

A chi-square test was performed for categorical variables summarized as counts and percentages. The Wilcoxon rank sum test was used for continuous variables summarized as mean and standard deviation. To analyze the comorbid factors associated with MI, we used a multivariable logistic regression model that involved the following variables: psoriasis vulgaris, diabetes mellitus, dyslipidemia, and hypertension. In this first analysis, we did not include sex and age in the model because of the lack of the data in a total population. Second, to analyze the association between psoriasis and MI in patients with one comorbidity or more including diabetes mellitus, dyslipidemia, and hypertension, we performed a sub-analysis with a multivariable logistic regression model that involved age, sex, psoriasis vulgaris, diabetes mellitus, dyslipidemia, and hypertension in adults (the age more than or equal to 20 years). In the subgroup analysis, we used risk-adjusting variables for excluding each

subgrouping factor without adjustment for multiple tests. We also evaluated the interactions between the subgroup factors and the effect of psoriasis for the MI. The adjusted odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. A two-tailed p value less than 0.05 was considered statistically significant in all analyses. Statistical analyses were performed using JMP pro software, version 13 (SAS Corp.).

Results

The comorbidities of this study population are shown in Table 1. Patients with psoriasis had a higher prevalence of hypertension, hyperlipidemia, diabetes mellitus, and MI. Figure 1 indicates the comorbidities of patients with psoriasis and as the figure shows, MI was present in 966 (0.85%) patients. The prevalence of MI in patients with hypertension, dyslipidemia, diabetes mellitus, and psoriasis vulgaris was 4.8% (794/16,476), 5.0% (459/9,236), 4.6% (531/11,555), and 2.7% (32/1197), respectively (Table 1).

By multivariate analysis, after adjusting for psoriasis vulgaris, diabetes mellitus, dyslipidemia, and hypertension, we established that psoriasis vulgaris was significantly associated with MI (adjusted OR: 1.87; 95% CI: 1.26–2.68; p=0.0022), along with hypertension (adjusted OR: 14.57; 95% CI: 12.12–17.58; p<0.0001), dyslipidemia (adjusted OR: 2.12; 95% CI: 1.84–2.44; p<0.0001), and diabetes mellitus (adjusted OR: 2.46; 95% CI: 2.13–2.84; p<0.0001) (Figure 2).

In the second analysis of 23,916 adult patients who had one or more comorbidities including diabetes mellitus, dyslipidemia, and hypertension, psoriasis vulgaris was still independently

associated with MI adjusted OR; 1.49; 95% CI: 1.02–2.18; p=0.0358, Table 2) after adjusting for diabetes mellitus, dyslipidemia, hypertension, sex, and age.

In subgroup analyses, there were no interactions between the subgrouping factors and the effect of PV on the presence of MI (Figure 3).

Discussion

In the present study, we demonstrated the independent association between MI and psoriasis vulgaris in a Japanese patient-population.

Many patients with psoriasis vulgaris have overlapping risk factors for MI. In the present study, psoriasis was independently associated with MI in a cohort of 113,065 patients and in a sub-population of 24,069 patients with one and more comorbidities in Japan. This result was consistent with research performed in Europe, North America, and Asia [14-22]. However, there were conflicting results in other published studies that did not show a significant relationship between psoriasis and MI [23-27]. In a large population-based Dutch cohort study, Wakkee et al. (2010), showed that the risk of MI was not significant in patients with psoriasis (HR: 0.94; 95% CI: 0.80–1.11) [25]. The presence or absence of arthritis is one reason why the discrepancies existed. [28]. Chin et al. and Ogdie et al. reported that psoriasis patients with arthritis had a greater risk of cardiovascular comorbidities or MI than psoriasis patients without arthritis [29, 30]. Other reasons for the conflicting results may be due to the severity and the duration of psoriasis. A recent study by Eqeberg et al. (2017), which included 61,603 patients with psoriasis and 4,300,085 controls, revealed a significant association

between MI and psoriasis only in patients with severe psoriasis (HR: 1.21, 95% CI: 1.07–1.37) [24]. Armstrong et al. (2012) indicated that patients who had psoriasis for over an 8-year period had a greater prevalence of CAD [9]. However, the association between myocardial infarction and psoriasis has been almost never studied in Japan. Future studies are necessary to research the general Japanese population and consider, age, sex, smoking, and psoriasis severity, duration, and treatment in order to show that psoriasis is truly an independent risk factor for myocardial infarction in the general Japanese population. In the present study, we could not assess the incidence of MI during the follow-up period due to the cross-sectional design. In addition, the severity of psoriasis was not mentioned in the data collected from the electrical medical record. However, after adjusting for available confounders, psoriasis was still independently associated with MI in a large Japanese population.

Psoriasis is a systemic inflammatory disease that mainly affects the skin. Inflammatory mediators produced by Type 1 helper T (Th1) and Type 17 helper T (Th17) cells cause systemic inflammation and vascular atherosclerosis [31-33]. Since the susceptibility to psoriasis may differ due to the genetic background [7-8] and the prevalence of psoriasis in

Japan is not high [13,34], the attributable risk of PV for MI may be small in Asian countries. However, the patients with PV should be carefully managed for controlling the atherosclerotic risks, especially myocardial infarction, the life-threatening disease condition, during clinical practice.

The present study has several limitations. First, the population in our study was not the general Japanese population, but a patient-population in a Japanese hospital. The prevalence of each disease in our study may be higher than that of the general Japanese population [34]. A nation-wide study would be helpful to generalize the results in this study. Second, we could not collect data regarding smoking, blood tests, and body weight; in addition, information on age and sex was disease-specifically extracted. This lack of data might have resulted in insufficient adjustment. Third, diagnostic codes consistent with the diseases may have included only registered codes acceptable to the Japanese health care insurance system. The ICD diagnosis codes have not been validated. However, Kubota et al surveyed demographic characteristics of PV using ICD-10 codes and they found the demographic findings were common to the whole population and dermatology/rheumatology department [34]. They suggested that all patients identified by the claims diagnosis codes in their study roughly

represented all patients with psoriasis who used healthcare services. However, we did not have the data of codes from which department the codes were reported. Fourth, it was possible that serious diseases including myocardial infarction might often accompany with the intensive systemic physical examination that revealed the existence of PV. Fifth, the information regarding the severity and treatment of psoriasis vulgaris was not collected. Finally, the time course of each disease was not taken into account because of the cross-sectional design. Larger, longitudinal cohort studies could address the cause-effect relationship between psoriasis and MI.

Conclusion

Psoriasis vulgaris was independently associated with the presence of MI within a patient-population in Japan.

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Disclosures

The Authors declare that there is no conflict of interest.

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Figure legends

Figure 1. Extraction of patients by international classification of diseases (ICD) -10 codes.

MI: Myocardial Infarction, HT: Hypertension, DLp: Dyslipidemia, DM: Diabetes Mellitus, PV: Psoriasis Vulgaris

Figure 2. The independent association between psoriasis and myocardial infarction after adjusting for hypertension, dyslipidemia, and diabetes mellitus. OR: odds ratio; CI: confidence interval.

Figure 3. Subgroup analysis. OR: odds ratio; CI: confidence interval.

Table 1. Baseline characteristics of patients with psoriasis

	With psoriasis			Without psoriasis		
	Total	MI		Total	MI	
Variables		Present	Absent		Present	Absent
Numbers	1197	32 (2.7%)	1165 (97.3%)	111868	934 (0.8%)	110934 (99.2%)
Age (y.o., mean, SD)	64.1, 18.9	63.8, 18.9	75.7, 12.7	n/a	74.7, 11.3	n/a
Male	762 (63.6%)	27 (84.3%)	735 (63.0%)	n/a	694 (74.3%)	n/a
Hypertension	288 (24.0%)	31 (96.8%)	257 (22.0%)	16188 (14.4%)	763 (1.6%)	15425 (13.9%)
Dyslipidemia	231 (19.2%)	22 (68.7%)	209 (17.9%)	9005 (8.0%)	437 (46.7%)	8568 (7.7%)
Diabetes	252 (21.0%)	17 (53.1%)	235 (20.1%)	11303 (10.1%)	514 (55.0%)	10789 (9.7%)

Abbreviations: MI = myocardial infarction, SD = standard difference, n/a = not available.

Table 2. Adjusted risk of myocardial infarction in adult patients who had one or more comorbidities including diabetes mellitus, dyslipidemia, and hypertension

Factors	Adjusted OR (95% CI)	P value
Age (1-y increment)	1.03 (1.02-1.04)	<0.0001
Male	3.21 (2.73-3.77)	<0.0001
Hypertension	4.94 (3.89-6.27)	<0.0001
Dyslipidemia	1.98 (1.72-2.28)	<0.0001
Diabetes Mellitus	1.79 (1.55-2.07)	<0.0001
Psoriasis	1.49 (1.02-2.18)	0.0358

OR: odds ratio; CI: confidence interval

Figure 1.

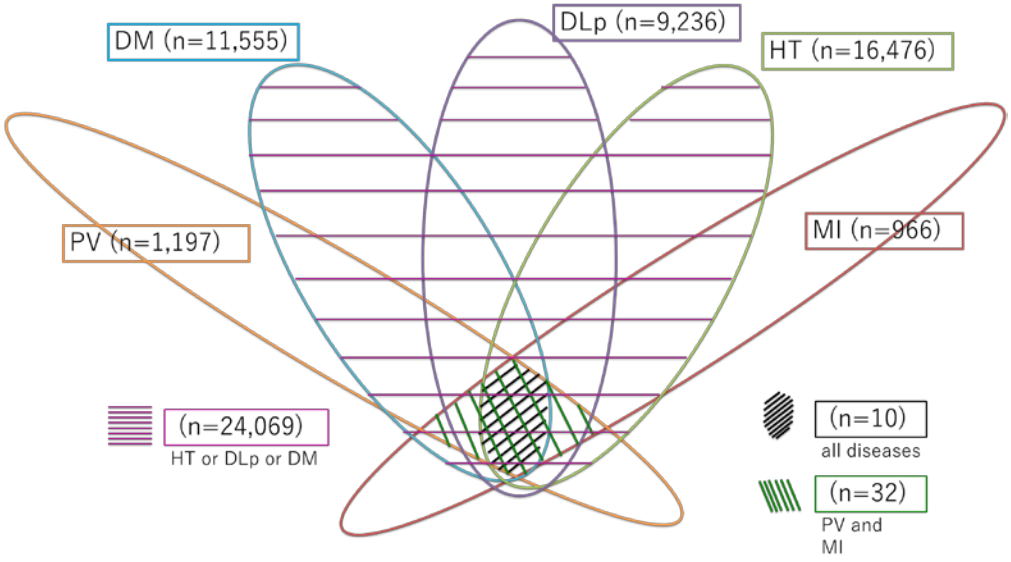
DM (n=11,555)
DLp (n=9,236)
HT (n=16,476)
PV (n=1,197)
MI (n=966)
(n=24,069)
HT or DLp or DM
(n=10)
all diseases
(n=32)
PV and
MI

Figure 2.

Factors	Adjusted OR (95%CI)	p value
Hypertension	14.57 (12.12-17.58)	<0.0001
Dyslipidemia	2.12 (1.84-2.44)	<0.0001
Diabetes mellitus	2.46 (2.13-2.84)	<0.0001
Psoriasis	1.87 (1.26-2.68)	0.0022

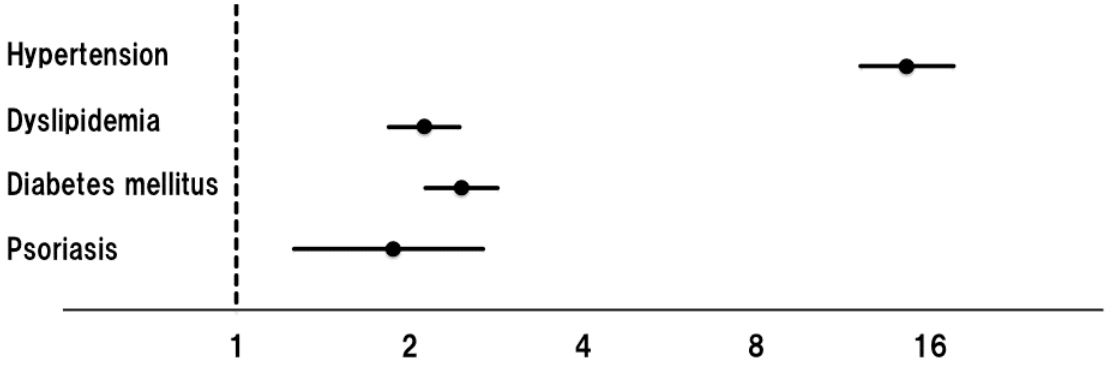

Figure 3.