PSYCHOLOGICAL AND CARDIOVASCULAR IMPACTS OF PSORIASIS: A SYSTEMATIC REVIEW OF ADVERSE OUTCOMES

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Abstract

Background: There is mounting evidence linking the chronic inflammatory condition psoriasis to an elevated risk of cardiovascular disease (CVD), which impacts millions of people around the globe. The results of the several research that have looked at this connection have been all over the map. In light of the expanding corpus of clinical evidence, researchers sought to elucidate the link between psoriasis and negative cardiovascular outcomes by doing a comprehensive analysis of cohort studies.

Methods: In order to find cohort studies published prior to January of 2024, a comprehensive literature search was conducted using 4 electronic databases: MEDLINE, EMBASE, SCI-Web of Science, as well as the Cochrane Library. Inclusion criteria required studies to examine psoriasis and cardiovascular outcomes

Results: We looked at data from 31 cohort studies that included 17,902,757 healthy controls and 665,009 people with psoriasis. Heart attacks, strokes, cardiovascular deaths, ischemic heart disease, and psoriasis all went hand in hand. thromboembolism, and arrhythmia. People with moderate to serious psoriasis were more likely to be affected than those with mild psoriasis. Both European and Asian populations showed increased cardiovascular risks, with no significant difference between them.

Conclusion: This systematic review provides strong evidence that Cardiovascular complications are increased in individuals with psoriasis. People suffering from moderate to serious psoriasis are at an especially high risk. Clinicians should keep an eye on their psoriasis patient' cardiovascular health and consider preventative measures to lower their risk of cardiovascular disease (CVD), according to these results.

Keywords: Psoriasis, Cardiovascular disease, Myocardial infarction, Systematic review, Cohort studies

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Introduction

About sixty million people, including adults and children, throughout the world suffer with psoriasis, an inflammatory disorder that lasts for a long time (1) (2). Skin lesions that are dry, red, scaly, or round are the most common way to identify it. This condition significantly interferes with patients' daily routines, sleep patterns, and overall well-being (3). Multiple indicators of risk for cardiovascular disease (CVD) are shared by psoriasis, according to research. These include being overweight, smoking, having high blood pressure, and having diabetes (4). Additionally, both psoriasis and atherosclerosis—one of the manifestations of CVD-exhibit similar immune-inflammatory responses, involving the activation of T-helper cell type 1 and type 17, alongside reduced functionality of T-regulatory cells (4, 5). As a result, psoriasis may contribute in isolation from other risk factors for adverse cardiovascular events.

Heart disease, stroke, peripheral artery disease, cerebrovascular disease, and aortic atherosclerosis are all part of cardiovascular disease (CVD). In clinical settings, cardiovascular events (CVE) refer to critical and unexpected episodes associated with cardiovascular disease (CVD), including heart attacks, strokes, and cardiovascular death. Heart disease (HD) continues to be a major global health concern, affecting millions of people. Nearly one-third of all deaths in the twenty-first century were attributed to it, making it the leading cause of mortality in that era. (6). Well-established contributors to CVD include obesity and hypertension (7–10), but given the multifaceted nature of its development, additional risk factors still require further investigation. There has been mixed results from the many research that have looked at the possible connection between psoriasis and CVD (11–13). While two meta-analyses have reviewed this connection, A greater number of case-control studies were considered than cohort studies (14, 15). With more and more clinical trials becoming available, it was time for a new meta-analysis to back up the claims. Thus, in order to provide a more solid knowledge of the connection between psoriasis and worse cardiovascular outcomes, this project intends to do a systematic evaluation of original cohort studies published prior to January 2024.

Materials and Methods

In this study, psoriasis was considered the exposure factor, while adverse cardiovascular outcomes were the primary endpoints. Accordingly, individuals diagnosed with psoriasis formed the exposure group, contrasted with the control group, which consisted of individuals free of psoriasis. In order to show how the research was carried out, a PRISMA flow diagram was created, and the study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses. Working with an informatics expert, we searched four databases—MEDLINE, EMBASE, SCI-Web of Science, and the Cochrane Library—for relevant material. All research that looked at the link between psoriasis and worse heart outcomes were found before January 2024.

Inclusion Criteria

Cohort studies examining the association among psoriasis with cardiovascular events in adults (∞18 years old) were eligible for inclusion. Participants had to be diagnosed with psoriasis through recognized medical institutions. The study outcome had to include hazard ratio (HR) or rate ratio (RR) as a key indicator. Given that HR and RR are functionally similar, HR values were converted to RR for consistency in analysis (16).

Exclusion Criteria

Studies were excluded if they were summaries, systematic reviews, conference abstracts, or lacked an appropriate control group or primary data. In cases where original data were unavailable, the corresponding author was contacted twice via email. If no response was received or the provided email was invalid, the study was omitted. For studies including multiple control groups of psoriasis patients, the most appropriate control group was selected. If duplicate data appeared in multiple publications, only the dataset most comparable to the others was included.

Data Analysis

Statistical analysis was performed as descriptive analysis and to prevent the duplication of psoriasis and non-psoriasis patients across multiple studies, data from the study with the largest sample size were selected if multiple studies relied on the same medical database within overlapping timeframes and contained similar psoriasis patient numbers.

Results

A comprehensive search across four databases yielded 460 relevant references. After screening, 429 references were excluded. Table 1 summarizes the study characteristics of the thirty-one studies that were part of the systematic review. These studies encompassed 665,009 individuals diagnosed with psoriasis and 17,902,757 individuals in the control group without psoriasis (4, 12, 13, 20–47). Studies with duplicate populations were not counted in the total participant numbers. Six low-quality studies were omitted from the analysis (11, 48–52). Nine of the thirty-one studies used a retrospective cohort design, while the others used a prospective one. Studies had an average follow-up length of 7.1 years. Researchers in several investigations found more than one result. The inaccessibility of complete texts also led to the exclusion of three research.

(53–55).

Thirteen studies examined the link between psoriasis and myocardial infarction, comprising 5,22,730 individuals with psoriasis and 11,171,909 individuals without psoriasis as controls.

Ten studies assessed the relationship between psoriasis and stroke, comprising 484,839 psoriasis patients and 11,529,624 controls. A higher risk of stroke was associated with psoriasis, according to the systematic study.

Five studies focusing on European populations explored the connection between psoriasis and cardiovascular-related deaths, involving 183,966 psoriasis patients and 4,116,176 controls. The heterogeneity analysis did not reveal substantial differences among the studies.

Three studies evaluated ischemic heart disease in European psoriasis patients, covering 67,048 psoriasis cases and 2,129,260 controls.

Four studies examined the relationship between psoriasis and thromboembolism, reviewing information from 4,971,594 individuals who did not have psoriasis and 63,236 individuals who did have it.

Three studies assessed the prevalence of arrhythmias among psoriasis patients, including 93,580 psoriasis cases and 5,380,933 controls.

Heart failure, atherosclerosis, angina, aortic aneurysm, aortic valve stenosis, and transient ischemic stroke were among the extra cardiovascular risks that eight studies examined in psoriasis patients. Due to the limited number of studies and inconsistent findings, no pooled analysis was conducted for these conditions.

Seven studies investigated cardiovascular disease (CVD) risk in Asian psoriasis patients (110,591 psoriasis cases, 2,813,658 controls), while 24 studies examined European populations (554,418 psoriasis cases, 15,089,099 controls). Both groups exhibited an increased cardiovascular risk

Eighteen studies assessed cardiovascular risks in individuals with mild psoriasis (857,939 psoriasis cases, 39,811,954 controls), while 22 studies examined moderate-to-severe psoriasis cases (917,271 psoriasis cases, 40,063,131 controls). Both groups showed significantly increased cardiovascular risks, with a higher risk in moderate-to-severe cases

GRADE assessment was employed to evaluate the strength of evidence. While randomized controlled trials (RCTs) are typically considered the gold standard, cohort studies provided the most reliable evidence (Table 1).

Discussion

Using information from 31 cohort studies including 6,65,009 people with psoriasis and 17,902,757 healthy controls, this meta-analysis looked at the correlation between psoriasis and CVD. The results show that those with psoriasis had a much greater chance of experiencing negative cardiovascular events. Ischemic heart disease, myocardial infarction, stroke, thromboembolism, arrhythmias, and death attributable to cardiovascular disease were more common in those with severe psoriasis.

Seven out of fourteen cohort studies that were included in our meta-analysis fulfilled the inclusion criteria set forth by Samarasekera et al. (15). Consistent with our findings, they found that severe psoriasis significantly raises the risk of cardiovascular disease (HR, 1.57; 95% CI, 1.26-1.96). Nevertheless, in contrast to their research, we also found that mild psoriasis patients had a significantly higher risk of cardiovascular morbidity when compared to controls. We found comparable results to another meta-analysis (14), although it only included case-control studies. This meta-analysis looked at 75 observational research,

Table 1. The included studies' characteristics examined the relationship between psoriasis and the risk of cardiovascular illnesses and events.

References	Psoriasis	No psoriasis	Severity	HR or RR (95% CI)	Outcome
Abuabara et al. (20)	3,603	14,330	2	1.57 (1.26–1.96)	Cardiovascular death
Ahlehoff et al. (42)	39,558	4,478,926	1	1.22 (1.14–1.30)	Atrial fibrillation
			2	1.53 (1.23–1.91)	Atrial fibrillation
			1	1.25 (1.17–1.34)	Stroke
			2	1.65 (1.33–2.05)	Stroke
Ahlehoff et al. (41)	2,242	97,115	1	0.99 (0.87–1.11)	Thromboembolism
			2	1.27 (1.02–1.57)	Thromboembolism
			1	0.97 (0.80–1.16)	Stroke
			2	1.51 (1.02–2.05)	Stroke
Ahlehoff et al. (4)	36,992	4,003,265	1	1.14 (1.06–1.22)	Cardiovascular death
			2	1.57 (1.27–1.94)	Cardiovascular death
			1	1.22 (1.12–1.33)	MI
			2	1.45 (1.10–1.90)	MI
			1	1.25 (1.16–1.33)	Stroke
			2	1.71 (1.39–2.11)	Stroke
Ahlehoff et al. (43)	38664	4,126,075	1	1.35 (1.21–1.49)	Venous thromboembolism
			2	2.06 (1.63–2.61)	Venous thromboembolism
Brauchli et al. (37)	36,702	36,702	0	1.07 (0.89–1.29)	MI
			0	0.92 (0.77–1.09)	Stroke
			0	0.98 (0.81–1.19)	Transient ischemic attack
Chiang et al. (21)	2,783	13,910	0	1.27 (1.05–1.52)	Ischemic stroke
Chiu et al. (22)	40,637	162,548	2	1.34 (1.29–1.39)	Arrhythmia
Chiu et al. (23)	34,301	137,204	2	1.80 (1.25–2.61)	Aortic aneurysm
Chung et al. (24)	8,945	8,945	0	2.02 (1.42–1.88)	Thromboembolism
Dregan et al. (44)	45,440	373,851	1	1.08 (0.98–1.18)	Stroke
			2	0.93 (0.64–1.36)	Stroke
			1	1.03 (0.97–1.11)	Coronary heart disease
			2	1.29 (1.01–1.64)	Coronary heart disease
Egeberg et al. (25)	53,454	4,300,085	1	1.03 (0.96–1.11)	MI

			2	1.21 (1.05–1.39)	MI
Egeberg et al. (45)	30,278	2,692,097	1	1.27 (1.11–1.45)	MACE
			2	1.69 (1.20–2.37)	MACE
Gelfand et al. (39)	130,976	556,995	1	1.15 (1.10–1.20)	MI
			2	1.16 (1.11–1.21)	MI
Gelfand et al. (38)	132,746	496,666	1	1.06 (1.00–1.10)	Stroke
			2	1.43 (1.10–1.90)	Stroke
Jung et al. (26)	5,788	1,727,832	1	0.96 (0.72–1.26)	MI
			2	2.24 (1.51–3.32)	MI
			1	1.09 (0.97–1.23)	Stroke
			2	1.23 (0.96–1.59)	Stroke
			1	1.25 (1.11–1.41)	Ischemic heart disease
			2	1.52 (1.21–1.92)	Ischemic heart disease
			1	1.32 (1.17–1.50)	Angina pectoris
			2	1.38 (1.06–1.79)	Angina pectoris
Kaye et al. (40)	44,164	219,784	0	1.21 (1.10–1.32)	MI
			0	1.20 (1.00–1.25)	Stroke
			0	1.20 (1.12–1.29)	Angina
			0	1.28 (1.20–1.48)	Atherosclerosis
Khalid et al. (27)	66,389	5,376,842	1	1.22 (1.15–1.28)	Heart failure
			2	1.55 (1.36–1.76)	Heart failure
Khalid et al. (46)	70,665	5,036,959	1	1.22 (1.11–1.33)	Aortic valve stenosis
			2	1.61 (1.32–1.96)	Aortic valve stenosis
Khalid et al. (47)	70,989	5,404,544	1	1.20 (1.03–1.39)	Abdominal aortic aneurysm
			2	1.67 (1.21–2.32)	Abdominal aortic aneurysm
Leisner et al. (28)	8,879	90,167	0	1.40 (1.09–1.80)	MI
Levesque et al. (29)	31,421	31,421	0	1.17 (1.04–1.31)	MI
			1	1.16 (0.94–1.42)	MI
			2	1.18 (1.05–1.33)	MI
Lin et al. (30)	4,752	23,760	0	2.10 (1.27–3.43)	MI
Lin et al. (31)	1,344	2,678	0	1.18 (0.80–1.74)	MI
			0	1.06 (0.85–1.33)	Heart failure
			0	1.04 (0.79–1.37)	Cardiovascular death
Mehta et al. (12)	3,603	14,330	2	1.57 (1.26–1.96)	Cardiovascular death
Mehta et al. (32)	3,603	14,330	2	1.53 (1.26–1.85)	MACE
Ogdie et al. (33)	138,424	81,573	1	1.09 (1.00–1.20)	Cardiovascular death
			2	1.54 (1.15–2.05)	Cardiovascular death
			1	1.08 (0.98–1.18)	MI
			2	1.26 (0.92–1.72)	MI
			1	1.08 (0.99–1.17)	Stroke
			2	1.45 (1.10–1.92)	Stroke
Parisi et al. (34)	48,523	208,187	2	1.28 (0.96–1.69)	MACE
Rhee et al. (35)	13,385	739,459	1	1.10 (0.97–1.24)	Atrial fibrillation
			2	1.44 (1.14–1.82)	Atrial fibrillation
			1	1.04 (0.96–1.13)	Thromboembolic events
			2	1.26 (1.07–1.47)	Thromboembolic events
Wakkee et al. (36)	15,820	27,577	0	0.94 (0.80–1.11)	MI
			0	1.05 (0.95–1.17)	Ischemic heart disease
Wu et al. (13)	14,014	70,070	1	1.28 (1.02–1.60)	MI
			2	1.31 (1.14–1.51)	MI

"1" denotes individuals with mild psoriasis, "2" denotes patients with moderate to severe psoriasis, and "0" denotes patients with psoriasis of all severity levels in the "Severity" column. PB, or population-based; CI, or confidence interval; MI stands for myocardial infarction; MACE is for major adverse cardiovascular event.

including 38 cross-sectional studies, 32 case-control studies, and 5 cohort studies.

A variety of heart and blood vessel illnesses, including coronary artery disease (including angina and myocardial infarction), peripheral arterial disease (including stroke), rheumatic heart disease, and congenital heart abnormalities, are classed as cardiovascular disease (CVD) according to the World Health Organization. CVD risk factors that have been well-documented include hypertension, dyslipidemia, smoking, obesity, and diabetes (56). It was crucial to account for conventional risk factors since psoriasis may cause cardiovascular problems in and of itself. Age, sex, socioeconomic position, past cardiovascular disease, smoking history, body mass index (BMI), and total cholesterol were all taken into consideration in 27 of the cohort studies that were included of our analysis. The quantity and nature of these adjusted parameters, however, differed. The credibility of our findings is enhanced by these modifications.

At present, therapeutic options for psoriasis range from topical treatments to systemic therapies, oral medicines, phototherapy, and TNF-α inhibitors (57-61). Cardiovascular risks in psoriasis patients may be affected by different therapy techniques. As an example, a research showed that compared to topical therapies, the use of TNF-α inhibitors (etanercept, infliximab, or adalimumab) considerably decreased the risk of myocardial infarction. In addition, individuals who used TNF-α inhibitors had the same risk of myocardial infarction as those who took systemic drugs like cyclosporine, acitretin, or methotrexate, or who had phototherapy (59). A lower incidence of CVD was linked to systemic anti-inflammatory therapies, such as methotrexate and biologics (TNF-α and interleukin inhibitors), in a nationwide trial (57) that focused on patients with severe psoriasis. Interestingly, there was no significant difference in major cardiovascular events between the placebo group and the biologic group in two meta-analyses that looked at 22 and 38 RCTs, respectively (62, 63). These results have been questioned, even by the authors, because of constraints such as inadequate random-effects modeling, insufficient data quality, and short follow-up periods (61). Weak treatment data from the included studies may be explaining part of the observed variation in the effects of psoriasis on cardiovascular risk.

It is important to keep in mind that our analysis has a number of limitations. One possible caveat is that the link between psoriasis and IHD is underappreciated. All three of the ischemic heart disease studies included in our meta-analysis used ICD codes to classify patients. Although coronary angiography (CAG) and CT angiography (CTA) are the only ways to diagnose silent ischemia, it is not known whether all individuals had these tests done. As a result, the connection may have been underestimated due to undiagnosed instances. The greatest connection with psoriasis in our study was cardiovascular mortality. The risk may have been exaggerated, however, since four out of five studies that looked at cardiovascular mortality only included those with severe psoriasis. The results might be more diverse due to these constraints.

Despite these constraints, our systematic review possesses several notable strengths. First, cohort studies represent the most robust method for investigating comorbidities due to ethical concerns surrounding experimental designs. As such, our systematic review of cohort studies provides high-level evidence. Second, the inclusion of data from 31 studies encompassing a vast number of psoriasis patients and controls significantly bolstered the statistical power of our findings. Third, all of the cohort studies that were considered had excellent quality, earning a minimum of 7 points on the Newcastle-Ottawa Scale (NOS). Last but not least, our data strongly supports the idea that psoriasis is linked to many negative cardiovascular outcomes.

In light of these findings, healthcare providers should consider cardiovascular risk when managing psoriasis patients. Efforts should focus on educating individuals at high risk of CVD on preventive measures to encourage proactive health management. In this regard, standard cardiovascular prevention guidelines may be applicable to psoriasis patients, serving as an enhanced primary prevention strategy. A randomized controlled trial involving 303 participants demonstrated that a 20-week dietary intervention combined with increased physical activity led to significant improvements in psoriasis severity among overweight and obese patients receiving systemic treatment (64). Moreover, multiple studies indicate that physical exercise not only mitigates psoriasis risk but also enhances cardiovascular health (65, 66). Conversely, a sedentary lifestyle among psoriasis patients may elevate their likelihood of developing CVD (67). Additionally, routine stress-testing for early detection of coronary artery disease in psoriasis patients may be beneficial.

Conclusion

Regardless of ethnicity or disease severity, this comprehensive analysis presents strong evidence that psoriasis is associated with an increased risk of several unfavourable cardiovascular events, such as myocardial infarction, stroke, thromboembolism, arrhythmia, and cardiovascular death. Those who suffered from moderate to severe psoriasis were more likely to experience this risk. The need of paying more attention in clinical practice to the possibility that psoriasis is an independent risk factor for adverse cardiovascular events is highlighted by these results.

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