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# Increased Risk of Adverse Cardiovascular Outcome in Psoriasis: A Retrospective Analysis Using a Large Database

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## Abstract

**Background:** Psoriasis, a chronic inflammatory skin condition, is linked to an increased risk of cardiovascular diseases due to shared inflammatory pathways. However, the direct impact of psoriasis on cardiovascular risk factors remains underexplored. This study investigates the relationship between psoriasis and cardiovascular events, including Myocardial Infarction (MI), stroke, heart failure, arrhythmias, and thromboembolic diseases.

**Methods:** A nationwide retrospective cohort study was conducted using de-identified Electronic Health Records (EHRs) from 93 healthcare organizations over 20 years. Two cohorts were analyzed: psoriasis patients and non-psoriasis controls, aged 18-60 years. Propensity Score Matching (PSM) balanced baseline characteristics, and the primary outcome was the occurrence of cardiovascular events within 10 years. Survival analyses and Risk Ratios (RR) were used to assess the relationship between psoriasis and cardiovascular outcomes.

**Results:** After matching, each cohort included 120,527 patients. Psoriasis patients had a significantly higher risk of cardiovascular outcomes, with a 28% increased risk of acute MI (RR: 1.28), 23% higher stroke risk (RR: 1.23), 40% higher heart failure risk (RR: 1.40), 60% higher arrhythmia risk (RR: 1.60), and 46% higher thromboembolism risk (RR: 1.46). Psoriasis patients also had higher risks of ischemic heart disease and transient ischemic attacks. Survival analyses showed lower survival probabilities for psoriasis patients across most outcomes.

**Conclusion:** Psoriasis is significantly associated with an increased risk of cardiovascular events, underscoring the need for proactive cardiovascular risk management in psoriasis patients.

**Keywords: Psoriasis; Cardiovascular Events; Myocardial Infarction (MI); Stroke; Heart Failure; Arrhythmias; Thromboembolic Diseases**

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## Background

Psoriasis is a chronic, immune-mediated inflammatory skin condition that affects approximately 2-3% of the global population, including 3% of adults in the United States [1, 2]. It manifests clinically as erythematous plaques with silvery scales, typically involving the extensor surfaces, scalp, and lumbosacral region [3]. At the cellular level, psoriasis is driven by dysregulated keratinocyte proliferation and immune system activation, particularly by T-lymphocytes and pro-inflammatory cytokines [3]. This leads to epidermal hyperplasia, parakeratosis, and chronic inflammation. Psoriasis is increasingly recognized as a systemic condition, with inflammatory involvement extending beyond the skin to affect multiple organ systems, particularly the cardiovascular system [4,5]. Epidemiological studies have consistently shown that patients with psoriasis are at significantly elevated risk for Cardiovascular Disease (CVD), including Myocardial Infarction (MI), stroke, heart failure, arrhythmias, thromboembolic events, and ischemic heart disease [2, 6, 7, 8].

The mechanistic link between psoriasis and CVD lies in shared inflammatory pathways. Key cytokines elevated in psoriatic inflammation - such as Tumor Necrosis Factor-$\alpha$ (TNF- $\alpha$), interleukin-6 (IL-6), IL-17, and IL-23 - are also known to drive vascular endothelial dysfunction, oxidative stress, and atherosclerosis development [4]. These pathways contribute to vascular inflammation, platelet 7-6activation, and disruption of lipid metabolism, amplifying cardiovascular risk [6, 7]. Psoriasis may act as a catalyst for cardiovascular disease through chronic low-grade systemic inflammation and adipose tissue dysfunction, contributing to insulin resistance and metabolic dysregulation [9,10]. Despite well-established associations, the direct role of psoriasis in driving cardiovascular risk remains uncertain, as many studies emphasize correlation rather than

causation.

To address these uncertainties, the present study investigates the relationship between psoriasis and cardiovascular outcomes using a large-scale, retrospective analysis of de-identified electronic health records from over 90 healthcare organizations. By employing propensity score matching to account for baseline differences, this study provides evidence that psoriasis is independently associated with a significantly increased risk of adverse cardiovascular outcomes, including myocardial infarction, stroke, heart failure, arrhythmias, thromboembolism, ischemic heart disease, Transient Ischemic Attack (TIA), and aortic stenosis. These findings underscore the need to reframe psoriasis as a systemic disease with significant cardiovascular implications.

## Methods

### Study Design

This study utilized a nationwide retrospective cohort design to investigate the incidence of cardiovascular outcomes in patients with psoriasis compared to those without the condition. De-identified Electronic Health Records (EHRs) were obtained from the TriNetX database, which contains over 20 years of clinical data. TriNetX is a global federated health research network that aggregates data from 93 Healthcare Organizations (HCOs), providing access to diagnoses, procedures, medications, lab values, and genomic information. To minimize bias and ensure comparability between groups, propensity score matching was employed to balance baseline characteristics. The primary outcome was defined as the occurrence of cardiovascular events within a 10-year period, and both survival analyses and Risk Ratios (RR) were used to evaluate the association between psoriasis and cardiovascular outcomes.

The analysis was conducted in two main phases. First, the cohorts were defined: Cohort 1 consisted of psoriasis patients aged 18 to 60 prior to December 31, 2018, while Cohort 2 included individuals of the same age range without psoriasis. The second phase involved setting up and running the analysis, which included defining the index event, the first qualifying encounter for inclusion as well as the observation window and outcome criteria. Cardiovascular outcomes were monitored from the day of the index event and followed over a 10-year period. The primary outcomes included acute Myocardial Infarction (MI), stroke, angina, heart failure, aortic stenosis, Transient Ischemic Attack (TIA), and venous thromboembolism.

### Cohort Construction

The study population was defined using specific inclusion and exclusion criteria to ensure a focused and relevant analysis. Individuals of both genders between the ages of 18 and 60 who had a diagnosis of psoriasis, as identified by specific ICD-10 codes, were included in the study. Individuals under the age of 18 or over the age of 60 were excluded, along with those who had a known history of cardiovascular disease prior to the index event. This included any prior diagnosis of acute Myocardial Infarction (MI), stroke, angina, heart failure, aortic stenosis, Transient Ischemic Attack (TIA), or venous thromboembolism. These criteria were applied to construct a clean baseline cohort for evaluating the relationship between psoriasis and future cardiovascular outcomes.

### Data analysis

Statistical analysis was performed using the TrinetX platform. Propensity score matching was employed to balance baseline characteristics between the two cohorts. The matched characteristics include age at index and gender. Before matching, Cohort 1 (psoriasis) had 129,928 patients and Cohort 2 (control) had 9,212,159 patients. After matching, both cohorts had 120,527 patients, matched based on similar characteristics (Figure 1). Measures of association analysis were utilized to see the risk of heart-related illnesses between the groups. The number of outcome events that occurred within the time window in each group was described, and the mean number of outcome events was calculated for those with outcomes during the study period using a number of instances analysis. The number of instances was grouped by visit, which counts any visit for the outcome as one, regardless of how many times it occurred. Additionally, Kaplan-Meier estimates were used to assess survival probability at the end of the study period, and hazard ratios were calculated using the same analysis.

### Ethical considerations

This retrospective study is exempt from informed consent. The data reviewed is a secondary analysis of existing data, does not involve intervention or interaction with human subjects, and is de-identified according to the de-identification standard defined in the HIPAA Privacy Rule.

## Results

This study investigates the association between cardiac risk factors and psoriasis using a large population database (Table 1).

After propensity score matching, each cohort included 120,527 patients. Analysis revealed that patients with psoriasis exhibited a consistently higher risk of adverse cardiovascular outcomes compared to matched controls.

For acute Myocardial Infarction (MI), both groups had a low absolute risk (0.3%), but psoriasis patients demonstrated a statistically significant 0.1% higher risk ($p$=0.001). The risk and odds ratios were both 1.28, indicating a 28% increased likelihood of MI in the psoriasis group. Survival analysis showed a marginally lower survival probability for psoriasis patients (99.31% *vs*. 99.41%), with a significant log-rank test ($p$=0.000). Stroke presented a similar pattern, with a 0.1% absolute risk difference and a 23% increased risk in the

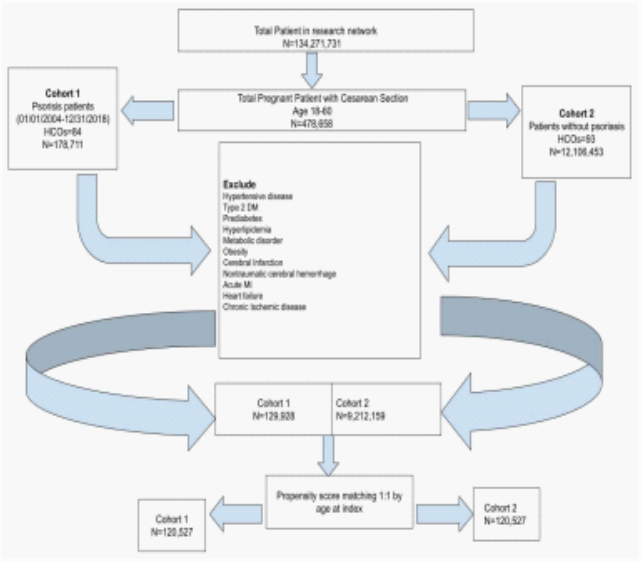
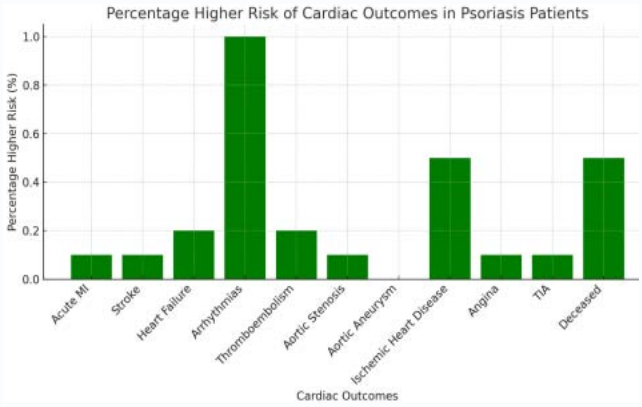


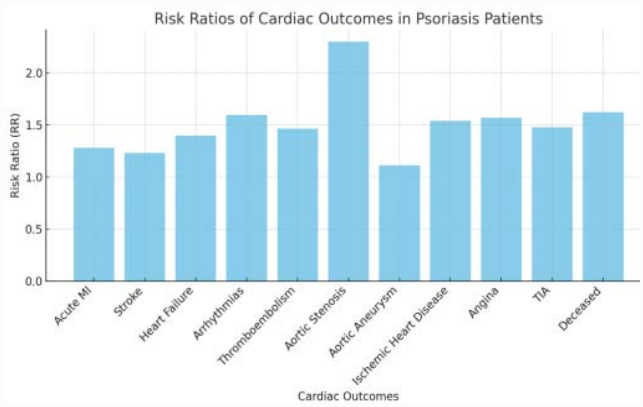

**Figure 1:** A flowchart of the cohort construction.

**Table 1:** Comparative Risk and Survival Outcomes for Cardiovascular Events in Psoriasis *vs.* Control Patients.

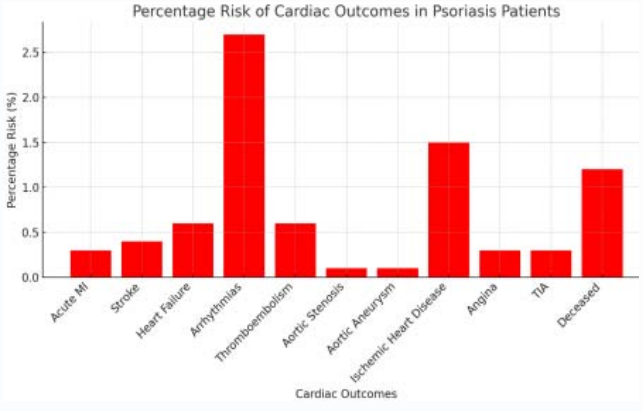
| Cardiovascular Outcome | Risk in Psoriasis (%) | Risk in Control (%) | Risk Difference (%) | Risk Ratio (RR) | Survival-Psoriasis (%) | Survival Control (%) |
|---|---|---|---|---|---|---|
| Acute MI | 0.3 | 0.3 | 0.1 | 1.28 | 99.31 | 99.41 |
| Stroke | 0.4 | 0.3 | 0.1 | 1.23 | 99.15 | 99.26 |
| Heart Failure | 0.6 | 0.4 | 0.2 | 1.4 | 98.81 | 98.95 |
| Arrhythmias | 2.7 | 1.7 | 1 | 1.6 | 94.86 | 96.35 |
| Thromoembolism | 0.6 | 0.4 | 0.2 | 1.46 | 98.73 | 99.01 |
| Aortic Stenosis | 0.1 | 0.1 | 0.1 | 2.3 | 99.79 | 99.89 |
| Aortic Aneurysm | 0.1 | 0.1 | 0 | 1.11 | - | - |
| Ischemic Heart Disease | 1.5 | 1 | 0.5 | 1.54 | 97 | 97.68 |
| Angina | 0.3 | 0.2 | 0.1 | 1.57 | - | - |
| TIA | 0.3 | 0.2 | 0.1 | 1.48 | - | - |
| All-Cause Mortality | 1.2 | 0.8 | 0.5 | 1.62 | 97.68 | 98.58 |



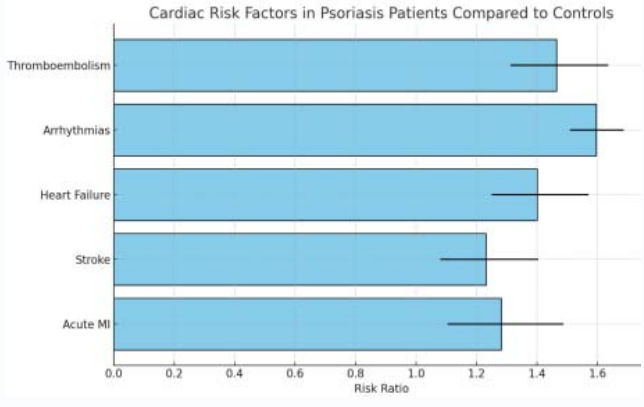

**Graph 1:** Percentage of Higher Risk of Cardiac Outcomes in Psoriasis Patients. Percentage increase in risk for various cardiac outcomes in psoriasis patients, displayed in green. This represents how much higher the risk is for psoriasis patients compared to controls for each condition.




**Graph 3:** Risk Ratios of Cardiac Outcomes in Psoriasis Patients. The risk ratios (RR) for various cardiac outcomes in psoriasis patients. It shows how the risk of these outcomes increases for patients with psoriasis compared to controls.




**Graph 2**: Percentage Risk of Cardiac Outcomes in Psoriasis Patients. The percentage risk of various cardiac outcomes in psoriasis patients, with each outcome's risk displayed in red. This shows the actual risk percentages for each condition.




**Graph 4**: Cardiac Risk Factors in Psoriasis Patients Compared to Controls.

psoriasis group (RR: 1.23; OR: 1.23; $p$=0.002). Survival probability was slightly lower in the psoriasis group (99.15% *vs.* 99.26%), and the difference was statistically significant ($p$=0.000). The risk of heart failure was 0.6% in psoriasis patients compared to 0.4% in controls, representing a 0.2% difference ($p$=0.000). Psoriasis patients were 40% more likely to develop heart failure (RR: 1.40; OR: 1.40), and survival analysis indicated lower survival (98.81% *vs.* 98.95%). Arrhythmias had the most pronounced absolute risk difference of 1%, with a risk of 2.7% in the psoriasis group and 1.7% in controls ($p$=0.000). The risk ratio was 1.60 and odds ratio 1.61, reflecting a 60% increased risk. Survival was notably reduced in psoriasis patients (94.86% *vs.* 96.35%), with a significant difference over time ($p$=0.020). The incidence of thromboembolism was 0.6% in the psoriasis cohort versus 0.4% in controls ($p$=0.000). The relative and odds ratios were

both 1.46, and survival analysis again showed a slight advantage for the control group (99.01% *vs*. 98.73%). For aortic stenosis, the absolute risk was low (0.1%) in both groups, but psoriasis patients had more than double the risk (RR and OR: 2.30), with a slightly lower survival rate (99.79% *vs*. 99.89%). In contrast, aortic aneurysm did not show a significant difference in risk or survival between the two groups (RR and OR: 1.11). Ischemic heart disease occurred in 1.5% of psoriasis patients compared to 1.0% of controls, representing a 0.5% difference ($p$=0.000). Psoriasis patients had a 54% increased risk (RR: 1.54), with lower survival (97.00% *vs*. 97.68%). Similarly, **angina** showed a 0.1% increased risk in the psoriasis group (RR: 1.57; OR: 1.57), though survival differences were not statistically significant ($p$=0.085). In cases of Transient Ischemic Attack (TIA), psoriasis patients had a 0.1% higher risk and a 48% increased relative risk (RR: 1.48; OR: 1.48), with a significant survival difference ($p$=0.009). Lastly, all-cause mortality was elevated in the psoriasis group, with a 0.5% higher mortality rate (1.2% *vs*. 0.8%) and a 62% increased risk (RR: 1.62; OR: 1.63). Survival was lower for psoriasis patients (97.68% *vs*. 98.58%), emphasizing the broader systemic burden of the disease. These findings highlight a consistent pattern of increased cardiovascular risk and slightly reduced survival across multiple endpoints in patients with psoriasis (Graph 1-4).

## Discussion

In this retrospective cohort study using a large, diverse population and a propensity score-matched design, we observed significantly elevated cardiovascular risks among patients with psoriasis. Notably, psoriasis was associated with a 28% increased risk of acute Myocardial Infarction (MI), 23% for stroke, and 40% for heart failure. Elevated risks were also seen for arrhythmias (60%), thromboembolism (46%), ischemic heart disease (54%), angina (57%), transient ischemic attack (TIA, 47%), and aortic stenosis (130%). These findings were further supported by survival analyses, which consistently demonstrated lower survival probabilities in the psoriasis cohort, particularly for ischemic heart disease, stroke, and thromboembolism. Among these outcomes, arrhythmias showed the highest relative increase, underscoring a significant and underrecognized risk. Of particular concern is Atrial Fibrillation (AF), the most common sustained cardiac arrhythmia, associated with increased morbidity and mortality across diverse populations [11]. A recent systematic review and meta-analysis confirmed that patients with psoriasis have an increased risk of developing AF, highlighting the need for regular cardiac monitoring, especially in individuals with moderate to severe disease [11].

Mechanistically, the chronic systemic inflammation of psoriasis is thought to create a pro-arrhythmic environment through several pathways. Inflammatory cytokines such as TNF-$\alpha$ and IL-6 contribute to electrical remodeling, fibrogenesis, and oxidative stress, promoting both structural and electrophysiological changes in atrial tissue [12, 13]. Notably, the NLRP3 inflammasome, a key mediator in both psoriasis and AF, has been implicated in cardiomyocyte inflammation and atrial conduction disturbances, potentially serving as a shared pathogenic node [13, 14]. These molecular insights help explain why psoriasis may confer an elevated arrhythmic burden independent of traditional cardiovascular risk factors.

Our findings align with prior literature on the cardiovascular burden of psoriasis. Garshick *et al*., [4] and Mehta *et al*., [9] describe a consistent association between psoriasis and Major Adverse Cardiovascular Events (MACE), while Gelfand *et al*., [8] identified even greater risks among younger patients. These findings further underscore the importance of proactive cardiovascular monitoring in this population to help prevent long-term adverse outcomes. The association between psoriasis severity and systemic inflammation is also supported by transcriptomic and imaging studies [15-18].

Beyond mechanistic overlap, lifestyle and behavioral patterns common among psoriasis patients - such as sedentary behavior, obesity, and smoking - may further exacerbate cardiovascular and arrhythmic risks. Recent evidence supports the role of exercise and weight reduction not only in mitigating Cardiovascular Disease (CVD) risk but also in reducing psoriasis severity. A 20-week intervention involving diet and physical activity improved both psoriasis outcomes and cardiovascular health in patients with systemic disease [19].

Looking forward, future care strategies must incorporate early screening for arrhythmias, particularly AF, as part of comprehensive cardiovascular risk assessment in psoriasis. This is especially critical given the rising global burden of AF and its association with stroke and heart failure [11]. Tools such as wearable ECG devices, inflammatory biomarkers (e.g., CRP, IL-6), and advanced imaging could facilitate early detection and risk stratification. Additionally, anti-inflammatory biologic therapies may offer dual benefit - reducing skin disease and cardiovascular complications through systemic immune modulation [13, 18].

This study has several limitations. First, while Propensity Score Matching (PSM) effectively balances observed characteristics between groups, it cannot account for unmeasured confounders such as diet, physical activity, or smoking, which may introduce residual bias. Second, PSM can result in data loss, as patients without suitable matches are excluded from the analysis, potentially reducing generalizability. Third, although we observed a pronounced increase in arrhythmia risk, we were unable to distinguish among arrhythmia subtypes (e.g., AF *vs*. ventricular arrhythmias), which limits clinical interpretability. Lastly, our reliance on coded EHR data may introduce diagnostic misclassification.

## Conclusion

This study provides compelling evidence that psoriasis, beyond its dermatologic manifestations, is a systemic condition with significant cardiovascular implications. By leveraging a large, nationally representative dataset and employing robust statistical methods, we have demonstrated that individuals with psoriasis face markedly higher risks of various cardiovascular events. These results underscore the necessity of rethinking psoriasis as a multi-system disorder. Moving forward, interdisciplinary approaches that integrate dermatologic care with cardiovascular risk surveillance and prevention may be critical in reducing long-term morbidity. Further research should aim to uncover the mechanistic pathways linking cutaneous and vascular inflammation and to evaluate whether early intervention in psoriasis can modify the trajectory of cardiovascular risk.

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