Unveiling the Hidden Shield: Methotrexate Emerges as a Cardio-Protector in Psoriasis—Insights from a Scoping Review

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INTRODUCTION

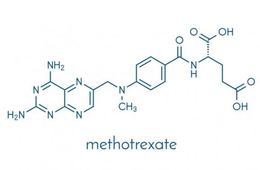
- Psoriasis, a chronic inflammatory skin condition affecting millions worldwide, presents a multifaceted challenge to patients and clinicians[1]. Research has consistently linked psoriasis with an elevated risk of cardiovascular diseases (CVD), including myocardial infarction, stroke, angina, and cardiac-related death[2].
- Methotrexate (MTX) is gaining attention for its potential cardio-protective effects[3].
- This scoping study aims to provide a nuanced understanding of MTX's impact on cardiovascular health within the context of psoriasis management.

METHODS

- The review adheres to PRISMA guidelines for scoping reviews and concentrates on English-language articles released from October 2013 to September 2023.
- Searches were conducted on PubMed, ScienceDirect, Cochrane Library, and Wiley Online Library using the keywords "psoriasis,“ “psoriasis arthritis’, "methotrexate," and "cardiovascular events."
- Manual searches were conducted on Google Scholar and clinical trial registries to identify relevant publications.
- 13 studies were included.

RESULTS

Cardiac-related risk profiles in psoriasis-treated patients with Methotrexate



Findings across various study designs involving 898,744 enrolled patients have ***consistently supported a low incidence rate of cardiac events (CEs)*** with no unexpected safety findings among patients receiving methotrexate over the last decade.

Study Design	Patient (#)	Age (y, mean ± SD)	Disease Duration (y, mean ± SD)	Time-points	Caridac Events Group	Cardiac-realted Outcomes n (%)	Authors, years
Randomized controlled Trial	52	42.1 ± 13.8	13.6 ± 12.6	Week 24	Cardiovascular Events	1 (1.9)	Reich et al., 2022
Retrospective Cohort	67	70.5 ± 4.6	30.3 ± 18.3	Week 36	Cardiovascular Events	1 (1.5)	Harr et al., 2022
	74	71.3 ± 5	22.1 ± 15.8	Week 52	Myocardial infarction	1 (1.4)	Piaserico et al., 2014
	1,153	46.3 ± 16.0	n/a	Week 144	CV death	28 (2.4)	Hong et al., 2021
					Other CVEs	0 (0.0)	
					Stroke	13 (1.1)	
	17,729	49.3 ± 13.5	n/a	Week 104	Angina	90 (1.0)	Wu et al., 2017
					Major CVEs	305 (3.6)	
					Myocardial infarction	89 (1.0)	
					Stroke	180 (2.1)	

Association of Methotrexate and Cardiac Events in patients with psoriasis

- ***Methotrexate*** may ***reduce*** the likelihood of various ***cardiac disorders*** and decrease cardiovascular disease risk by lowering E-selectin and VCAM-1 levels.
- Comparative studies show a lower hazard risk for major cardiac events in methotrexate-treated psoriasis patients than those on other medications and ***reduced cardiovascular and cerebrovascular risks*** in psoriasis patients without arthritis.
- These collective findings underscore methotrexate's pivotal role in comprehensive psoriasis management, highlighting its substantial cardiovascular benefits.

Study Design	Control Group	Patient (#)	Age (y, mean ± SD)	Time-points	Caridac Events Group	Cardiac-realted Outcomes n (%)	Authors, years
Prospective Cohort	Baseline	25	46.7 ± 12.2	Week 12	Cardiovascular Events	A significant reduction in VCAM-1 and E-selectin levels**, suggesting decrease CVD risk	Zdanowska et al., 2020
Meta-analysis	Baseline or MTX-naive	7,615	≥18 years	Week 52	Major CVEs	Decreased risk (OR= 0.7, 0.70-0.77)***	Vecchis et al., 2016
Retrospective Cohort	Mild disease	824,059	46.3 ± 16.0	Week 144	Major CVEs	No protected effect (HR=1.1, 0.55-1.36)	Hong et al., 2021[7]
Prospective Cohort	Adalimumab	5,393	44.2 (35-54)	Year 12	Major CVEs	No elevated risk (HR= 1.1, 0.34–3.28)	Rungapiromnan et al., 2020
Retrospective	Retinoids	19,797	47.3 ± 15.6	12 years (2000-2012)	CV death	Reduced risk (HR,0.8, 0.66–0.85)*	Tsai et al., 2021
					Heart failure	No effect of heart disease (HR=0.9, 0.71–1.06)*	
					Major CVEs	Reduced risk (HR=0.8, 0.76–0.94)*	
					Stroke	No elevated effect (H=1.1, 0.89–1.27)	
Retrospective Cohort	Not MTX, not RET	7,429	11-80 years	Week 520	Cardiovascular Events	Reduced risk in PsO patients (HR=0.4, 0.20–0.76)**, while having no effect on PsA patients (HR=0.8, 0.33–1.89)	Chin et al., 2013
					Cerebrovascular events	Reduced risk in PsO patients (HR=0.4, 0.19–0.95)*, while having no effect on PsA patients (HR=0.6, 0.20–1.95)	
Retrospective Cohort	TNFi	3,704	51.3 ± 13.4	Week 208	Myocardial infarction	No different: IR: 4.9 vs 5.4	Shaaban et al., 2018
	Topical therapy	3,704	51.3 ± 13.4		Myocardial infarction	Significantly lower: IR: 5.4 vs 12.3	
Retrospective Cohort	Other therapies	1,601	51.2	Week 72-156	Major CVEs	Reduced risk (HR= 0.5, 0.26–0.97)*	Ahlehoff et al., 2013
		7,525	50.2 ± 15.3	Week 260	CV death	Reduced risk (HR= 0.6, 0.42–0.76)***	Ahlehoff et al., 2015
					Major CVEs	Reduced risk (HR= 0.5, 0.34–0.83)**	

CONCLUSIONS

- **Methotrexate** demonstrates significant cardiovascular protective effects in psoriasis patients. Multiple studies indicate ***reductions in major cardiovascular events and mortality***.
- Its ***cost-effectiveness*** compared to biological agents makes methotrexate a compelling therapeutic option, particularly beneficial in resource-limited settings.
- Methotrexate's dual benefit ***addresses both dermatological and cardiovascular*** psoriasis management aspects, as well as emphasizes its importance in optimizing patient care and healthcare resource allocation.
- Further research should explore its long-term cardiovascular benefits in psoriasis management.

REFERENCES

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