Tumour necrosis factor alpha blockade is associated with sustained regression of carotid intima-media thickness for patients with active psoriatic arthritis: a 2-year pilot study

We have reported that psoriatic arthritis (PsA) patients without overt cardiovascular diseases have evidence of premature atherosclerosis as indicated by an increased carotid intima-media thickness (IMT).[1] Whether an increase in IMT reflects current (but reversible) inflammation of the vessel wall rather than more permanent structural vessel changes in PsA has never been assessed. We undertook a prospective, observational study to determine whether a 12-week treatment of tumour necrosis factor alpha (TNFα) blockers may reduce IMT in patients with active PsA, and whether the changes in IMT can be sustained in patients who were continued on long-term TNFα blockers.

Twenty consecutive PsA patients with active disease were recruited to receive TNFα blockers. After 12 weeks, nine patients continued (group 1) while 11 patients discontinued TNFα blockers due to financial constraints (group 2). Twenty PsA patients who were naive to TNFα blockers were recruited as controls (group 3). Patients were prospectively followed for 2 years. IMT was measured by carotid ultrasound at baseline, 12 weeks (groups 1 and 2) and at the last visit.

At 12 weeks, a significant reduction in the maximum IMT in groups 1 and 2 and also the mean IMT in group 2 was observed (table 1). After a mean follow-up of 24.7±3.9 months, the maximum IMT continued to show significant reduction only in group 1. In contrast, the change in IMT in group 2 became statistically insignificant, while significant progression in the mean IMT was observed in group 3. There was a trend suggesting that the rate of change in the mean IMT may be different between the three groups.

This is the first longitudinal study on the progression of IMT in patients with PsA. The results of this study showed that short-term TNFα blockade significantly slowed the progression of atherosclerosis in PsA patients with active disease, and further regression of the maximum IMT was possible only in patients who were continued on long-term TNFα blockers, suggesting that effective suppression of inflammation in patients with high-grade inflammation may potentially reverse early atherosclerotic lesions. We cannot exclude the possibility of IMT reduction by other potent immunosuppressants including methotrexate, as over 50% of patients in both groups 1 and 2 were on concomitant methotrexate, and methotrexate therapy has been associated with a decrease in cardiovascular disease events in patients with rheumatoid arthritis.[2]

The major limitation of this study included the small sample size and the open-label study design. The inclusion of patients who can afford their own payment for TNFα blockers after the first 3 months may also introduce a selection bias. The higher baseline mean and maximum IMT in group 3 was unexpected because the disease activity and inflammatory markers were lower. Nonetheless, the natural progression of this group may be higher regardless of therapy. Because of the small sample size, only maximum IMT showed significant regression in group 1 as the mean IMT values are more reproducible but are less sensitive to change, whereas the maximum IMT values are more sensitive to change but are less reproducible,[3] and may be more susceptible to outliers. Based on the current finding, a future randomised study with 18 patients in each group will be required to detect a significant difference in the maximum IMT between the two groups with a power of 80% and and α value of 0.05.

Notwithstanding all the limitations, this study provides preliminary evidence supporting the hypothesis that potent immunosuppressants, including TNFα blockers, may prevent the progression of IMT in PsA by effective suppression of inflammation. Longer-term follow-up of the IMT from future randomised controlled trials of TNFα blockers in PsA patients would be warranted to confirm our findings.

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Table 1 Changes in the IMT in the three groups

	Group 1	Group 2	Group 3	p Value
Mean IMT (mm)				
Baseline	0.70 (0.63–0.74)	0.71 (0.60–0.73)	0.79 (0.74–0.83)	0.010*
3 Months	0.68 (0.64–0.73)	0.67 (0.62–0.70) †	–	
2 Years	0.63 (0.59–0.75)	0.67 (0.62–0.74)	0.82 (0.71–0.86) †	
Maximum IMT (mm)				
Baseline	0.81 (0.70–0.90)	0.78 (0.71–0.84)	0.90 (0.81–1.15)	0.013*
3 Months	0.80 (0.70–0.89) †	0.74 (0.70–0.79) †	–	
2 Years	0.75 (0.65–0.85) †	0.78 (0.70–0.82)	0.87 (0.82–1.12)	
Annualised rate of change, mean (95% CI) (mm/year)				
Mean IMT	−0.0137 (−0.0381 to 0.0106)	−0.0069 (−0.0294 to 0.0156)	0.0129 (0.0001 to 0.0257)	0.058‡
Maximum IMT	−0.0223 (−0.0392 to −0.0054)	−0.0167 (−0.0487 to 0.0153)	−0.0077 (−0.0317 to 0.0163)	0.713‡

Data are expressed as median (interquartile range). Group 1, psoriatic arthritis (PsA) patients continued on tumour necrosis factor (TNF) blockers; Group 2, PsA patients discontinued TNF blockers after 3 months; Group 3, TNF blocker-naive PsA patients.
*Kruskal–Wallis test comparing differences at baseline between the three groups.
†$p<0.05$ using Wilcoxon signed ranks test comparing changes with baseline.
‡Analysis of variance test comparing differences between the three groups.
IMT, intima-media thickness.

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