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学位論文の題名	<p>A Comparative analysis of two interferon-<math>\gamma</math> releasing assays to detect past tuberculosis infections in Japanese rheumatoid arthritis patients</p> <p>(日本人関節リウマチ患者における結核既感染評価のためのクオンティフェロン®TBゴールドとT-スポット®-TBの有用性の比較検討)</p> <p>Mod Rheumatol. (accepted for publication)</p>
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Patients with rheumatoid arthritis (RA) receiving immunosuppressive disease modifying anti-rheumatic drugs (DMARDs), especially tumor necrosis factor (TNF) inhibitors, are at higher risk of developing active TB from LTBI than those not receiving immunosuppressive treatment [Keane J, Gershon S, Wise RP, et al. Tuberculosis associated with infliximab, a tumor necrosis factor alpha-neutralizing agent. *N Engl J Med* 2001;345:1098–104.]. When total or CD4-positive lymphocytes in peripheral blood are suspected to be low due to aggressive RA treatment with methotrexate (MTX) and/or biologics, it remains unclear whether these IGRAs can be used reliably without increasing the number of false negative or indeterminate result. To compare the utility of QuantiFERON-TB Gold in tube (QFT-GIT) and T-SPOT.TB assays (T-SPOT.TB) to detect past tuberculosis infection, here we evaluated the IFN- $\gamma$  responses to TB-antigens of two IGRAs in Japanese RA patients receiving MTX and/or biologics.

We compared the sensitivities and specificities, the rates of indeterminate results, and the rates of positive results in patients with total and low CD4-positive lymphocyte counts of both assays simultaneously performed on 68 rheumatoid arthritis patients receiving MTX, in whom 33 had evidence of past tuberculosis infection by chest computed tomography and the other had neither history of tuberculosis exposure nor abnormalities in chest computed tomography.

The sensitivities, specificities and the rates of indeterminate results of QFT-GIT were 21.2%, 100%, and 4.4%, and those of T-SPOT.TB were 21.9%, 100%, and 1.5%, respectively. The overall agreement of both assays was good ( $\kappa=0.68$ ). In patients with past tuberculosis infection, there are significant positive linear trends in positive rates of both assays across ranges of larger numbers of total and CD4-positive lymphocyte counts.

In conclusion, Both assays were equally useful with high specificities, but may falsely identify past tuberculosis infection owing to low sensitivities. In patients with low total and CD4-positive lymphocyte counts, both assays might give higher rates of false negative results.