Factors Influencing Discrepancies Between the QuantiFERON-TB Gold in Tube Test and the Tuberculin Skin Test in Korean Patients with Rheumatic Diseases

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Objectives: To estimate the positivity and agreement between QuantiFERON-tuberculosis (TB) gold in tube test (QFT-GIT) and tuberculin skin test (TST) according to underlying rheumatic diseases and to identify the influencing factors on discrepancies between the 2 tests.

Methods: Among the 757 patients who underwent both QFT-GIT and TST simultaneously from September 2008 to November 2010, patients with indeterminate QFT-GIT results ($n = 21$), with active ($n = 11$) or suspicious ($n = 1$) findings for tuberculosis on a chest radiograph, were excluded. Finally, 724 patients were recruited for this study: 497 patients with rheumatoid arthritis (RA), 198 with ankylosing spondylitis (AS), and 29 with juvenile rheumatoid arthritis (JRA). The agreement between the 2 tests was estimated by Cohen's κ and factors influencing discrepancies were identified using multivariate analysis.

Results: The positivity of QFT-GIT was higher in RA than AS or JRA (30.2%, 16.2%, and 3.4%, respectively). In contrast, TST positivity was highest in AS compared to RA and JRA (45.5%, 28.2%, and 17.2%, respectively). The agreement between the 2 tests was low in all patients ($\kappa = 0.285$). The only predictor of a discrepancy between the 2 tests was older age. Factors associated with discordant QFT-GIT-negative/TST-positive results were female [odds ratio (OR) = 2.33, confidence interval (CI) 1.11 to 4.89] and AS (OR = 3.12, CI 1.44 to 6.79), whereas a discordant QFT-GIT-positive/TST-negative result was associated with glucocorticoid use (OR = 2.44, CI 1.24 to 4.81).

Conclusions: The agreement between the 2 tests is low; therefore, it would be better to perform both tests than to use any 1 test alone for the detection of LTBI in TB-endemic regions. Female and underlying AS are related to being QFT-GIT-negative/TST-positive, and the use of glucocorticoid is associated with being QFT-GIT-positive/TST-negative.

 Semin Arthritis Rheum 42:424-432

Keywords: *QuantiFERON-TB gold in tube test, tuberculin skin test, latent tuberculosis infection, tumor necrosis factor inhibitor, rheumatic disease*

Patients with inflammatory diseases are at increased risk of developing serious infections. Among them, tuberculosis (TB) is still a major concern and extremely prevalent in patients with rheumatologic diseases due to immune dysregulation and the immunosuppressive agents used in the treatment of these patients (1). It has been reported that patients with rheumatoid arthritis (RA) or ankylosing spondylitis (AS) are 4 times more likely to develop TB than the general population (2,3).

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This study was supported by the research fund of Hanyang University (HY-2009-000-0000-0969).

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 0049-0172/13/$-see front matter
http://dx.doi.org/10.1016/j.semarthrit.2012.07.001

Tumor necrosis factor (TNF) inhibitors are widely used for the treatment of rheumatologic diseases because of their effectiveness and relatively good safety profile (4). However, the reactivation of latent *Mycobacterium tuberculosis* infection (LTBI) is a major concern associated with TNF inhibitor use and the risk of new infection of TB increases after using TNF inhibitors (5-8). Therefore, it is recommended that all patients who are candidates for treatment with TNF inhibitors should be screened for *M tuberculosis* infection before initiating treatment (9,10).

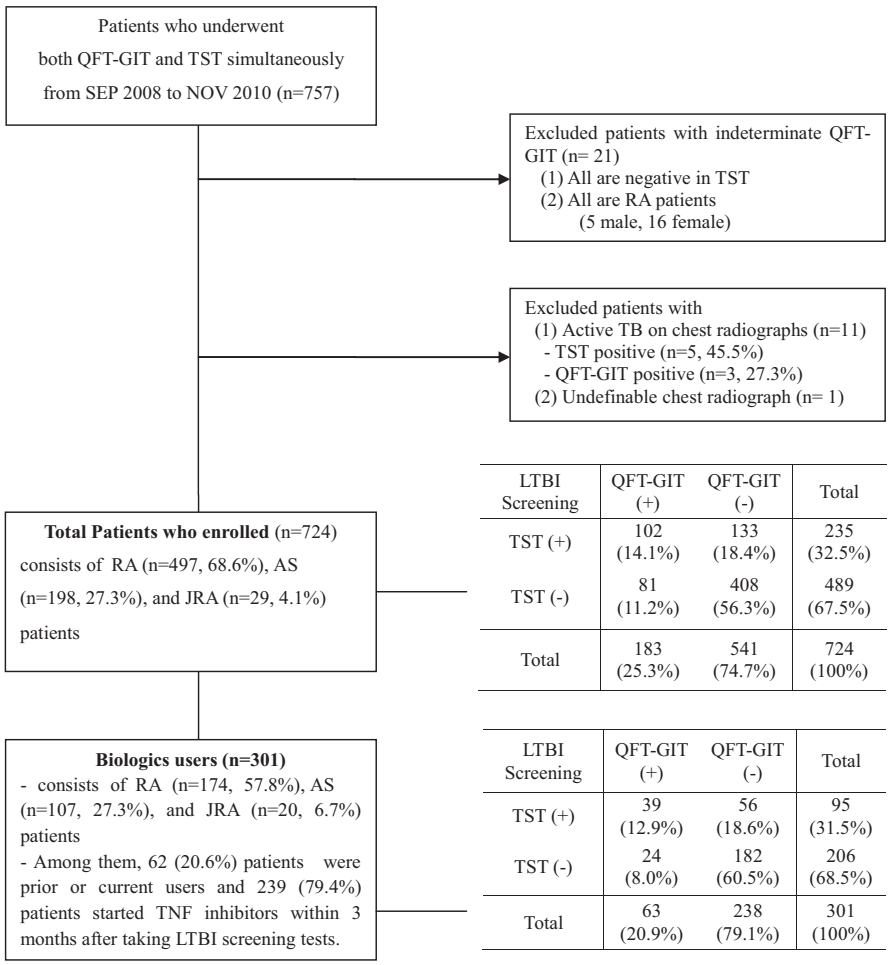
To evaluate the presence of LTBI, we usually use the tuberculin skin test (TST) and interferon-γ release assays (IGRAs). Currently, there are 3 [T-SPOT.TB, QntiFERON-TB gold, and QuantiFERON-TB gold in tube test (QFT-GIT)] commercially available kits of IGRAs. Although these are valuable tests for screening for LTBI, the diagnostic accuracy varies according to the patient population (11), and the concordance rate between TST and QFT-GIT is known to be low (12-14). This is the reason practice guidelines were recently revised to recommend performing both tests for patients eligible for TNF inhibitor treatment and to treat for LTBI in those with either positive TST or QFT-GIT results (15). However, the agreement between the 2 screening tests for LTBI may be influenced by socioeconomic and medical factors as well as the presence of comorbid diseases in each patient.

In this study, we aimed to estimate the agreement between QFT-GIT and TST when screening for LTBI and to measure the difference in the positivity of both tests among patients who were candidates for TNF inhibitor treatment. In addition, we sought to identify factors influencing discrepancies between QFT-GIT and TST results in Korean patients with rheumatologic diseases.

MATERIALS AND METHODS

Study Population

A total of 757 patients who underwent both QFT-GIT and TST simultaneously from September 2008 to November 2010 at a single tertiary academic hospital were selected for the study. We retrospectively collected data from March 2011 to April 2011 and the minimum interval between the screening LTBI and data collection was 3 months, which allowed us to identify the patients treated with TNF inhibitors (Fig. 1). Among the 757 patients, patients with indeterminate QFT-GIT results (n = 21), patients with active tuberculosis (n = 11), or findings suspicious for tuberculosis (n = 1) on a chest radiograph



LTBI Screening	QFT-GIT (+)	QFT-GIT (-)	Total
TST (+)	102 (14.1%)	133 (18.4%)	235 (32.5%)
TST (-)	81 (11.2%)	408 (56.3%)	489 (67.5%)
Total	183 (25.3%)	541 (74.7%)	724 (100%)

LTBI Screening	QFT-GIT (+)	QFT-GIT (-)	Total
TST (+)	39 (12.9%)	56 (18.6%)	95 (31.5%)
TST (-)	24 (8.0%)	182 (60.5%)	206 (68.5%)
Total	63 (20.9%)	238 (79.1%)	301 (100%)

Figure 1 Flow chart of patient enrollment (n = 757).