Performance of QuantiFERON TB Gold Test Compared With the Tuberculin Skin Test for Detecting Latent Tuberculosis Infection in Lung and Heart Transplant Candidates

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Abstract

Objectives: Evaluation for latent tuberculosis infection is advised before organ transplant. The interferon-gamma release assay has been shown to be more specific than the tuberculin skin test for screening for latent tuberculosis infection. We compared the tuberculin skin test and QuantiFERON-TB Gold In-Tube test for screening for latent tuberculosis infection and agreement between the tests in heart and lung transplant recipients before transplant.

Materials and Methods: Fifty-five adult patients who had been evaluated for heart and lung transplant between September 2011 and September 2012 at Masih Daneshvari Hospital in Iran were prospectively enrolled. We performed the tuberculin skin test and QuantiFERON-TB Gold In-Tube test.

Results: Of the 55 patients, 3 (5%) had positive tuberculin skin test results, and 11 (20%) had positive QuantiFERON-TB Gold In-Tube test results. Agreement between the tuberculin skin test and QuantiFERON-TB Gold In-Tube test was fair (Kappa=0.061; 95% CI: -0.185-0.307) (P = .56).

Conclusions: The positivity for QuantiFERON-TB Gold In-Tube test was greater than the positivity for the tuberculin skin test, and QuantiFERON-TB Gold In-Tube test more accurately determined the risk for latent tuberculosis infection. However, a further longitudinal study is necessary to verify that the QFT-G test would predict developing tuberculosis after heart and lung transplant.

Key words: Transplant, Tuberculin skin test, Interferon-gamma release assay, Tuberculosis

Introduction

Tuberculosis (TB) is a significant infection affecting organ transplant recipients.1,2 Development of TB occurs in transplant recipients 20 to 74 more than it does in the general population. Management of TB in this group is challenging, because there can be atypical clinical symptoms, and therapy may lead to potential toxicity or interactions with immunosuppressive medications.1,3–5 Accordingly, the American Society of Transplantation has suggested that all transplant recipients should be screened for TB infection, including previous exposure to Mycobacterium TB, chest radiograph, and a tuberculin skin test (TST) before transplant.6 However, performing the TST regarding identifying latent TB infection in organ transplant candidates has been deemed suboptimal because of the high risks of anergy, false-negative
results, and possible false-positive outcomes from Bacillus Calmette–Guérin (BCG) vaccination.3,4

We performed the TST and QFT-GIT before heart and lung transplant where a moderate incidence of TB and BCG vaccination is mandatory.7 We compared the results of the TST and QFT-GIT as a means for screening for latent TB infection, and we determined the agreement between the TST and QFT-GIT in this group of patients before transplant.

Materials and Methods

Patients were selected from heart or lung transplant candidates at the National Research Institutes of Tuberculosis and Lung Diseases between September 1, 2011, and September 1, 2012. The study was approved by the Ethical Review Committee of the institute. All protocols conformed with the ethical guidelines of the 1975 Helsinki Declaration. Informed consent was obtained from all subjects.

A whole-blood Interferon Gama Release Assay (IGRA) in reaction to Early Secreted Antigenic Target 6 and Culture Filtrate Protein 10 antigens was performed, and IFN-G was measured via enzyme-linked immunosorbent assay. According to the manufacturer’s instructions, the first, and every patient’s specimens—each containing 1 mL of whole blood—was poured into 3 separate tubes. The specimens were incubated in 37°C for 24 hours. Then the tubes were centrifuged at 2000 to 3000 rpm/minute for 15 minutes. The supernatant was frozen at -20°C. One tube served as the negative control containing only heparin. The second tube was the test tube holding Early Secreted Antigenic Target 6 and Culture Filtrate Protein 10 antigens. Gamma interferon released in each tube was measured by enzyme-linked immunosorbent assay. According to the manufacturer’s instructions, the first, and every patient’s specimens—each containing 1 mL of whole blood—was poured into 3 separate tubes. The specimens were incubated in 37°C for 24 hours. Then the tubes were centrifuged at 2000 to 3000 rpm/minute for 15 minutes. The supernatant was frozen at -20°C. One tube served as the negative control containing only heparin. The second tube served as the positive control, with added phytohemagglutinin as the mitogen, and the third tube was the test tube holding Early Secreted Antigenic Target 6 and Culture Filtrate Protein 10 antigens. Gamma interferon released in each tube was measured by enzyme-linked immunosorbent assay, and the measurements were read with QFT-GIT software. Indeterminate results, defined as a negative result in the positive control tube (mitogen tube) were identified. The TST was performed by injecting 0.1 mL of purified protein derivative intradermally into the forearm. The transverse induration size in millimeters was measured by a trained nurse 48 to 72 hours after induration. Values equal to or greater than 10 mm were defined as a positive TST result.

Statistical analyses were performed with SPSS software (SPSS: An IBM Company, version 11.5, IBM Corporation, Armonk, NY, USA). Agreement between the QFT-GIT and the TST was calculated using Kappa Test.

Results

A total of 55 organ transplant patients were recruited from September 2011 to September 2012. All patients had a history of being vaccinated by BCG. Of the 55 patients who entered the study, 47 were male (85%), and 8 were female (15%) (mean age, 37 ± 1.7; range, 14-63 y). Thirty-six (65%) were candidates for heart transplant and 19 (35%) were scheduled for lung transplant. A total of 43 (78%) had negative and 11 (20%) had a positive result for QFT-GIT and 1 (2%) patient had an intermediate test. A positive TST was detected in 3 patients (5%).

Of the positive QFT-GIT group, only 1 patient had a concomitant positive latent TB infection test, and among the positive latent TB infection patients, we found just 1 of our cases had a positive QFT-GIT simultaneously (Tables 1-3). Additionally, the Kappa agreement between the QFT-G and the TST was 0.061 (95% CI: -0.185-0.307) (P = .56).

| Table 1. QFTG and Tuberculin Skin Test Results Among 55 Patients |
|-------------|------------------|------------------|------------------|
| QFTG        | Tuberculin Skin Test | Positive | Negative | Total |
| Positive    | 1 (2%)            | 10 (18%)        | 11 (20%)        |
| Negative    | 2 (4%)            | 41 (76%)        | 43 (80%)        |
| Total       | 3 (6%)            | 51 (94%)        | 54 (100%)       |

Abbreviations: QFTG, QuantiFERON-TB Gold In-Tube test
*One patients with an intermediate QFTG result was excluded in our result.

| Table 2. QFTG and Tuberculin Skin Test Results Among Heart Transplant Candidates |
|-------------|------------------|------------------|------------------|
| QFTG        | Tuberculin Skin Test | Positive | Negative | Total |
| Positive    | 0                 | 9 (25%)          | 9 (25%)          |
| Negative    | 0                 | 27 (75%)         | 27 (75%)         |
| Total       | 0                 | 36 (100%)        | 36 (100%)        |

Abbreviations: QFTG, QuantiFERON-TB Gold In-Tube test

| Table 3. QFTG and Tuberculin Skin Test Results Among Lung Transplant Candidates |
|-------------|------------------|------------------|------------------|
| QFTG        | Tuberculin Skin Test | Positive | Negative | Total |
| Positive    | 1 (6%)            | 1 (6%)           | 2 (11%)          |
| Negative    | 2 (11%)           | 14 (18%)         | 16 (89%)         |
| Total       | 3 (16%)           | 15 (23%)         | 18 (100%)        |

Abbreviations: QFTG, QuantiFERON-TB Gold In-Tube test
*One patients with an intermediate QFTG result was excluded in our result.
Discussion

Pretransplant screening of candidates for TB infection is suggested with either the TST or one of the IGRAs. To date, performance of QFT-GIT in detecting latent TB infection in heart and lung transplant patients has not been entirely investigated. We demonstrated that positive results for QFT-GIT were more frequent than they were for the TST in heart and lung transplant candidates, and that agreement between the 2 tests was fair. Positive results for QFT-GIT were seen in 11 patients (20%), and positive results for the TST were seen in 3 (5%). The fact that positive results for QFT-GIT were more common than for the TST was consistent with earlier reports on the TST and IGRAs in immunocompromised patients or transplant candidates. These results proposed that QFT-GIT may be more sensitive than the TST in transplant candidates. Most positive QFT-GIT results were seen in heart transplant candidates compared with one positive among lung recipient candidates. Additionally, the fair agreement between the TST and QFT-GIT was consistent with previous studies in immunocompromised patients. The TST alone might miss 50% to 78% of latently infected individuals who may eventually reactivate their infection. On the other hand, the specificity of IGRAs has been between 67.4% to 98.1% in the immunocompetent population.

Only 5% of evaluated patients had a positive TST, despite prior BCG vaccination in all of our subjects during childhood, which might potentially lead to false-positive TST results. Our data are low compared with previous reports that show a 24% positive outcome.

According to the available data from the World Health Organization, Iran is a country with a moderate incidence for TB. Early detection and treatment of latent TB infection, particularly in high-risk individuals (eg, transplant candidates) should be a high priority in TB management.

A meta-analysis of studies comparing IFN-γ release assays with the TST indicated that agreement between tests was generally good, with κ values between 0.57 and 0.70. Conversely, we observed no agreement in our pretransplant populations. Given that the TST can be influenced by prior BCG vaccination, the results from our investigation and others could lend support to the recommendation that IGRA may be preferable to TST when diagnosing latent TB infection in populations with a high vaccination rate.

Our study also had some limitations. The sample size is relatively small. Because of the limited accessibility to the QFT-GIT testing tools, which in return, would hamper interpreting the results as general conclusions, we recommend the findings of this preliminary study be investigated with a large sample size and with subject recruitment on a multicenter scale.

In conclusion, QFT-GIT was found to be a more accurate tool in detecting latent TB infection. Detecting latent TB infection in heart and lung transplant individuals showed a poor agreement between QFT-GIT and the TST. Our study revealed that prior BCG vaccination had a minimal influence on the TST results in our patients.

References


