Nephrol Dial Transplant (2009) 24: 2252–2257
doi: 10.1093/ndt/gfp030
Advance Access publication 13 February 2009

The value of QuantiFERON®TB-Gold in the diagnosis of tuberculosis among dialysis patients

Tsuyoshi Inoue, Taichi Nakamura, Ai Katsuma, Shoichi Masumoto, Eri Minami, Daisuke Katagiri, Taro Hoshino, Maki Shibata, Manami Tada and Fumihiko Hinoshita

Division of Nephrology, International Medical Center of Japan, Tokyo, Japan

Correspondence and offprint requests to: Tsuyoshi Inoue; E-mail: tsuyoshi313@hotmail.com

Abstract

Background. It is difficult to diagnose tuberculosis (TB) in dialysis patients because of the high rate of extrapulmonary TB in these patients compared with the general population. Recently, a new diagnostic test called QuantiFERON (QFT) has been developed and shown promise as a diagnostic tool for active TB diseases and latent TB infection.

Methods. We examined 162 dialysis patients admitted to a single institute, including 8 patients with active TB, and evaluated the utility of this test in dialysis patients.

Results. Among 162 dialysis patients, positive QFT results occurred in 28 (17.3%), negative QFT results occurred in 95 (58.6%) and indeterminate QFT results occurred in 39 (24.1%). All eight active TB patients had positive QFT results, and none of the 95 patients with negative results had active TB. Among 23 patients with a history of active TB, 10 (43.5%) had positive results. Although the indeterminate rate was relatively high, no patient with an indeterminate result had active TB. Factors such as shorter duration of dialysis, lower lymphocyte count and higher white blood cell count were associated with indeterminate results. Among 105 cases after excluding the patients with previous TB or indeterminate results, the sensitivity of the QFT is 100% (8 of 8) and the specificity is 89.7% (87 of 97 cases).

Conclusions. Our data suggest that the QFT test is a useful supplementary tool for the diagnosis of active TB even in dialysis patients. Negative and indeterminate results on this test may be used to exclude the presence of active TB.

Keywords: diagnosis; dialysis; extrapulmonary TB; QuantiFERON; tuberculosis

Introduction

Tuberculosis (TB) is a common life-threatening infection worldwide, and approximately 2 million deaths and 9 million new cases are reported annually [1]. Haemodialysis patients are 6–25 times more likely to develop TB than other members of the community, primarily due to the impaired cellular immunity that occurs in chronic renal failure [2–4]. In addition, compared with the general population, the rate of extrapulmonary TB among all TB cases was reported to be high—from 38% to >80%—in dialysis patients. The mortality rate of TB in dialysis patients ranges from 17 to 75%, indicating that it is crucial to diagnose and treat TB in these patients as soon as possible [5]. A delay in diagnosis or treatment might lead to deterioration in the patient's nutritional status, a well-known negative prognostic factor in dialysis patients. To date, many patients have undergone treatment without a definite diagnosis of TB due to the difficulties of diagnosing TB in dialysis patients. However, as the treatment for TB is extensive, it would be preferable to have a positive diagnosis before beginning a treatment regimen.

Many methods have been used to diagnose TB, including acid-fast bacilli smear, culture, polymerase chain reaction (PCR), imaging studies, histological examination and various invasive procedures. However, these techniques have not satisfied clinical demands, and a new, quick and useful diagnostic tool for TB is needed.

The recently developed interferon-γ release assays (IGRAs) using *Mycobacterium tuberculosis*-specific antigens, early secreted antigenic target 6 (ESAT-6) and culture filtrate protein 10 (CFP-10) have shown promise as alternative diagnostic tools for latent TB infection (LTBI) and active TB. However, published data assessing the use of these tests in immunocompromised populations, particularly dialysis patients, are limited. One report examined the use of QuantiFERON (QFT; Cellestis Ltd, Carnegie, Victoria, Australia) in dialysis patients, but the value of QFT in diagnosing active TB was not investigated [6]. In addition, most studies focus on pulmonary TB as opposed to extrapulmonary TB [7,8]. This study compared the results of QFT results with clinical conditions and evaluated the value of QFT in dialysis patients.

We chose QFT for this study because it is the only commercially used IGRA in Japan. Although we previously reported results of a pilot study on the use of QFT for diagnosing extrapulmonary TB in dialysis patients, that study included a small number of patients [9]. The present study included more patients and thus has additional clinical relevance.

Subjects and methods

Study population

We examined QFT in dialysis patients with end-stage renal disease aged 18 or older. All patients were admitted to the International Medical Center of Japan, Tokyo, Japan, which is one of the largest national hospitals with an isolation ward for TB and a dialysis facility. They were hospitalized between April 2006 and June 2008 for reasons including suspected active TB, fever or inflammation of unknown origin, unilateral pleural effusion and abnormal lung shadows. Physicians decided to use the QFT depending on the medical situation (usually suspected TB disease, fever of unknown origin or the need to rule out TB). Patients who underwent the QFT test were enrolled in the present study. All patients provided oral or written informed consent. The procedures were in accordance with the Helsinki Declaration of 1975.

QuantiFERON test

Blood samples were obtained just before dialysis in haemodialysis patients, and at any time in peritoneal dialysis patients. The QFT test was performed according to the manufacturer's recommendations, and test results were evaluated according to the guidelines of the Centers for Disease Control and Prevention for using the QFT test [10] as follows: the test consisted of a negative control (a 'nil' well; whole blood without antigens or mitogen), a positive control (a 'mitogen' well; whole blood stimulated with the mitogen phytohaemagglutinin) and two sample wells (whole blood stimulated with either ESAT-6 or CFP-10). Whole-blood specimens were incubated for 18 h (overnight) at 37°C in a humidified atmosphere. The IFN-γ level of the nil well was considered to be the background value and was subtracted from the values for the mitogen well and the antigen-stimulated wells. The test result was considered positive, and TB infection suspected if the IFN-γ level in the sample well after stimulation with ESAT-6 and/or CFP-10 was >0.35 IU/ml (after subtraction of the value for the nil well) irrespective of the result for the positive control well. The test result was considered negative with no possibility of TB infection if the IFN-γ level was <0.35 IU/ml on both antigen wells and if the IFN-γ level of the positive control well (after subtraction of the value for the nil well) was >0.5 IU/ml. The test result was considered indeterminate and impossible to interpret if the IFN-γ level was <0.35 IU/ml in both antigen wells and <0.5 IU/ml in the positive control well, or if the IFN-γ level was below half of the negative control well in both antigen wells and >0.7 IU/ml in the negative control well.

Tuberculin skin testing (TST)

After venipuncture, patients underwent routine Mantoux TST with 0.1 ml (5 TU) of tuberculin-purified protein derivative (NIHON BCG supply, Tokyo, Japan). TSTs were read 48–72 h later by a physician. Induration of 5 mm was considered a positive TST result.

Status of TB infection

We classified TB infection into three categories: active TB, previous TB and non-TB. For all patients, we collected demographic, clinical, radiologic and microbiologic data. Physicians routinely carried out complete blood counts, blood chemistries including CRP, chest radiographs, history taking, general physical examinations and epidemiologic surveys (self-reported history of active TB, self-reported contact with an active case of TB, occupational history). When we suspected active TB based on these routine examinations, we added sputum and/or stomach fluid smear, culture, PCR, enhanced chest CT scans and enhanced abdominal CT scans. Depending on the situation, we also performed pleural effusion examinations (including smear, culture, adenosine deaminase), lymph node biopsy or positron emission tomography. Patients were finally classified as having active TB if either culture was positive for *Mycobacterium tuberculosis* or the experienced physician decided that the patients suffered from TB based on clinical findings, patient history, imaging study, histology indicating mycobacterial infection (i.e. granulomatous necrosis or identification of acid-fast bacilli) and the patients responded clinically and radiologically to anti-TB treatment.

We classified patients who had a history of TB treatment (recorded in charts or history taking) or who had some radiological evidence of TB as previous TB patients. Patients with no current or previous active TB or treatment were classified as non-TB patients.

Table 1. Demographics of study subjects

Patients (*N*)	162
Age (years; mean ± SD)	65.4 ± 12.0
Sex (M/F)	97/65
Haemodialysis/peritoneal dialysis	156/6
Duration of dialysis (months; range)	42.4 (0–468)
Cause of renal disease	
Diabetic nephropathy	74
Nephrosclerosis	22
Chronic glomerulonephritis	21
Collagen disease	10
Vasculitis	7
Drug nephropathy	3
Other	14
Unknown	9
Past history of TB	25
Immunosuppressive treatment	21

Table 2. Reasons for hospital admission (no. of patients)

Fever or inflammation of unknown origin	16
Unilateral pleural effusion	10
Pneumonia	10
Abnormal lung shadow	7
Heart failure (including ischaemic heart disease)	18
Stroke	5
Infection (except pneumonia)	7
Malignancy	6
Bone fracture	8
Vascular access problem	3
Disturbance of consciousness	3
Initiation of dialysis	37
Others	32

Primary renal disease

Primary renal diseases were classified into seven categories: diabetic nephropathy, nephrosclerosis, chronic glomerulonephritis, collagen disease, vasculitis, drug nephropathy and other.

Statistical analysis

We calculated proportions of positive, negative and indeterminate results across active TB, non-TB and previous TB patients. A logistic regression analysis was applied to investigate what parameters determined indeterminate QFT results in our cohort. The following variables were considered: age, sex, duration of dialysis, haemoglobin, WBC, lymphocyte count, albumin, blood urea nitrogen, creatinine, calcium, phosphate, CRP, body temperature, body mass index, existence of diabetes mellitus, hyperlipidaemia and use of immunosuppressive drugs. A *P*-value <0.05 was considered significant. We performed all analyses with JMP version 6.0 (SAS Institute Inc., Cary, NC, USA).

Results

One hundred and sixty-two patients (97 men and 65 women; mean age 65.4 years) underwent QFT tests (Table 1). The mean duration of dialysis was 42.4 months (range, 0–468 months), and 37 patients had just started dialysis. All patients were admitted to our hospital; reasons for admission are shown in Table 2. Forty-three patients had highly suspected active TB with symptoms including persistent fever of unknown origin or inflammation, unilateral pleural effusion, pneumonia and abnormal lung shadow. Among them, eight cases (18.6%) of active TB were diagnosed after admission.

Table 3. Results of QFT in dialysis patients

	Active TB	Non-TB	Previous TB	Total
Positive results	8	10	10	28
Negative results	0	87	8	95
Indeterminate results	0	34	5	39
Total	8	131	23	162

Among the 162 dialysis patients, QFT results were positive in 28 (17.3%), negative in 95 (58.6%) and indeterminate in 39 (24.1%). Eight (28.6%) of 28 patients with a positive result had active TB. Ten (35.7%) of these 28 patients had a history of TB disease and 10 (35.7%) did not have active or previous TB. None of the 95 patients with a negative result had active TB disease. Eighty-seven (91.6%) of 95 patients with negative results did not have a history of active or previous TB, and the remaining 8 patients (8.4%) had a history of TB. All 39 patients (24.1%) with indeterminate results showed a positive control failure on QFT-TB results (IFN-γ <0.5 IU/ml). None of them had active TB. Thirty-four (87.2%) of 39 patients did not have any history of active or previous TB, and 5 patients (12.8%) had a history of previous TB (Table 3).

Of the 28 patients with positive QFT results, 8 had active TB. Among these eight patients, four had tuberculous lymphadenitis, two had tuberculous pleuritis and two had pulmonary TB (Table 4). In both pulmonary TB patients, active TB was easily diagnosed using sputum smear, PCR and culture. On the other hand, a detailed investigation was needed to diagnose extrapulmonary TB in six patients with active TB. Four of the six extrapulmonary TB cases presented as fever of unknown origin, and two showed pleural effusion, although the cause was difficult to determine. In one patient, tuberculous lymphadenitis was confirmed by autopsy. This case presented with fever of unknown origin and was diagnosed as para-aortic tuberculous lymphadenitis in advance by enhanced abdominal CT scan and response to TB treatment. Only one of eight was TST positive. This is consistent with the recent report that showed the lack of utility of TST in diagnosing active TB [11]. Among the 23 patients with a history of active TB, 10 (43.5%) had a positive result, 8 (34.8%) had a negative result and 5 (21.7%) had an indeterminate result on the QFT test.

It is difficult to interpret QFT results in patients with previous TB or indeterminate QFT results. So, when we excluded indeterminate results and/or previous TB, we were left with 105 cases. Among the 105 cases after excluding the patients with previous TB or indeterminate results, the sensitivity of the QFT is 100% (8 of 8) and the specificity is 89.7% (87 of 97 cases). The positive predictive value is 44.4% (8 of 18), and the negative predictive value is 100% (87 of 87).

Table 5 shows the association between risk factors and indeterminate QFT results. Univariate analysis revealed an association between indeterminate results and shorter duration of dialysis, decreased albumin levels, increased white blood cell count (WBC) and increased C-reactive protein (CRP) levels. Multivariate analysis revealed that a decreased lymphocyte count and the absence of hyperlipidaemia were also associated with indeterminate results.

Table 4. Details of eight cases with active tuberculosis and positive QFT results

Age (years)	Sex	Reason for dialysis	Duration of dialysis	Clinical problem	Focus of tuberculosis infection	ESAT-6	CFP-10	Mitogen	TST
65	M	DM	6 years and 9 months	FUO	Tuberculous lymphadenitis (LN at right axilla)	0.04	1.89	0.26	Negative
79	M	DM	Dialysis just started	FUO	Tuberculous lymphadenitis (para-aortic LN, abdomen)	1.66	0.03	6.70	Positive
69	M	DM	5 years and 7 months	PE	Tuberculous pleuritis (right side)	−0.01	0.72	16.01	Negative
75	F	DM	1 month	FUO	Tuberculous lymphadenitis (LN at right clavicular fossa)	13.21	0.1	2.69	Negative
63	M	Nephrosclerosis (HTN)	4 years and 3 months	PE	Tuberculous pleuritis (right side)	10.05	0.02	0.86	Negative
73	M	Nephrosclerosis (HTN)	9 years and 7 months	FUO	Tuberculous lymphadenitis (para-aortic LN, abdomen)	0.91	0.00	1.40	Negative
76	M	CGN	2 years and 11 months	Abnormal lung shadow	Pulmonary tuberculosis (right side)	1.85	3.14	1.42	Negative
61	M	DM	8 years and 3 months	Abnormal lung shadow	Pulmonary tuberculosis (right side)	0.09	1.93	12.32	Negative

ESAT-6, early secreted antigenic target 6; CFP-10, culture filtrate protein; DM, diabetes mellitus; FUO, fever of unknown origin; LN, lymph node; PE, pleural effusion; HTN, hypertension; CGN, chronic glomerulonephritis, TST, tuberculin skin testing.

Table 5. Univariate and multivariate analyses of indeterminate QFT results

	Univariate		Multivariate	
	Odds ratio (95% CI)	*P*-value	Odds ratio (95% CI)	*P*-value
Age (years)	1.01 (0.98–1.04)	0.45	0.99 (0.93–1.04)	0.73
Female	0.91 (0.43–1.91)	0.80	3.76 (0.82–17.18)	0.086
Duration (months)	0.98 (0.97–0.99)	0.006	0.94 (0.90–0.98)	0.005
Haemoglobin (g/dl)	0.94 (0.74–1.19)	0.60	1.52 (0.95–2.42)	0.078
WBC (/μl/1000)	1.12 (1.00–1.25)	0.045	1.56 (1.14–2.14)	0.005
Lymphocyte (/μl/100)	0.89 (0.80–1.00)	0.053	0.79 (0.66–0.95)	0.015
Albumin (g/dl)	0.28 (0.14–0.56)	0.0003	0.19 (0.042–0.88)	0.034
BUN (mg/dl)	0.99 (0.98–1.01)	0.62	0.97 (0.94–1.00)	0.15
Creatinine (mg/dl)	0.88 (0.76–1.00)	0.067	1.16 (0.83–1.63)	0.36
Calcium (mg/dl)	1.24 (0.85–1.82)	0.25	1.11 (0.47–2.58)	0.80
Phosphate (mg/dl)	0.91 (0.73–1.14)	0.43	1.00 (0.67–1.50)	0.98
CRP (mg/dl)	1.06 (1.00–1.12)	0.033	1.04 (0.88–1.22)	0.62
Body temperature (°C)	1.39 (0.74–2.63)	0.29	0.39 (0.10–1.58)	0.19
BMI (kg/m^2)	0.98 (0.87–1.09)	0.75	1.06 (0.87–1.28)	0.54
Diabetes mellitus	1.10 (0.53–2.27)	0.78	0.71 (0.20–2.54)	0.60
Hyperlipidaemia	0.90 (0.37–2.20)	0.83	0.19 (0.03–0.97)	0.046
Immunosuppressive drug	0.90 (0.31–2.64)	0.86	0.11 (0.01–1.06)	0.056

Discussion

Our findings indicate that QFT is a useful test to diagnose active TB in dialysis patients, as all active TB patients showed positive QFT results, and no patient with a negative or indeterminate result had active TB. These results are consistent with our previous report [9]. This study focused on dialysis patients, who are likely to develop active TB as well as extrapulmonary TB. Among the eight active TB patients in this study: six (75%) had extrapulmonary TB (four had tuberculous lymphadenitis and two had tuberculous pleuritis) and two (25%) had pulmonary TB. The regular occurrence of extrapulmonary TB among TB cases in this study supports the findings of a previous study [5].

Except for eight active TB cases, no active TB cases were found among subjects with positive QFT results, even after detailed investigations. However, two cases who had positive QFT results but who were initially ruled out from having active TB developed active TB during the follow-up period. This indicates that we need to rule out the existence of active TB when QFT results are positive. Moreover, even if we cannot confirm active TB after a positive QFT test result, we should carefully follow up these cases. On the other hand, none of the 95 patients with negative QFT results had active TB, allowing us to use negative results of this test to rule out active TB. In addition, cases with indeterminate results might be regarded as negative because no cases with indeterminate results had active TB. Considering that indeterminate results can be treated the same as negative results, we suggest that the sensitivity of QFT is 100% (8 of 8) and its specificity is 87.0% (134 of 154 cases). It is difficult to interpret QFT results in patients with previous TB or indeterminate QFT results. However, when we excluded indeterminate results without previous TB ($n = 34$) and previous TB cases ($n = 23$), we were left with 105 cases. In this case, the sensitivity of the QFT is the same (100%) and specificity is 89.7% (87 of 97 cases).

There is one study that compared the results of QFT in two groups among dialysis patients who did or did not have a close contact with an active pulmonary TB case. The total number of patients included in the study was 96, and none of them had a history of TB. Among the 96 cases, 2 had indeterminate results (2.1%), and after excluding these two patients, 55 cases had contacts and 39 did not. Any patient who shared dialysis time with the active pulmonary TB patient was 'contact'; 16 of 55 contacts (29.1%) were QFT positive and 5 of the 39 non-contacts (12.8%) were QFT positive. In this report, the authors concluded that QFT results were more closely associated with recent TB exposure than positive TST were. Compared to this report, our study showed a higher frequency of intermediate results (24.1 versus 2.1) and a similar rate of QFT-positive results (17.3% versus 22.3%) [6].

In terms of previous TB, the percentage of positive QFT results in patients with previously treated TB but without active TB has been reported to be 36.6% in the general population ($n = 134$) [12]. The present study showed a rate of 43.5% (10/23) in dialysis patients. There has been no previous report that suggests that QFT can be used to differentiate between previous and current TB. Therefore, the high percentage of positive QFT results makes it difficult to determine whether these patients have active or previous TB.

Previous studies have suggested high rates of indeterminate results among immunocompromised patients. Indeterminate results have been reported in 10.8% of patients with malignant disease ($n = 74$), 27.8% of patients undergoing immunosuppressive treatment ($n = 72$), 3.8% of patients with diabetes mellitus ($n = 52$) [13] and 5.1% of patients with HIV infection ($n = 294$) [14]. In routine use of the QFT test for outpatients or inpatients with suspected TB (active or latent), two studies reported that 11% ($n = 383$) [15] and 21.4% ($n = 318$) [16] had indeterminate results. Only a few studies on indeterminate results among dialysis patients have been reported [13,16,17]. The incidence of indeterminate results ranged from 2 to 40%, and appeared to depend on whether they were outpatients or inpatients, had primary renal diseases and whether complications were

present [13,16,17]. Our study showed that 24.1% of patients had indeterminate results, which is consistent with previous reports.

Little is known about which factors influence indeterminate results. Lower $CD4^+$ count, lymphocytopenia, older age, female sex, diabetes mellitus, cancer chemotherapy and immunosuppressive treatment have been previously reported to be associated with indeterminate results [8,14,16,18,19], and our study confirmed one of these risk factors and revealed some additional risk factors (Table 5). In general, immunity is compromised within 1 year after starting dialysis [17], and most TB cases are diagnosed in haemodialysis patients prior to or within the first 6 months of dialysis [20,21]. These reports support our results that a shorter duration of dialysis increases indeterminate results. Among HIV patients, lower $CD4^+$ cell counts were reported to be associated with decreased IFN-γ response to the positive control and to both TB antigens [14,22]. In addition, indeterminate results in elderly patients were shown to be caused by lymphocytopenia due to underlying diseases [18]. Lymphocytopenia causes a decrease in the production of IFN-γ and a low mitogen QFT level [23]. Increased WBC and CRP also seem to be caused by severe underlying diseases such as infection and could correlate with lymphocytopenia and result in positive control failures. It is thus possible that lower serum albumin levels and the absence of hyperlipidaemia may increase indeterminate results, because dialysis patients tend to suffer from malnutrition in general, which may compromise the immune system. We could not confirm any relationship between diabetes mellitus and indeterminate results in this study. Immunosuppressive treatments have been reported to increase indeterminate results [13]. In our study, however, there was an opposite trend in that a lower indeterminate QFT rate was observed in patients taking immunosuppressive drugs. A higher indeterminate QFT rate in female patients was reported in one study, although the reason for these findings was not elucidated [19]. One report showed a female predominance among dialysis TB patients despite a higher frequency of male than female patients reported with TB in general [24]. However, no gender differences in QFT results were found in our study. In summary, some variables appear to be associated with indeterminate results, but no case with indeterminate results had active TB. Taken together, indeterminate results may be interpreted as negative results, and the high rate of indeterminate results seen do not hinder the use of the QFT in diagnosing active TB, even in dialysis patients.

Because there is no diagnostic gold standard for LTBI, we could not assess the sensitivity and specificity of QFT for this disease state. The only diagnostic standard for LTBI is the eventual development of active TB, and the predictive value for progression of TB can be ascertained only through longitudinal cohort studies that follow clinical outcomes of tested individuals. In the present study, one case of non-TB (ESAT-6 0.96 IU/ml, CFP-10 −0.01 IU/ml) and one case of previous TB (ESAT-6 0.96 IU/ml, CFP-10 0.77 IU/ml) developed active TB during follow-up (7 months later and 6 months later, respectively). Both cases had positive QFT results and thus a higher possibility of experiencing LTBI, so it would be advisable to administer prophylactic anti-TB drugs to these patients. Few studies have shown that QFT-positive individuals later develop active TB [25,26]. One report showed that patients with positive QFT results had a high possibility of developing TB (14.6%), and all of these cases responded strongly to a QFT assay, with IFN-γ levels >10 IU/ml [27]. Therefore, QFT-positive cases should be carefully followed up for a long time, even if no active TB is revealed.

Our study has several limitations. First, the number of active TB patients was small, which makes it difficult to evaluate the diagnostic value of QFT. Second, we analysed only hospitalized patients. These patients often have other severe diseases that could influence QFT results. Third, we could not reach a definite conclusion on how to interpret the high incidence of indeterminate QFT results due to the lack of cases. Finally, our follow-up period was relatively short (up to two and a half years), and we can neither fully analyse nor say much about cases with positive QFT results and no active TB during the study period. Further studies are needed to resolve these limitations.

In conclusion, our data suggest that the QFT test is a useful supplementary tool for the diagnosis of active TB, and that negative results may be used to exclude active TB in dialysis patients. Results also suggest that the QFT test is valuable in detecting extrapulmonary TB, which can be difficult to diagnose. In spite of the high rate of indeterminate QFT results in our study, no patient with indeterminate results had active TB. This might mean that we can consider indeterminate results among dialysis patients as negative results and rule out active TB in these patients.

Conflict of interest statement. None declared.

References

1. Kang YA, Lee HW, Hwang SS *et al*. Usefulness of whole-blood interferon-γ enzyme-linked immunospot assay in the diagnosis of active pulmonary tuberculosis. *Chest* 2007; 132: 959–965
2. Wauters A, Peetermans WE, Van Den Brande P *et al*. The value of tuberculin skin testing in haemodialysis patients. *Nephrol Dial Transplant* 2004; 19: 433–438
3. Habesoglu MA, Torun D, Demiroglu YZ *et al*. Value of the tuberculin skin test in screening for tuberculosis in dialysis patients. *Transplant Proc* 2007; 39: 883–886
4. Passalent L, Khan K, Richardson R *et al*. Detecting latent tuberculosis infection in hemodialysis patients: a head-to-head comparison of the T-SPOT.TB test, and an expert physician panel. *Clin J Am Soc Nephrol* 2007; 2: 68–73
5. Hussein MM, Mooij JM, Roujouleh H. Tuberculosis and chronic renal disease. *Semin Dial* 2003; 16: 38–44
6. Winthrop KL, Nyendak M, Calvet H *et al*. Interferon-γ release assays for diagnosing *Mycobacterium tuberculosis* infection in renal dialysis patients. *Clin J Am Soc Nephrol* 2008; 3: 1357–1363
7. Ravn P, Munk ME, Andersen AB *et al*. Prospective evaluation of a whole-blood test using mycobacterium tuberculosis-specific antigens ESAT-6 and CFP-10 for diagnosis of active tuberculosis. *Clin Diagn Lab Immunol* 2005; 12: 491–496
8. Baba K, Sørnes S, Hoosen AA *et al*. Evaluation of immune responses in HIV infected patients with pleural tuberculosis by the QuantiFERON®TB-Gold interferon-gamma assay. *BMC Infect Dis* 2008; 8: 35–42
9. Inoue T, Nakamura T, Katagiri D *et al*. The usefulness of QuantiFERON®TB-2G for the diagnosis of tuberculosis in dialysis patients. *J Jpn Soc Dial Ther* 2008; 41: 65–70

10. Mazurek GH, Jereb J, Lobue P *et al*. Guidelines for using the QuantiFERON®TB-Gold test for detecting *Mycobacterium tuberculosis* infection, United States. *MMWR Recomm Rep* 2005; 54: 49–55
11. Resić H, Dizdarević Z, Corić A *et al*. Evaluation of clinical presentation and prognosis of tuberculosis in patients undergoing hemodialysis. *Acta Med Croatica* 2008; 62: 65–68
12. Kawabe Y. Application and problems of QuantiFERON®TB-2G for tuberculosis control programs—(2) clinical use of QuantiFERON®TB-2G. *Kekkaku* 2007; 82: 61–66
13. Kobashi Y, Mouri K, Obase Y *et al*. Clinical evaluation of QuantiFERON TB-2G test for immunocompromised patients. *Eur Respir J* 2007; 30: 945–950
14. Luetkemeyer AF, Charlebois ED, Flores LL *et al*. Comparison of an interferon-γ release assay with tuberculin skin testing in HIV-infected individuals. *Am J Respir Crit Care Med* 2007; 175: 737–742
15. Ferrara G, Losi M, D'Amico R *et al*. Use in routine clinical practice of the two commercial blood tests for diagnosis of infection with *Mycobacterium tuberculosis*: a prospective study. *Lancet* 2006; 367: 1328–1334
16. Ferrara G, Losi M, Meacci M *et al*. Routine hospital use of a new commercial whole blood interferon-γ assay for the diagnosis of tuberculosis infection. *Am J Respir Crit Care Med* 2005; 172: 631–635
17. Harada T, Sakata H, Yasumori R *et al*. Tuberculosis in patients undertaking hemodialysis. *Kekkaku* 1989; 64: 47–54
18. Kobashi Y, Mouri K, Yagi S *et al*. Clinical utility of the QuantiFERON TB-2G test for elderly patients with active tuberculosis. *Chest* 2008; 133: 1196–1202
19. Chee CBE, Gan SH, KhinMar KW *et al*. Comparison of sensitivities of two commercial gamma interferon release assays for pulmonary tuberculosis. *J Clin Microbiol* 2008; 46: 1935–1940
20. Taskapan H, Utas C, Oymak FS *et al*. The outcome of tuberculosis in patients on chronic hemodialysis. *Clin Nephrol* 2000; 54: 134–137
21. Andrew OT, Schoenfeld PY, Hopewell PC *et al*. Tuberculosis in patients with end-stage renal disease. *Am J Med* 1980; 68: 59–65
22. Brock I, Ruhwald M, Lundgren B *et al*. Latent tuberculosis in HIV positive, diagnosed by the *M. Tuberculosis* specific interferon-γ test. *Respir Res* 2006; 7: 56–64
23. Kobashi Y, Fukuda M, Yoshida K *et al*. An indeterminate QuantiFERON TB-2G response for military tuberculosis, due to severe pancytopenia. *J Infect Chemother* 2007; 13: 414–417
24. Christopoulos AI, Diamantopoulos AA, Dimopoulos PA *et al*. Male-female differences in the risk of tuberculosis in dialysis patients. *Int Urol Nephrol* 2008
25. Brock I, Munk ME, Kok-Jensen A *et al*. Performance of whole blood IFN-gamma test for tuberculosis diagnosis based on PPD or the specific antigens ESAT-6 and CFP-10. *Int J Tuberc Lung Dis* 2001; 5: 462–467
26. Harada N, Nakajima Y, Higuchi K *et al*. Screening for tuberculosis infection using whole-blood interferon-gamma and mantoux testing among Japanese healthcare workers. *Infect Control Hosp Epidemiol* 2006; 27: 442–448
27. Diel R, Loddenkemper R, Meywald-Walter K *et al*. Predictive value of a whole blood IFN-γ assay for the development of active tuberculosis disease after recent infection with *Mycobacterium tuberculosis*. *Am J Respir Crit Care Med* 2008; 177: 1164–1170

Received for publication: 23.10.08; Accepted in revised form: 15.1.09