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Thyroid Function as a Predictive Factor in Outcomes of Renal Transplantation

Farzanehsadat Minoo[1, 2] Azam Alamdari[1,2], Ali Ghafari[1,2*]

1 Nephrology Research Center, Tehran University of Medical Sciences. Tehran, Iran

2 Center of Excellence in Nephrology

Corresponding author: Ali Ghafari, Assistant Professor of Nephrology ,Nephrology Research Center, Tehran University of Medical Science, Tehran, Iran., Email address: ghaf_ali *Mailing address: Nephrology Research Center, Nephrology Department, Imam Khomeini hospital, Tehran, Iran*

Keywords

Abstract

Background - Bi-directional link between renal and thyroid dysfunctions was identified previously. The present study evaluated free triiodothyronine (FT3), free thyroxine (FT4), and thyroid-stimulating hormone (TSH) concentration before renal transplant relative to kidney allograft function.

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1. Introduction

Although renal allograft outcomes have improved with modern immunosuppression, its loss remains a great dilemma with up to 3-fold increased risk of death, immunological sensitization which is an obstacle for retransplantation, lower quality of life and increased costs (1). The identification of predictive factors in renal transplantation can help us to decline the rate of graft loss. However, to date, no reliable simple parameter has been found to predict the long term outcomes.

A mutual interaction between thyroid and renal function has been found. On one side, thyroid hormones can influence kidney function directly through their effects on glomerular filtration, electrolyte pumps, secretory and absorptive capacity of tubuli, and kidney structure. Moreover, the impact of thyroid hormones on cardiovascular function can indirectly affects the kidney function via decreasing renal blood flow (2). On the other side, it appears that kidney has a significant role in synthesis, secretion, metabolism, and elimination of thyroid-stimulating hormone (TSH). Studies indicated that individuals who suffer from end-stage renal disease are prone to elevated TSH levels, reduced TSH responses to thyroid-releasing hormone (TRH), and reduced serum levels of total and free triiodothyronine (T3) and thyroxine (T4) (3).

Overall, our purpose is to investigate the association between thyroid and renal functions due to renal allograft to understand if thyroid hormones can be considered as a predictive factor in kidney transplants.

[Abstract Continued…]

Methods - Fifty consecutive kidney graft recipients were entered in this cohort study. FT3, FT4, and TSH were measured on the day before transplantation. Correlations between these variables and transplant kidney function and graft survival were assessed.
Results - Significant correlation between pretransplant FT3 and transplant kidney function as well as one year graft survival was observed. Pretranslant serum levels of FT4 associated with one year transplant kidney function.
Conclusion FT3 and with less extent FT4 may be used as predictive factor for outcomes of renal transplantation.
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2. Patients and Methods

2.1 *Patients*

This is a prospective cohort study of individuals undergoing allograft renal transplantation who were referred to Imam Khomeini hospital complex affiliated to Urumia University of Medical Sciences between April 5, 2015 and October 5, 2015. The exclusion criteria were age less than 18 years, multi-organ transplant, and prior history of thyroid dysfunction (before recognition of renal failure) or thyroid malignancy.

2.2 *Methods*

Serum levels of thyroid hormones including TSH, free T3 (FT3), and free T4 (FT4) were measured in our studied group one day before renal transplant and using immunosuppressive medications. The patients were followed up for one year after transplantation and factors related to kidney function were assessed in one, six, and twelve months after kidney replacement. Those included delayed graft function (DGF), graft loss, and serum levels of creatinine (Cr).

2.3 *Statistical analysis*

Results of metric variables were presented as means and standard deviations (SD). Also, for statistical analysis, independent T-test was used. Regarding graft survival, Kaplan-Meier estimator was performed. Descriptive variables were described using percentage and to compare, Chi-square was used. The obtained data were analyzed by SPSS V.16 software and the statistical significance was set at P-value of <0.05.

3. Result

Our sample included 50 individuals with 31 males (62%) and 19 females (38%). The mean age (SD) of our participants was 42.10 (14.89). Among these 50 patients, 34 of them had normal levels of FT3 while 16 of them had decreased levels (mean (SD): 2.7 (0.62)). Furthermore, 7 and 10 people were reported to have decreased levels of FT4 and TSH, respectively (mean of FT4 (SD): 1.00 (0.24); mean of TSH (SD): 2.41 (2.04)).

DGF was assessed before kidney replacement in all of our cases and using Chi-square reported no significant correlation between pretransplant levels of FT3, FT4, and TSH with this parameter (P-value<0.05) (Table 1).

After renal replacement, 5 cases of our sample quit the study and 45 remained. Regarding the function of transplanted kidney, in the first step, glomerular filtration rate (GFR) of participants was measured in the first and sixth months after allograft and the results of each patient were compared. Overall a positive association was indicated between FT3 before renal transplant and function of replaced kidney (P-value: 0.04). However, no correlation was observed between FT4 and TSH with level changes of GFR. In the next step, GFR levels of the first and twelfth months after transplant were compared. Positive correlation was reported between pretransplant FT3 and FT4 levels with function of transplanted kidney (P-value: 0.01 and 0.03, respectively) (Table 1).

The relationship between one year graft survival and pretransplant thyroid hormones was also assessed in our study. Statistical analysis revealed that FT3 was associated with one year graft survival (X^2: 5.37 , P-value: 0.03). but no such correlation was observed considering FT4 and TSH (Table 1).

4. Discussion

In this study, we realized that the decreased pretransplant levels of FT3 statistically associated with increased risk of short- and long-term allograft kidney dysfunction. Besides, it was identified that FT3 level could be an important predictive factor for one year graft survival. Decreased pretransplant FT4 levels also correlated with long-term kidney dysfunction. In line with our trial, one study identified that pretransplant FT3 levels were useful to estimate the risk for renal graft failure (4). Another study with 46 kidney graft recipients reported a significant negative association between serum FT3 levels and Cr; while no correlation was observed between FT4 or TSH and Cr (5). A cross-sectional study with 136 subjects also concluded that the presence of low serum FT3 levels correlated with worse kidney graft function, anemia, body mass index (BMI), and serum sodium (6). Of interest, recent evidence indicated that decreased thyroid function is negatively correlated with other types of transplantations too (7).

The underlying mechanisms of this association are not yet clear. A causality mechanism may somewhat justify this association. As we mentioned, thyroid dysfunction has an independent role in renal failure and may affect the function of allograft kidney. That is why some evidence suggested that supplementary thyroid hormone therapy should be considered in kidney transplant recipients (5). A shared risk factor is another possible mechanism for this relationship. Cytokines are a group of small proteins with a major role in cell signaling in the immune system but also increasingly recognized in pathogenesis of various systemic disorders such as neurological, psychiatric and skin diseases (8). It has been realized that pro-inflammatory cytokines like interleukin (IL)6 have a considerable role in thyroid dysfunction. In fact, increased levels of pro-inflammatory mediators observed in people with decreased levels of thyroid hormones (9). On the other side, the negative impact of inflammation on renal allograft outcome was reported in previous trials. A recent study demonstrated that urinary chemokines may predict the long-term outcome of kidney replacement (10). Therefore, the above-mentioned association between pretransplant serum FT3 levels and transplanted kidney function or its survival may be confounded by elevated levels of cytokines. According to the small number of our cases and other studies, the coincidental event should still not be underestimated.

Small sample and short-term follow-up were the main limitations of our study. Evaluation of the size of thyroid in our studied group could also give us more hints about the association between thyroid and transplanted renal functions. Furthermore, using other tools like resistance index through the performance of color doppler in the renal arteries could give us better sight about kidney function.

In conclusion, pretransplant serum levels of FT3 and with less extent FT4 may be a useful tool to predict the function and survival of renal allograft.

Table 1. The correlation between thyroid hormones and factors related to allograft kidney

	DGF	Allograft kidney function (during 1 to 6 months)	Allograft kidney function (during 1 to 12 months)	One year graft survival
FT3	7 patients with negative DGF and decreased FT3 levels 11 patients with negative DGF and normal FT3 levels 32 patients with positive DGF and decreased FT3 levels 23 patients with positive DGF and normal FT3 levels	11 patients with decreased GFR and decreased FT3 levels 11 patients with decreased GFR and normal FT3 levels 4 patients with increased GFR and decreased FT3 levels 19 patients with increased GFR and normal FT3 levels*	12 patients with decreased GFR and decreased FT3 levels 12 patients with decreased GFR and normal FT3 levels 3 patients with increased GFR and decreased FT3 levels 18 patients with increased GFR and normal FT3 levels*	In patients with decreased FT3 levels mean (SD): 9.70 (0.60) In patients with normal FT3 levels mean (SD): 11.37 (0.60) X^2: 5.37 P-value: 0.03*
FT4	2 patients with negative DGF and decreased FT4 levels 16 patients with negative DGF and normal FT4 levels 5 patients with positive DGF and decreased FT4 levels 27 patients with positive DGF and normal FT4 levels	2 patients with decreased GFR and decreased FT4 levels 20 patients with decreased GFR and normal FT4 levels 5 patients with increased GFR and decreased FT4 levels 18 patients with increased GFR and normal FT4 levels	6 patients with decreased GFR and decreased FT4 levels 18 patients with decreased GFR and normal FT4 levels 1 patients with increased GFR and decreased FT4 levels 20 patients with increased GFR and normal FT4 levels*	X^2: 0.80 P-value: 0.30
TSH	5 patients with negative DGF and decreased TSH levels 13 patients with negative DGF and normal TSH levels 5 patients with positive DGF and decreased TSH levels 27 patients with positive DGF and normal TSH levels	3 patients with decreased GFR and decreased TSH levels 19 patients with decreased GFR and normal TSH levels 7 patients with increased GFR and decreased TSH levels 16 patients with increased GFR and normal TSH levels	6 patients with decreased GFR and decreased TSH levels 18 patients with decreased GFR and normal TSH levels 4 patients with increased GFR and decreased TSH levels 17 patients with increased GFR and normal TSH levels	X^2: 1.30 P-value: 0.20

* Statistically correlated

DGF: delayed graft function; GFR: glomerular filtration rate; FT3: free triiodothyronine; FT4: free thyroxine; TSH: thyroid-stimulating hormone

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