# Expansion and Characterization of Treg Populations from Korean Kidney Transplant Recipient

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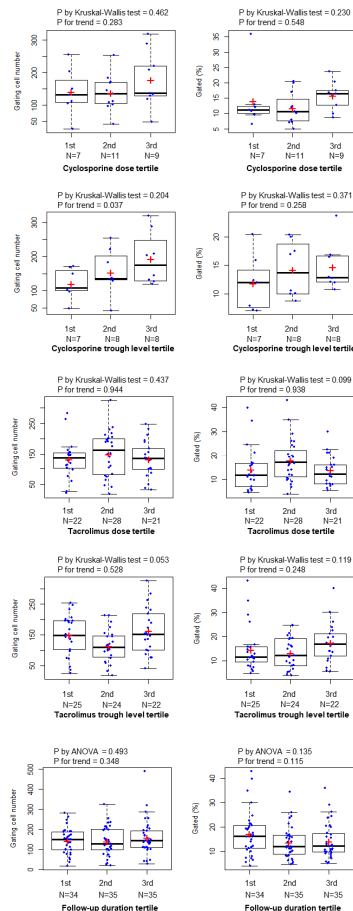**이병현[1], 김예나[1,2], 박영찬[1], 신호식[1,2], 정연순[1,2], 임학[1,2]**

**Background/Aims:** The development of immunosuppressants has enabled remarkable progress in kidney transplantation (KT). However, current immunosuppressants cannot achieve induction of immune tolerance and their nonspecific immunosuppressive effects result in many adverse effects. Regulatory T cells (Tregs) play crucial roles in controlling allospecific immune responses. This study evaluated the distribution of Tregs and their effects on kidney allograft function in Korean KT recipients.

**Methods:** We enrolled 144 KT recipients with stable graft function between 1989 and 2018. Differentiation and expansion of Tregs were studied by flow cytometry to compare the Tregs subpopulations. Tregs were defined as CD4+CD25highCD127low/-FoxP3+ cells.

**Results:** Among the 144 patients, 75 patients (65.8%) were males and mean follow-up period was 144.3 ± 111.5 months. All patients received calcineurin inhibitors as maintenance immunosuppressants. Patients with follow-up period more than 144.3 months tended to have more gating Tregs numbers than that in shorter follow-up period (92.3 ± 142.4 vs. 50.1 ± 76.4, p = 0.061, respectively). There were no significant differences in Tregs subpopulations between patients with serum creatinine more than 1.5 md/dL and patients with serum creatinine less than 1.5 mg/dL. In terms of the number of Tregs, when the trough level of tacrolimus was at an appropriate level, the number of Tregs tended to be higher than that of Tregs when the trough level of tacrolimus was low or high, and the organ function of the transplant was also stable.

**Conclusions:** Tregs counts may be associated with transplant outcomes considering that there is a relationship between these cells and kidney graft function.

**2차 명단**



| | Gating cell number | P value | Gated (%) | P value |
|---|---|---|---|---|
| Male (n=73) | 76.7 ± 129.5 | 0.295 | 29.1 ± 22.4 | 0.078 |
| vs. Female (n=40) | vs. 56.6 ± 73.5 | | vs. 37.6 ± 27.1 | |
| LDKT (n=85) | 75.6 ± 121.5 | 0.113 | 32.0 ± 24.1 | 0.640 |
| vs. DDKT (n=23) | vs. 44.5 ± 72.1 | | vs. 34.7 ± 26.7 | |
| Follow-up duration ≤ 147.5 months (n=57) | 50.6 ± 76.9 | 0.073 | 36.4 ± 27.9 | 0.060 |
| vs. Follow-up duration > 147.5 months (n=56) | vs. 89.0 ± 138.5 | | vs. 27.8 ± 19.5 | |
| Tacrolimus (n=70) | 49.3 ± 69.4 | 0.095 | 34.3 ± 26.2 | 0.378 |
| vs. Cyclosporine (n=39) | vs. 94.7 ± 158.1 | | vs. 29.9 ± 21.4 | |
| MMF (n=73) | 65.0 ± 121.7 | 0.558 | 33.2 ± 25.3 | 0.515 |
| vs. No MMF (n=40) | vs. 78.1 ± 95.8 | | vs. 30.1 ± 22.8 | |
| PDN (n=79) | 58.1 ± 89.6 | 0.181 | 34.1 ± 25.8 | 0.194 |
| vs. No PDN (n=34) | vs. 96.3 ± 152.4 | | vs. 27.6 ± 20.3 | |
| Tacrolimus/MMF/PDN (n=49) | 44.0 ± 66.4 | 0.427 | 36.8 ± 26.8 | 0.459 |
| vs. Cyclosporine/MMF/PDN (n=9) | vs. 88.9 ± 158.8 | | vs. 29.7 ± 20.7 | |
| Median tacrolimus level ≤ 5.7 ng/ml (n=35) | 56.9 ± 72.7 | 0.363 | 31.7 ± 21.4 | 0.530 |
| vs. Median Tacrolimus level > 5.7 ng/ml (n=35) | vs. 41.7 ± 66.1 | | vs. 36.8 ± 30.5 | |
| Mean tacrolimus level ≤ 5.8 ng/ml (n=39) | 57.6 ± 73.3 | 0.266 | 30.9 ± 20.6 | 0.053 |
| vs. Mean Tacrolimus level > 5.8 ng/ml (n=31) | vs. 38.9 ± 63.8 | | vs. 38.5 ± 31.9 | |
| Median tacrolimus dose ≤ 2.5 mg (n=36) | 46.6 ± 62.5 | 0.963 | 37.6 ± 25.7 | 0.614 |
| vs. Median tacrolimus dose > 2.5 mg (n=22) | vs. 45.7 ± 80.2 | | vs. 33.9 ± 30.1 | |
| Mean tacrolimus dose ≤ 2.6 mg (n=36) | 46.6 ± 62.5 | 0.963 | 37.6 ± 25.7 | 0.614 |
| vs. Mean tacrolimus dose > 2.6 mg (n=22) | vs. 45.7 ± 80.2 | | vs. 33.9 ± 30.1 | |
| Median cyclosporine level ≤ 87.7 ng/ml (n=20) | 53.5 ± 111.1 | 0.095 | 32.0 ± 22.8 | 0.530 |
| vs. Median cyclosporine level > 87.7 ng/ml (n=19) | vs. 138.1 ± 189.3 | | vs. 27.7 ± 20.3 | |
| Mean cyclosporine level ≤ 98.1 ng/ml (n=23) | 52.9 ± 105.5 | 0.078 | 30.7 ± 21.9 | 0.776 |
| vs. Mean cyclosporine level > 98.1 ng/ml (n=16) | vs. 154.8 ± 201.1 | | vs. 28.7 ± 21.4 | |
| Median cyclosporine dose ≤ 100 mg (n=18) | 119.8 ± 197.7 | 0.401 | 36.3 ± 21.6 | 0.010 |
| vs. Median cyclosporine dose > 100 mg (n=12) | vs. 66.2 ± 110.5 | | vs. 17.0 ± 12.7 | |
| Mean cyclosporine dose ≤ 106.7 mg (n=18) | 119.8 ± 197.7 | 0.401 | 36.3 ± 21.6 | 0.010 |
| vs. Mean cyclosporine dose > 106.7 mg (n=12) | vs. 66.2 ± 110.5 | | vs. 17.0 ± 12.7 | |
| Creatinine ≤ 1.2 mg/dl (n=79) | 65.2 ± 111.3 | 0.527 | 32.4 ± 24.1 | 0.856 |
| vs. Creatinine > 1.2 mg/dl (n=34) | vs. 79.9 ± 117.6 | | vs. 31.5 ± 25.5 | |
| Creatinine ≤ 1.5 mg/dl (n=96) | 67.6 ± 111.9 | 0.647 | 33.0 ± 24.6 | 0.382 |
| vs. Creatinine > 1.5 mg/dl (n=17) | vs. 81.2 ± 121.1 | | vs. 27.3 ± 23.3 | |
| Total cholesterol ≤ 172.8 mg/dl (n=53) | 90.6 ± 140.6 | 0.044 | 32.3 ± 25.1 | 0.886 |
| vs. Total cholesterol > 172.8 mg/dl (n=52) | vs. 45.8 ± 74.8 | | vs. 33.0 ± 24.9 | |
| Non-HBV (n=95) | 72.8 ± 117.0 | < 0.001 | 30.8 ± 23.1 | 0.134 |
| vs. HBV (n=7) | vs. 12.4 ± 13.0 | | vs. 55.2 ± 37.0 | |