

# TREMOR AFTER RENAL TRANSPLANT: NEUROLOGICAL SIDE EFFECT OF CALCINEURIN INHIBITORS

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**Objective:** To assess prevalence, phenomenology, and putative pathophysiology of tremor in patients under treatment with different immunosuppressive drugs following kidney transplantation.

**Background:** Neurologic complications are a significant cause of morbidity during immunosuppression after transplantation [1,2]. Tremor is one of the commonest symptoms in immunosuppressed transplanted patients [1,2,3]. Nevertheless, there are no systematic studies assessing its prevalence and characteristics in this population.

**Materials and Methods:** One-hundred-twenty consecutive patients (46 women, 74 men; mean age, 57.1±12.8 years) who underwent kidney transplantation were enrolled. Sixty-six were treated with tacrolimus (34 with the prolonged-release formulation and 32 with the immediate-release formulation), 32 with ciclosporin A and the remaining 23 with other non-calcineurin inhibitors drugs. All subjects were neurologically evaluated by evaluators blinded to treatment allocation. Specifically, the Fahn-Tolosa-Marin (FTM) Tremor Rating Scale and the Scale for the Assessment and Rating of Ataxia (SARA) were used. A neuropathy score was also gathered.

**Results:** Fifty-one (77.3 %) patients in the tacrolimus groups reported to be affected by tremor, 17 (53.2 %) in the ciclosporin group, and 2 (9.1%) in the non-calcineurin inhibitors group. FTM rating score was significantly higher in the tacrolimus than in the non-calcineurin inhibitors ( $p < 0.0001$ ) and ciclosporin A group ( $p = 0.02$ ). Postural and action tremor were the commonest components and tremor more frequently affected the arms. ADL were significantly more impaired in tacrolimus group compared to each others ( $p = 0.002$ ). SARA and neuropathy scores were similar between groups. There was a significant correlation between FTM score and SARA ( $\rho = 0.526$ ,  $p < 0.0001$ ). No difference between drug assumption formulation were disclosed.

**Discussion:** Calcineurin inhibitors (mostly tacrolimus, regardless of the formulation) are a common cause of tremor in transplanted patients. Tremor has a strong impact on daily life activities. The correlation between the FTM and SARA scores suggests a centrally-acting mechanism underpinning the development of tremor.

**Conclusion:** While preliminary, our results suggest it might be worth to switch transplanted patients who develop tremor, according to its severity and impact on ADL, to non-calcineurin inhibitors.

No difference in terms of sex, age, family history for ND, smoking ( $p > 0.05$ )

Group	Female	Male	Tremor NO	Tremor YES	Total
Non Calcineurin Inhibitors	0	16	20 (90.9%)	2 (9.1%)	22
Adgraf / Prograf	1	41	15 (22.7%)	51 (77.3%)	66
Ciclosporin A	2	17	15 (46.8%)	17 (53.2%)	32

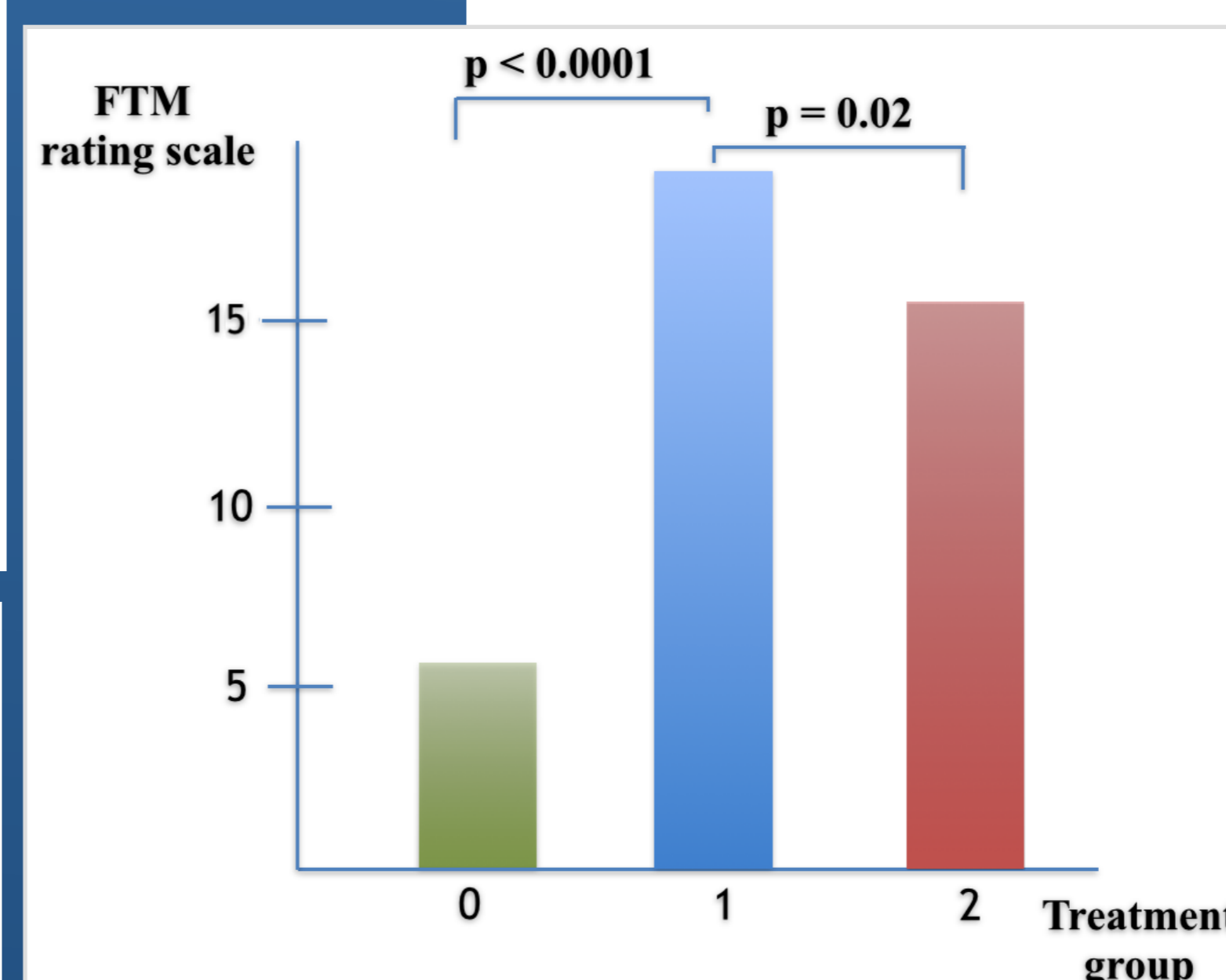
$p < 0.0001$

## Head Tremor ( $p = 0.19$ )

1 34/66 (51.5%)  
2 12/32 (37.5%)  
0 6/22 (27.2%)

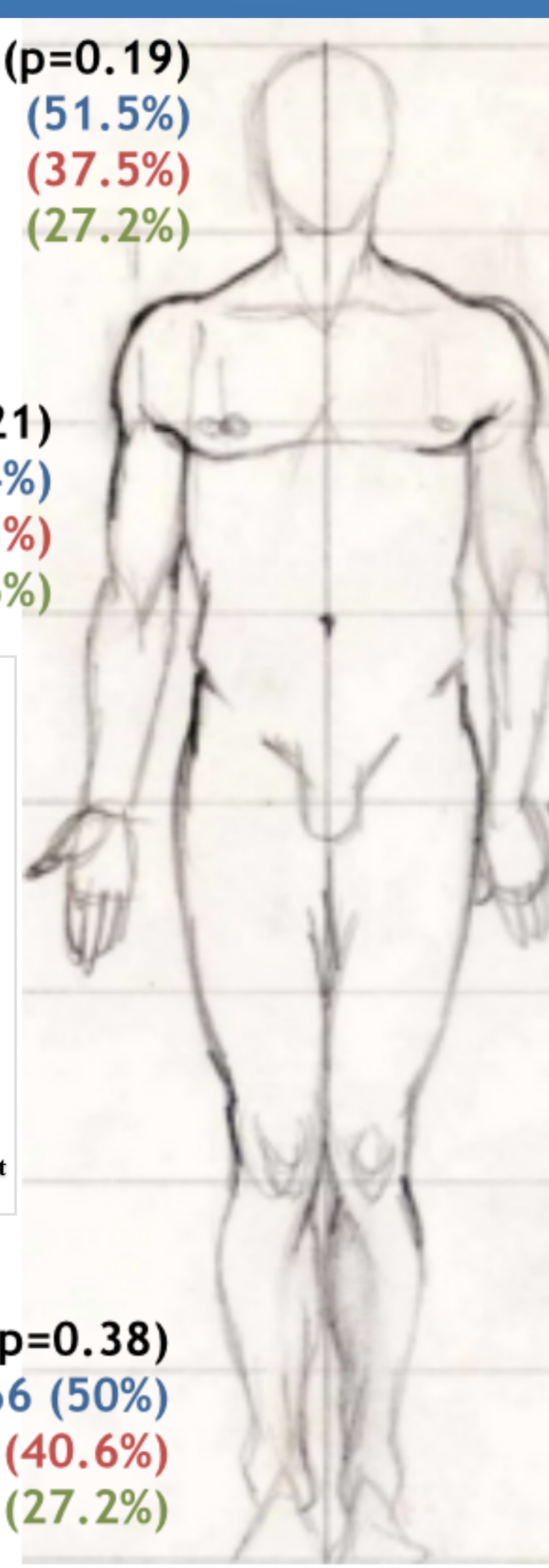
## Arm Tremor ( $p = 0.21$ )

1 61/66 (92.4%)  
2 27/32 (84.3%)  
0 14/22 (63.6%)



## Leg Tremor ( $p = 0.38$ )

1 33/66 (50%)  
2 13/32 (40.6%)  
0 6/22 (27.2%)



[1] W.O. Bechstein, Neurotoxicity of calcineurin inhibitors: impact and clinical management, *Transpl Int.* 13 (2000) 313-326.

[2] R.A. Walker, J.A. Brochstein, Neurologic complications of immunosuppressive agents, *Neurol. Clin.* 6 (1988) 262-278.

[3] G. Al Ghamdi, A. Awada, D.Z. Tanimu, S. O. Huraib, S. A. Romeh, K. Quadri, Neurological Disorders in Renal Transplant Recipients, *Saudi J. Kidney Dis. Transplant* 9 (1999) 435-439.