

# DIFFERENCES IN CLINICAL OUTCOMES, SIDE EFFECTS AND QUALITY OF LIFE IN PATIENTS TREATED WITH CYCLOSPORINE AND TACROLIMUS-BASED IMMUNOSUPPRESSIVE REGIMENS

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## Background

Post-transplant patient quality of life (QOL) is affected by a number of different factors. A nationwide patient registry has been established to evaluate QOL and determine the effects of immunosuppressive regimens on patient outcomes.

## Methods

Patients were contacted directly at national meetings, through transplant centers, and patient support groups and invited to participate in the registry. All transplant patients age 16 and over were eligible to enroll. Patients completed a 100-item self-administered questionnaire consisting of questions about patient demographics, organ functioning, and other post-transplant outcomes (Table 1). Side effects associated with immunosuppression including emotional, life/role, mobility and gastrointestinal distress were measured using the Memphis survey. General QOL was measured by the SF-12.

Table 1. PORTEL survey domains

Domain	Questions/Instruments
Health Factors	- Organ function - Medications - Hospitalizations
Social Factors	- Socioeconomic status - Social support - Productivity
Major Health Events	- Rejection episodes - Adverse events
Major Life Events	- Family changes - Employment
QOL and Related Outcomes	- Physical appearance (Modified Bergner) - SF-12 (generic) - Memphis Survey (disease specific)

## Results

Data were analyzed from the first 722 patients who entered the registry between 1/7/2000 and 7/10/2001. Patients reported the use of the following immunosuppressive agents: cyclosporine (54.6%), tacrolimus (40.2%), and steroids (76.3%) (Table 2).

Table 2. Transplant type and immunosuppressive medications (n=722)

Transplant Type		
Single Transplant		
Heart	141	19.5%
Kidney	296	41.0%
Liver	141	19.5%
Lung	38	5.3%
Pancreas	6	0.8%
Intestine	0	0%
Total repeat transplants	68	9.4%
All other transplants	32	4.4%
<b>Immunosuppressive Medications</b>		
Azathioprine/Imuran	152	21.1%
Cyclosporine/Neoral/SangCya	394	54.6%
MMF/CellCept	312	43.2%
Prednisone	551	76.3%
Rapamycin/Rapamune	29	4.0%
FK506/Prograf/Tacrolimus	290	40.2%

Patients on tacrolimus-based regimens were younger (47.3 vs 51.7 years; p<0.001) and had received transplants more recently (2.6 vs 5.7 years; p<0.001) compared to patients on cyclosporine-based regimens (Table 3).

Table 3. Demographics by regimen

	All (n=722)	%	Cyclo (n=385)	%	Tacro (n=283)	%	p-value
Mean Age (yrs)	49.73		51.66		47.34		p < 0.001
Time since txp (yrs)	4.5		5.7		2.6		p < 0.001
Gender							
Female	336	46.5%	159	41.3%	147	51.9%	
Male	377	52.2%	223	57.9%	131	46.3%	p < 0.01

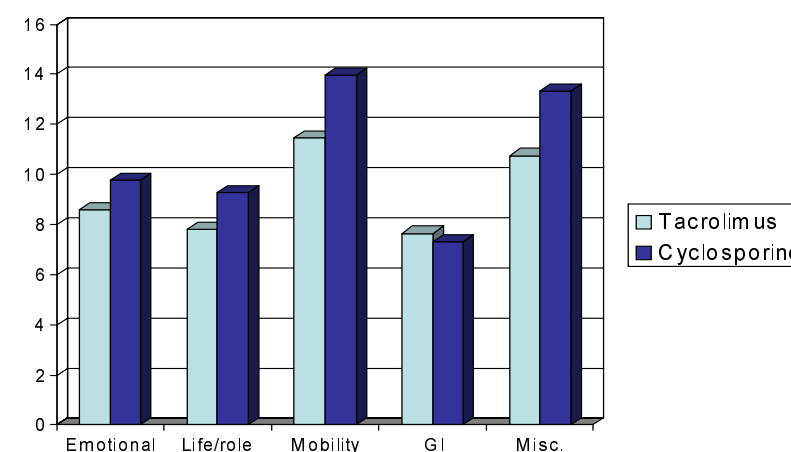
When grouped by immunosuppressive regimen, there were no differences between the groups in terms of patients reporting good to excellent organ function, treatment for rejection, infection, and over-immunosuppression. There were differences in the reported rate of comorbidities between the two groups with patients on a cyclosporine-based regimens reporting a significantly greater likelihood of being treated for high cholesterol (40.8% vs. 22.3%, p<0.001) and high blood pressure (73% vs. 50.5%, p<0.001) in the last 6 months compared to patients on a tacrolimus-based regimen (Table 4).

Table 4. Clinical outcomes by regimen

	All (n=722)	%	Cyclo (n=385)	%	Tacro (n=283)	%	p-value
Rejections (1 or more episodes)	63	8.7%	27	7.0%	31	11.0%	NS
Infections (1 or more episodes)	125	17.3%	72	18.7%	48	17.0%	NS
Immunosuppression (1 or more episodes)	79	10.9%	42	10.9%	36	12.7%	NS
Diabetes	139	19.3%	77	20.0%	52	18.4%	NS
High blood pressure	456	63.2%	281	73.0%	143	50.5%	P<0.001
High cholesterol	241	33.4%	157	40.8%	63	22.3%	P<0.001
Osteoporosis	160	22.2%	96	24.9%	53	18.7%	NS

Compared to tacrolimus patients, patients on cyclosporine-based regimens reported more frequent and severe side effects in the mobility and miscellaneous (including high blood pressure, enlarged gums, hair growth) Memphis subscales. In addition, cyclosporine patients reported greater overall side effect severity and more severe side effects affecting life roles (Figure 1).

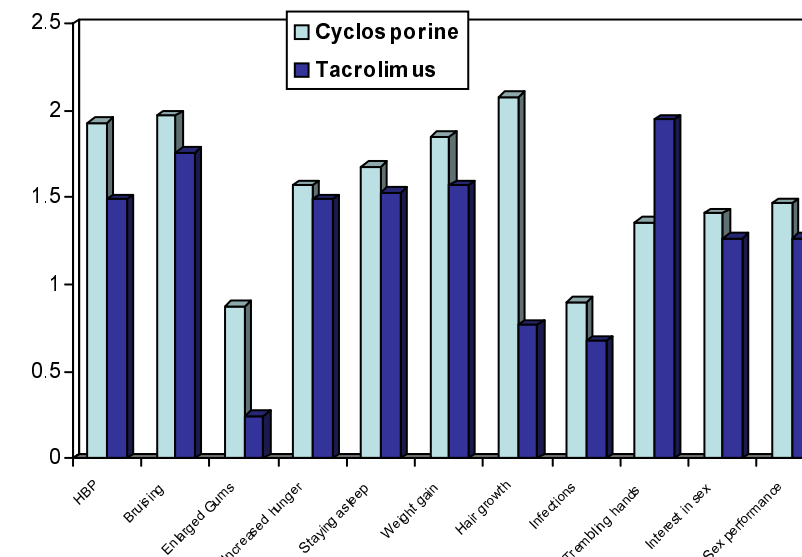
Figure 1. Memphis severity subscale scores



Note: Significant differences for life/role, mobility and miscellaneous (p<0.05).

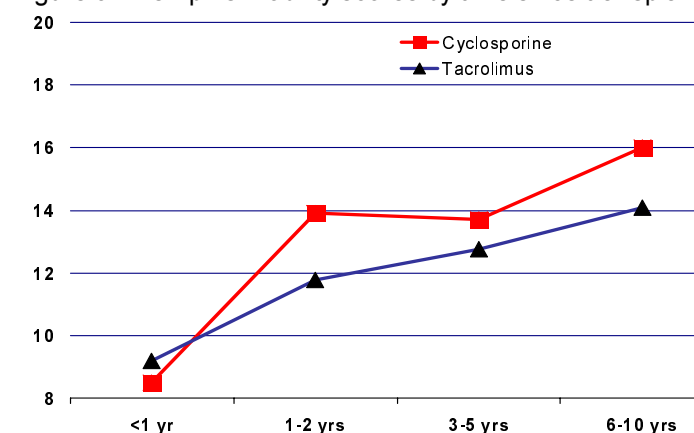
Patients on tacrolimus-based regimens reported significantly fewer problems with high blood pressure (1.5 vs. 1.9, p<0.001), enlarged gums (0.3 vs. 0.9, p<0.001), staying asleep (1.5 vs. 1.7, p<0.05), hair growth (0.8 vs. 2.1, p<0.001), and infections (0.7 vs. 0.9, p<0.01), but significantly more problems with trembling hands (2.0 vs. 1.4, p<0.001) than patients on cyclosporine-based regimens (Figure 2).

Figure 2. Memphis miscellaneous frequency item scores



Older patients and patients who were treated with immunosuppressives for longer periods of time reported more frequent and more severe side effects related to mobility.

Figure 3. Memphis mobility scores by time since transplant and regimen



Note: Differences significant at all time intervals except <1 yr.

Multiple stepwise regression models were constructed to identify the predictors of mental (MCS scores) and physical (PCS scores) QOL. The strongest predictors of the MCS score were the frequency and severity of problems with emotional burden, living status, income, social support and age. Recipients with higher (better) mental QOL scores reported fewer and less severe problems with emotional burden, were not living alone, had an income of greater than \$10,000, had more than adequate social support and were older than the average patient in the sample. Overall, these variables explained approximately 60% of the variability in the MCS scores. The predictors of the PCS score were problems with mobility, life/role responsibilities, emotional burden, work status and the total weighted frequency score of the Memphis Survey. Patients with higher (better) physical QOL scores reported less trouble with problems with mobility and life/role responsibilities, were able to work full or part-time and had a more favorable overall side effect profile.

## Conclusion

Tacrolimus-based regimens are associated with fewer and less severe side effects than cyclosporine-based regimens. This study establishes a relationship between patient-reported symptom experience, which is sensitive to immunosuppressive regimen, and overall QOL.