

# Patient-related factors affecting the initial tacrolimus trough level after kidney transplantation

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**BACKGROUND:** In general, the recommended tacrolimus (Tc) initial dose is calculated per kg of body weight and fixed at 0.1 mg/kg/dose BID. Some observations suggest that in selected groups of patients such dosing may result in Tc toxicity in the early posttransplant period.

The aim of our study was to find the factors influencing the first measured Tc trough level after kidney transplantation.

**PATIENTS AND METHODS:** We performed the retrospective analysis (2000-2013) of 468 consecutive kidney transplant recipients initially treated with immunosuppressive regimen containing tacrolimus BID, mycophenolate, and steroids. As concomitant antifungal treatment interferes with tacrolimus metabolism, patients receiving ATG induction or simultaneous pancreas-kidney transplant, routinely treated by fluconazole, were excluded from the analysis. The mean age of transplanted patients (n=380) was 46±14 (range years 17-76). The analysis included the first assessment of Tc trough levels and patient-related factors that might affect the pharmacokinetics of Tc.

**RESULTS:** The mean initial Tc dose was 0.095±0.015 mg/kg BID. The analysis revealed that recipient's age and BMI, but not pretransplant diabetes, gender or residual diuresis, are explaining the variability of initial Tc trough level.

Recipients ≥60 years old had 55% greater Tc initial trough levels than those ≤40 years (Table 1).

Higher concentrations were also observed in overweight [15.2 (14.0-16.5) ng/ml] and obese [16.9 (13.2-20.5) ng/ml] than normal weight [12.5 (11.6-13.4) ng/ml] and underweight [10.9 (8.1-13.7) ng/ml] patients (ANOVA <0.001). The association between Tc trough level and BMI was independent from the influence of age.

The percentage of the initial Tc troughs >15 ng/ml was significantly higher in overweight and especially in obese (Fig 1) and in the oldest subgroup of patients (Table 1, Fig 2).

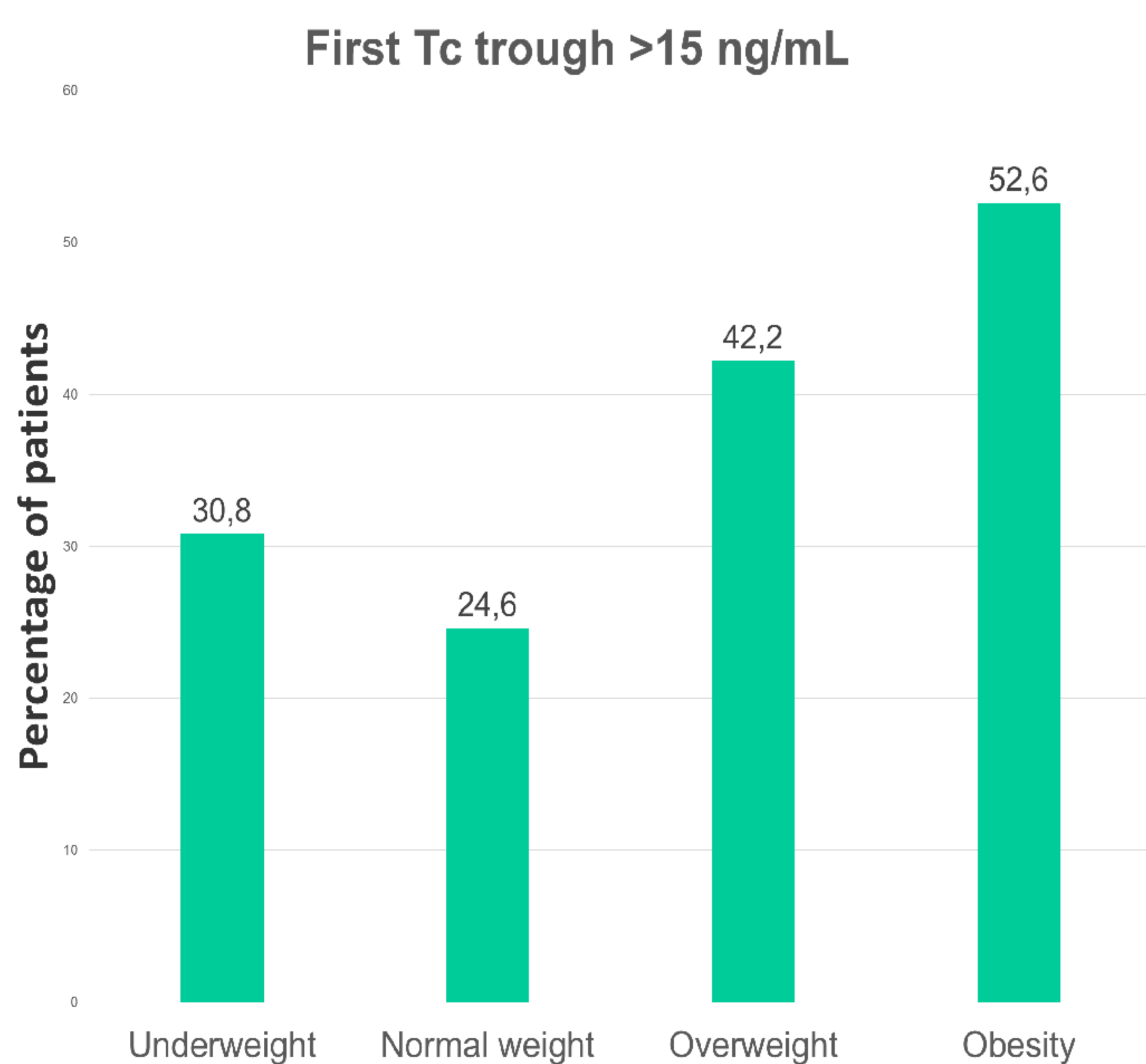
Additionally, there was no significant influence of early graft function on Tc trough level [IGF: 12.8 (11.4-14.2), SGF: 13.6 (12.5-14.7), DGF: 13.7 (12.4-15.1) ng/ml, NS].

**Table 1. Characteristics of patients stratified to three groups according to the recipient's age at transplantation**

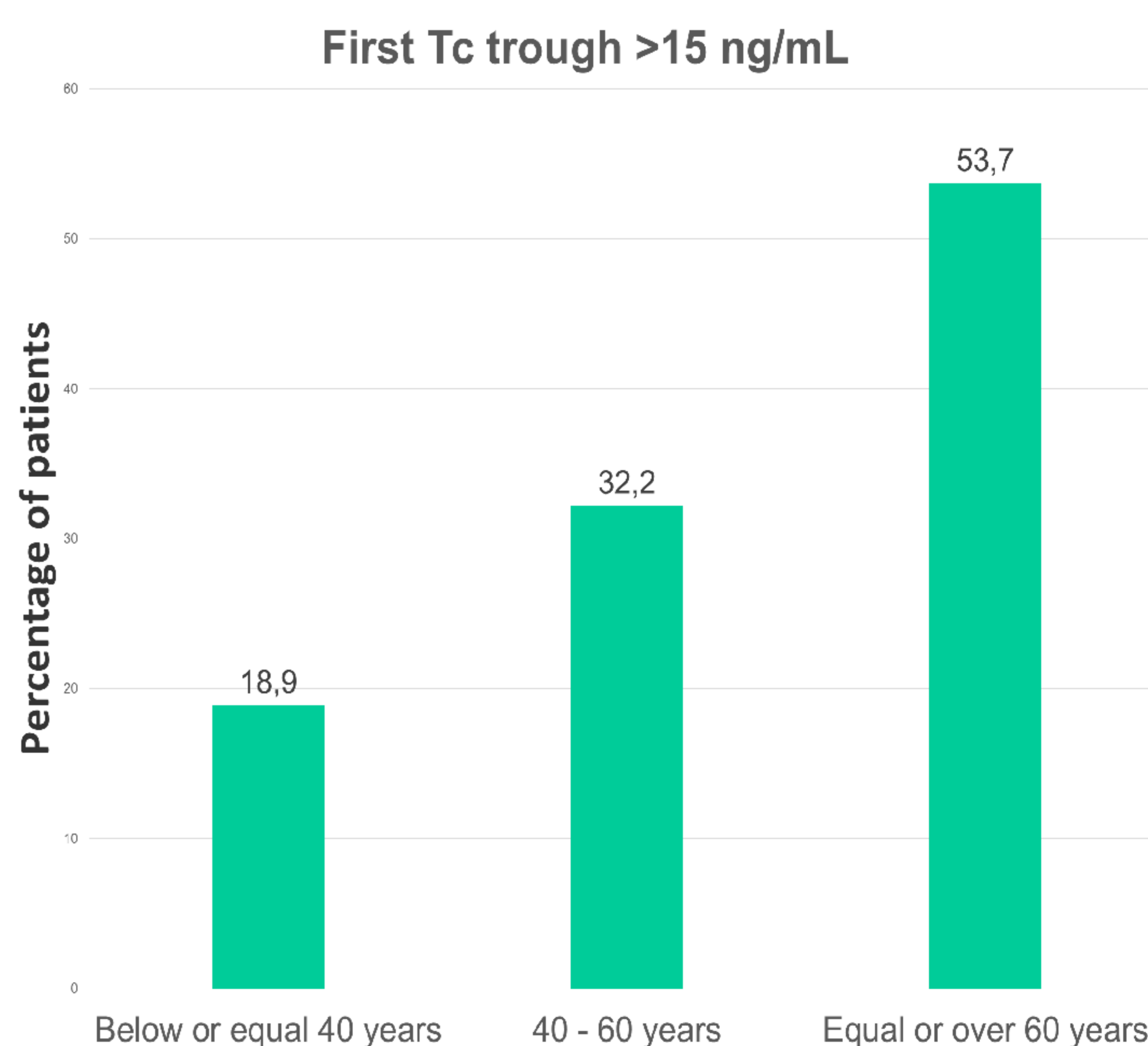
	Total n=380	Age ≤40 n=127	Age 40-60 n=171	Age ≥60 n=82	ANOVA
<b>At transplantation</b>					
Gender [M/F]	252/128	81/46	116/55	55/27	n.s.
BMI [kg/m <sup>2</sup> ]	24.0 (23.6-24.4)	22.2 (21.5-22.8)	24.7 (24.2-25.2)	25.3 (24.5-26.1)	<0.001
Overweight/obese [%]	33.9/5.1	16.7/3.2	42.0/4.7	43.8/8.7	<0.001
Dialysis vintage [mo]	41 (37-44)	42 (36-48)	40 (35-46)	39 (35-43)	n.s.
Residual diuresis [ml]	633 (538-727)	604 (427-781)	657 (510-805)	622 (444-801)	n.s.
Hypertension [%]	88.9	88.2	88.3	91.4	n.s.
Diabetes [%]	8.2	3.9	9.9	11.0	0.05
Coronary artery disease [%]	10.9	1.0	8.3	37.2	<0.001
MACE [%]	13.4	3.1	12.9	30.5	<0.001
CIT [h]	18 (17-19)	18 (16-19)	19 (17-20)	18 (17-20)	n.s.
First transplant [%]	82.6	75.6	81.3	96.3	<0.001
HLA mismatch class I	2.3 (2.2-2.4)	2.1 (2.0-2.3)	2.3 (2.2-2.5)	2.3 (2.0-2.6)	n.s.
HLA mismatch class II	0.7 (0.6-0.7)	0.7 (0.6-0.8)	0.7 (0.6-0.8)	0.6 (0.5-0.8)	n.s.
<b>Initial immunosuppressive regimen</b>					
Basiliximab [%]	18.7	19.7	17.5	19.5	n.s.
Tc initial dose [ng/day]	13.0 (12.8-13.3)	12.3 (11.9-12.8)	13.6 (13.1-14.0)	13.0 (12.5-13.7)	n.s.
Tc initial dose [ng/kg]	0.19 (0.19-0.19)	0.20 (0.19-0.20)	0.19 (0.18-0.19)	0.18 (0.18-0.19)	0.02
Tc first trough level [ng/ml]	13.6 (12.9-14.3)	10.7 (9.7-11.7)	14.2 (13.2-15.3)	16.6 (15.0-18.2)	<0.001
First Tc trough >15 ng/ml [%]	32.4	18.9	32.2	53.7	<0.001

Data are mean and 95% CI (in the brackets) or frequencies. BMI: body mass index, MACE: major adverse cardiovascular events, CIT: cold ischaemia time; HLA: human leukocyte antigen, Tc: tacrolimus.

**Fig. 1**



**Fig. 2**



**CONCLUSIONS:** The reduction of recommended fixed Tc initial dose should be considered in the older and overweight/obese kidney transplant recipients. Such a strategy may help to increase the group of patients, not exceeding the recommended tacrolimus trough level during first days after kidney transplantation.