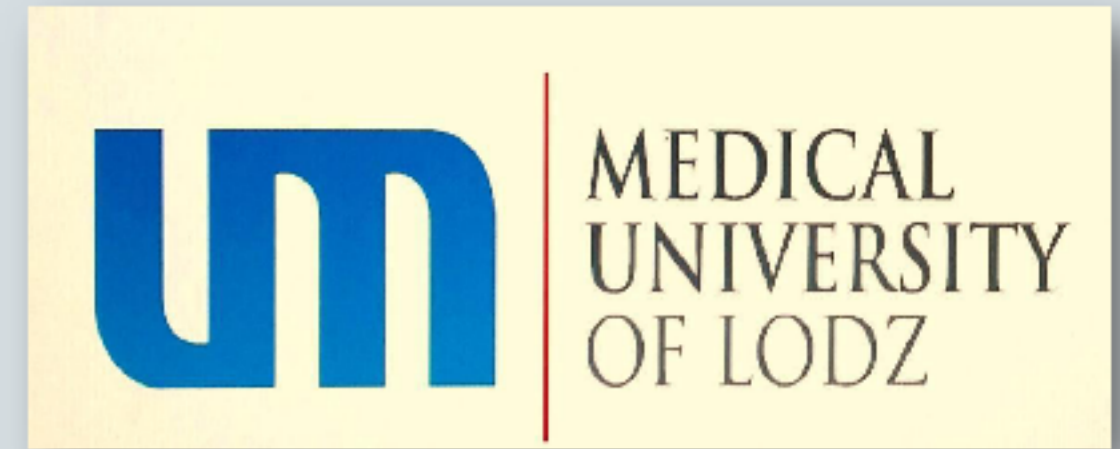


Effects of concomitant immunosuppressive and protein pump inhibitor therapy on the prevalence of gastrointestinal symptoms in patients late after kidney transplantation



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Introduction: Gastrointestinal (GI) symptoms are highly prevalent in kidney transplant recipients (KTx) and may adversely affect their quality of life. Although the use of immunosuppressive drugs has been recognized as the main cause of GI symptoms after KTx other medications such as proton pump inhibitors (PPI) that are commonly used for gastroprotection have also been implicated in GI symptoms. In contrast to early post-transplant period little is known about the causes, prevalence and perpetuation of GI symptoms in long-term KTx patients.

Aim: to compare the pattern of GI symptoms in clinically stable patients late after KTx treated or not treated with PPI.

Methods and patients: The study comprised 100 KTx recipients (66 men and 34 women, age 49±12 years, mean time after transplantation 56±46 months). All subjects completed Gastrointestinal Symptoms Rating Scale (GSRS) and the Quality of Life Questionnaire SF-8. History and current treatment was analyzed based on medical records. A coefficient of variation (CoV) was used to express the variability of a concentration of a given immunosuppressant during the last 6 measurements.

Results: 65% of the patients did not notice any change in the prevalence of GI symptoms after kidney transplantation, 25% reported an increase and 7% a decrease. Most commonly reported symptoms were borborygmus (27%), flatulence (23%), abdominal distension (18%), urgent need of defecation (17%), heartburn, acid reflux and eructation (13%). These GI side effects resulted in isolated or multiple omission of medication dose in only 6% of subjects. Most of patients (85%) did not self-modified the therapy administered by their physicians. PPIs were chronically used by 50% of patients and sporadically by 33%. The immunosuppressive regimen was associated with the pattern of GI symptoms. Tacrolimus-treated patients had higher GSRS score (meaning more prevalent symptoms) than cyclosporine A - treated (GSRS score 7.4 5.4 vs. 4.6 3.6; p=0.019). GSRS score was higher in patients on maintenance therapy with PPIs (GSRS score 7.8 5.5 vs. 4.6 3.0; p=0.013). The sum of items representing diarrhea in the GSRS scale (increased passage of stools, loose stools, defecation – urgent need, incomplete evacuation) was significantly higher in PPI treated patients than in subject not treated with PPI (2.3 2.2 vs. 1.3 1.9; p=0.04). Mean CoV of calcineurin inhibitor blood concentration was tended to be higher in patients on PPI therapy than in those without PPI (0.32 0.315 vs. 0.22 0.08; p=0.13) (Fig. 2). A significant correlation between Quality of Life Questionnaire SF-8 and GSRS score was found only in women (r=0.57; p<0.001) (Fig. 1) The differences in mean GSRS score in the groups of patients with PPI or without PPI therapy are shown in table 1.

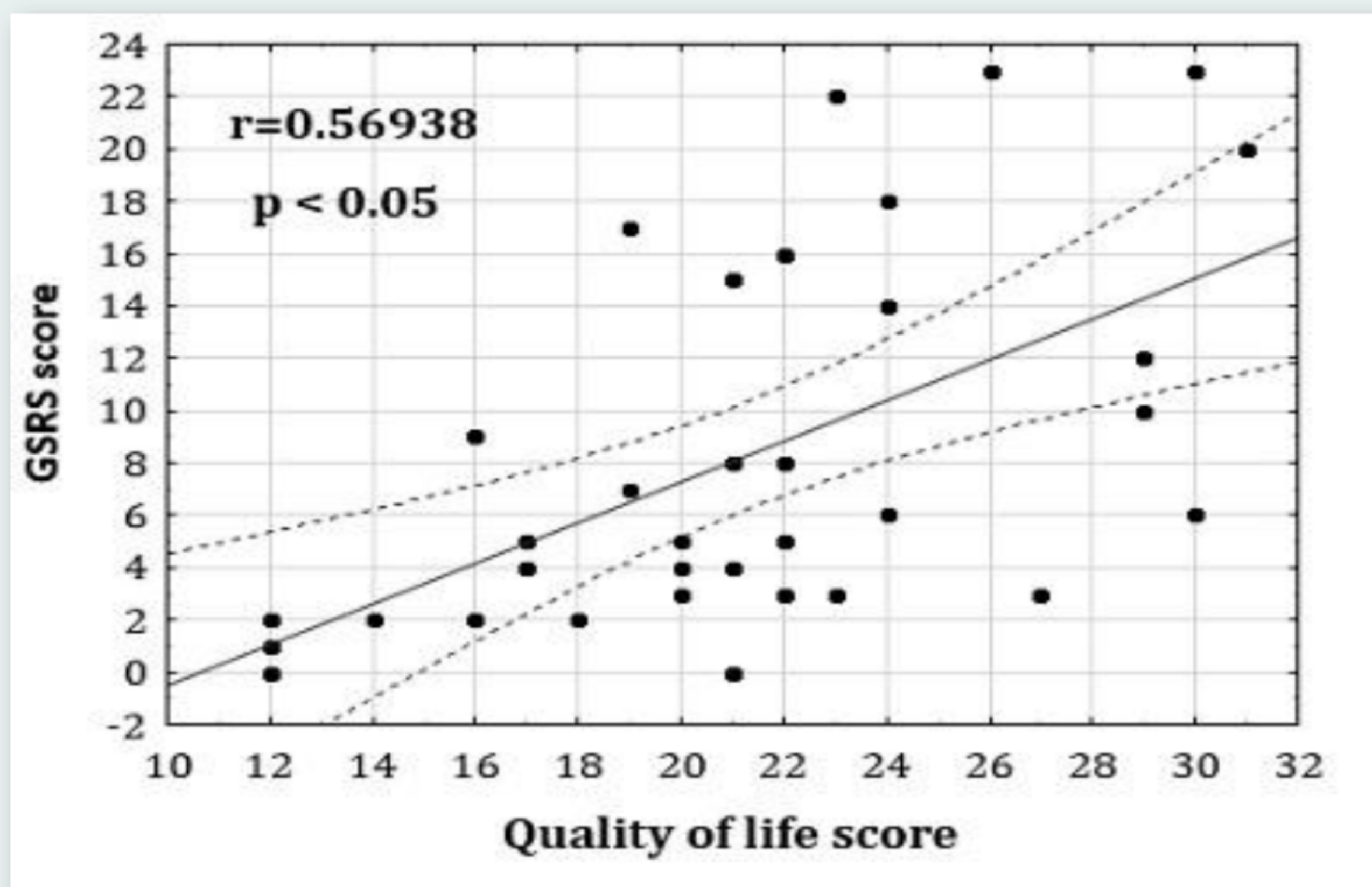


Fig.1. A correlation between Quality of Life score and GI symptoms intensity in group of women.

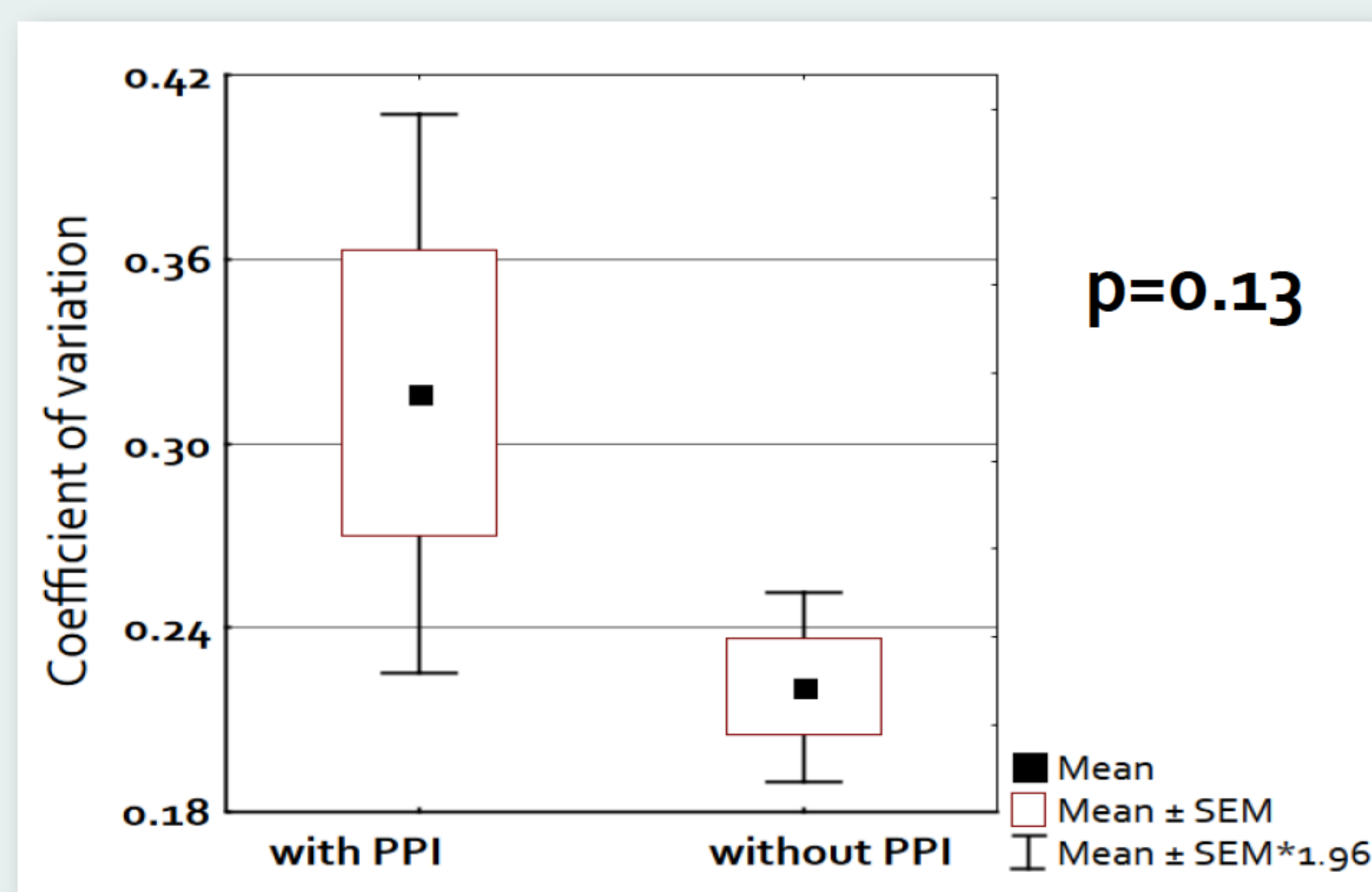


Fig.2. Coefficient of variation of calcineurin inhibitor blood concentration in patients treated with or without PPI.

Type of gastrointestinal symptom	Mean GSRS score in patients treated with PPI	Mean GSRS score in patients not treated with PPI	p value
1. Abdominal pain	0.28	0.05	0.023
2. Heartburn	0.56	0.41	0.436
3. Acid reflux	0.56	0.41	0.436
4. Sucking sensation	0.30	0.32	0.902
5. Nausea and vomiting	0.34	0.09	0.052
6. Borborygmus	1.00	0.41	0.003
7. Abdominal distention	0.78	0.36	0.067
8. Eructation	0.56	0.41	0.411
9. Increased flatus	0.80	0.59	0.324
10. Decreased passage of stools	0.44	0.45	0.937
11. Increased passage of stools	0.56	0.23	0.067
12. Loose stools	0.52	0.27	0.123
13. Hard stools	0.38	0.32	0.716
14. Defecation – urgent need	0.68	0.27	0.042
15. Incomplete evacuation	0.58	0.41	0.323

Table 1. Differences between GSRS score in patients using and not-using proton pump inhibitors.

Conclusion: Although the pattern of GI symptoms after kidney transplantation is mostly dependent on immunosuppressive regimen chronic PPI use may increase the prevalence of GI symptoms in particular diarrhea in patients late after KTx.