

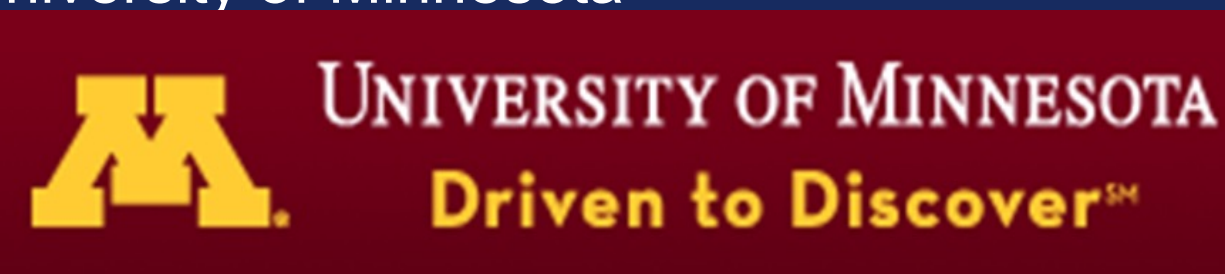
Dietary intake and mycophenolate mofetil-related diarrhea following kidney transplantation

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INTRODUCTION

- Mycophenolate mofetil (MMF) is associated with diarrhea.
- Recipients developing diarrhea are generally managed with lower MMF daily doses or dividing the same daily dose into three times a day dosing.
- Shorter dosing intervals are associated with reduced adherence to immunosuppression and poorer outcomes.

HYPOTHESIS

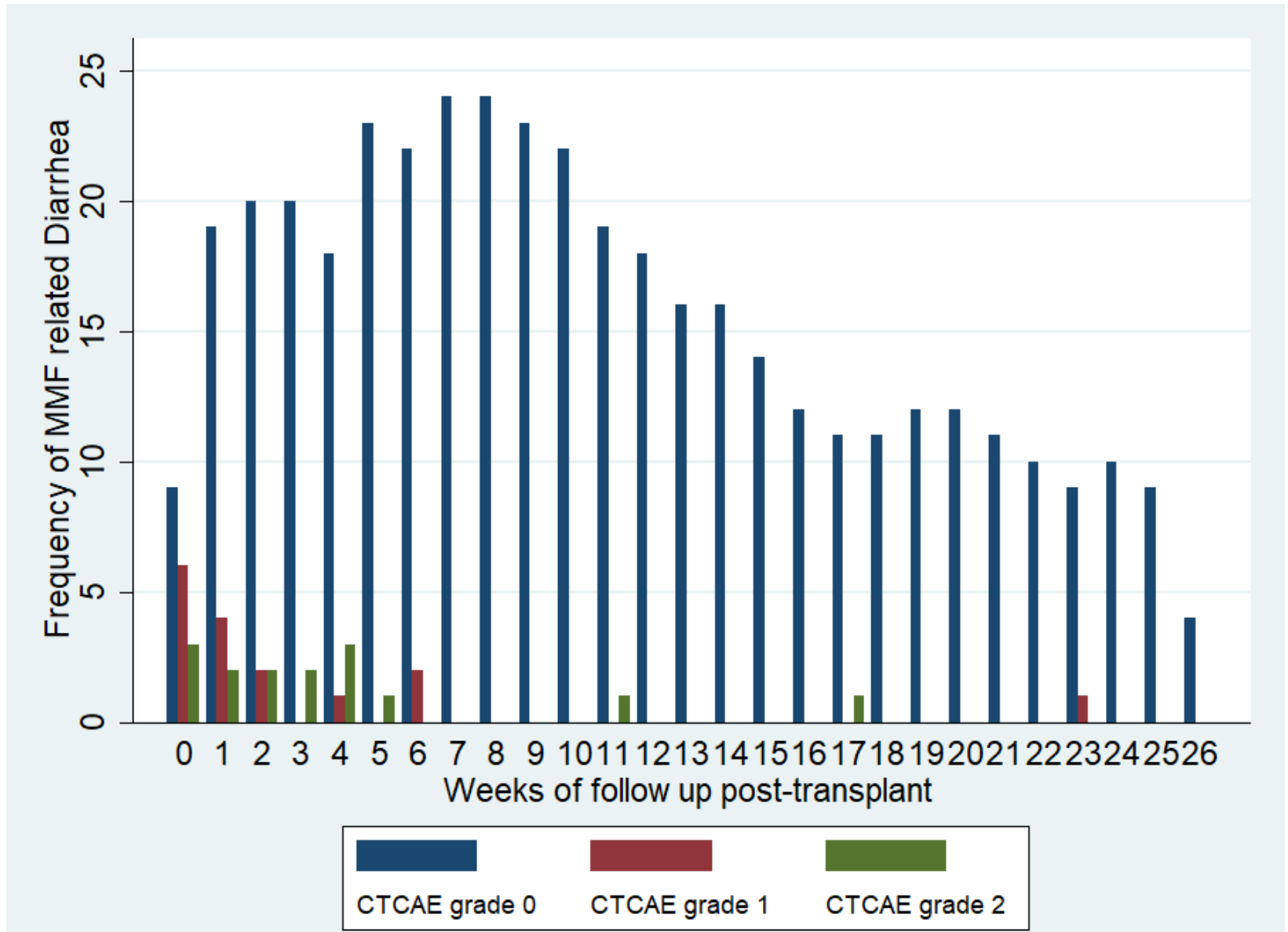
- We hypothesized that dietary fiber or “fermentable oligo-, di-, mono-saccharides and polyols” (FODMAP) intake post-transplantation would be associated with MMF-related diarrhea.

METHODS

- The Microbiome and Immunosuppression in Kidney Transplantation (MISSION) study assessed diarrhea posttx using a HIPPA compliant text-based survey (Mosio, Inc , Seattle, WA).
- Short bi-weekly text message surveys were sent to participants receiving MMF and Tacrolimus 6 months post-transplant to collect diarrhea information. Data from first 12 participants is presented.
- Diarrhea events were defined using the V 5.0 definition of the National Cancer Institute's Common Terminology Criteria for Adverse Events (CTCAE).
- Diarrhea events of CTCAE grade 2 (increase of 4-6 stools per day compared to the previous week) in the first 30 days post transplant was the primary outcome.
- A baseline 48-hour food recall was collected one-week post-transplant in each participant using the Nutrition Data System for Research (NDSR). FODMAP subgroups were our exposure of interest due to their association with diarrhea in previous studies.

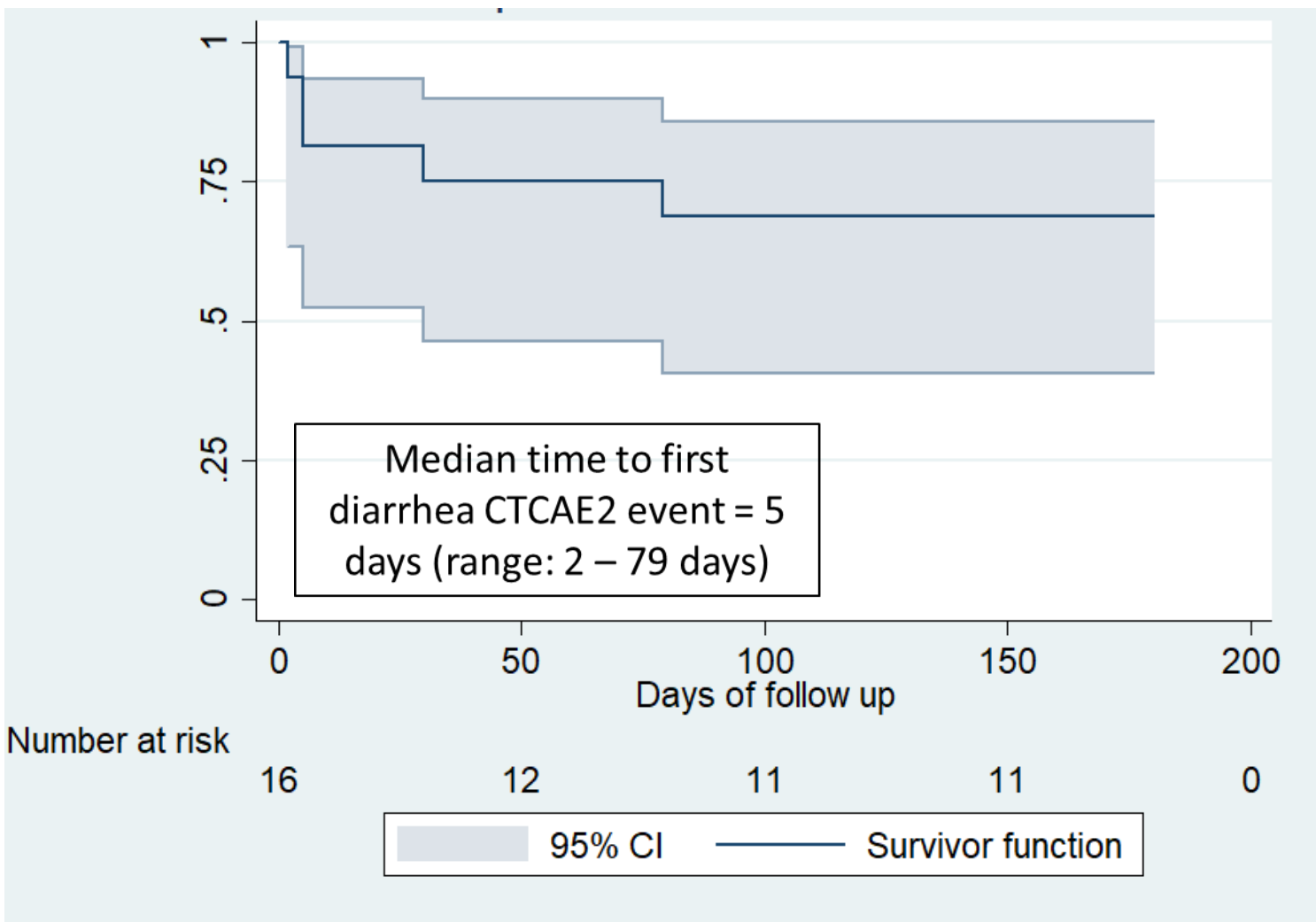
RESULTS

Figure 1: Frequency of MMF-related diarrhea during the first 6 months of follow up



During the first 6 months of follow up, we observed 15 CTCAE grade 1 (3.6% of responses) and 16 CTCAE grade 2 (3.3% of responses) diarrhea events. The majority of diarrhea events (73%) occurred in the first 30 days of follow up.

Figure 2: Kaplan Meier curve for Diarrhea events of CTCAE grade 2+ events during follow up



Data represent the Kaplan Meier estimates for the time to first severe diarrhea event over the first 6 months of follow up. 80% of the reported CTCAE grade 2 diarrhea events occurred in the first 30 days of follow up.

Table 1: Demographic & clinical characteristics of the study participants

Variable	CTCTAE grade 2 diarrhea		
	Did not develop diarrhea in the first month (N=8)	Developed diarrhea in the first month (N=4)	total (N=12)
Male, n(%)	5 (61.5%)	3 (75.0%)	8 (66.67%)
Caucasian, n(%)	6 (75.0%)	3 (75.0%)	9 (75.0%)
Living Donor, n(%)	4 (50.0%)	3 (75.0%)	7 (58.33%)
Former smoker, n(%)	4 (50.0%)	2 (50.0%)	6 (50.0%)
Diabetes pre-transplant, n(%)	2 (25.0%)	2 (50.0%)	4 (33.3%)
bmi, mean (sd)	27.8 (2.6)	29.2 (4.0)	28.3 (3.0)

Table 2: Intake of diet characteristics and FODMAP subgroups between patients with and without diarrhea in the 30 days following 48-hour dietary recall.

	Did not develop diarrhea in the first month (N=8)	Developed diarrhea in the first month (N=4)	P-value (t-test)
	Median (Min, Max)	Median (Min, Max)	
Fiber (g/day)	15.4 (3.8, 55.6)	19.5 (15.3, 22)	0.88*
Soluble Fiber (g/day)	5.2 (0.9, 14.4)	5.8 (2.7, 7.0)	0.7
Insoluble Fiber (g/day)	10.4 (2.9, 37.9)	14 (10.8, 15.5)	0.96*
Mannitol (g/day)	0.2 (0.02, 0.49)	0.46 (0.43, 0.47)	0.01*
Sorbitol (g/day)	0.01 (0.00, 0.40)	0.03 (0.00, 0.10)	0.18*
Fructose (g/day)	12.3 (1.7, 24.8)	10.0 (3.9, 15.9)	0.71
Lactose (g/day)	5.9 (0.1, 40.8)	13.6 (9.6, 26.2)	0.78
Percent Calories from Fat (%)	39.9 (23.1, 51.5)	33.2 (29.5, 50.3)	0.5
Percent Calories from Protein (%)	15.8 (9.8, 22.9)	17.0 (12.8, 23.9)	0.55
Poly-Sat fat ratio	1.1 (0.3, 2.6)	0.7 (0.2, 1.2)	0.27

*Satterthwaite p-value due to unequal variance

CONCLUSIONS

- 73% of the reported diarrhea events (CTCAE grade 1 & grade 2) and 80% of the reported CTCAE grade 2 events occurred within the first 30 days of follow up.
- These preliminary findings suggest an increased dietary intake of polyols may contribute to the development of MMF related diarrhea.
- Similar to other FODMAPs components, mannitol and sorbitol have an osmotic action in the small intestine and are readily fermented by colonic bacteria, leading to altered bowel habits.
- The prospective collection of diarrhea, nutrition and microbiome data will contribute to future interventions to reduce incidence of MMF-related diarrhea in kidney transplantation.

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