ORIGINAL RESEARCH

Gastrointestinal Symptoms and Nutritional Status in Women and Men on Maintenance Hemodialysis

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Objective: The main objective was to investigate whether the prevalences of nausea, vomiting, diarrhea, and reduced appetite varied by gender in maintenance hemodialysis (MHD) patients. We also evaluated whether these symptoms explain female–male difference in nutritional status.

Design: Cross section of baseline data of the Prospective Study of the Prognosis in Chronic Hemodialysis Patients.

Setting: Dialysis units in the city of Salvador, Brazil.

Patients: Three hundred ninety-seven men and 287 women with more than three months on MHD.

Predictor Variable: Gender.

Outcome Measures: The patient's self-reported nausea, vomiting, diarrhea, and reduced appetite. The malnutrition–inflammation score (MIS) was used to assess nutritional status.

Results: The prevalence of symptoms was 24.3% for reduced appetite, 19.7% for nausea, 12.3% for vomiting, and 3.5% for diarrhea. In a logistic regression model with adjustments for age, diabetes, congestive heart failure, hemoglobin, albumin, Kt/V, and years on dialysis, women were found to have significantly higher odds of reduced appetite (odds ratio [OR] = 1.97), nausea (OR = 1.90), and vomiting (OR = 2.21). MIS was 5.41 ± 3.18 for women and 4.66 ± 3.28 for men ($P = .002$) corresponding to a percentage difference of 13.86%. The female-male difference reduced by more than half after excluding the gastrointestinal symptoms component and by approximately 65% after excluding both the gastrointestinal symptoms and the dietary intake components from the MIS.

Conclusions: The results suggest that the prevalences of nausea, vomiting, and reduced appetite are higher in women than in men on MHD. These gastrointestinal symptoms and perhaps their detrimental effects on dietary intake may partially explain a poorer nutritional status in MHD women.

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DESPITE IMPROVEMENTS IN the treatment of patients with advanced chronic kidney disease, gastrointestinal symptoms frequently occur in these patients even after starting maintenance dialysis.[1-4] The prevalence of these symptoms tends to be higher soon after initiating dialysis and, depending on the symptoms noted, has been reported to be as high as 79%.[2] Nausea, vomiting, diarrhea, and reduced appetite may contribute to reduce the nutritional status of patients with chronic diseases.[5-8] Whereas poor appetite, nausea, and vomiting may reduce food intake, diarrhea may impair nutrient absorption. The presence and the severity of these specific symptoms are used to determine scores of 2 nutritional tools widely used for hemodialysis patients: the subjective global assessment (SGA) score and the malnutrition–inflammation score (MIS).[9-11]

Previous studies in the general population have indicated that the prevalence of gastrointestinal symptoms is higher for women than for men.[12-15] There is a lack of studies, however, to compare the prevalence of these symptoms in patients on maintenance hemodialysis (MHD) patients. The present study was developed to assess whether there were differences between women and men in the prevalences of persistent nausea, vomiting, diarrhea, and reduction in appetite among prevalent patients on MHD. Additionally, we compared women and men on nutritional status by using different versions of the MIS, a complete version with 10 components, a 9-component version without the gastrointestinal symptoms component, and an 8-component version without the gastrointestinal symptoms and the dietary intake components.

Methods

Study Design and Subjects

A cross-sectional analysis was performed using baseline data of MHD patients enrolled from May 2005 to January 2008 in the Prospective Study of the Prognosis of Chronic Hemodialysis Patients (PROHEMO), conducted at dialysis units in Salvador, Brazil.[16] From an original sample of 743 patients, 59 (21 women and 38 men) were on MHD for a period of ≤3 months, and 684 (287 women and 397 men), for a period of >3 months. The data of these 684 prevalent MHD patients were used for the main analysis of present study. Among these patients, 46 were on dialysis for >3 to <6 months; 190 patients, for 6 to 24 months; and 448 patients for >2 years. The number of prevalent patients by hemodialysis shift was 237 in the morning, 238 in the afternoon, and 209 in the evening. The Research Ethics Committee of the School of Medicine of the Federal University of Bahia approved the study protocol. All patients provided written informed consent for study participation.

Variables

The main outcome (dependent) variables were the patient's self-reported nausea, vomiting, diarrhea, and reduced appetite. MIS was also treated as outcome variable. Gender was the main predictor (independent) variable of interest for the assessment of associations with gastrointestinal symptoms and MIS. Age, diabetes, congestive heart failure, dialysis dose by single pool Kt/V, years on dialysis, serum hemoglobin, and serum albumin were treated as potential confounders for these associations. The number of years on dialysis was also treated as potential effect modifier of the association between gender and each of the 4 symptoms.

Data Collection and Definitions

Demographic data, laboratory results, clinical variables, and prescription of binders were abstracted from medical records and supplemented by information provided by the patient and by attending nephrologists. As part of the nutritional questionnaire, patients were asked about the presence of nausea, vomiting, diarrhea, and reduced appetite. The question was formulated to capture symptoms that were present daily or weekly for at least 4 weeks. The patients were interviewed on a dialysis day, in nonfasting conditions, in the morning, afternoon, or evening, depending upon the hemodialysis shift.

The MIS was used as a proxy for protein-energy nutritional status. MIS takes into account the interplay of several factors on nutritional status, including reduced protein and caloric intake, hypercatabolism, and inflammation.[10,17] It is a more comprehensive nutritional tool than its predecessors, that is, the SGA and the dialysis malnutrition score.[17] MIS comprises the 7 components of the SGA tool (weight change, dietary intake, gastrointestinal symptoms, functional capacity, comorbidities related to nutritional status, 2 components of a brief physical examination about fat store, and muscle wasting) and 3 additional

non-SGA components, that is, body mass index (BMI), serum albumin, and total iron-binding capacity. Each of the 10 components of MIS has 4 levels of severity from 0 (normal) to 3 (severely abnormal).

As the association between years on dialysis and outcomes is complex and highly dependent on prevalence of comorbidities,[18] the comorbidity component of MIS was determined by a recently developed method that does not include the number of years on dialysis.[10] The sum of the 10 MIS components can range from 0 to 30, with a higher score indicating a more severe degree of protein-energy nutritional status. In addition to the original MIS that is composed of 10 components, we also used reduced versions of MIS, 1 version with 9 components that did not include the gastrointestinal symptoms component and another version with 8 components that did not include both the gastrointestinal symptoms and the dietary intake components. We used different versions of MIS to assess possible influence of gastrointestinal symptoms and dietary intake on the comparisons of MIS between women and men.

The diagnoses of diabetes mellitus and congestive heart failure were based on information provided by the attending nephrologists. In general, the diagnosis of diabetes was made before the initiation of maintenance dialysis. Typically, the diagnosis of heart failure in the patients treated in the dialysis units from PROHEMO is based on findings of clinical examination (dyspnea on exertion, ventricular filling gallop, rales) and chest radiograph (cardiomegaly, pulmonary venous congestion), after ruling out differential diagnoses. Dialysis dose was assessed by the average of 3 consecutive measures of single-pool Kt/V.[19] Serum albumin and hemoglobin values were based on predialysis measurements. Serum albumin concentration was determined by the bromocresol green method.

Statistical Analyses

The Student *t* test for independent samples was used to compare means between women and men when the assumption of normal distribution was met. The Mann–Whitney test was used to compare means of the each version of MIS (the complete version with 10 components and the reduced version with 9 and 8 components) between women and men. Also, for each version of MIS, the percentage difference between the means of MIS in women and men was calculated dividing the absolute difference of the 2 means by the observed higher mean value and multiplying the obtained result by 100%. The Fisher exact test was used to compare proportions.

To compare the odds of symptoms between women and men, logistic regression was used with adjustments for age, diabetes, congestive heart failure, dialysis dose, years on dialysis, serum hemoglobin, and serum albumin, even when the female–male difference in the characteristics was not statistically significant. A model was also used that included hemodialysis shift (morning, afternoon, or evening) in addition to previous variable.

The Bonferroni post hoc test[20] was used to correct the *P* values for 4 comparisons between women and men for nausea, vomiting, diarrhea, and reduced appetite. Bonferroni-corrected *P* values less than .0125 (i.e., .05/4) were considered statistically significant. To assess whether the female–male comparison for each symptom was modified by the length of time on dialysis before study enrollment, separate multivariable logistic regression models were developed that included an interaction term between gender and years on dialysis.[21] The Hosmer–Lemeshow goodness-of-fit test was used to assess whether the predicted values were consistent with the observed values. The statistical analysis was performed using the SPSS version 16.0 for Windows (SPSS Inc, Chicago, IL).

Results

As compared with the 684 prevalent MHD patients (>3 months on MHD) selected for the main analysis of the study, the 59 incident MHD patients (≤3 months on MHD) were older (mean age 53.8 ± 13.8 years vs. 48.4 ± 14.1 years, $P = .005$), presented higher MIS (6.9 ± 4.3 vs. 5.0 ± 3.3, $P = .046$) and were more often diabetic (44.1% vs. 18.9%, $P < .001$). Incident patients had also lower means of serum concentrations of albumin (3.7 ± 0.71 g/dL vs. 4.0 ± 0.5 g/dL, $P = .002$), creatinine (8.4 mg/dL vs. 10.2 mg/dL, $P < .001$), and hemoglobin (8.5 ± 1.5 g/dL vs. 10.2 ± 1.7 g/dL, $P < .001$). The prevalence of the assessed self-reported symptoms in incident and prevalent patients were, respectively, 27.1% and 24.1% for reduced appetite ($P = .637$), 20.3% and 19.7% for nausea ($P = .866$), 10.2% and 12.6% for vomiting ($P = .685$), 11.9% and

3.5% for diarrhea ($P = .008$), and 44.1% and 38.1% for the presence of at least 1 of the 4 symptoms ($P = .403$).

Table 1 shows the comparisons of characteristics between women and men, restricted to prevalent patients, that is, those for ≥3 months on MHD. Mean age was lower for women than for men, 46.9 ± 14.0 years versus 49.4 ± 14.1 years ($P = .024$). Mean Kt/V was 1.55 ± 0.22 for women and 1.41 ± 0.19 for men ($P < .0005$). The prevalence of diabetes was 19.9% for women and 18.1% for men ($P = .569$), and the prevalence of congestive heart failure was 11.8% for women and 12.3% for men ($P = .845$). The means of serum hemoglobin, serum albumin, and serum creatinine were significantly lower for women than for men. The median number of years on dialysis (approximately 3.3 years) was similar for men and women. Phosphate binder was the only oral medication with data available for analysis. The percentage of patients with a prescription of sevelamer or calcium-based phosphate binder was similar between women (77.5%) and men (81.4%). The median number of pills/day of phosphate binders was 5 among women and 6 among men. These data are not shown in Table 1.

Among prevalent patients, the prevalence of at least 1 of the assessed symptoms was similar among those on MHD for >3 to <6 months (prevalence of 41.3%), 6 to 24 months (prevalence of 37.9%), and >24 months (prevalence of 37.8%), $P = .896$. It was observed, however, that patients receiving hemodialysis in the morning had a higher prevalence of nauseas (23.2% vs. 17.9%, $P = .106$) and vomiting (18.1% vs. 9.6%, $P = .002$). The percentage of patients reporting diarrhea was 3.0% for patients receiving hemodialysis in the morning and 3.8% for those receiving hemodialysis in the evening or afternoon ($P = .640$). Also, the frequencies of reduced appetite did not vary by hemodialysis shift (about 24.0%, $P = .923$). These data are not shown in tables.

The prevalence of nausea, vomiting, diarrhea, and reduced appetite in men and women with more than 3 months on MHD are shown in Table 2. Compared with men, women more frequently reported reduced appetite (31.4% vs. 19.1%, $P < .0005$), nausea (26.1% vs. 15.1%, $P < .0005$), and vomiting (18.5% vs. 8.3%, $P < .0005$). The prevalence of diarrhea was 2.1% in women and 4.5% in men ($P = .087$). The differences between women and men did not change substantially after adjustment for potential confounders.

By using the responses for the dietary intake component of MIS, we indentified patients with suboptimal solid dietary intake or reduced caloric intake. The percentage of patients with suboptimal solid dietary intake or reduced caloric intake was almost 70% higher in women (15.7%) than in men (9.3%), $P = .012$. As compared with patients with no alteration in food or caloric intake, those with a reduction in intake of food or calorie had a significantly higher prevalence of reduced appetite (74% vs. 17.4%, $P < 0.001$), nausea (35.4% vs. 17.6%, $P < .001$), and vomiting (23.2% vs. 11.1%, $P = .002$). These associations followed the same patterns in women and men. These data are not shown in the Table.

In Table 2 the odds of presenting at least 1 assessed symptom were 89% higher for women than for men (OR = 1.89, 95% confidence interval (CI) = 1.34 to 2.65, $P < .0005$) in the

Table 1. Characteristics of the Sample of Prevalent Hemodialysis Patients

Characteristics*	Women n = 287	Men n = 397	*P* Value†	All n = 684
Age, years	46.9 ± 14.0	49.4 ± 14.1	.024	48.4 ± 14.1
Diabetes (%)	19.9	18.1	.569	18.9
Congestive heart failure (%)	11.8	12.3	.845	12.1
Hemoglobin, g/dL	10.1 ± 1.6	10.4 ± 1.7	.025	10.2 ± 1.7
Albumin, g/dL	3.88 ± 0.47	4.03 ± 0.52	<.0005	3.96 ± 0.5
Creatinine, mg/dL	9.57 ± 3.00	11.42 ± 3.41	<.0005	10.64 ± 3.37
Body mass index‡	22.37 ± 4.06	22.71 ± 3.56	.249	22.57 ± 3.78
Phosphate binder prescription (%)‡	77.5	81.4	.245	79.8
Kt/V	1.55 ± 0.22	1.41 ± 0.19	<.0005	1.47 ± 0.21
Years on dialysis	3.33	3.29	.992	3.30

*Quantitative variables are expressed as mean ± SD, except for years on dialysis that is expressed by the median value.

†The statistical tests compare women and men. The Mann–Whitney (MW) test was used to compare women and men based on years on dialysis. The Student *t* test or the Fisher exact test was used for the other variables.

‡Number of missing data: 1 for body mass index and 7 for phosphate binder prescription.

multivariable logistic regression model with adjustments for age, diabetes, congestive heart failure, hemoglobin, albumin, Kt/V and years on dialysis. The adjusted odds of symptoms were approximately two-fold higher in women for reduced appetite (OR = 1.97, 95% CI = 1.34 to 2.88, $P = .001$), nausea (OR = 1.90, 95% CI = 1.26 to 2.87, $P = .002$), and vomiting (OR = 2.21, 95% CI = 1.34 to 3.64, $P = .002$). The odds ratios related to these symptoms changed slightly with additional adjustment for hemodialysis shift in models that already included, diabetes, congestive heart failure, hemoglobin, albumin, Kt/V, and years on dialysis. The differences between women and men for each of these symptoms remained statistically significant after Bonferroni correction for multiple comparisons (i.e., each $P < .0125$).

In the multivariable logistic regression, older age was independently associated with lower odds of nausea (OR per 10 years of age = 0.86, 95% CI = 0.74 to 0.99, $P = .041$) and vomiting (OR per 10 years of age = 0.80, 95% CI = 0.67 to 0.96, $P = .018$). Diabetes was independently associated with higher odds of vomiting (OR = 2.16, 95% CI = 1.18 to 3.95, $P = .012$). The patterns of these associations of age and diabetes with the assessed symptoms were similar between women and men. Dialysis dose by Kt/V was not independently associated (adjusted OR approximately 1.00) with appetite, nausea, or vomiting, both in women and men. A marginally significant adjusted association was observed between higher Kt/V and lower odds of diarrhea (OR per 0.2 unit higher Kt/V = 0.67, 95% CI = 0.43 to 1.04, $P = .076$). These data are not shown in Table 2.

In separate multivariable logistic regression models using nausea, vomiting, diarrhea, and reduced appetite, and the presence of at least 1 of these symptoms as the outcome variable, no significant coefficient of interaction was observed between gender and years on dialysis. The *P* values for these interaction coefficients were .851 for reduced appetite, .724 for nausea, .432 for vomiting, .160 for diarrhea, and .432 for the presence of at least 1 of the assessed symptoms. These data are not shown in Table 2.

Table 3 shows comparisons between women and men for the mean values of the complete version (the 10-component MIS) and the reduced versions of the MIS. The means of the complete version of MIS were significantly ($P = .002$) higher for women (5.41 ± 3.18) than for men (4.66 ± 3.28). The mean values for the reduced versions were also higher for women, but the differences were not statistically significant ($P > .05$). The percentage difference in the mean values between women and men for the complete version of MIS was 13.86%. The percentage difference between women and men in the mean values reduced by more than half (from 13.86% to 6.44%) after excluding the gastrointestinal symptoms component to determine the 9-component MIS. A reduction of approximately 65% (from 13.86% to 4.84%) in the percentage difference was observed after excluding both the gastrointestinal symptoms component and the dietary intake component to determine the 8-component MIS.

Discussion

In the present study, approximately 1 of 3 patients on MHD for >3 months reported at least 1 of the assessed symptoms, that is, nausea,

Table 2. Associations Between Gender and Gastrointestinal Symptoms in Prevalent Hemodialysis Patients

	% Reporting Symptoms		Odds Ratio Comparing Women and Men (95% Confidence Interval); *P* Value*	
Symptoms	Women	Men	Unadjusted	Adjusted†
Reduced appetite	31.4	19.1	1.93 (1.36-2.75); <.0005	1.97 (1.34-2.88); .001
Nausea	26.1	15.1	1.99 (1.36-2.91); <.0005	1.90 (1.26-2.87); .002
Vomiting	18.5	8.3	2.50 (1.57-3.98); <.0005	2.21 (1.34-3.64); .002
Diarrhea	2.1	4.5	0.45 (0.18-1.15); .087	0.50 (0.19-1.34); .168
At least one of the symptoms	47.4	31.2	1.98 (1.45-2.72); <.0005	1.89 (1.34-2.65); <.0005

*The *P* values for nausea, vomiting, and reduced appetite remained statistically significant after Bonferroni correction for 4 comparisons ($P < .0125$).

†Odds ratios were adjusted for age, diabetes, congestive heart failure, hemoglobin, albumin, Kt/V, and years on dialysis. All *P* values for the Hosmer–Lemeshow goodness-of-fit test >.2.

Table 3. Comparisons Between Women and Men on the Complete and Reduced Versions of the Malnutrition–Inflammation Score

Versions of MIS*	Mean ± SD		Absolute Difference in Scores	Percentage Difference in Scores	*P* Value†
	Women	Men			
10-component MIS	5.41 ± 3.18	4.66 ± 3.28	0.75	13.86	.002
9-component MIS	4.50 ± 2.79	4.21 ± 3.02	0.29	6.44	.082
8-component MIS	4.34 ± 2.68	4.13 ± 2.98	0.21	4.84	.135

*MIS = malnutrition–inflammation score. The 9-component MIS does not include the gastrointestinal component, and the 8-component MIS does not include the gastrointestinal component and the dietary intake component.

†*P* values were determined by the Mann–Whitney test.

vomiting, diarrhea, and reduced appetite. The percentage of patients who reported at least 1 of these symptoms was higher among those with ≤3 months on MHD than among prevalent patients with more than 3 months on MHD, but the difference was not statistically significant. The only statistically significant difference in the prevalence of the assessed symptoms by time on dialysis was for diarrhea. The observed prevalence of diarrhea was more than 3 times higher for incident MHD patients than for prevalent MHD patients.

In the main analysis restricted to patients with more than 3 months on MHD, the prevalences of nausea, vomiting, and reduced appetite were higher for women than for men. The differences between women and men in the odds of these symptoms were not modified by the number of years on dialysis and remained statistically significant after adjustments for age, diabetes, congestive heart failure, serum hemoglobin, serum albumin, dialysis dose, and years on dialysis. It is interesting to note the observed prevalence of nausea and vomiting in patients receiving hemodialysis in the morning. However, additional adjustment for dialysis shift did not change the differences between women and men in the odds of these symptoms.

The finding of greater prevalence of reduced appetite in women observed in the present study is in agreement with previous observations from the international Dialysis Outcomes and Practice Patterns Study (DOPPS) that included more than 14,000 prevalent MHD patients.[3] DOPPS found significantly greater prevalence of reduced appetite in women than in men, both with and without adjustments for numerous potential confounders. In a study of 223 prevalent hemodialysis patients, Carrero et al. have also described a higher prevalence of reduced appetite in women than in men.[22] The importance of appetite as a contributor to malnutrition in MHD patients is supported by results of DOPPS and smaller studies conducted in dialysis settings that have shown associations of reduced appetite with indicators of poorer nutritional status among those patients.[3,5,8,22]

Diarrhea was the symptom with the lowest prevalence among the 4 symptoms assessed in the present study. In contrast to nausea, vomiting, and reduced appetite, the prevalence of diarrhea was higher in men than in women, but the difference was not statistically significant. Smaller studies among hemodialysis patients have also failed to show differences in the prevalence of diarrhea between women and men.[1,2,4] The data from larger studies in the general population are conflicting regarding gender differences in diarrhea.[14,15,23]

Our results suggest that the observed female–male differences in appetite, nausea, vomiting, and dietary intake play a role in explaining a poorer nutritional status in women than in men on MHD. The percentage difference between women and men in the mean values of MIS was much higher in version that included all 10 components than in the reduced version that did not include the gastrointestinal symptoms component. The percentage difference between women and men was even smaller for the MIS version that did not include both the gastrointestinal symptoms component and the dietary intake component. As gastrointestinal symptoms and dietary intake are subjective measures based on patient's report, we cannot rule out the possibility that the female–male differences in appetite, nausea, and vomiting were partly related to a higher propensity of women to disclose their discomfort. Apparently, women tend to report more often both somatic and psychological symptoms than men, but it is not clear whether this is due to biological, social, or behavioral factors.[24] Nevertheless, the presence of the assessed symptoms and the dietary intake reported by MHD patients may help to identify those with poor nutritional status and at higher risk of malnutrition.

In addition to gender, age and diabetes were also independently and significantly associated with the assessed symptoms. The study suggests that the odds of vomiting are higher for diabetic patients and the odds of both nausea and vomiting are higher for younger patients, independently of the effects of potential confounders. The directions of these associations were similar for women and men. Similar to previous studies, we did not find associations between a higher dialysis dose and lower frequencies of nausea, vomiting, and reduced appetite among men and women treated by standard hemodialysis 3 times weekly.[3,25] This finding might be explained by the negative effect of higher dialysis dose via increased ultrafiltration rate on postdialysis fatigue and the exacerbation of symptoms, particularly reduction in appetite during the period of dialysis recovery.[3,26,27]

One limitation of the present study is the restriction of the analysis to only appetite, nausea, vomiting, and diarrhea. Although there is a strong rationale to support a systematic evaluation of hemodialysis patients for the presence of these symptoms owing to their potential contribution to malnutrition, it is also interesting to assess other symptoms reported to be more prevalent in hemodialysis patients than among community controls, for example, dyspepsia, persistent abdominal pain, heartburn, and constipation.[1] Unfortunately, the study could not assess the reasons for the observed differences in symptoms between women and men. One factor that deserves to be evaluated as possible explanation for the differences in symptoms between women and men, particularly reduced appetite, is delayed gastric emptying (or gastroparesis). There is evidence that gastroparesis due to autonomic neuropathy contributes to poor appetite and reduced nutritional status among dialysis patients.[28,29] Moreover, there are data to indicate that gastroparesis is more frequent in women than in men.[30,31] Another factor that could potentially contribute to the assessed symptoms and other symptoms in hemodialysis patients, such as dyspepsia and constipation, is the use of medication. As shown previously, the large number of oral medications that are prescribed for MHD patients is a factor independently associated with higher odds of reduced appetite.[3] Unfortunately, data on pill medication prescription were available in the present study only for phosphate binder. However, phosphate binder seems to be the most important contributor to pill burden in maintenance dialysis patients.[32] In a study using data of maintenance dialysis patients treated in different geographic areas of the United States, it was shown that phosphate binders accounted for about one-half of the daily pill burden.[33] In our study, the prescribed number of pills/day of phosphate binders was very similar between women and men. Thus, it is unlikely that pill burden may fully explain the higher odds of nausea, vomiting, and reduced appetite in women than in men.

Considering the evidence that inflammation plays a pivotal role in appetite and nutritional status among patients with chronic kidney disease,[22,34–37] it is interesting to assess whether biological mediators of inflammation, such as interleukin 6 and TNF-alpha, account for difference in appetite between women and men in the population on MHD. However, a lower serum concentration of albumin was observed in women than in men, a finding that might be partially mediated by inflammation.[38] Metabolic acidosis is a disturbance linked with inflammation in maintenance dialysis patients that deserves to be evaluated as potential mediator of associations with appetite and nutritional status.[39,40] Unfortunately, it was not possible to evaluate the influence of metabolic acidosis in our results because plasma bicarbonate and pH were not available.

Another missing piece of information in the present study was the status of the patients regarding residual renal function (RRF). As shown previously, patients with RRF have, in general, lower inflammation and better nutritional status.[41,42] These studies have not shown differences in RRF by gender; however, they have not assessed the possibility of a differential effect of RRF on inflammation and nutritional status between women and men. Studies are also needed to assess a possible mediating effect of higher serum leptin concentrations on gender differences in appetite and nutritional status. This possibility is supported by previous observations indicating that serum leptin concentration is higher in women than in men and that higher levels of leptin are associated with poor appetite and worse nutritional status in chronic kidney disease and maintenance dialysis patients.[43,44]

The indicator of nutritional status used in the present study, the MIS, is a comprehensive tool that considers recommendations of the National Kidney Foundation Kidney Disease Outcomes Quality Initiative of using a panel of measures to assess protein-energy nutritional status.[45] However,

the additional use of specific measures of body composition will provide an even more comprehensive evaluation of nutritional status. For the ongoing new phase of PROHEMO, we will determine data on body composition by near-infrared analysis using FUTREX-62, conicity index, and skinfold anthropometry.

Encouraging evidence from clinical studies provides support for specific interventions to reduce gastrointestinal symptoms and prevent malnutrition in MHD patients.[46-50] If effective interventions are targeted to MHD patients most in need, they are likely to narrow the female–male gaps in gastrointestinal symptoms and nutritional status.[46-50] Nausea, vomiting, and reduced appetite in patients with chronic renal failure may be related to the intake of specific types of foods.[48,49] Moreover, the susceptibility to nausea and vomiting seems to be more strongly related to aversion to certain types of foods in women than in men.[50] Thus, nutrition counseling and behavioral interventions may help to prevent malnutrition in MHD patients as a whole and reduce the gender gap in nutritional status by guiding those with nausea, vomiting, or reduced appetite toward food choices that are more suitable for both their appetite and nutritional requirements. Pharmacological interventions and dialysis prescription may also play a role in controlling gastrointestinal symptoms and improving nutritional status. A previous study, for example, showed that the use of prokinetic medications in hemodialysis patients with gastroparesis is efficacious in improving appetite and increasing serum albumin concentration.[46] Whereas higher dialysis dose in patients treated by conventional thrice-weekly hemodialysis with fixed session length of approximately 4 hours has not been associated with improved appetite, hemodialysis with slower ultrafiltration rate and daily hemodialysis may reduce postdialysis fatigue, which may contribute toward improving appetite and nutritional status.[47,51]

In conclusion, the results indicate a higher prevalence of nausea, vomiting, and reduced appetite in women than in men on MHD. These gastrointestinal symptoms and perhaps the detrimental effects of these symptoms on dietary intake may partially explain a poorer nutritional status in MHD women.

Practical Application

The results are consistent with a major role of gastrointestinal symptoms in the nutritional status of MHD patients. It is shown that the higher prevalence of nausea, vomiting, and poor appetite accounts for the poorer nutritional status in women than in men on MHD. The study supports a greater emphasis on early identification and treatment of gastrointestinal symptoms to reduce the prevalence of malnutrition and the observed gender gap in nutritional status among MHD patients.

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