Predictor factors of peritoneal dialysis-related peritonitis

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Abstract

Introduction: Peritonitis remains a major complication of peritoneal dialysis (PD). **Objective:** Evaluate peritonitis incidence, etiology and outcome in cronic PD patients. **Methods:** A retrospective cohort study was carried out on 330 patients (mean age of 53 ± 19 years) who had been treated by PD in a dialysis center in Aracaju/SE, Brazil between January 1st, 2003 and December 31th, 2007. Data of patients with and without peritonitis were compared using Student's t-test, chi-squared statistic and multiple logistic regression. **Results:** There were 213 peritonitis among 141 patients (1.51 episode/patient) resulting in a rate of 28.44 patient/episode/month (0.42 patient/episode/year). *Staphylococcus aureus* was the most frequent micro-organism isolated (27.8%), followed by Escherichia coli (13.4%) and 32.5% were culture-negative peritonitis. A greater risk of peritonitis was identified at the patients with hypoalbuminemia [relative risk (RR) = 2.0; 95% confidence interval (CI) = 1.21 – 3.43; p < 0,01], < 4 school years (RR = 2.15; CI = 1.09–4.24; p = 0.03) and catheter's exit site infection (RR = 2.63; IC = 1.57 – 4.41; p < 0.01). There were no significant difference among gender, age, family income, diabetes mellitus, type of dialysis treatment, type of catheter and its surgical implant. **Conclusions:** Hypoalbuminemia, low schooling and catheter's exit site infection were associated with greater risk to peritonitis. Although peritonitis rate follow international pattern, prophylactic strategies are recommended.

Keywords: kidney failure chronic, peritoneal dialysis, peritonitis.

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Introduction

Peritoneal dialysis (PD) is an accepted and widely used form of renal replacement therapy (RRT), peritonitis being its main complication.[1,2]

Sociodemographic[3,4,5] and nutritional[6,7] factors, climatic circumstances,[8] *diabetes mellitus*,[3,5,6,7] PD modality,[9] and the presence of peritoneal catheter tunnel or exit site infection (PCESI) have been reported as possible risk factors associated with the development of peritonitis.[10,11]

Although occurring with an increasing frequency, due to the development of specific programs,[1,2] peritonitis represents one of the major reasons for hospitalization and dialysis technique failure,[10,12,13] and remains as the main cause of death in patients treated with PD.[1,11] Its prevention is, thus, of fundamental importance for a successful dialysis program.[1] This article aimed at assessing the possible predictive factors of peritonitis in patients on a PD program, and at comparing the findings with indicators described in the literature.

Method

This was a retrospective study of a cohort of 330 chronic renal patients belonging to the PD program of the Nephrology Clinic of the State of Sergipe (Clinese), in the city of Aracaju. The patients had undergone dialysis therapy for at least 30 uninterrupted days from January 1st, 2003, to December 31st, 2007.

At that dialysis center, the Y connection system PD (Baxter Hospitalar) is used, with implantation of the peritoneal catheter (Tenckhoff, Swan Neck Tenckhoff or Swan Neck Missouri) by use of a trocar or microlaparotomy. Cefalotin is routinely

used in surgery as antibiotic prophylaxis and immediately at the beginning of therapy or after break-in, depending on the need for emergency dialysis treatment. At the time, neither antibiotic prophylaxis of peritonitis or of exit site infections was prescribed, nor routine search for *Staphylococcus aureus* nasal carriers was performed.

Each patient provided the following information: clinical and demographic profile; history of the dialysis treatment; catheter history; infectious complications inherent in treatment; and laboratory tests at the beginning of PD therapy. The patient's age at the beginning of PD was considered for data analysis. Patients on automated peritoneal dialysis (APD) and on continuous ambulatory peritoneal dialysis (CAPD) were not separated into different groups. Peritoneal catheter exit site infection was defined by the presence of purulent secretion, with or without skin erythema in the pericatheter region.[10,14] If a certain patient had more than one peritoneal catheter, the catheter present at the time of the peritonitis episode was considered when analyzing that particularity, or the catheter with the longest time of stay, for individuals who did not have that complication.

The peritonitis episodes were assessed regarding their incidence, causative agents, and possible predictive factors related to their development. Diagnosis was confirmed by the simultaneous occurrence of at least two of the following criteria: abdominal pain; cloudy peritoneal effluent; leukocyte count in the dialysate > 100/μL; and positive culture of the peritoneal fluid.[14] Peritonitis rate was calculated through the number of episodes as a function of time of exposure to the dialysis technique, according to the recommendations of the International Society for Peritoneal Dialysis (ISPD).[10] For determining the predictors of peritonitis, patients were divided into two groups, depending on the presence (141 patients – 42.7%) or absence (189 patients – 57.3%) of peritonitis, and the first episode of peritonitis was considered.

Data Analysis

The data obtained were checked and submitted to statistical analysis by using the programs Epi Info 2005, version 3.3.2, and Statistical Package for Social Sciences (SPSS) 16.0 for Windows (SPSS Inc., Chicago, Illinois). The significance level adopted for rejecting the null hypothesis was $p < 0.05$.

The statistical comparisons between the continuous variables and the calculations of the means were performed by using Student t test. The percentages of the categorical variables (presence or absence of peritonitis) were compared by use of the two-tailed chi-square test. To further explore the individual effects of the predictors involved in the peritonitis episodes, a logistic regression model was built through the analysis of multiple variables (adjusted by the Hosmer-Lemeshow test), including sociodemographic factors and the variables that had $p < 0.25$ in the non adjusted analysis.

Results

The mean age of the 330 patients studied at the beginning of the dialysis therapy was 53 ± 19 years. Their general characteristics are shown in Table 1.

In those patients, 381 peritoneal catheters were implanted (1.15/patient), and the Tenckhoff type predominated (59.8%). Forty-four patients (11.5%) used more than one catheter during the period. All catheters of the Swan Neck type were implanted through microlaparotomy, and those of the Swan Neck Tenckhoff type, through trocar. Most of those of the Tenckhoff type (95.2%) were implanted through trocar.

Peritonitis occurred in 141 individuals (42.7%), in a total of 213 episodes (1.51/patient). The overall peritonitis rate for the period studied was one episode every 28.4 months (0.42 episode/patient/year). Of the patients with peritonitis, 90 (63.8%) had an episode; 34 (24.1%), two; 13 (6.1%), three; and four patients (1.8%), four episodes.

Table 2 shows the distribution of the cases of peritonitis as a function of the etiologic agent identified in culture. Gram-positive and Gram-negative microorganisms – 55 episodes each – were the most frequent, and *Staphylococcus aureus* was the commonest agent isolated in the series (54 episodes – 25.4%). The negative culture rate was 32.5% (63 cases). Culture was not performed in 19 opportunities (8.9%).

Peritoneal catheter exit site infection was identified in 136 patients (42.1%), 73 of whom (53.7%) later developed peritonitis. In 28 (38.4%) of those peritonitis episodes, *Staphylococcus aureus* was the causative agent. Peritonitis due to *Staphylococcus aureus* following PCESI represented 50.9% of the episodes from which that microorganism was isolated.

The following predictors of peritonitis were identified through univariate analysis (Table 3): starting RRT through PD ($p = 0.02$); serum albumin < 3 g/dL at the beginning of PD ($p = 0.03$); and presence of PCESI ($p < 0.01$). The male sex showed statistical tendency towards the development of peritonitis ($p = 0.08$),

Table 1 General characteristics of the patients undergoing peritoneal dialysis (N = 330)

Variables	Frequency	%
Sex		
Male	168	50.9
Female	162	49.1
Age (years)		
< 65	237	71.8
≥ 65	93	28.2
Origin		
City of Aracaju	130	39.4
Inner State/other States	200	60.6
Educational level (n = 322)		
Illiterate	102	31.7
Literate	145	45.0
Complete elementary school	25	7.8
Complete high school	43	13.3
Complete university	7	2.2
Monthly family income (n = 316)		
Up to 1 minimum wage	158	50.0
From 1 to 5 minimum wages	118	37.4
From 5 to 10 minimum wages	32	10.1
More than 10 minimum wages	8	2.5
Underlying disease* (n = 206)		
Diabetic nephropathy	94	45.7
Hypertensive nephrosclerosis	55	26.7
Chronic glomerulonephritis	23	11.2
Polycystic kidneys	10	4.8
Obstructive uropathy	10	4.8
Chronic pyelonephritis	6	2.9
Other etiologies	8	3.9
Diabetes mellitus		
Yes	120	36.4
No	210	63.6
Initial serum albumin (n = 319)		
< 3.0 g/dL	116	36.4
≥ 3.0 g/dL	203	64.6
Initial modality of dialysis		
Peritoneal dialysis	171	51.8
Hemodialysis	159	48.2
Mode of the initial dialysis		
Elective	53	16.1
Non-elective	277	83.9
Type of peritoneal catheter		
Swan Neck	95	28.8
Double Tenckhoff cuff	196	59.4
Swan Neck Tenckhoff	39	11.8
Implantation type		
Trocar	226	68.5
Microlaparotomy	104	31.5
Catheter exit site infection		
Yes	136	41.2
No	194	58.8

* The underlying disease was not identified in 124 patients (37.5%).

Table 2 Distribution of the episodes of peritonitis in patients on peritoneal dialysis as a function of the identified etiological agent (N = 194)

Identified etiological agent	Frequency	%
Gram-positive (n = 55)		
Staphylococcus aureus	54	27.8
Staphylococcus epidermidis	1	0.5
Gram-negative (n = 55)		
Escherichia coli	26	13.4
Klebsiela sp.	8	4.1
Pseudomonas sp.	10	5.2
Enterobacter sp.	7	3.6
Proteus sp.	1	0.5
Alcaligenes sp.	3	1.5
Fungus (n = 6)		
Candida albicans	5	2.5
Others	1	0.5
Others	15	7.7
Negative culture	63	32.5

Culture was not performed in 19 episodes (8.9%).

while the use of the Swan Neck Tenckhoff catheter provided protection ($p < 0.01$).

In the analysis with multiple variables (Table 4), the following independent peritonitis predictors were identified: serum albumin < 3 g/dL at the beginning of therapy ($p < 0.01$); PCESI ($p < 0.01$); and less than four years of schooling ($p = 0.03$). Monthly family income ≥ 5 minimum wages ($p = 0.06$) and beginning RRT through PD ($p = 0.06$) showed statistical tendency.

Discussion

Peritonitis rates have been decreasing in the past years due to advances in PD techniques.[1,2,15] Nevertheless, peritonitis still remains as the major cause of therapeutic failure, in addition to sometimes culminating in patient's death.[1,10,11,13,15]

In an observation period of five years, 330 patients belonged to the PD program of the dialysis center studied for at least 20 uninterrupted days, 171 of whom (51.8%) began RRT with PD.

On December 31st, 2007, 31.67% of the dialysis patients at that institution were on PD. That percentage was proportionally higher than the North-American (8.8%)16 and national (10.6%)[17] means, similar to the mean in Holland (30%)[18], and lower than the 74% reported in Mexico, the major user of PD worldwide.[7] This reflects our police of impartially presenting the available therapies, allowing patients and their families to freely choose in situations with no contraindication to any method. The fact that 51.8% of the patients had PD as their first dialysis modality emphasizes that observation. The suppressed demand for RRT and the sympathy of the professionals working at the institution for the method can have contributed to the magnitude of the PD program, making Sergipe the State that proportionally has the greatest percentage of patients on that dialysis modality in the country.[17]

Data have revealed that patients of this study have characteristics similar to those described in other Brazilian series regarding sociodemographic and clinical indicators.[19] The percentage of elderly (28.2%) and patients living away from the dialysis center (60.6% live in the countryside or other States) is high, most patients are illiterate or have not completed elementary school (76.7%), and their monthly family income is lower than five minimum wages (87.4%). The lack of access to conservative treatment of most patients has hindered the identification of the underlying disease in 37.5% of the cases and has contributed, along with problems of vascular access to hemodialysis, to the high index of therapy beginning as an emergency indication (83.9%).

Table 3 Statistic univariate analysis of possible predictive factors of peritonitis in patients undergoing peritoneal dialysis (n = 330)

Characteristics	General population	Peritonitis Yes	Peritonitis No	p
	330 (100%)	141 (42.7%)	189 (57.3%)	-
Sex				
Male	168 (50.9%)	64 (45.4%)	104 (55.0%)	0.08
Female	162 (49.1%)	77 (54.6%)	85 (45.0%)	
Age				
< 65 years	237 (71.8%)	100 (70.9%)	137 (72.5%)	0.75
≥ 65 years	93 (28.2%)	41 (29.1%)	52 (27.5%)	
Educational level*				
Up to 4 years of scho oling	247 (76.7%)	110 (79.7%)	137 (74.5%)	0.26
More than 4 years of schooling	75 (23.3%)	28 (20.3%)	47 (25.5%)	
Income				
Up to 5 minimum wages	276 (87.3%)	116 (85.3%)	160 (88.9%)	0.34
More than 5 minimum wages	40 (12.7%)	20 (14.7%)	20 (11.1%)	
Origin				
City of Aracaju	130 (39.4%)	61 (43.3%)	69 (36.5%)	0.21
Inner State/other States	200 (60.6%)	80 (56.7%)	120 (63.5%)	
Underlying disease				
Diabetic nephropathy	94 (28.5%)	44 (31.2%)	50 (26.5%)	0.34
Hypertensive nephrosclerosis	55 (16.7%)	20 (14.2%)	35 (18.5%)	0.29
Chronic glomerulonephritis	23 (7.0%)	10 (7.1%)	13 (6.9%)	0.93
Polycystic kidneys	10 (3.0%)	2 (1.4%)	8 (4.2%)	0.14
Obstructive uropathy	10 (3.0%)	4 (2.8%)	6 (3.2%)	0.85
Chronic pyelonephritis	6 (1.8%)	2 (1.4%)	4 (2.1%)	0.63
Other etiologies	8 (2.4%)	3 (2.1%)	5 (2.6%)	0.76
Undetermined	124 (37.6%)	57 (40.4%)	67 (35.4%)	0.35
Initial modality of dialysis				
Peritoneal dialysis	171 (51.8%)	83 (58.9%)	88 (46.6%)	0.02
Hemodialysis	159 (48.2%)	58 (41.1%)	101 (53.4%)	
Mode of the initial dialysis				
Non-elective	277 (83.9%)	123 (87.2%)	154 (81.5%)	0.15
Elective		53 (16.1%)	18 (12.8%)	35 (18.5%)
Diabetes mellitus	120 (36.4%)	56 (39.7%)	64 (33.9%)	0.27
Catheter exit site infection	136 (41.2%)	73 (51.8%)	63 (33.3%)	0.0007
Type of catheter				
Swan Neck	95 (28.8%)	46 (32.6%)	49 (25.9%)	0.18
Double Tenckhoff cuff	196 (59.4%)	86 (61%)	110 (58.2%)	0.60
Swan Neck Tenckhoff	39 (11.8%)	9 (6.4%)	30 (15.9%)	0.008
Type of implantation				
Trocar	226 (68.5%)	90 (63.8%)	136 (72.0%)	0.11
Microlaparotomy	104 (31.5%)	51 (36.2%)	23 (28.0%)	
Initial serum albumin				
< 3 g/dL	116 (36.4%)	59 (43.1%)	57 (31.3%)	0.03
≥ 3 g/dL	203 (63.6%)	78 (56.9%)	125 (68.7%)	

*Illiterate and literate are included in the educational level up to 4 schooling years; more than 4 schooling years includes complete elementary school level, complete high school, and complete university.

Table 4 Statistical analysis with multiple variables of possible predictive factors of peritonitis in patients undergoing peritoneal dialysis

Risk factors	Odds ratio	95% CI*	p
Male sex (*versus* female)	0.73	0.44 – 1.21	0.23
Age of starting RRT** ≥ 65 years (*versus* < 65 years)	1.12	0.63 – 1.98	0.70
Educational level up to 4 years of schooling*** (*versus* ≥ 4 years)	2.15	1.09 – 4.24	0.03
Income ≥ 5 minimum wages (*versus* < 5 minimum wages)	2.23	0.97 – 5.12	0.06
Origin from the city of Aracaju (*versus* inner state)	1.61	0.92 – 2.79	0.09
Start with peritoneal dialysis (*versus* hemodialysis)	1.61	0.97 – 2.68	0.06
Non-elective start (*versus* elective)	1.99	0.97 – 4.11	0.06
Catheter exit site infection	2.63	1.57 – 4.41	< 0. 01
Implantation through microlaparotomy (*versus* trocar)	0.37	0.07 – 1.95	0.24
Swan Neck Tenckhoff catheter (*versus* other catheters)	0.55	0.10 – 2.95	0.48
Serum albumin < 3 g/dL (*versus* ≥ 3 g/dL)	2.03	1.21 – 3.43	< 0.01

* CI = 95% confidence interval; ** RRT – renal replacement therapy; *** up to 4 years of schooling includes illiterate and literate; more than 4 years of schooling includes complete elementary school, complete high school, and complete university.

Despite the unfavorable sociodemographic and clinical characteristics, 141 patients (42.7%) had peritonitis, summing up to 213 episodes, and the peritonitis rates are in accordance with the international recommendations and the reports of current series.[6,13,20,21,22] According to the ISPD, the goal of a dialysis center is peritonitis rates lower than one episode every 18 months (0.67 episode/patient/year).10 Fernandes *et al.*,[20] in a large national multicenter study (Brazilian Peritoneal Dialysis Multicenter Study – BRAZPD), have reported a peritonitis rate of one episode every 30 months, while Moraes *et al.*,[22] when describing 25-year cumulative data, have reported one episode every 14.63 months in the city of Curitiba, in the State of Paraná. It is worth emphasizing that, as the latter study relates to a prolonged experience, that rate encompasses all the evolution of PD connections. When analyzing data separately and for five-year intervals, the authors have reported one episode of peritonitis for every 3.38 patients/month from 1980 to 1985, and one episode for every 17.64 patients/month from 2000 to 2005, better representing the results obtained with current connections.[22]

Analysis of the information about the etiologic agent of peritonitis was partially hindered because culture was not performed in 8.9% of the cases. This may be justified by the fact that 200 patients (60.7%) lived away from the dialysis center, and sometimes their first visit to a health care service and the beginning of the antimicrobial therapy occurred at non-reference hospitals. National authors have reported rates of culture non-performance ranging from 7% to 22.7%.[2,23]

Most international authors have described Gram-positive microorganisms as the major causative agents of peritonitis, *Staphylococcus epidermidis* being the

most frequent.[5,21,24] Latin-American authors 4,22 have reported *Staphylococcus aureus* as the major etiologic agent. In our series, the same proportion of Gram-positive and Gram-negative agents (55 episodes each) was found, *Staphylococcus aureus* being the most frequently isolated microorganism (27.8%), and *Escherichia coli* (13.4%) and *Klebsiela* sp. (9.7%) the most frequently identified Gram-negative microorganisms. Although Barretti *et al*.[2] and Kavanagh *et al*.[13] have also reported higher prevalence of *Escherichia coli*, that distribution varies.[2] The results of that study regarding the prevalence of fungi in positive cultures (2.8%) are similar to those reported by other researchers.[21,22,24]

The peritoneal fluid cultures of 63 episodes of peritonitis (32.5%) were negative, a value greater than that recommended in the ISPD guidelines (< 20%).10 Moraes *et al*.[22] and Lima *et al*.[25] have reported negative culture rates of 26% and 33.7%, respectively. According to Barretti *et al*.,[2] a factor that can contribute to a high frequency of negative cultures is the fact that reference laboratories do not comply with some recommendations of the ISPD[10] regarding culture specimen collection and inoculation. Nevertheless, in that series, the rate of cure of peritonitis with negative culture was similar to the rate of cure of episodes caused by Gram-positive agents, 77.8% and 83.6%, respectively, as reported by Mujais.[21] As suggested by Fernandes *et al*.,[20] our predominance of *Staphylococcus aureus*-caused peritonitis can be due to the high rate of negative cultures, which can hide the presence of other microorganisms that prevail in most studies, such as coagulase-negative *Staphylococcus*.

Sociodemographic variables have been considered as possible risk factors associated with the unfavorable evolution of dialysis patients, more specifically regarding the variations in quality of life scores, peritonitis, and mortality.[2,3,4,5,26,27,28] Diabetic nephropathy, advanced age, lower family income, and lower educational level have been associated with worse prognosis in some reports.[3,5,26,27,28] In our case series, beginning treatment at advanced age, being diabetic, or having a monthly family income lower than five minimum wages were not associated with the development of peritonitis. However, in accordance with Aslam *et al*.[3] and Chow *et al*.,[5] low educational level was identified as a risk factor in the analysis through multiple variables.

Hypoalbuminemia, at the beginning of treatment, is associated with a higher chance of developing peritonitis, in accordance with the reports of other authors.[3,5,6] Hypoalbuminemia, here defined as albumin < 3.0g/dL, was identified in 36.4% of the patients admitted to the program and in 43.1% of those developing peritonitis, and could have been associated with the low socioeconomic level of the population, as well as with the late referral to a nephrologist.

The benefit of one type of catheter over another has not been conclusively demonstrated by randomized and prospective studies.[10,29,30] A comparison of 107 Swan Neck Missouri catheters and 153 Tenckhoff catheters implanted in 236 patients at the same center from December 2000 to June 2005 has shown no differences in survival and prevalence of the major causes of failure. Based on this, from 2007 on, the institution began to adopt the routine use of the Swan Neck Tenckhoff catheter, implanted by a nephrologist through trocar.[31] Univariate analysis has shown that the Swan Neck Tenckhoff catheter provided protection against the development of peritonitis, but that was not confirmed after logistic regression. Maybe the still nonrepresentative number of that type of catheter may have hindered the observation of any difference.

Previous catheter tunnel infection and PCESI have shown to be the major independent risk factors for the development of peritonitis, being associated with a 2.6-time increase in the occurrence of that complication. The elevated incidence of peritonitis in patients who had previously had PCESI can relate to the fact that, at that time, no antimicrobial agent was used at our institution for the prophylaxis of peritonitis or PCESI. Lima *et al*.[25] have reported a PCESI-related peritonitis rate of 35.7% at a service where routine prophylaxis with mupirocin is not performed, to avoid the appearance of multiresistant *Staphylococcus aureus*.[25] Moreira *et al*.32 have shown a significant reduction in the incidence of peritonitis in patients using mupirocin. Takei[33] has reported that the use of mupirocin reduced the colonization by *Staphylococcus aureus* at catheter exit site and nasal mucosas. Barretti *et al*.[2] have reported that the daily use of mupirocin at the catheter exit site reduced the peritonitis rate from 1/16.2 episode/patient/month to 1/24.2 episode/patient/month, and was associated with changes in the epidemiological profile, with a strong reduction in the prevalence of peritonitis caused by *Staphylococcus aureus*. Piraino *et al*.[34] have reported an overall reduction in the peritonitis rate with the use of topical gentamicin, mainly due to the reduction in peritonitis caused by Gram-negative agents from 0.52 to 0.34 episode/year. Those authors have also reported a 63% reduction in the risk of infectious complications due to *Staphylococcus aureus* because of the use of mupirocin.

Climatic factors were not assessed in this study, but in the northeastern region of Brazil, the weather is hot and humid during almost the entire year. Szeto *et al*.8 have shown a higher incidence of catheter infection in countries of hot and humid weather because of the accumulation of sweat and dirt around the catheter exit site. That explanation has also been provided by Stinghen, Barretti, and Pecoits-Filho,[15] who have recommended that maintaining the catheter and the exit site orifice drier can help to reduce the incidence of infections in tropical countries.

The present study has some limitations, such as the fact that the analysis was retrospective and limited to a single center, and, thus, the particularities of the study should be carefully considered before results can be generalized. In addition, measuring serum albumin at the beginning of the PD treatment to infer the patient's nutritional status should be considered with reservation, because that is not a reliable marker and neither serial measurements nor values immediately prior to episodes of peritonitis were considered. Finally, it is worth emphasizing that, when considering a possible association of peritoneal catheter tunnel or exit site infection with the occurrence of peritonitis, no interval between the two events was observed, which does not allow a cause-effect relation to be established.

Conclusion

Hypoalbuminemia, low educational level, and catheter exit site infection have shown to be independent predictive factors of peritonitis.

Although the socioeconomic level has been historically considered a contraindication for PD, this was not a limiting factor, because in the study population, even with unfavorable sociodemographic and clinical indicators, the peritonitis rates observed were within the international recommendations. Finally, considering the high penetration of *Staphylococcus aureus* as an etiological agent, prophylactic strategies in *Staphylococcus aureus* nasal carriers and for PCESI, as currently recommended by the international guidelines, should be universally applied.

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