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Original Article

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The Relationship Between Mucociliary Clearance Time and Peritonitis Frequency in Patients Receiving Peritoneal Dialysis

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ABSTRACT

Background: The present study sought to explore the association between nasal mucociliary clearance time (MCT) and the frequency of peritonitis among patients with chronic kidney disease (CKD) treated by peritoneal dialysis (PD).
Methods: This cross-sectional study enrolled 24 patients with CKD treated by PD and 24 healthy volunteers. Nasal mucociliary function was assessed using the saccharin transit time test. In this procedure, a saccharin particle with a 1 mm diameter was meticulously placed on the anteromedial surface of the inferior nasal concha. The 2 groups were compared based on their mean MCT. Within the patient group, the number of peritonitis cases in the last year was evaluated, and the correlation between MCT and the occurrence of peritonitis was analyzed.
Results: The patient group consisted of 15 females and 9 males, with a mean age of 52.6 years. The control group included 14 females and 10 males, with a mean age of 47.5 years. The mean duration of PD among the followed cohort was 20 months, ranging from 3 to 190 months. The comparison of mean MCT between patients with a history of peritonitis and those without peritonitis did not reveal a statistically significant difference (P = .333). However, the neutrophil-to-lymphocyte ratio was significantly elevated in the group exhibiting prolonged MCT (P = .046).
Conclusion: Although this study found no statistically significant direct relationship between peritonitis incidence and MCT, the research aimed to evaluate MCT as a potential indicator of susceptibility to respiratory tract infections, which play a role in the development of peritonitis.
Keywords: Mucociliary clearance, peritoneal dialysis, peritonitis, saccharin transit time

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INTRODUCTION

Beyond serving as an airway barrier, mucus and its mechanical clearance constitute an innate defense mechanism for the respiratory system.[1] The mucous layer, the airway surface liquid (ASL), and cilia are fundamental components of mucociliary clearance (MCC). Cilia exhibit parallel and perpendicular movement capacity relative to the airway surface.[2,3] Their coordinated beating in waves propels pathogens and particulate matter out of the airways, which functions efficiently in healthy individuals. Within the respiratory epithelium, cilia interact with the ASL, while a low-viscosity periciliary layer facilitates the effective clearance of the airway.[4]

Determining mucociliary clearance time (MCT) is a significant method for assessing the adequacy of the airway defense system. Efforts have been made to develop standardized measurement techniques, such as lung gamma scintigraphy following aerosol inhalation and induced coughing.[5] However, the widespread applicability of this method is limited due to its cost. The saccharin

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transit time (STT) test is the preferred measurement due to its ease of administration and repeatability. A normal clearance time of 20 minutes is generally accepted for this test.[6] Studies evaluating the transit of wood charcoal, possessing similar properties to saccharin, from the nasal cavity to the oropharynx have also been conducted, reporting a normal MCT of 14 minutes.[7] The overarching goal is to accurately assess mucociliary activity, as this provides insight into the effectiveness of the respiratory tract's defense barrier.

The peritoneum is an extensive serous membrane exhibiting both epithelial and mesenchymal characteristics, encompassing a variety of functions. Approximately 1 L of peritoneal fluid is produced daily to lubricate the peritoneal surfaces and facilitate the exchange of substances and immune cells between the peritoneal fluid and plasma. This fluid contains a diverse array of immune cells, including macrophages, natural killer cells, lymphocytes, eosinophils, mesothelial cells, and mast cells.[8] Peritoneal dialysis (PD) induces both morphological and functional adaptations in the peritoneum, including inflammation, thickening of the submesothelial stroma, progressive fibrosis, and angiogenesis, ultimately leading to a loss of filtration capacity.[9]

The pathogenesis of peritonitis in PD is amplified by factors encompassing insufficient adherence to hand hygiene protocols and the occurrence of nasal and respiratory tract infections. Crucially, the efficiency of MCC mechanisms is integral to impeding the development of respiratory tract infections.[10] Based on this understanding, the study aimed to evaluate the relationship between the incidence of peritonitis and mucociliary activity function in this patient population.

MATERIAL AND METHODS

Study Population and Recruitment

The research began following the acquisition of ethical approval from Karatay University (March 7, 2024/025). The study obtained informed consent from all participating patients and healthy volunteers. Forty patients with chronic kidney disease (CKD) treated by PD at a nephrology clinic were initially matched with 40 volunteers exhibiting similar demographic characteristics (age and gender) between March and June. Both the patient and volunteer groups were subsequently referred for routine examination at the ear, nose, and throat (ENT) clinic. The following criteria served as grounds for exclusion from the study: allergic rhinitis, nasal polyps, septal deviation, a history of nasal surgery, chronic lung disease, current smoking, or the presence of an upper respiratory tract infection within the preceding month. Following the application of these exclusion criteria, a total of 24 patients and 24 control participants met the eligibility requirements and were included in the final analysis.

MAIN POINTS

- This study aims to assess the link between mucociliary clearance time and peritonitis concerning its impact on patient outcomes in critical care.
- The aim is to investigate the relationship between inflammatory markers and mucociliary function in patients undergoing peritoneal dialysis.
- This study aims to evaluate the clinical utility of measuring nasal mucociliary clearance time.

Assessment of Nasal Mucociliary Clearance Time

Nasal MCT was assessed using the STT. Before the test, participants abstained from eating or drinking for 1 hour and gently cleared their nasal passages. Measurements were taken under controlled environmental conditions (20-24°C, 45%-60% humidity). During the test, participants were instructed to avoid actions that could affect measurements, such as nose blowing, coughing, or sneezing, as well as eating or drinking. Each participant's head was positioned in a 10-degree flexion. A 1 mm sodium saccharin particle was carefully placed approximately 1 cm posterior to the anterior medial border of the inferior nasal concha. Participants maintained their posture, breathed normally through their mouth, and swallowed freely. The time from saccharin placement until the perception of a sweet taste was recorded in minutes using a calibrated stopwatch.[11]

Determination of Peritonitis History

The PD patients included in the study were managed with Continuous Ambulatory Peritoneal Dialysis. The average daily dialysate volume was 8 L/day. Regarding the dialysate solutions, icodextrin was used for nocturnal exchanges in all patients, while daytime exchanges primarily utilized 1.36% and 2.27% glucose solutions.

The history of peritonitis in the PD patients over the preceding year was determined through a comprehensive review of their electronic medical records, clinical findings documented during consultations, and relevant laboratory data. Diagnosis of peritonitis was established based on the presence of any 2 of the following criteria:

- Clinical symptoms consistent with peritonitis, including abdominal pain and/or the presence of cloudy dialysate effluent.
- Dialysate white blood cell count exceeding 100/μL or 0.1×10^9/L (after a minimum dwell time of 2 hours) with a differential count showing >50% polymorphonuclear leukocytes.
- A positive result from dialysate culture.[12]

Statistical Analysis

Following data collection, the information was entered into the SPSS software package (Statistical Package for the Social Sciences, version 22.0, IBM Corp., Armonk, NY, USA) for statistical analysis. Descriptive statistics for continuous variables are presented as mean ± standard deviation (SD) for parameters exhibiting a normal distribution, while numerical parameters

that did not conform to a normal distribution are presented as median (minimum-maximum) or median (interquartile range). Categorical variables are expressed as frequencies (n) and percentages (%). The Chi-square test was employed for pairwise comparisons of categorical variables. The independent samples *t*-test was used when the data distribution was normal, whereas the Mann–Whitney *U*-test was applied for non-normally distributed data. Pearson correlation analysis was performed for normally distributed data, and Spearman's rank-order correlation was used for non-normally distributed data to assess their relationship with the presence of MCT. A *P* value of less than .05 (*P* < .05) was considered indicative of statistical significance.

RESULTS

The mean age of the PD patients with was 52 years, with 62.5% being female. The mean age of the control group was 47.5 years, with 58.3% female. The primary diseases of the patients were as follows: hypertension (37.4%), diabetes mellitus (29.2%), polycystic kidney disease (4.2%), and other etiologies (29.2%). The mean duration of PD was 20 months, ranging from 3 to 190 months. The MCT was found to be 10.5 minutes in the patient group and 11 minutes in the control group (see Table 1).

The patients were divided into 2 groups based on a median MCT value of 10.5. The frequency of peritonitis was numerically higher in the patients with MCC above 10.5, but this was insignificant (*P* = .333). However, the neutrophil-to-lymphocyte ratio (N/L ratio) was found to be significantly higher in the group with shorter MCTs (*P* = .046) (see Table 2).

In the correlation analysis, a statistically significant negative correlation was found between MCT and calcium (*r* = −0.487, *P* = .016). Additionally, this moderate correlation was illustrated with a non-linear correlation curve (Figure 1).This indicates that as MCT values increase, calcium levels tend to decrease. However, no significant correlation was observed between MCT and peritonitis (*P* = .206) or systolic blood pressure (*P* = .063). Similarly, the correlations between MCT and diastolic blood pressure (*P* = .522), creatinine (*P* = .600), blood urea nitrogen (*P* = .873), phosphorus (*P* = .328), and sodium (*P* = .921) were not statistically significant (see Table 3).

Table 1. Baseline Characteristics of the Patient and Control Groups

	Patient (n = 24)	Control (n = 29)	*P*
Age (years)	52 ± 14.9	47.5 ± 8.6	.124
Gender (%)	M 9 (37.5) F 15 (62.5)	M 12 (41.4) F 17 (58.6)	.851
MCT (minutes)	10.5 (5-24)	11 (2-22)	.499
BMI	22.5 (19-36.8)	25.9 (19-38.4)	
Comorbidity (%) DM HT ADPKD Other	 7 (29.2) 9 (37.4) 1 (4.2) 7 (29.2)		
Dialysis vintage (months)	20 (3-190)		

M, male; F, female; MCT, mucociliary clearance time; BMI, body mass index; DM, diabetes mellitus; HT, hypertension; ADPKD, autosomal dominant polycystic kidney disease.

Table 2. Comparison of Patients' Laboratory and Clinical Parameters According to Mucociliary Clearance Times

Parameters	MCT ≤ 10.5 minutes (n = 12)	MCT > 10.5 minutes (n = 12)	*P*
Age (years)	47.8 ± 16.4	57.5 ± 12.2	.112
SBP (mmHg)	131 ± 25.4	151.8 ± 28.2	.070
DBP (mmHg)	81.8 ± 10.9	85.4 ± 15.1	.503
BMI	22.5 (19-36.8)	25.9 (19-38.4)	.418
Dialysis Vintage h (months)	15.5 (3-185)	24.5 (4-190)	.707
UF (mL)	1550 (500-7000)	1375 (0-2700)	.954
Cre (mg/dL)	6.14 ± 2.14	6.74 ± 3.87	.644
Na^{+}(mmol/L)	135.8 ± 5.3	136.4 ± 6.1	.805
Ca^{2+}(mg/dL)	8.7 ± 0.8	8.2 ± 0.4	.057
P_i (mg/dL)	3.9 ± 0.7	4.5 ± 0.8	.100
PTH (png/dL)	285.5 (99-965)	415 (109-834)	.386
CRP (mg/dL)	8.5 (1-321)	4.15 (0.6-71)	.272
WBC (10^3/μL)	7100 ± 1383.6	7039.4 ± 1900.8	.930
N (10^3/μL)	4970.8 ± 1367.8	4400.8 ± 1227.8	.294
L (10^3/μL)	1360.8 ± 625.8	1783.3 ± 626.2	.112
N/L	3.54 (1.50-12.90)	2.53 (1.50-5.80)	.046
Peritonitis (once a year)	3 (25%)	5 (41.9%)	.333
Non-Peritonitis (once a year)	9 (75%)	7(58.3%)	
Respiratory tract infection (once a year)	7 (58.3%)	8 (66.7%)	.500
Non-respiratory tract infection (once a year)	5 (41.7%)	4 (33.3%)	

BMI, body mass index; Ca^{+2}, Calcium; Cre, creatinine; CRP, C-reactive protein; DBP, diastolic blood pressure; L, lymphocyte; MCT, mucociliary clearance time; N, neutrophil; Na^{+}, Sodium; N/L, neutrophil lymphocyte ratio; P_i, inorganic phosphate; PTH, parathyroid hormone; SBP, systolic blood pressure; UF, ultrafiltration; WBC, white blood cell.
SD, range, or % have been used where appropriate.

DISCUSSION

The respiratory and peritoneal cavities, while distinct, share potential pathways for inflammation and immune dysregulation. Impaired MCC, indicative of a compromised local defense mechanism in the respiratory tract, might be associated with a

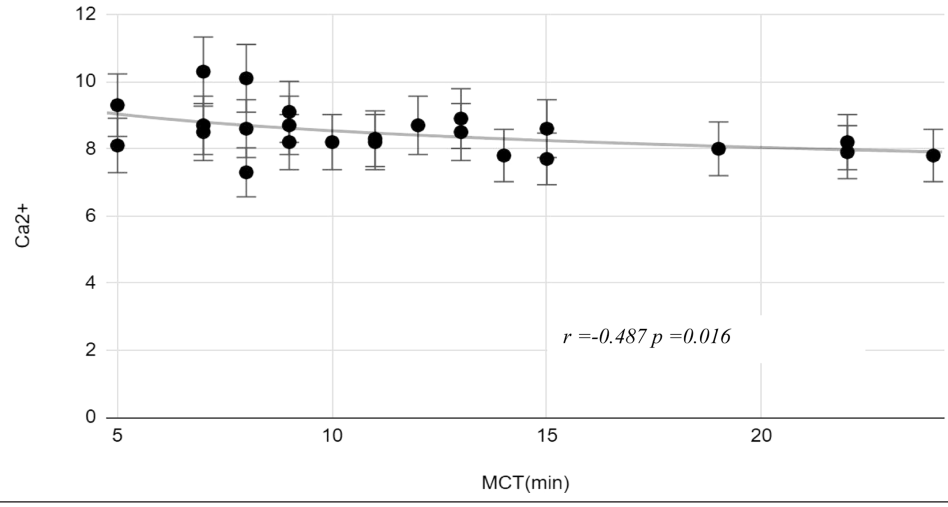

Figure 1. The Correlation of Ca^{2+} with MCTMCT, Mucociliary clearance time, Ca^{+2}, Calcium.

more systemic inflammatory state or altered immune responses that could potentially influence peritoneal defense mechanisms. Upon reviewing the literature, the study appears to be the second prospective study to investigate the relationship between peritonitis and MCC. A prospective study by Vural et al[13] conducted between May 2014 and July 2017 reported a positive correlation between peritonitis frequency and prolonged MCT. In contrast, while the study observed a numerical increase in peritonitis incidence in the patients with longer MCTs, this difference did not reach statistical significance. While the study screened patients' medical histories for peritonitis incidence within the last year, Vural et al collected 3 years of patient data. In this context, excluding factors that could influence MCT might be challenging due to the longer follow-up period. However, a higher number of peritonitis cases were diagnosed in their study. Due to the study's retrospective peritonitis data and prospective MCC measurements, it's not possible to claim a direct causal relationship for the observed association. Prospective studies are needed to determine whether peritonitis affects MCC or if impaired MCC directly contributes to the development of peritonitis.

Table 3. Correlation Analysis for MCT

Parameters (n = 24)	**R**	***P***
Age, years	0.287	.134
SBP (mmHg)	0.385	.063
DBP (mmHg)	0.137	.522
BMI	0.001	.996
Dialysis Vintagehistory (months)	−0.092	.669
UF (mL)	−0.096	.656
BUN (mg/dL)	0.34	.873
Cre (mg/dL)	0.113	.600
Na^+	0.021	.921
Ca^{2+} (mg/dL)	−0.487	.016
P_i mg/dL	0.209	.328
PTH (png/dL)	0.020	.924
CRP (mg/dL)	−0.151	.481
WBC (10^3/µL)	0.024	.911
N (10^3/µL)	−0.135	.528
L (10^3/µL)	0.287	.174
N/L	−0.172	.423
Peritonitis	0.268	.206

BMI, body mass index; BUN, blood urea nitrogen; Ca+2, calcium; Cre, creatinine; CRP, C-reactive protein; DBP, diastolic blood pressure; L, lymphocyte; N, neutrophil; Na+, sodium; N/L, neutrophil lymphocyte ratio; Pi, inorganic phosphate; PTH, parathyroid hormone; SBP, systolic blood pressure; UF, ultrafiltration; WBC, white blood cell.

In measurements conducted via the STT, the normal MCT has been previously reported as 20 minutes, as mentioned.[6] Also, the study by Kucur et al reported a mean MCT of 12.51 minutes in patients with CKD.[14] In the study, the mean clearance time for the control group was found to be 11 minutes. The inability to detect a significant difference between the patient and control groups could be attributed to the inclusion of a control group exhibiting clearance times lower than the established normal value.

Prolonged MCT was observed in hypocalcemic patients with CKD treated by PD. Cellular calcium signaling has been reported to influence inflammatory responses, mucus secretion, and MCC in the airways. Disruption in calcium signaling can lead to a prolongation of clearance time.[15]

The most significant finding of this study was the statistically significant elevation of the NLR in patients with shorter MCTs. The NLR is a well-established systemic inflammatory marker. Neutrophil degranulation and the subsequent release of inflammatory mediators perpetuate inflammation, leading to impaired MCC. Consequently, it has been hypothesized that

neutrophil-targeted therapies may offer benefits in modulating inflammation and improving MCC.[16] It is possible that chronic inflammation, potentially stemming from uremia or the PD procedure itself, could negatively impact mucociliary function. Conversely, impaired MCC might contribute to a pro-inflammatory state through increased susceptibility to (even subclinical) respiratory infections or altered immune regulation.

The lack of statistically significant differences in other clinical and laboratory parameters between the groups, despite the significant finding regarding NLR, suggests that the impact of MCT on these specific variables might be less pronounced or require larger sample sizes to detect. The probable small number of patients receiving PD necessitates multi-center studies with extensive cohorts.

The limitations of this study were identified as its single-center design, the small sample size, the reduced patient enrollment during March-June due to allergic reactions and respiratory tract infections, and the lack of optimized data on humidity and temperature levels, which could potentially influence MCC. Another significant limitation of the study is the discrepancy between the data collection methods for peritonitis and MCC. This difference in data collection prevents us from establishing a direct causal relationship between the 2 variables, underscoring the need for future longitudinal studies to explore this dynamic more thoroughly.

In conclusion, this study provides preliminary evidence suggesting a potential association between prolonged MCT and systemic inflammation, as indicated by a significantly higher NLR, in PD patients . While other clinical parameters did not show statistically significant differences, the observed trends warrant further investigation in larger, prospective studies to elucidate the underlying mechanisms and the clinical significance of these findings. Future research should also aim to explore the potential role of interventions targeting mucociliary function in improving outcomes for PD patients, particularly regarding inflammation and infection risk.

Data Availability Statement: The data that support the findings of this study are available on request from the corresponding author.

Ethics Committee Approval: Ethical committee approval was received from the Ethics Committee of Karatay University (Approval no: 025; Date: 07.03.2024).

Informed Consent: Informed consent was obtained from patients who agreed to take part in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – B.D.; Design – B.D.; Supervision – B.D.; Resources – B.D.; Materials – B.D.; Data Collection and/or Processing – B.D.; Analysis and/or Interpretation – B.D.; Literature Search – B.D.; Writing Manuscript – B.D.; Critical Review – B.D.

Declaration of Interests: The authors have no conflict of interest to declare.

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