www.mednet.gr/archives
ARCHIVES OF HELLENIC MEDICINE: ISSN 11-05-3992

ORIGINAL PAPER
ΕΡΕΥΝΗΤΙΚΗ ΕΡΓΑΣΙΑ

The association between serum calcium levels and the calcium-to-phosphate ratio and their potential impact on the incidence of peritonitis in patients undergoing peritoneal dialysis

ARCHIVES OF HELLENIC MEDICINE 2025, 42(3):347–356
ΑΡΧΕΙΑ ΕΛΛΗΝΙΚΗΣ ΙΑΤΡΙΚΗΣ 2025, 42(3):347–356

J.K. Fajar,[1,2]
A. Rifai,[3]
N. Samsu,[3]
A. Gunawan[3]

[1]Brawijaya Internal Medicine Research Center, Department of Internal Medicine, Faculty of Medicine, Universitas Brawijaya, Malang
[2]Medical Research Unit, Deka Institute, Malang
[3]Division of Nephrology & Hypertension, Department of Internal Medicine, Faculty of Medicine, Universitas Brawijaya, Malang, Indonesia

OBJECTIVE **To investigate the association between serum calcium levels and the calcium-to-phosphate ratio and the susceptibility to peritoneal dialysis (PD)-related peritonitis.** METHOD **A retrospective analysis was undertaken at Saiful Anwar General Hospital, Malang, Indonesia. Data encompassing the period from July 2019 to July 2021 were extracted from medical records utilizing a standardized pilot form. Subsequent to this, a subgroup analysis was conducted to evaluate corrected calcium employing the formula proposed by Portale, Payne, Jain, and Ferrari in relation to the risk of peritonitis associated with PD. The correlation between calcium levels, calcium-to-phosphate ratio, and the likelihood of PD-related peritonitis was examined through the multiple logistic regression analysis.** RESULTS **An analysis was conducted on 123 patients undergoing PD during the study period, with 20 instances of PD-related peritonitis observed. Serum calcium levels equal to or exceeding 8.25 mg/dL were associated with a 6.71-fold increased risk of PD-related peritonitis. Concurrently, an elevated calcium-to-phosphate ratio demonstrated an augmented risk of PD-related peritonitis. In a sub-group analysis, corrected calcium levels, determined by the formulas of Portale and Jain, exhibited superior sensitivity and specificity in predicting the incidence of PD-related peritonitis. Furthermore, the corrected calcium-to-phosphate ratio, calculated using the formula proposed by Ferrari, demonstrated the highest Youden index for predicting PD-related peritonitis.** CONCLUSIONS **Increased concentrations of calcium and an elevated calcium-to-phosphate ratio may elevate the susceptibility to PD-related peritonitis in PD patients, underscoring the significance of calcium as a key predictor for PD-related peritonitis.**

Συσχέτιση μεταξύ των επιπέδων ασβεστίου στον ορό και της σχέσης ασβεστίου προς φωσφορικό καθώς και η πιθανή επίδρασή τους στην επίπτωση της περιτονίτιδας σε ασθενείς που υποβάλλονται σε περιτοναϊκή κάθαρση

Περίληψη στο τέλος του άρθρου

Key words

Calcium
Calcium-to-phosphate ratio
Peritoneal dialysis
Peritonitis
Predictor

Submitted 12.1.2024
Accepted 16.3.2024

The inception of peritoneal dialysis (PD) occurred in 1959.[1] Peritoneal dialysis (PD) has the potential to yield favorable outcomes in individuals with end-stage renal disease by mitigating the risk of complications and enhancing overall quality of life.[2] The implementation of PD comes with various challenges, with PD-related peritonitis being one notable hurdle.[3] In accordance with global data, the frequency of PD-related peritonitis was estimated to fall within the range of 1.1 to 1.3 episodes per patient per year of treatment. Additionally, the mortality rate associated with this condition exhibited a variability from 4% to 16%.[4] The predominant challenge in the management of PD-related peritonitis resides in its multifactorial etiology, where the onset of peritonitis is intricately linked to an array of factors such as malnutrition, immunosuppression, low socioeconomic status, psychosocial determinants, and disorders pertaining to bone mineral metabolism,[5] involving the disruption of calcium homeostasis.[6]

Calcium homeostasis is a physiological process directed by hormonal activities that regulate the transport of calcium in the gut, kidney, and bone. In this context, an imbalance in calcium plays a crucial role in inducing pathological

conditions in these three areas (the gut, kidney, and bone).[7] In the context of renal disease, this pathological condition is termed chronic kidney disease-mineral bone disease (CKD-MBD), characterized by an increased risk of fractures in a negative balance and, conversely, an elevated risk of vascular calcification and cardiovascular-related deaths in a positive balance.[8] In the context of PD, there is evidence suggesting a correlation between vascular calcification and an elevated risk of peritonitis.[9] Furthermore, calcium functions as a second messenger in the signaling pathway of lymphocytes,[10] a critical cell in immunity.[11] Maintaining a balance between intracellular and extracellular calcium levels is crucial for sustaining the immune response. When intracellular calcium levels are low and extracellular calcium levels are high, it implies that lymphocytes may be in a resting state, posing an elevated risk of infection.[10] Hence, in individuals undergoing PD, a positive calcium balance theoretically poses a risk of infection, including peritonitis. Presently, there is limited evidence assessing the role of calcium in individuals with PD-related peritonitis. Therefore, the principal objective of this study was to investigate the association between calcium levels, calcium-to-phosphate ratio, and the likelihood of PD-related peritonitis.

MATERIAL AND METHOD

Study design and patients

A retrospective investigation was carried out at Saiful Anwar General Hospital in Malang, Indonesia, utilizing a total sampling method. All PD patients treated at our facility between August 2019 and July 2021, aged 18 years and above, were deemed eligible for participation in the study. Exclusion criteria encompassed individuals with a history of parathyroid hormone disorders, including adenoma or hyperplasia of the gland, and those diagnosed with multiple endocrine neoplasia syndrome. Relevant information was extracted from medical records through the use of a standardized pilot form. The study obtained approval from the local Ethical Committee of RSUD Dr Saiful Anwar hospital (no 400/033/K.3/102.7/2021), and given the retrospective nature of our data analysis, the requirement for written informed consent was exempted. Our study protocols adhered to the principles delineated in the Helsinki Declaration and were guided by the checklist outlined in Strengthening the Reporting of Observational Studies in Epidemiology (STROBE), ensuring compliance with standardized guidelines.[12] The STROBE checklist is provided in the supplementary file.[13]

Study covariates

The predictor covariates in the study comprised calcium levels and calcium-to-phosphate ratio. Additionally, a sub-group analysis was conducted to evaluate corrected calcium levels and corrected calcium-to-phosphate ratio. Corrected calcium levels were calculated following the Portale formula: calcium level+(0.8×[4-albumin]); Payne formula: calcium level+[4–serum albumin (g/dL)]; Jain formula: calcium level+0.8×[3–serum albumin (g/dL)]; and Ferrari formula: calcium level+1.6×[4–serum albumin (g/dL)]+0.56×[1.5–0.32×Pho (mg/dL)].[14]

The primary outcome measure in the study was the occurrence of PD-related peritonitis. Additionally, we conducted an assessment of the association between the incidence of PD-related peritonitis and various patient characteristics, including age, gender, body weight, body height, mid-upper arm circumference (MUAC), body mass index (BMI), educational level, smoking history, comorbidities (diabetes mellitus, hypertension, renal stone, renal cyst, chronic lung disease, ischemic heart disease, and stroke), as well as laboratory parameters (hemoglobin levels, leukocyte levels, hematocrit levels, platelet levels, neutrophil levels, lymphocyte levels, urea levels, creatinine levels, sodium levels, potassium levels, and chloride levels).

Statistical analysis

To appraise the normality of numeric covariates, we applied the Kolmogorov-Smirnov test. A p-value surpassing 0.05 was interpreted as indicative of a normal distribution. Employing multiple logistic regression analysis, we assessed the homogeneity of demographic data, clinical characteristics, and laboratory data among distinct groups. A p-value exceeding 0.05 denoted homogeneous distribution of data across these groups. We employed multiple logistic regression with the enter method to determine the association between calcium levels, calcium-to-phosphate ratio, and the risk of PD-related peritonitis. In our analysis, a significance level of $p<0.05$ was considered statistically significant. To ascertain effect estimates, we calculated the odds ratio (OR) and 95% confidence interval (95% CI) for categorical covariates, while for numeric covariates, we determined the mean difference (MD). Receiver Operating Characteristic (ROC) analysis was employed to ascertain the optimal thresholds for calcium levels, corrected calcium, and calcium-to-phosphate ratio. The cut-off point corresponding to the highest Youden index was considered the optimal threshold. The Statistical Package of Social Sciences software (SPSS Inc, Chicago, IL), version 17.0 was utilized for data analysis.

RESULTS

Patients' characteristics

A total of 239 PD patients were initially enrolled, with 116 individuals subsequently excluded due to incomplete medical records, specifically pertaining to the absence of calcium level assessments. Ultimately, a refined pool of 123 PD patients underwent analysis, and 20 individuals

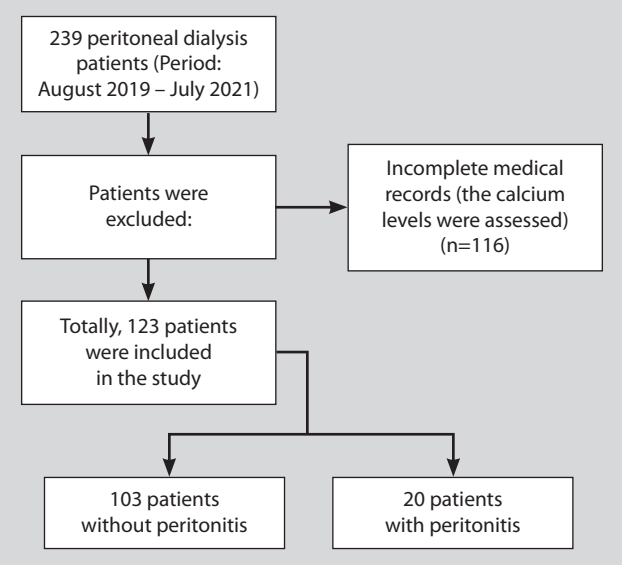

Figure 1. A flow chart of patient selection in the present study.

(16.3%) developed peritonitis. In our study, figure 1 elucidates the procedural flowchart outlining the meticulous patient selection process. Additionally, table 1 presents the intricate characteristics of the patients incorporated into our analytical framework. Comprehensive details of the data can be found in the supplementary file.[13]

Association of calcium level and calcium-to-phosphate ratio and the risk of PD-related peritonitis

Our results revealed that among PD patients, those with elevated calcium levels exhibited a heightened risk of peritonitis (MD: 0.59; 95% CI: 0.13; 1.05) (fig. 2A). Furthermore, an increased risk of peritonitis was noted in PD patients with an elevated calcium-to-phosphate ratio (MD: 0.41; 95% CI: 0.12; 0.71) (fig. 3A). In a sub-group analysis employing the corrected calcium calculation formula, our findings indicated that heightened corrected calcium levels derived from the formulas of Portale (fig. 2B), Payne (fig. 2C), Jain (fig. 2D), and Ferrari (fig. 2E) were linked to an elevated risk of peritonitis among PD patients (fig. 4A). Regarding the corrected calcium-to-phosphate ratio, our results substantiated that an elevated risk of peritonitis in PD patients was observed in individuals with an increased corrected calcium-to-phosphate ratio, calculated using the formulas of Portale (fig. 3B), Payne (fig. 3C), Jain (fig. 3D), and Ferrari (fig. 3E). The MDs for these formulations were 0.46, 0.48, 0.44, and 0.55, respectively. The summary of the association between calcium levels and calcium-to-phosphate ratio and the risk of PD-related peritonitis is outlined in table 2.

The cut-off point of calcium level and calcium-to-phosphate ratio and the risk of PD-related peritonitis

Our data implies that among PD patients, those with calcium levels ≥8.25 mg/dL and a calcium-to-phosphate ratio ≥1.88 exhibit elevated risks of peritonitis, with odds ratios of 6.71 and 2.55, respectively, compared to individuals with calcium levels <8.25 mg/dL and a calcium-to-phosphate ratio <1.88. In the subgroup analysis, elevated levels of corrected calcium, calculated using the formulas of Portale, Payne, Jain, and Ferrari, with thresholds of ≥8.74 mg/dL, ≥8.84 mg/dL, ≥7.94 mg/dL, and ≥8.94 mg/dL, respectively, were linked to an increased risk of PD-related peritonitis (fig. 4B). Among these formulas, the Portale and Jain formulations exhibited the highest Youden index (J: 144.34). The corrected calcium-to-phosphate ratio, as determined by the Portale (≥2.26), Payne (≥2.31), Jain (≥2.08), and Ferrari (≥2.14) formulas, demonstrated an association with an elevated risk of PD-related peritonitis (fig. 4D). Notably, the Ferrari formula yielded the highest Youden index (J: 124.58). The overview of the optimal cut-off points for calcium and calcium-to-phosphate ratio in forecasting the risk of PD-related peritonitis is delineated in table 3.

DISCUSSION

Our investigation revealed that calcium levels and the calcium-to-phosphate ratio could serve as significant indicators of peritonitis in PD patients. These findings align with previous study, which emphasized the elevation of calcium levels as a crucial characteristic in peritonitis among individuals undergoing PD.[15] Another study confirmed that higher risk of peritoneal calcification, a common condition associated with PD-related peritonitis[16] was found in patients with increased levels of calcium.[17] Additionally, heightened calcium levels, reduced phosphate levels, and diminished parathyroid hormone levels have been shown to be pivotal factors in the progression of PD-related peritonitis.[18] Nonetheless, a study indicated that heightened calcium levels were linked to the accelerated deterioration of renal function in hemodialysis patients.[19] Hence, it is comprehensible that elevated levels of calcium and calcium-to-phosphate ratio were more prevalent in patients experiencing PD-related peritonitis in our investigation.

In the sub-group analysis, the corrected calcium levels following the Portale and Jain formulas exhibited the highest Youden index, indicating that these formulas are deemed to have the best sensitivity and specificity in predicting the incidence of peritonitis among patients with PD. Conversely, for the corrected calcium-to-phosphate ra-

Table 1. Baseline characteristics of patients included in our study.

Characteristics	Peritonitis (n=20) n (%)	Non-peritonitis (n=103) n (%)	p-value
Age (years), mean±SD	42.0±18.0	43.0±14	0.7810
Male	16 (80.0)	68 (66.0)	0.2260
BW (kg), mean±SD	59.1±18.3	59.1±11.9	1.0000
BH (cm), mean±SD	157.0±12.9	160.0±10.5	0.2610
MUAC (cm), mean±SD	27.3±1.6	27.0±3.0	0.6640
BMI (kg/m^2), mean±SD	23.4±5.7	23.0±4.3	0.7190
Nutritional status (BMI)			
Severe malnutrition	3 (15.0)	3 (2.9)	0.0390
Malnutrition	2 (10.0)	10 (9.7)	0.9680
Normal	6 (30.0)	63 (61.2)	0.0140
Overweight	4 (20.0)	14 (13.6)	0.4610
Obesity	5 (25.0)	13 (12.6)	0.1600
Educational levels			
None	1 (5.0)	3 (2.9)	0.6340
Elementary school	8 (40.0)	14 (13.6)	0.0070
Junior high school	4 (20.0)	17 (16.5)	0.7040
Senior high school	6 (30.0)	45 (43.7)	0.2600
University	1 (5.0)	24 (23.3)	0.0960
Smoking	3 (15.0)	26 (25.2)	0.3300
Comorbidity			
Diabetes mellitus	6 (30.0)	26 (25.2)	0.6580
Hypertension	20 (100.0)	103 (100.0)	1.0000
Renal stone	5 (25.0)	17 (16.5)	0.3680
Renal cyst	2 (10.0)	5 (4.9)	0.3740
Chronic lung disease	1 (5.0)	9 (8.7)	0.5810
Ischemic heart disease	1 (5.0)	10 (9.7)	0.5080
Stroke	0 (0.0)	4 (3.9)	0.6830
Laboratory findings			
Hemoglobin (g/dL), mean±SD	8.8±1.5	8.7±1.4	0.7730
Leukocyte (cells/µL), mean±SD	8156.3±2013.9	7982.9±2847.9	0.7950
Hematocrit (%), mean±SD	27.7±7.2	25.1±5.2	0.0560
Platelet (cells/µL), mean±SD	268100.0±84208.0	252456.0±80518.0	0.4300
Neutrophile, mean±SD	5615.5±1851.6	5767.3±2765.9	0.8140
Lymphocyte, mean±SD	1527.0±595.1	1285.5±462.7	0.0420
NLR, mean±SD	4.2±2.1	5.5±4.8	0.2360
PLR, mean±SD	192.2±80.8	220.6±104.9	0.2520
Urea (mg/dL), mean±SD	94.4±37.2	112.4±56.9	0.1750
Creatinine (mg/dL), mean±SD	9.5±3.7	12.5±11.3	0.2410
Sodium (mmoL/L), mean±SD	133.8±2.8	133.6±4.9	0.8600
Potassium (mmoL/L), mean±SD	3.7±0.6	4.0±1.0	0.1950
Chloride (mmoL/L), mean±SD	102.7±4.8	100.2±11.2	0.3280

SD: Standard deviation, BW: Body weight, BH: Body height, MUAC: Mid-upper arm circumference, BMI: Body mass index, NLR: Neutrophil-to-lymphocyte ratio, PLR: Platelet-to-lymphocyte ratio

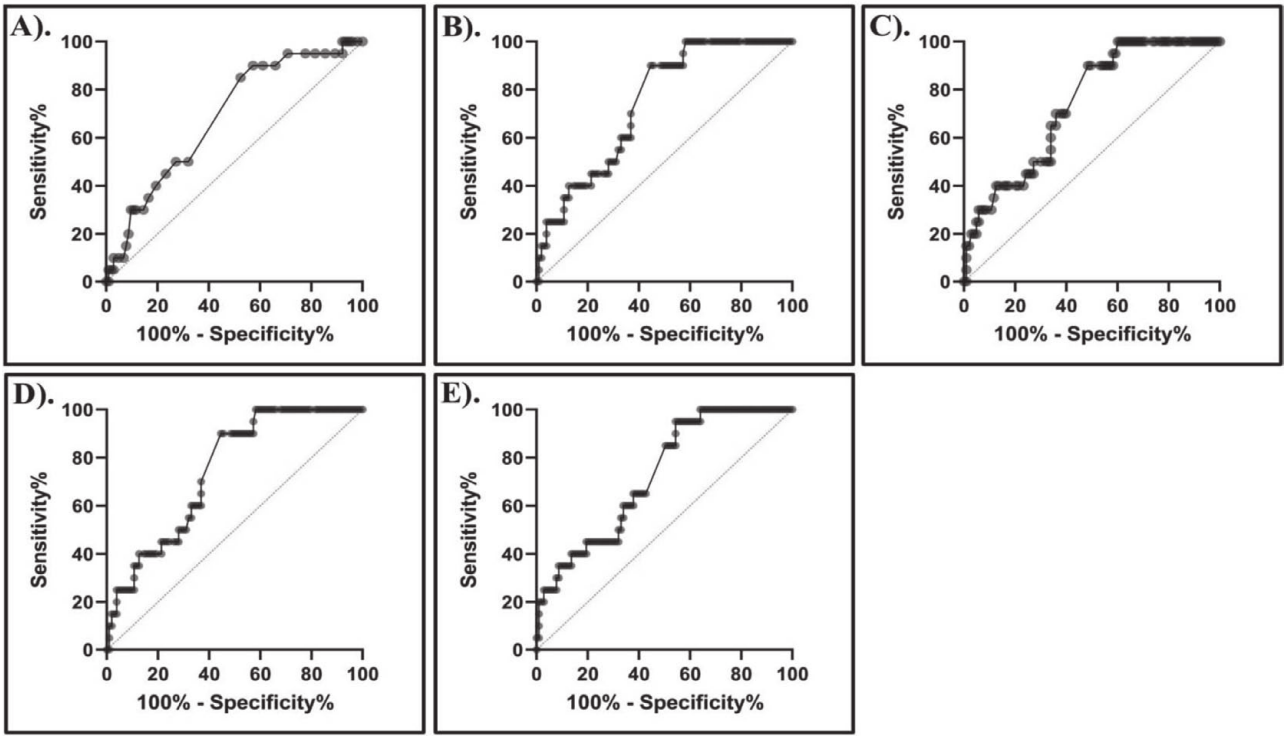

Figure 2. The Receiver Operating Characteristic (ROC) between calcium levels and the risk of peritonitis among patients with peritoneal dialysis. (A) Calcium levels. (B) Corrected calcium levels (Portale). (C) Corrected calcium levels (Payne). (D) Corrected calcium levels (Jain). (E) Corrected calcium levels (Ferrari).

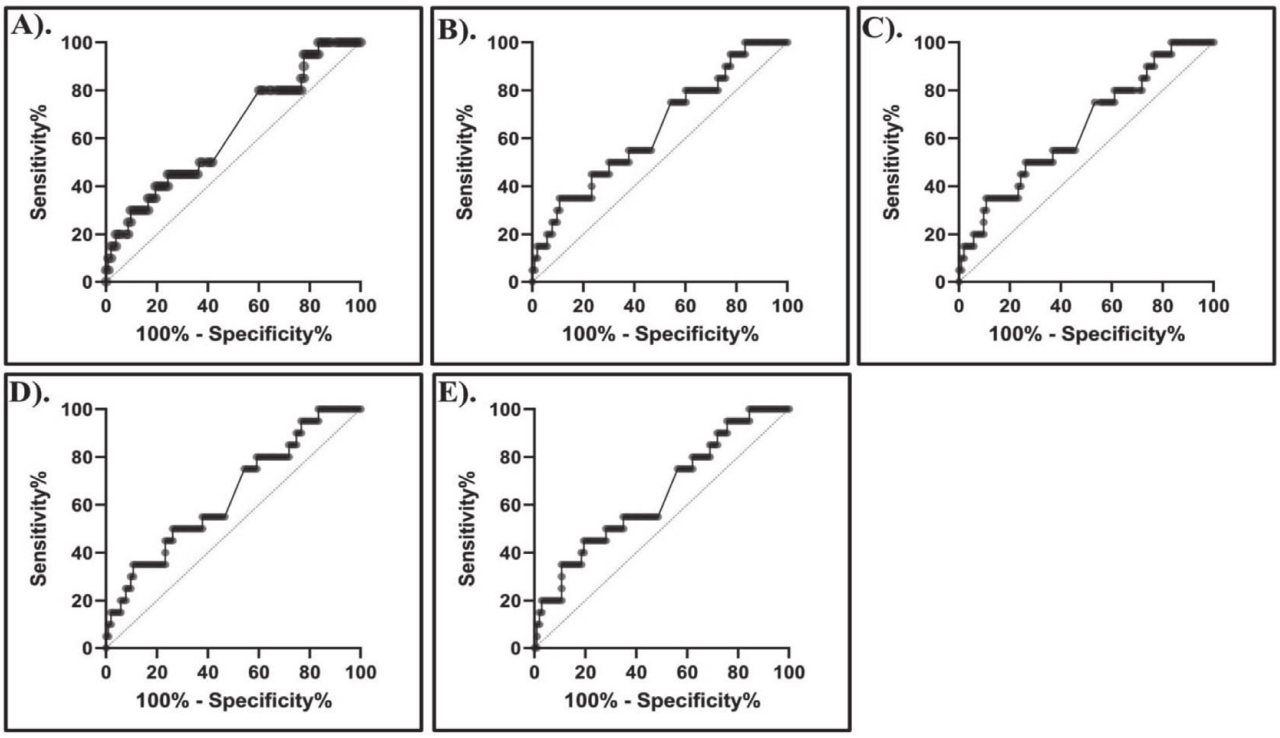

Figure 3. The Receiver Operating Characteristic (ROC) between calcium-to-phosphate ratio and the risk of peritonitis among patients with peritoneal dialysis. (A) Calcium-to-phosphate ratio. (B) Corrected calcium (Portale)-to-phosphate ratio. (C) Corrected calcium (Payne)-to-phosphate ratio. (D) Corrected calcium (Jain)-to-phosphate ratio. (E) Corrected calcium (Ferrari)-to-phosphate ratio.

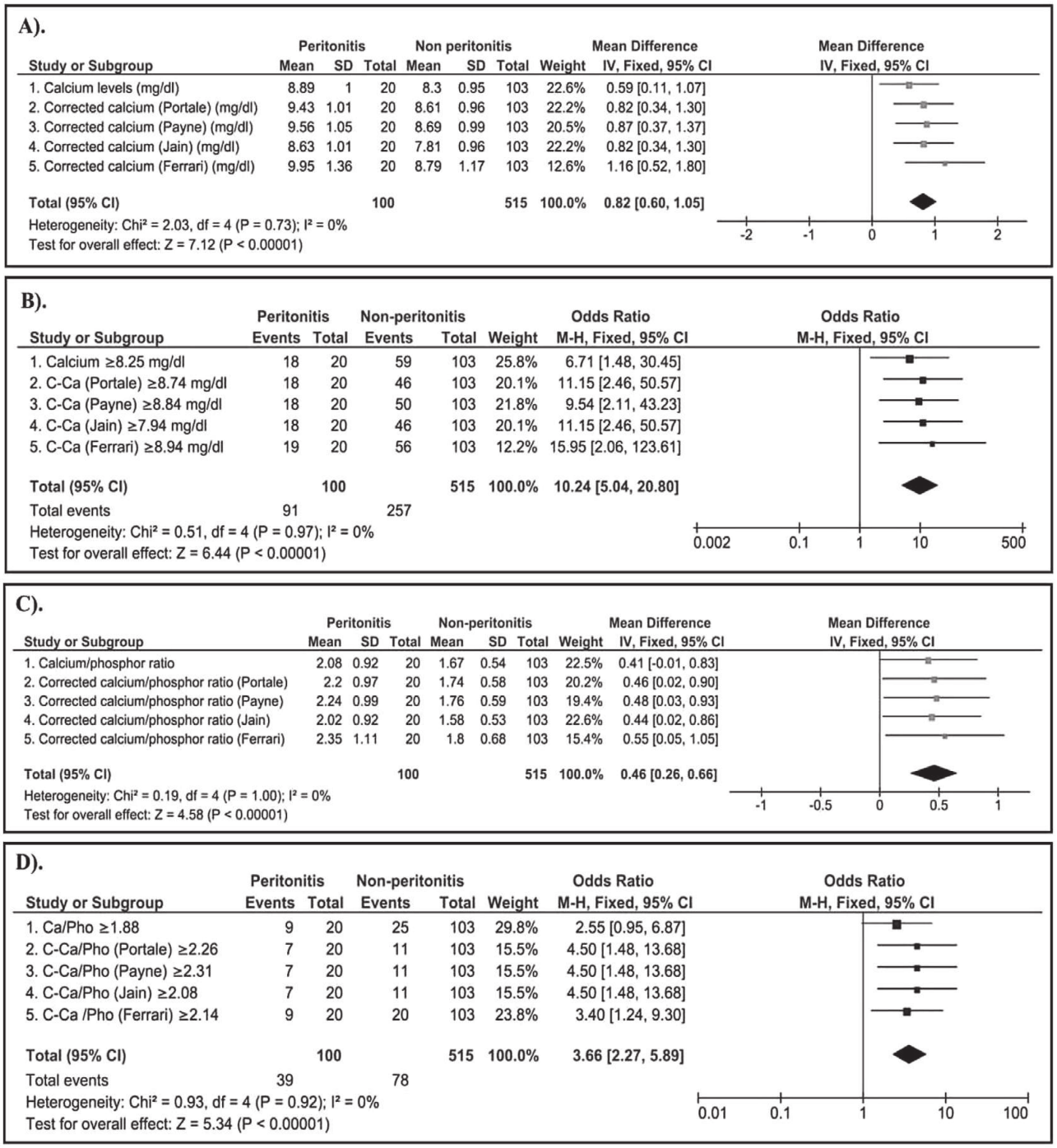

Figure 4. The cumulative comparison between the potential risk of peritonitis and the levels of calcium (A), calcium level cut-off (B), calcium-to-phosphate ratio (C), and the cut-off of calcium-to-phosphate ratio (D).

tio, the Ferrari formula demonstrated the highest Youden index. These conflicting findings may necessitate further exploration. However, the perspective of previous study should also be considered to determine which formula is suitable for application in the context of renal failure. A study by Kaku et al evaluated the Portale, Payne, Jain, and Ferrari formulas in hemodialysis patients and determined that the Ferrari formula had the highest accuracy in predicting actual calcium levels in individuals with advanced chronic kidney disease.[14] Additionally, previous investigations have suggested that the calculation of corrected calcium levels should encompass not only

Table 2. The summary of the association between calcium levels and the risk of peritonitis among patients with peritoneal dialysis.

Parameters	Peritonitis (n=20) Mean±SD	Non-peritonitis (n=103) Mean±SD	MD	95% CI	p-value
Calcium (mg/dL)	8.89±1.00	8.30±0.95	0.59	0.13, 1.05	0.0120
Corrected calcium (Portale) (mg/dL)	9.43±1.01	8.61±0.96	0.82	0.36, 1.28	0.0010
Corrected calcium (Payne) (mg/dL)	9.56±1.05	8.69±0.99	0.87	0.39, 1.35	0.0001
Corrected calcium (Jain) (mg/dL)	8.63±1.01	7.81±0.96	0.82	0.36, 1.28	0.0010
Corrected calcium (Ferrari) (mg/dL)	9.95±1.36	8.79±1.17	1.16	0.58, 1.74	0.0001
Calcium-to-phosphate ratio	2.08±0.92	1.67±0.54	0.41	0.12, 0.71	0.0060
Corrected calcium-to-phosphate ratio (Portale)	2.2±0.97	1.74±0.58	0.46	0.15, 0.78	0.0040
Corrected calcium-to-phosphate ratio (Payne)	2.24±0.99	1.76±0.59	0.48	0.16, 0.80	0.0030
Corrected calcium-to-phosphate ratio (Jain)	2.02±0.92	1.58±0.53	0.44	0.15, 0.73	0.0030
Corrected calcium-to-phosphate ratio (Ferrari)	2.35±1.11	1.8±0.68	0.55	0.18, 0.92	0.0030

SD: Standard deviation, MD: Mean difference, CI: Confidence interval

Table 3. Sub-group analysis of the association between the calcium levels cut-off and the risk of peritonitis among patients with peritoneal dialysis.

Parameters	Peritonitis (n=20)	Non-peritonitis (n=103)	Sensitivity (%)	Specificity (%)	Youden index	OR	95% CI	p-value
The cut-off of calcium levels								
Calcium (≥8.25 versus <8.25 mg/dL)	18 (90.0)	59 (57.3)	90.00	42.72	131.72	6.71	1.48, 30.45	0.0140
Corrected calcium (Portale) (≥8.74 versus <8.74 mg/dL)	18 (90.0)	46 (44.7)	90.00	55.34	144.34	11.15	2.46, 50.57	0.0020
Corrected calcium (Payne) (≥8.84 versus <8.84 mg/dL)	18 (90.0)	50 (48.5)	90.00	51.46	140.46	9.54	2.11, 43.23	0.0030
Corrected calcium (Jain) (≥7.94 versus <7.94 mg/dL)	18 (90.0)	46 (44.7)	90.00	55.34	144.34	11.15	2.46, 50.57	0.0020
Corrected calcium (Ferrari) (≥8.94 versus <8.94 mg/dL)	19 (95.0)	56 (54.4)	95.00	45.63	139.63	15.95	2.06–123.61	0.0080
The cut-off of calcium-to-phosphate ratio								
Calcium-to-phosphate ratio (≥1.88 versus <1.88)	9 (45.0)	25 (24.3)	45.00	75.73	119.73	2.55	0.95–6.87	0.0630
Corrected calcium-to-phosphate ratio (Portale) (≥2.26 versus <2.26)	7 (35.0)	11 (10.7)	35.00	89.32	123.32	4.50	1.48–13.69	0.0080
Corrected calcium-to-phosphate ratio (Payne) (≥2.31 versus <2.31)	7 (35.0)	11 (10.7)	35.00	89.32	123.32	4.50	1.48–13.69	0.0080
Corrected calcium-to-phosphate ratio (Jain) (≥2.08 versus <2.08)	7 (35.0)	11 (10.7)	35.00	89.32	123.32	4.50	1.48–13.69	0.0080
Corrected calcium-to-phosphate ratio (Ferrari) (≥2.14 versus <2.14)	9 (45.0)	20 (19.4)	45.00	80.58	124.58	3.40	1.24–9.30	0.0170

Data were presented in n (%)

OR: Odds ratio, CI: Confidence interval

albumin but also phosphate, particularly in individuals with chronic renal disease.[20] In this context, the Ferrari formula may be considered as the appropriate choice for calculating corrected calcium levels in individuals with renal failure.

The rationale behind the involvement of calcium in the pathogenesis of PD-related peritonitis remains unclear. Various potential mechanisms could be postulated. Initially, the theory of systemic immune dysregulation could establish a link between calcium levels and the susceptibility to PD peritonitis.[21] It has been documented that heightened levels of calcium, along with elevated

parathyroid hormone levels, may influence the intracellular signaling of immune cells. Consequently, this could contribute to a diminished phagocytic capability of polymorphonuclear cells.[22] Furthermore, elevated calcium levels and parathyroid hormone have been implicated in influencing the malnutrition-inflammation complex, thereby heightening susceptibility to infection.[23] Secondly, the potential link between increased calcium levels and the risk of PD-related peritonitis may be attributed to the theory of vascular calcification. Elevated calcium levels may contribute to the excessive deposition of calcium in the vascular system, affecting both the intimal and medial layers.[24,25] In individuals undergoing PD, this condition could be characterized as peritoneal calcification.[9] In this context, a heightened inflammatory response may ensue within the peritoneum, involving intricate interactions among vascular smooth muscle cells, interleukin 6, and tumor necrosis factor alpha. The accumulation of these pro-inflammatory cytokines is acknowledged to instigate an inflammatory cascade in the peritoneal milieu, thereby precipitating peritonitis.[26]

In the light of current knowledge, our study stands as a pioneering exposition elucidating the contributory role of calcium in forecasting the proclivity towards peritonitis in patients subjected to PD. The discerned significance of calcium levels as a cardinal metric in gauging susceptibility to PD-related peritonitis underscores the potential for its integration into prognostic models for outcome prediction in PD patients. Furthermore, the utilization of the Ferrari formula for deriving corrected calcium levels in the calculation of corrected calcium-to-phosphate ratio may augment prognostic precision for peritonitis in the PD patient. The study furnishes delineated cut-off thresholds for calcium levels and calcium-to-phosphate ratio, wherein the identified cut-off point for calcium levels, notably below the upper limit of normal, accentuates the necessity for meticulous calcium level monitoring to mitigate peritonitis risk in PD patients. Nonetheless, it is imperative to underscore the need for further investigations across diverse geographical contexts to validate these precise cut-off points scientifically.

This study is accompanied by several limitations that merit detailed consideration. Firstly, the omission of relevant confounding factors, such as parathyroid hormone (PTH), vitamin D, and metabolic parameters, from the analysis introduces a notable constraint, limiting the comprehensive evaluation of calcium levels. Secondly, the relatively modest sample size and disproportionate distribution between case and control groups raise concerns regarding the potential for spurious positive outcomes. Thirdly, the retrospective study design imparts a lower level of evidence, necessitating the implementation of a prospective study with a larger sample size to enhance evidentiary robustness. Lastly, the reliance on medical records for data retrieval introduces a potential for information gaps, probably affecting the precision of the study's conclusions.

In conclusion, our study underscores the significance of considering calcium levels as a key predictive factor in the development of PD-related peritonitis. The utilization of the Ferrari formula for calculating corrected calcium levels, particularly in the context of determining the corrected calcium-to-phosphate ratio, emerges as a judicious approach due to its superior sensitivity and specificity in predicting the incidence of PD-related peritonitis. These findings contribute valuable insights into the prognostic landscape for PD patients, warranting further exploration and validation in diverse clinical settings.

AUTHOR CONTRIBUTION

Idea/concept: JKF. Design: JKF. Control/supervision: AR, NS, AG. Data collection/processing: JKF. Extraction/analysis/interpretation: JKF. Literature review: JKF. Writing the article: JKF. Critical review: AR, NS, AG. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

ΠΕΡΙΛΗΨΗ

Συσχέτιση μεταξύ των επιπέδων ασβεστίου στον ορό και της σχέσης ασβεστίου προς φωσφορικό καθώς και η πιθανή επίδρασή τους στην επίπτωση της περιτονίτιδας σε ασθενείς που υποβάλλονται σε περιτοναϊκή κάθαρση

J.K. FAJAR,[1,2] A. RIFAI,[3] N. SAMSU,[3] A. GUNAWAN[3]

[1]Brawijaya Internal Medicine Research Center, Department of Internal Medicine, Faculty of Medicine, Universitas Brawijaya, Malang, [2]Medical Research Unit, Deka Institute, Malang, [3]Division of Nephrology and Hypertension, Department of Internal Medicine, Faculty of Medicine, Universitas Brawijaya, Malang, Ινδονησία

Αρχεία Ελληνικής Ιατρικής 2025, 42(3):347–356

ΣΚΟΠΟΣ Η διερεύνηση της συσχέτισης μεταξύ των επιπέδων ασβεστίου στον ορό και της αναλογίας ασβεστίου προς φωσφορικό, καθώς και της πιθανής επίδρασής τους στην περιτονίτιδα που σχετίζεται με περιτοναϊκή κάθαρση (ΠΚ). **ΥΛΙΚΟ-ΜΕΘΟΔΟΣ** Διενεργήθηκε μια αναδρομική ανάλυση στο Γενικό Νοσοκομείο Saiful Anwar, Malang, της Ινδονησίας. Τα δεδομένα κάλυπταν την περίοδο Ιουλίου του 2019 έως τον Ιούλιο του 2021 και εξήχθησαν από ιατρικά αρχεία χρησιμοποιώντας ένα τυποποιημένο πιλοτικό έντυπο. Στη συνέχεια, διεξήχθη μια ανάλυση για την αξιολόγηση του διορθωμένου ασβεστίου εφαρμόζοντας τον τύπο που προτείνεται από τους Portale, Payne, Jain και Ferrari σε σχέση με τον κίνδυνο εμφάνισης περιτονίτιδας η οποία σχετίζεται με ΠΚ. Η συσχέτιση μεταξύ των επιπέδων ασβεστίου, της αναλογίας ασβεστίου προς φωσφορικό και της πιθανότητας περιτονίτιδας σχετιζόμενης με ΠΚ εξετάστηκε μέσω ανάλυσης πολλαπλής λογιστικής παλινδρόμησης**. ΑΠΟΤΕΛΕΣΜΑΤΑ** Μελετήθηκαν 123 ασθενείς που υποβλήθηκαν σε ΠΚ κατά την περίοδο της μελέτης, με 20 παρατηρημένες περιπτώσεις περιτονίτιδας σχετιζόμενης με ΠΚ. Επίπεδα ασβεστίου στον ορό ≥8,25 mg/dL συσχετίστηκαν με 6,71 φορές αυξημένο κίνδυνο περιτονίτιδας σχετιζόμενης με ΠΚ. Ταυτόχρονα, η αυξημένη αναλογία ασβεστίου προς φωσφορικό έδειξε αυξημένο κίνδυνο περιτονίτιδας σχετιζόμενης με ΠΚ. Σε μια ανάλυση υποομάδας, τα διορθωμένα επίπεδα ασβεστίου, που προσδιορίστηκαν από τους τύπους Portale και Jain, έδειξαν μεγαλύτερη ευαισθησία και ειδικότητα στην πρόβλεψη της συχνότητας περιτονίτιδας που σχετίζεται με ΠΚ. Επί πλέον, η διορθωμένη αναλογία ασβεστίου προς φωσφορικό, που υπολογίστηκε εφαρμόζοντας τον τύπο που προτείνει η Ferrari, έδειξε υψηλότερο δείκτη Youden για την πρόβλεψη περιτονίτιδας σχετιζόμενης με ΠΚ. **ΣΥΜΠΕΡΑΣΜΑΤΑ** Αυξημένες συγκεντρώσεις ασβεστίου και αυξημένη αναλογία ασβεστίου προς φωσφορικό μπορεί να αυξήσουν την ευαισθησία σε περιτονίτιδα σχετιζόμενη με ΠΚ σε ασθενείς με ΠΚ, υπογραμμίζοντας τη σημασία του ασβεστίου ως βασικού προγνωστικού παράγοντα για περιτονίτιδα που σχετίζεται με ΠΚ.

Λέξεις ευρετηρίου: Ασβέστιο, Περιτοναϊκή κάθαρση, Περιτονίτιδα, Πρόγνωση, Σχέση ασβεστίου-φωσφόρου

References

1. BLAGG CR. The early history of dialysis for chronic renal failure in the United States: A view from Seattle. *Am J Kidney Dis* 2007, 49:482–496
2. CHUASUWAN A, POORIPUSSARAKUL S, THAKKINSTIAN A, INGSATHIT A, PATTANAPRATEEP O. Comparisons of quality of life between patients underwent peritoneal dialysis and hemodialysis: A systematic review and meta-analysis. *Health Qual Life Outcomes* 2020, 18:191
3. ALWAKEEL JS, ALSUWAIDA A, ASKAR A, MEMON N, USAMA S, ALGHONAIM M ET AL. Outcome and complications in peritoneal dialysis patients: A five-year single center experience. *Saudi J Kidney Dis Transpl* 2011, 22:245–251
4. SZETO CC. Peritonitis rates of the past thirty years: From improvement to stagnation. *Perit Dial Int* 2014, 34:151–153
5. KERSCHBAUM J, KÖNIG P, RUDNICKI M. Risk factors associated with peritoneal-dialysis-related peritonitis. *Int J Nephrol* 2012, 2012:483250
6. PAZIANAS M, MILLER PD. Current understanding of mineral and bone disorders of chronic kidney disease and the scientific grounds on the use of exogenous parathyroid hormone in its management. *J Bone Metab* 2020, 27:1–13
7. KEUNG L, PERWAD F. Vitamin D and kidney disease. *Bone Rep* 2018, 9:93–100
8. GALLANT KMH, SPIEGEL DM. Calcium balance in chronic kidney disease. *Curr Osteoporos Rep* 2017, 15:214–221
9. PALOIAN NJ, GIACHELLI CM. A current understanding of vascular calcification in CKD. *Am J Physiol Renal Physiol* 2014, 307:F891–F900
10. VIG M, KINET JP. Calcium signaling in immune cells. *Nat Immunol* 2009, 10:21–27
11. LENEY-GREENE MA, BODDAPATI AK, SU HC, CANTOR JR, LENARDO MJ. Human plasma-like medium improves T lymphocyte activation. *iScience* 2020, 23:100759
12. VON ELM E, ALTMAN DG, EGGER M, POCOCK SJ, GØTZSCHE PC,

VANDENBROUCKE JP ET AL. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: Guidelines for reporting observational studies. *Br Med J* 2007, 335:806–808

13. FAJAR JK. Supplementary files: The association between calcium levels and calcium-to phosphor ratio and the risk of peritonitis among patients with peritoneal dialysis. *Figshare* 2021, 1:1
14. KAKU Y, OOKAWARA S, MIYAZAWA H, ITO K, UEDA Y, HIRAI K ET AL. Approximation of corrected calcium concentrations in advanced chronic kidney disease patients with or without dialysis therapy. *Nephron Extra* 2015, 5:39–49
15. RODRIGUEZ-OSORIO L, FERNANDEZ-FERNANDEZ B, MARTIN-CLEARY C, ORTIZ A. Increasing serum calcium levels and recent return from transplantation as clues to the tuberculous nature of refractory peritoneal dialysis peritonitis. *J Postgrad Med* 2014, 60:200–201
16. AGARWAL A, YEH BM, BREIMAN RS, QAYYUM A, COAKLEY FV. Peritoneal calcification: Causes and distinguishing features on CT. *AJR Am J Roentgenol* 2004, 182:441–445
17. HUANG JW, LIEN YC, YANG CY, LIU KL, FANG CC, WU CK ET AL. High peritoneal KT/V and peritonitis rates are associated with peritoneal calcification. *PLoS One* 2013, 8:e71636
18. LIAO CT, ZHENG CM, LIN YC, WU MY, LIN YF, HSU YH ET AL. Aberrant serum parathyroid hormone, calcium, and phosphorus as risk factors for peritonitis in peritoneal dialysis patients. *Sci Rep* 2021, 11:1171
19. JANMAAT CJ, VAN DIEPEN M, GASPARINI A, EVANS M, QURESHI AR, ÄRNLÖV J ET AL. Lower serum calcium is independently associated with CKD progression. *Sci Rep* 2018, 8:5148
20. KAKU Y, OOKAWARA S, MIYAZAWA H, ITO K, UEDA Y, HIRAI K ET AL. New method for the approximation of corrected calcium concentrations in chronic kidney disease patients. *Ther Apher Dial* 2016, 20:46–52
21. HAUSER AB, STINGHEN AEM, KATO S, BUCHARLES S, AITA C, YUZAWA Y ET AL. Characteristics and causes of immune dysfunction related to uremia and dialysis. *Perit Dial Int* 2008, 28:S183–S187
22. PERRY HM 3rd, CHAPPEL JC, BELLORIN-FONT E, TAMAO J, MARTIN KJ, TEITELBAUM SL. Parathyroid hormone receptors in circulating human mononuclear leukocytes. *J Biol Chem* 1984, 259:5531–5535
23. DUKKIPATI R, KOVESDY CP, COLMAN S, BUDOFF MJ, NISSENSON AR, SPRAGUE SM ET AL. Association of relatively low serum parathyroid hormone with malnutrition-inflammation complex and survival in maintenance hemodialysis patients. *J Ren Nutr* 2010, 20:243–254
24. RIVARA MB, RAVEL V, KALANTAR-ZADEH K, STREJA E, LAU WL, NISSENSON AR ET AL. Uncorrected and albumin-corrected calcium, phosphorus, and mortality in patients undergoing maintenance dialysis. *J Am Soc Nephrol* 2015, 26:1671–1681
25. CHEN NX, MOE SM. Vascular calcification: pathophysiology and risk factors. *Curr Hypertens Rep* 2012, 14:228–237
26. JONO S, SHIOI A, IKARI Y, NISHIZAWA Y. Vascular calcification in chronic kidney disease. *J Bone Miner Metab* 2006, 24:176–181

Corresponding author:

J.K. Fajar, Brawijaya Internal Medicine Research Center, Department of Internal Medicine, Faculty of Medicine, Universitas Brawijaya, Malang 65145, Indonesia
e-mail: gembyok@gmail.com