Peritoneal dialysate effluent and serum CA125 concentrations in stable peritoneal dialysis patients

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ABSTRACT

INTRODUCTION: CA125 in peritoneal dialysis (PD) effluent dialysate has been used as a surrogate biomarker for the health of the peritoneum in PD patients. However CA125 is synthesised by epithelial cells and as such is not specific for the peritoneum, and most studies have only measured peritoneal CA125, without serumCA125 values. As such we wished to determine the factors which influenced PD effluent CA125 in a large contemporaneous cohort.

METHODS: We measured dialysate effluent CA125 in PD patients attending for routine assessment of peritoneal membrane function with a peritoneal equilibration test (PET), with corresponding serum CA125.

RESULTS: Serum and dialysate CA125 were measured in 205 PD patients; 59.0 ±16.8 years, median PD treatment 3 (2-20) months, 59% male, 42.4% diabetic, with 31.2% treated by continuous ambulatory peritoneal dialysis, 22% by automated overnight peritoneal dialysis cycler (APD) and 46.8% by APD with a day time exchange. The median serum CA125 was 21 (13-38) U/ml, with an effluent 4 hour PD PET effluent of 20 (11.5-36.5) U/ml. PET PD effluent dialysate was associated with PET dialysate total protein (β 12.9,$p<0.001$), serum CA125 (β 0.109, $p=0.002$), residual renal function (β 0.53,$p=0.018$) and age (β 0.145, $p=0.042$) and negatively with the number of PD cycles/day (β -2.19, $p=0.001$). There was no association with prior peritonitis episodes.

CONCLUSION: PD effluent CA125 concentrations were associated with peritoneal protein losses and increased by the usage of higher glucose dialysates to compensate for loss of residual renal function.

INTRODUCTION

The peritoneum is lined by a single layer of epithelial cells, which are protected by a mucous barrier formed from a combination of secreted and transmembrane highly glycosylated glycoproteins which create a hydrophilic, lubricating environment protecting the apical cell surface with a mucous coating from foreign particles and invading bacteria. Cancer antigen 125 (CA125), also termed Mucin 16, is the largest of the transmembrane glycoproteins, and binds to mesothelin, a glycophosphatidylinositol glycoprotein, expressed by the peritoneal mesothelium.

In routine clinical practice serum CA125 is used both as a screening test for ovarian cancer, and also to monitor the response to chemotherapy. However as CA125 is produced by the cells lining the peritoneum, effluent dialysate CA125 has been proposed to reflect mesothelial cell mass in stable peritoneal dialysis (PD) patients [1,2]. However inflammation within the peritoneal cavity will potentially cause an increase in dialysate CA125 concentrations and some reports have reported that effluent CA125 concentrations can increase during an episode of PD peritonitis and then fall with resolution of the infection [3,4], although this has not been confirmed in all studies [5].

More recently peritoneal dialysate effluent CA125 has been used as a biomarker of the general health of peritoneal epithelium, with reports of falling or low CA125

concentrations in patients who develop encapsulating peritoneal sclerosis [6,7], and increasing peritoneal effluent CA125 concentrations when patients were switched from standard peritoneal dialysates to more bio-compatible solutions [8].

These studies have reported on peritoneal dialysate effluent concentrations or production rates, but did not report on peritoneal CA125 in relation to serum concentrations. It has been assumed that peritoneal dialysate effluent CA125 is predominantly produced within the peritoneum, with minimal contribution from that in the blood. However systemic or local peritoneal inflammation could lead to an increase in protein transfer from the vascular compartment to the peritoneal cavity [9]. As such we wished to determine which factors affected the ratio of peritoneal dialysate to serum CA125 in stable PD patients

PATIENTS and METHODS

We prospectively measured serum and peritoneal CA125 in a cohort of stable 205 adult patients treated by peritoneal dialysis, when they attended for routine clinical assessment of peritoneal membrane function. No patient had been diagnosed with an episode of PD peritonitis in the preceding 3 months prior to attending for assessment of peritoneal membrane function. A standardised four-hour peritoneal equilibration test (PET) was performed by infusion of 2 litres of 2.27% dialysate solution over 10 minutes, with the patients in supine position [10]. Patients also brought in samples from their weighed spent dialysate bags so that PD adequacy could be calculated, along with a corresponding 24-hour urine collection to determine residual renal function. Peritoneal dialysate creatinine and sodium were corrected for the glucose content of the peritoneal dialysate effluent [11], and

serum albumin by the bromcresol green method, haemoglobin by a standard analyzer [12], , and serum C reactive protein (CRP) by the same method as the UK National Amyloid Centre. Serum total protein by a modified biuret method (colorimetric assay based on divalent copper reacting in alkaline solution with protein peptide bonds to form a characteristic purple-coloured biuret complex, measuring increased absorbance at 546 nm), and peritoneal dialysate protein using pyrogallol red which complexes with proteins in an acid environment containing molybdate ions, and measuring absorbance at 600nm [9]. Serum beta-2-microglobulin was measured by rate nephelometry (www.Dako.com, Image 800 analyser, Beckman Coulter, High Wycombe, UK) [13]. Serum and peritoneal dialysate effluent CA125 were measured using a sandwich immunoassay with chemi-luminescence detection (Roche Diagnostics Modular Analytics E170 analyser). Dietary protein intake was estimated using the Randerson equation to obtain a normalised protein nitrogen appearance rate (nPNA) [14]. Patient weight and measurement of intracellular and extracellular water by multifrequency bioimpedance (InBody 720, Seoul, South Korea), using a standardised protocol [15,16]. Patient co-morbidity was scored using the Stoke-Davies grading scales [17].

This retrospective audit complied with both the local Royal Free Hospital Research and Development office and the UK NHS guidelines for clinical audit and service development, available at http://www.hra.nhs.uk/documents/2013/09/defining-research.pdf, and http://www.gov.uk/government/publications/health-research-ethics-committees-governance-arrangements

STATISTICAL ANALYSIS

Data is presented as a mean ± standard deviation, or median and inter-quartile range unless otherwise stated. Standard analysis included Chi square testing with Yates's correction, t test, Man Whitney U test and anova with appropriate Bonferonni or Dunn's testing post analysis. Spearman correlation analysis was performed to identify factors associated with serum and peritoneal CA125. Multiple linear correlation was undertaken in a step backward fashion, including all variables with a $p<0.1$, with nonparametric variables log transformed and then excluding variables which were not significant unless they improved model fit. Statistical analysis was performed with GraphPad (GraphPad version 6.0, Prism, San Diego USA and SPSS, version 22.0, Univ Chicago, Chicago, USA). Statistical significance was taken at $p < 0.05$.

RESULTS

The mean age was 59.0 ±16.8 years, median peritoneal dialysis vintage 3 (2-20) months, with 59% male, 42.4% diabetic, and 42.9% Caucasoid. 31.2% of patients were treated by continuous ambulatory peritoneal dialysis (CAPD), 22% by automated overnight peritoneal dialysis cycler (APD) and 46.8% by APD with a day time exchange. Mean patient weight was 73.4 ±16.9 kg, body mass index 26.4±5.4 kg/m^2. The median serum CA125 was 21 (13-38) U/ml, with an effluent 4 hour peritoneal dialysate of 20 (11.5-36.5) U/ml following a 4 hour 2.0 litres 22.7 g/dl glucose peritoneal dialysate exchange. The median number of episodes of PD peritonitis per patient was 0 (0-1).

The median ratio of dialysate to serum CA125 measured during the PET test was 0.96 (0.53-1.5). As PD effluent CA125 has been used as a biomarker of peritoneal mesothelial cell health, we divided patients into those who had a peritoneal dialysate to serum CA125 ratio of <1.0 compared to those with a ratio of ≥ 1.0 (table 1). Those patients with a low D/S ratio had both lower dialysate effluent CA125 and higher serum concentration (Figure 1). Patients with higher D/S CA125 ratios were larger in size, had greater residual renal function, and lower prescription of higher glucose and 7.5% icodextrin dialysates. The ratio of dialysate to serum CA125 was associated with 4 hour PET dialysate total protein (Figure 2), body surface area (r=0.17,p=0.014) and residual renal function (r=0.14, p=0.43). 45 patients (42.5%) of those with a low D/P CA125 ratio had suffered a previous episode of peritonitis, which was not different to31 (31.1%) for those with a ratio of ≥1.0. There was no association with estimated dietary protein intake, serum albumin or C reactive protein.

45 patients (22%) of patients used a neutral pH, bicarbonate containing twin bag glucose containing dialysate. There were no differences in serum CA125 (23 (12-238) vs 21 (14-39) U/ml), or 4 hour dialysate CA125 (17 (10-28) vs 21 (12-38) U/ml), or the ratio (0.95 (0.52-1.39) vs 0.97 (0.54-1.65). However patients using the more biocompatible dialysate had longer dialysate vintage (28 (14-38) vs 3 (2-14) months, p<0.001, and more used 22.7 g/l glucose dialysates (14/31) vs (59/101), X2=3.67, p=0.039.

To determine which variables were associated with peritoneal and serum dialysate CA125, simple univariate analysis was performed (tables 1 and 2). Peritoneal dialysate effluent CA125 was associated with patient age, use of CAPD, residual renal function, faster

peritoneal transport status, greater peritoneal protein transport and serum CA125 concentrations. Peritoneal dialysate effluent CA125 was lower in those using more 22.7% glucose dialysates, APD cycler therapy, and greater peritoneal dialysis small solute clearance. Whereas serum CA125 was associated with peritoneal dialysate CA125, CAPD rather than APD usage, faster peritoneal transport, and negatively with larger body size (table 2). Multivariate linear analysis was then undertaken in a step backward fashion, eliminating those variables which were not statistically significant, unless they improved model fit. We found that dialysate effluent CA125 was associated with PET protein, fewer PD cycles, serum CA125, residual renal function and age (table 3). Whereas serum CA125 was associated with both the ratio of dialysate to serum protein loss (β 559, standard error 117, F value 23.0, t value 4.8, 95% confidence limits 329 to 790, p=0.000), and the number of peritoneal dialysis cycles per day (β -3.5, standard error 1.2, F value 7.7, t value -2.8,95% confidence limits -5.9 to—1.0, p=0.006),with a r^2 model fit of 0.35,and adjusted r^2 value of 0.32.

There was no association between dialysate CA125 nor the ratio of dialysate to serum CA125 and previous peritonitis episodes (p=0.45 and 0.25 respectively). PD CA125 for patients with no previous peritonitis was 21 (13-38) U/l compared to those with one previous episode 18 (10-32) U/l and those with 2 or more episodes 15 (9-25) U/l, with corresponding serum concentrations of 21 (13-38) vs 27 (17-49) and 17 (10-26) U/l respectively.

DISCUSSION

Peritoneal dialysate effluent CA125 has been reported to decrease with longer duration of peritoneal dialysis treatment [18]. Peritoneal mesothelial cells constitutively express CA125 on their apical cell membrane [19], and reduced CA125 expression has been reported to be associated with epithelial to mesenchymal transformation which occurs with increasing exposure to peritoneal dialysates [20]. However in our cross sectional study, the duration of peritoneal dialysis treatment was not associated with peritoneal dialysate CA125 concentrations on univariate analysis, and this may be due to analyzing patients who had been treated for a shorter period.

Previous studies have reported either no differences in peritoneal dialysate effluent CA125 concentrations with icodextrin usage [21], or greater CA125 with less biocompatible neutral pH, bicarbonate containing dialysates [8]. Our study of more than 200 patients is the largest cross sectional cohort of peritoneal effluent dialysate CA125 to be reported. We found that there was an effect of peritoneal dialysis prescription and peritoneal dialysates. Although larger patients would be expected to have a larger peritoneal surface area, we found no association between size and peritoneal dialysate CA125, although there was a univariate association with body fat mass. Patients using the standard four daily exchanges with CAPD had higher PD effluent CA125 concentrations, compared to those using increasing number of overnight cycles with APD based prescriptions, and those with the lower D/P CA125 ratios used less 22.7 g/l dextrose and icodextrin dialysates. Whereas there are reports on CA125 increasing with PD peritonitis [3], we did not find any association between peritoneal CA125 and previous episodes of peritonitis.

Residual renal function was also observed to be associated with increasing PD effluent CA125 concentrations, and as such PD effluent CA125 falls with loss of residual renal function, which is associated with longer peritoneal dialysis treatment, greater requirement for peritoneal small solute clearance and peritoneal ultrafiltration, with greater usage of higher glucose dialysates. Although we did not observe any differences in PD effluent CA125 concentrations in those using standard compared to patients using more biocompatible dialysates; those using the biocompatible dialysates had longer duration of peritoneal dialysis treatment, greater loss of residual renal function and greater user of higher glucose containing dialysates, which may explain the similar results, as a reduction in residual renal function was associated with an increased the use of higher glucose containing dialysates and icodextrin.

We noted that patients with greater PD effluent CA125 concentrations also had greater total peritoneal dialysate protein losses. PD protein loss may reflect local intraperitoneal inflammation, with increased large pore transport [22]. This is supported by the association of PD effluent CA125 and faster peritoneal transport associated with increased peritoneal creatinine transport, in keeping with earlier reports [23]. This relationship between faster transport and increased peritoneal protein transport in patients starting peritoneal dialysis has been reported by others [24], but may be lost with longer duration of therapy. We also recorded an effect of increasing patient age. Elderly patients are more at risk of sarcopenia, which may be associated with inflammatory conditions [25] and loss of muscle mass [26,27]. However, this association with peritoneal CA125 may be confounded by more elderly patients in our study being treated with CAPD than APD cyclers.

Whereas many reports have concentrated on PD effluent CA125, we also measured the corresponding serum CA125. Although it may be expected that serum CA125 would increase as residual renal function declines, we found no such association. Similarly whereas it may be expected that larger patients with greater cell mass would have a higher serum CA125, we observed lower serum CA125 concentrations in our larger patients with greater body cell mass. We did however note on univariate analysis that increased peritoneal dialysate small solute clearances, and greater use of peritoneal dialysates were associated with lower serum values, and conversely faster transport status was associated with lower serum CA125 concentrations. This would suggest that peritoneal dialysis may affect serum CA125 concentrations.

Whereas there a number of reports examining peritoneal clearances of large serum proteins [28,29], we were unable to find studies examining whether there was any relationship between dialysate and serum CA125. CA125 is a large molecule of around 220,000 D, and as such would be expected to have slow transport into the peritoneal cavity [28,29]. We found that serum CA125 concentrations were associated with PD effluent values on both univariate and multivariable analyses, suggesting that PD effluent CA125 may not only depend upon local production and secretion, but could also be possibly affected by serum concentrations. Larger protein transport may be increased in patients recently starting peritoneal dialysis [24]. We observed an association between higher serum CA125 concentrations with fewer peritoneal dialysis exchanges, and greater peritoneal large pore transport. It has been reported that peritoneal losses of some large serum proteins, such as vitamin D binding protein and haptoglobin can lead to significant losses with reduced serum

concentrations [30]. To explore this further we analysed the ratio of dialysate effluent CA125 to serum CA125. The ratio of dialysate to serum CA125 was higher for larger patients, as larger patients would be expected to have a larger peritoneal surface area with a corresponding greater mesothelial cell mass. However those patients with an increased dialysate to serum CA125 ratio not only had an increased peritoneal CA125 but also a lower serum CA125. Patients with a higher dialysate to serum CA125 ratio had greater residual renal function, which would potentially imply greater renal clearance. Patients with more residual renal function generally have lower extracellular fluid [31], which would in keeping with the higher serum albumin concentration observed, and suggest that the lower serum CA125 was not due to a dilution effect. As the group with the lower dialysate to serum CA125 ratio had less residual renal function they were prescribed higher concentrations of glucose dialysates and icodextrin [32]. Heat sterilisation of glucose dialysates leads to the production of glucose degradation products; including formaldehyde, acetaldehyde, furaldehyde, methylglyoxal, glyoxal and 3-deoxyglucosone [33], which increase with higher concentrations of glucose so exposing peritoneal mesothelial cells to these potentially toxic substances, with a reduction in peritoneal CA125.

The normal serum reference range for serum CA125 is below 35 U/ml [34]. As such more than 25% of our healthy peritoneal dialysis cohort had raised serum levels. However it should be recognised that CA125 can also be produced by epithelial tissues elsewhere in the body including ovary, lung, pancreas, breast, stomach, and gall bladder. None of our patients had a diagnosis of epithelial cell cancer, or benign conditions including endometriosis or pelvic inflammatory disease, and equally no patient has been subsequently found to have ovarian or

other malignancy. Those patients with the lower dialysate/serum ratio were more likely to have increased serum CA125. However this may have been due to the lower residual renal function in this group, with reduced renal clearance, which is in keeping with previous observations of higher serum CA125 concentrations in both healthy peritoneal dialysis [35] and haemodialysis populations [36] compared to normal control subjects.

Although CA125 in spent peritoneal dialysate is used as a surrogate biomarker for assessing the health of the peritoneum, in our cross sectional study predominatly of patients recently starting peritoneal dialysis, we observed that there was an association between peritoneal and serum CA125 concentrations. We noted that peritoneal concentrations were affected by increased peritoneal protein transport, fewer peritoneal dialysis exchange cycles and residual renal function, with loss of residual renal function leading to increased usage of higher glucose concentration dialysates.

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REFERENCES

1. Koomen GCM, Betjes MGH, Zemel D, Krediet RT, Hoek FJ. Dialysate cancer antigen (CA) 125 is a reflection of the peritoneal mesothelial mass in CAPD patients. Perit Dial Int. 1994;14:132–61.
2. Visser CE, Brouwer-Steenbergen JJ, Betjes MG, Koomen GC, Beeleen RH, Krediet RT. Cancer antigen 125: a bulk marker for the mesothelial mass in stable peritoneal dialysis patients. Nephrol Dial Transplant. 1995;10:64–9
3. Pannekeet MM, Zemel D, Koomen GC, Struijik DG, Krediet RT. Dialysate markers of peritoneal tissue during peritonitis and in stable CAPD. Perit Dial Int. 1995;15:217–25

4. Elsurer R, Afsar B, Sezer S, Ozdemir FN. Peritoneal cells at admission: do they have prognostic significance in peritonitis? Ren Fail. 2010;32(3):335–42
5. Panorchan K, Davenport A. Diagnostic and prognostic role of peritoneal CA 125 in peritoneal dialysis patients presenting with acute peritonitis. BMC Nephrol. 2014; 15:149
6. Sampimon DE, Korte MR, Barreto DL, Vlijm A, de Waart R, Struijk DG, Krediet RT. Early diagnostic markers for encapsulating peritoneal sclerosis: a case-control study. Perit Dial Int. 2010 Mar-Apr;30(2):163-9
7. Habib AM, Preston E, Davenport A. Risk factors for developing encapsulating peritoneal sclerosis in the icodextrin era of peritoneal dialysis prescription. Nephrol Dial Transplant. 2010;25(5):1633–8
8. Jones S, Holmes CJ, Krediet RT, Mackenzie R, Faict D, Tranaeus A, Williams JD, Coles GA, Topley N; Bicarbonate/Lactate Study Group. Bicarbonate/lactate-based peritoneal dialysis solution increases cancer antigen 125 and decreases hyaluronic acid levels. Kidney Int. 2001;59(4):1529-38
9. Rajakaruna G, Caplin B, Davenport A. Peritoneal protein clearance rather than faster transport status determines outcomes in peritoneal dialysis patients. Perit Dial Int. 2015. pdi.2013.00217. PMID: 25082839
10. Twardowski ZJ, Nolph KD, Khanna R, Prowant BF, Ryan LP, Moore. HL, Neilson MP. Peritoneal Equilibration Test. Perit Dial Bull 1987;7:138-47
11. Persaud J, Thomas M, Davenport A. Indirect ion selective electrode methods potentially overestimate peritoneal dialysate sodium losses. Ther Apher Dial. 2014;18(4):321-5
12. Booth J, Pinney J, Davenport A. Changes in red blood cell size and red cell fragmentation during haemodialysis. Int J Artif Organs. 2010;33(12):900-5
13. Oates T, Pinney JH, Davenport A. Haemodiafiltration versus high-flux haemodialysis: Effects on phosphate control and erythropoietin response. Am J Nephrol. 2011;33(1):70-5
14. Randerson DH, Chapman GV, Farell PC. Amino acid and dietary status in CAPD patients. In Peritoneal Dialysis, edited by Atkins RC, Farell PC, Thomson N, Edinburgh, Scotland, Churchill-Livingstone, 1981, pp 180-191
15. Davenport A, Willicombe M. Comparison of fluid status in patients treated by different modalities of peritoneal dialysis using multi-frequency bioimpedance. Int J Artif Organs. 2009;32(11):779-86
16. Davenport A, Willicombe M. Hydration status does not influence peritoneal equilibration test ultrafiltration volumes. Clin J Am Soc Nephrol. 2009;4(7):1207-12
17. Davies SJ, Phillips L, Naish PF, Russell GI. Quantifying comorbidity in peritoneal dialysis patients and its relationship to other predictors of survival. Nephrol Dial Transplant 2002; 17: 1085-1092.
18. Fusshöller A, Grabensee B, Plum J. Effluent CA 125 concentration in chronic peritoneal dialysis patients: influence of PD duration, peritoneal transport and PD regimen. Kidney Blood Press Res. 2003;26(2):118-22

19. Li FK, Davenport A, Robson RL, Loetscher P, Rothlein R, Williams JD, Topley N. Leukocyte migration across human peritoneal mesothelial cells is dependent on directed chemokine secretion and ICAM-1 expression. Kidney Int. 1998;54(6):2170-83
20. Do JY, Kim YL, Park JW, Chang KA, Lee SH, Ryu DH, Kim CD, Park SH, Yoon KW. The association between the vascular endothelial growth factor-to-cancer antigen 125 ratio in peritoneal dialysis effluent and the epithelial-to-mesenchymal transition in continuous ambulatory peritoneal dialysis. Perit Dial Int. 2008;28 Suppl 3:S101-6
21. Parikova A, Zweers MM, Struijk DG, Krediet RT. Peritoneal effluent markers of inflammation in patients treated with icodextrin-based and glucose-based dialysis solutions. Adv Perit Dial. 2003;19:186-90
22. Heaf JG. Peritoneal transport: getting more complicated. Nephrol Dial Transplant. 2012;27(12):4248-51
23. Rodrigues A, Martins M, Santos MJ, Fonseca I, Oliveira JC, Cabrita A, Melo e Castro J, Krediet RT. Evaluation of effluent markers cancer antigen 125, vascular endothelial growth factor, and interleukin-6: relationship with peritoneal transport. Adv Perit Dial. 2004;20:8-12
24. Struijk DG, Krediet RT, Koomen GC, Boeschoten EW, Hoek FJ, Arisz L. A prospective study of peritoneal transport in CAPD patients. Kidney Int. 1994;45(6):1739-44
25. Zhang R, Ren YP. Protein-energy wasting and peritoneal function in elderly peritoneal dialysis patients. Clin Exp Nephrol. 2012;16(5):792-8
26. Fürstenberg A, Davenport A. Assessment of body composition in peritoneal dialysis patients using bioelectrical impedance and dual-energy x-ray absorptiometry. Am J Nephrol. 2011;33(2):150-6
27. Davies SJ, Davenport A. The role of bioimpedance and biomarkers in helping to aid clinical decision-making of volume assessments in dialysis patients. Kidney Int. 2014;86(3):489-96
28. Krediet RT, Zuyderhoudt FM, Boeschoten EW, Arisz L. Alterations in the peritoneal transport of water and solutes during peritonitis in continuous ambulatory peritoneal dialysis patients. Eur J Clin Invest. 1987;17(1):43-52
29. Douma CE, de Waart DR, Struijk DG, Krediet RT. Are phospholipase A2 and nitric oxide involved in the alterations in peritoneal transport during CAPD peritonitis? J lab Clin Med. 1998;132(4):329-40
30. Wang HY, Tian YF, Chien CC, Kan WC, Liao PC, Wu HY, Su SB, Lin CY. Differential proteomic characterization between normal peritoneal fluid and diabetic peritoneal dialysate. Nephrol Dial Transplant. 2010;25(6):1955-63
31. Fan S, Sayed RH, Davenport A. Extracellular volume expansion in peritoneal dialysis patients. Int J Artif Organs. 2012;35(5):338-45
32. McCafferty K, Fan S, Davenport A. Extracellular volume expansion, measured by multifrequency bioimpedance, does not help preserve residual renal function in peritoneal dialysis patients. Kidney Int. 2014;85(1):151-7
33. Sitter T, Sauter M. Impact of glucose in peritoneal dialysis: saint or sinner? Perit Dial Int 2005; 5:415-421

34. Nossov V, Amneus M, Su F, Lang J, Janco JM, Reddy ST, Farias-Eisner R. The early detection of ovarian cancer: from traditional methods to proteomics. Can we really do better than serum CA-125?. Am. J. Obstet. Gynecol. 2008; 199 (3): 215–23
35. Camci C, Büyükberber S, Tarakçioğlu M, Adam SM, Camci C, Türk HM, Büyükberber N, Balat O. The effect of continuous ambulatory peritoneal dialysis on serum CA-125 levels. Eur J Gynaecol Oncol. 2002;23(5):472-4.
36. Yu X, Xu X, Ye Z. Effect of renal function and hemodialysis on the serum tumor markers in patients with chronic kidney disease. Front Med China. 2007;1(3):308-11

Figure 1. Peritoneal equilibrium test 4 hour dialysate effluent CA125 concentration and corresponding serum CA125 concentrations. Patients divided according to dialysate to serum ratios. Median and interquartile ranges. * p<0.001

Figure 2. Pearson univariate correlation between peritoneal equilibrium test 4 hour dialysate effluent CA125 concentration corrected for ultrafiltration volume and peritoneal equilibrium test 4 hour dialysate total protein concentration.

Table 1. Comparison of those patients who had an increase in extracellular (ECW)/total body water (TBW) at the time of first peritoneal transport assessment (PET) compared to ECW/TBW prior to peritoneal dialysis (PD) training compared to those with a stable or falling ECW/TBW. Stoke-Davies co-morbidity grade (12), intracellular water (ICW). Serum albumin (albumin), C reactive protein (CRP). Creatinine clearance (CrCl). PD modality –over-night cycler (APD), continuous peritoneal dialysis (CAPD). Dialysate (D), plasma (P). Data expressed as mean ±SD, median (IQR) or percentage. P values <0.05 provided

variables	D/P CA125 < 1.0	D./P CA125 ≥1.0	P value
number	106	99	
Age years	58.0 ±18.0	61.0 ±15.0	
Male %	58.5	59.6	
Diabetic %	54.5	59.6	
Caucasian %	42.5	43.4	
South Asian %	18.9	19.2	
Afro-Caribbean %	30.2	30.3	
Davies grade 0 %	27.4	34.3	

Davies grade 1 %	61.3	53.5	
Davies grade 2 %	10.4	12.1	
Weight kg	70.0 ±15.7	77.0 ±17.5	0.003
Body mass index kg/m^2	25.2 ±4.9	27.6 ±5.5	0.001
Body surface area m2	1.80 ±0.24	1.90 ±0.26	0.010
ECW/TBW ratio	0.397 ±0.015	0.394 ±0.012	
CAPD %	34.0	28.3	
APD %	16.0	28.3	
CCPD %	50.0	43.4	
Peritoneal dialysis treatment months	3 (2-23)	3 (2-17)	
Kt/V urine	1.0(1.0-2.0)	1.0 (1.0-2.0)	
Kt/V PD	1.17 ±0.57	2.65 ±1.16	
24 hour PD UF ml	513(200-879)	400 (150-876)	
Urine l creat/wk	32 (9.0-69.)	55 (29-89)	0.001
Urine creatinine clearance ml/min	3 (1-7)	5 (3-9)	0.005
Urine output ml/day	746 (233-1433)	1156 (588-1784)	0.003
PD l creat/wk	32 (17.8-47.5)	33.6 (20.9-46.2)	
7.5% icodextrin l/day	2.0 (0-2.0)	1.0 (0-2.0)	0.037
22.7 g/l dialysate l/day	1.0 (0-6)	0 (0-4.4)	0.044
4 h D/Pcreatinine	0.73 ±0.13	0.73 ±0.14	
4 h D/Pglucose	0.33 ±0.09	0.33 ±0.09	
4 h D/Pprotein	0.12 ±0.22	0.13 ±0.01	
PET UF volume ml	200 (100-400)	200 (100-400)	
PET PD protein g/l	0.68 ±0.44	0.84 ±0.55	0.002
Haemoglobin g/l	110.0 ±17.0	109 ±15.0	
Sodium mmol/l	137.0 ±4.0	138.0 ±4.0	0.046
Serum urea mmol/l	18.0 ±6.0	20 ±5.0	0.046
Serum creatinine umol/l	642 (456-875)	575(414-760)	
Serum albumin g/l	36.0 ±5.0	38.0 ±4.0	0.003
C reactive protein mg/l	4 (1-11)	3 (1-7)	
Serum glucose mmol/l	5.6 (4.8-9.2)	5.8 (4.8-8.5)	
Serum β2M mg/l	24.9 ±13.6	22.4 ±8.6	0.009

Table 4. Linear multiple correlation analysis for PET dialysate CA125. Final variables -4 hour PET effluent dialysate protein (PET protein), number of peritoneal dialysis cycles/day (PDcycles), residual renal function as combined 24 hour urea and creatinine clearance (RRF). Tandarderror (SE),95% confidence limits (95% CL). Model fit r^2=0.47, adjusted r^2=0.45.

variable	β value	SE	F value	t value	95% CL	p value
PET protein	12.9	2.3	31.7	5.6	8.4 to 17.4	0.000
PD cycles	-2.19	0.62	12.3	-3.6	-3.4 to -0.96	0.001
Serum CA125	0.11	0.04	9.4	3.1	0.04 to 0.18	0.002
RRF	0.53	0.22	5.1	2.4	0.92 to 0.96	0.018

Age	0.15	0.07	4.2	2.1	0.01 to 0.28	0.042

table 2. Univariate Spearman analysis to determine variables associated with Dialysate effluent CA125.

variable	r value	p value
β2 microglobulin mg/l	-0.423	0.000
Weekly Kt/Vurea peritoneal	-0.396	0.000
22.7 g/l glucose l/day	-0.395	0.000
RRF ml/min/1.73m^2	0.395	0.000
PD cycles/24 hours	-0.390	0.000
Urinary Litres creatinine cleared/wk	0.388	0.000
Weekly Kt/V urine	0.378	0.000
CAPD	0.359	0.000
24 hour urine volume ml	0.348	0.000
PET protein g/l	0.347	0.000
PET D_4/P protein	0.347	0.000
Serum CA125 U/l	0.319	0.000

PET D_4/P creatinine	0.309	0.000
Age years	0.243	0.005
Peritoneal dialysis Litres creatinine cleared/wk	-0.232	0.000
Racial origin	-0.201	0.038
24 hour peritoneal ultrafiltration volume litres	-0.196	0.005
7.5% Icodextrin usage l/day	0.187	0.007
Body Fat mass kg	0.182	0.015
Automated peritoneal dialysis cycler	-0.141	0.040

table 3. Univariate Spearman analysis to determine variables associated with serum CA125.

variable	r value	p value
Peritoneal dialysis Cycles/day	-0.39	0.000
CAPD	0.331	0.000
PET 4 hour dialysate CA125	0.319	0.000
7.5% Icodextrin usage l/day	0.295	0.000
PET D_4/P creatinine	0.254	0.000
PET D_4/P protein	0.254	0.000
Extracellular water/total body water ratio	0.252	0.005
Intracellular water Litres	-0.236	0.014
Body cell mass kg	-0.227	0.002
Automated peritoneal dialysis cycler	-0.224	0.001
Lean muscle mass kg	-0.211	0.004
Serum sodium mmol/l	-0.197	0.005
Davies co-morbidity score	0.161	0.021
Weekly Kt/Vurea peritoneal	-0.191	0.007
Peritoneal dialysis Litres creatinine cleared/wk	-0.184	0.009
Peritoneal dialysis ultrafiltration litres/day	-0.184	0.019

Weight kg	-0.184	0.008
Serum albumin g/l	-0.178	0.010
Extracellular water volume l	-0.174	0.019
Body surface area kg/1.73m2	-0.169	0.006
β2 microglobulin mg/l	-0.169	0.047
Haemoglobin g/l	0.147	0.035