Third Day

Friday, December 18
Clinical and Pathological Prognostic Indicators of IgA Nephropathy in Iranian Patients

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Introduction. Immunoglobulin A (IgA) nephropathy is the most common cause of primary glomerulonephritis with slow progression to end-stage renal disease (ESRD) in up to 40% of the patients.

Methods. A retrospective cohort study of patients with biopsy proven IgA nephropathy was performed in our center from 1997 to 2008. We tried to determine the clinical and pathological data that was associated with the prognosis of the disease. Clinical characteristics at the time of renal biopsy and follow-up were reviewed. Severity of histology was quantified as grade 1 to 3.

Results. There were 70 IgA nephropathy patients and 46 were men. The average age of the patients at biopsy time was 39 ± 12.1 years. During the median 23.5 (range, 6 to 130 months) months of follow-up, 10 patients progressed to ESRD and no patient died. Median time of progression to ESRD was 107 (range, 62 to 152 months) months. The renal survival was 94% at one year, 91% at 3 years, and 88% at 5 years. A higher histological grade of IgA nephropathy was associated with higher baseline age (P = 0.003), higher mean arterial pressure (P = 0.01), greater serum creatinine (P < 0.001), more 24-hour urine protein excretion (P = 0.002), and higher number of ESRD events (P < 0.001). Odds ratio of ESRD events for patients older than 50 years was 13.5 (CI: 95% 2.9-61.7, P = 0.003) and for daily proteinuria more than 3 g/24h was 13.1(2.5-69.2, P = 0.002). We had no ESRD event in patients with grade II pathology, and odds ratio for grade III versus II was 12 (2.2-64.5, P = 0.004). ESRD events were also more common in male and hypertensive patients but not at significant level.

Conclusion. Although the number of studied patients and median time of follow-up in our study is limited, we showed that kidney biopsy and risk stratification of different factors at baseline in IgA nephropathy are useful for predicting the prognosis and probably appropriate intervention.

Looking for a New Marker in Renal Osteodystrophy, Time for a Change?

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Introduction. Validity of serum PTH as a surrogate marker of bone turnover in patients with chronic kidney disease is limited by several factors such as relative resistance of bone to PTH action, hyperphosphatemia, diabetic status, gender, age, race, and vitamin D analogue action on PTH-bone axis. Urinary N-telopeptide X (NTx), a bone collagen degradation product, expressed as bone collagen equivalents (BCE) per mM of creatinine (NTx/Cr ratio), is routinely used to estimate bone turnover in patients with osteoporosis. The purpose of this study is to evaluate NTx as a marker of bone turnover in renal osteodystrophy.

Methods. We studied the relationship between BSAP, PTH, and 2nd morning void urine NTx/Cr in 37 CKD out-patients.

Results. In a multivariate model, PTH had a positive correlation with BSAP (r = 0.60, P < 0.005) and U-NTx/Cr (r = 0.43, P < 0.04), after adjusting for age, gender, GFR, serum phosphorus, corrected calcium, and race. However, the strongest correlation was found between the two direct markers of bone resorption and formation (U-NTx vs. BSAP; r = 0.80; P < 0.0001), suggesting tight coupling of bone resorption and formation in CKD. The effect of gender on U-NTx/Cr was studied in a multivariate model after adjusting for age, race, GFR, serum calcium, phosphorus, and PTH. Females had higher U-NTx/Cr.

Conclusion. Our findings indicate that urinary NTx, a promising marker of bone resorption in CKD patients, exhibits a strong positive correlation with other markers used to assess renal osteodystrophy such as PTH and BSAP. Unlike PTH and BSAP, urine NTx also measures bone loss secondary to osteoporosis.

Effects of L-Carnitine and Alpha-Tocopherol on Acute Ureteral Obstruction-Induced Disturbances of Renal Function, Oxidative Balance, and Energy Metabolism in Anaesthetized Rats

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Introduction. L-carnitine is a facilitating cofactor for mitochondrial oxidation of fatty-acids as well as a scavenger of free-radicals, and alpha-tocopherol is the most potent antioxidant. This study investigated the improving effects of these compounds on renal oxidative stress, suppressed energy metabolism as well
as hemodynamic and excretory dysfunctions at early hours following release of acute unilateral ureteral obstruction (UUO).

Methods. The left ureter was legated in anaesthetized rats, in which L-carnitine, alpha-tocopherol or their vehicles (saline and olive oil, respectively) were injected in four different groups. Each rat was re-anesthetized and cannulated, and then ureteral legation was released after 24 hours of UUO-induction. Thereafter, urine from both kidneys was separately collected during a 60-minute clearance period, and then under 30-mm paraffin for half an hour. Finally, both kidneys were removed and preserved at -80°C for future measurements of their ATP and ADP amounts, as well as their levels of malondialdehyde (MDA) and ferric reducing/antioxidant power (FRAP). There were also sham and control groups (n = 8 to 10 in each group).

Results. Post-obstructed kidney of vehicle-treated groups in comparison to equivalent kidney of sham group had decreases of about 40% in ATP, 60% in ATP/ADP, 40% in FRAP, 25% in urinary Pco2 (P < 0.01-0.001), 27% in creatinine clearance, 74% in absolute Na-excretion, 93% in absolute K-excretion, 95% in effective free-water reabsorption, 77% in urine flow rate, and 64% in urine osmolality (P values < 0.001), but increases of about 65% in MDA (P < 0.001), 65% in ADP (P < 0.05), and 13% in urinary pH (P < 0.001). L-carnitine could improve oxidative stress and suppressed energy metabolism and alpha-tocopherol only prevented oxidative stress; however, neither of the compounds did not have any effect on disturbed renal functional variables of the post-obstructed kidney.

Conclusion. Hence, oxidative stress and defect of energy metabolism are not involved in the development of disturbances in renal hemodynamic, excretory functions, and urine concentrating ability during acute UUO.

O504
Intensive Tandem Cryofiltration Apheresis and Hemodialysis in Patients with Hepatitis C Associated Cryoglobulinemia
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Introduction. Forty-nine patients with cryoglobulinemia have been treated using 1350 cryofiltration apheresis procedures (CFA). Thirty-nine patients (78%) had mixed type, of which, 36 (90%) had Type II cryoglobulinemia. Thirty-one (83%) with mixed cryoglobulinemia developed renal failure. Most had Type II associated with Hepatitis C virus.

Methods. Two critically ill patients with Type II cryoglobulinemia and renal failure requiring both CFA and HD were transferred to our institution. They were treated with intensive tandem CFA/HD. For HD, 2008 E, Fresenius, and F50 dialyzer was used. For CFA, Spectra plasma separation, Gambro and Cryofilter from Pall Medical with 4.3 micron pore size made of polyvinyl chloride and acrylonitile membrane were used. For cryoprecipitation, thermoregulator made in our institution was used to cool the plasma to 4 degree C. Plasma was warmed to 37 degrees C. Cryoglobulin measured as cryocrit. Cryofilter compatibility was measured by C3a and C5a compliments. Immunoglobulins, albumin, fibrigen, cryoprecipitate, BUN, and Cr were measured before and after the procedures. Sieving coefficient for plasma proteins was measured by pre and post plasma analysis. Clinical score of patients’ symptoms was life threatening, severe, moderate, and mild with given scores of 4,3,2, and 1, respectively.

Results. Patient JFR had 10 CFA/HD procedures in 12 days. WJF had 18 CFA/HD in 30 days. No complement activation, technical difficulties, or no unusual hypotensive episodes were observed. Sieving coefficients for IgG, IgA, IgM, Alb, and fib were greater than 90%. Cryoprecipitate was removed 73% of cryoglobulin. Average clinical score of patients’ symptoms dropped from severe (3) to less than mild (1) after 10 procedures. Tandem CFA and HD were both preformed in 4 hours instead of 7.5 hours if they were done separately. The extra primer and citrate given for CFA were removed by HD. No albumin replacement fluid was required. Nursing and procedure time was almost 50% preserved. More than one plasma volume could be processed with the same cryofilter.

Conclusion. Intensive tandem CFA/HD was safe even in critically ill patients. No compliment activation or adverse events were observed. Tandem CFA/HD was effective to remove 73% of the cryoglobulin and conserved 90% of the plasma protein. No coagulation factor or immunodifficiency required. No replacement fluid required. The procedure saved time and expense because of less staff time and no albumin solution required.

O505
WNK1 Kinase Investigation in Human Essential Hypertension
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Introduction. WNK1 affects p38 mitogen-activated protein kinase (MAPK) which it’s signaling cascade is an important pathway for key cellular mechanisms of diverse cardiovascular pathologies, including inflammation. Inflammatory triggers include oxidized lipoproteins,
hypertension and diabetes. Due to difficulty in detection of WNK products, we designed to investigate the serum levels of p38, WNK1 and p38 mRNA expression and presence of WNK1 and p38 protein in peripheral blood mononuclear cells (PBMCs) in Iranian patients with essential hypertension.

Methods. Serum and PBMCs of 50 patients with essential hypertension were isolated from peripheral blood. Serum levels of p38 were measured by enzyme linked immuno sorbent assay (ELISA). The expression of WNK1 and p38 mRNA was examined in PBMCs by real-time reverse transcriptase polymerase chain reaction (RT-PCR). The presence of WNK1 and p38 protein was determined by western blotting analysis.

Results. Serum levels of p38 increase in patients with essential hypertension versus controls. mRNA expression of p38 also increase in the patients comparing with healthy individuals. Presence of WNK1 and p38 was also determined.

Conclusion. Results of this study indicate that p38 plays an important role in the inflammation due to essential hypertension. WNK1 and p38 up-regulation suggest that they may be used as an effective factor in diagnosis of essential hypertension.

O506 The Effect of Ramadan Fasting in Urinary Risk Factors of Stone Formation

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Introduction. Urinary stone formation is a common, troublesome, and costly medical problem. Even though dehydration could aggravate stone formation, the effect of fluid and diet restriction on stone formation is questionable. The purpose of this study is to evaluate the effect of fluid and diet restriction in Ramadan fasting on urinary factors of stone formation in recurrent calcium stone formers.

Methods. We selected 37 recurrent calcium stone-former males between 30 and 55 years old. All patients were evaluated for blood tests, sonography, urinalysis, urine culture, and 24-h urine collection for calcium, citrate, oxalate, uric acid, magnesium, phosphate, potassium, creatinine, and sodium before and during Ramadan fasting. In Ramadan, 24-h urine was collected in 2 containers one for the first 20h (U1) and second for the last 4h (U2 as concentrated urine). The values of stone-precipitating solutes as well as inhibitory factors were measured in all specimens and the results were compared.

Results. Total excretion of calcium in 24-h urine during fasting (U1+2) was significantly lower than non-fasting [U3; 151.55 mg/d ± 68.82 and 261.14 mg/d ± 65.19, 95% CI of diff. (62.74 to 156.42; P < 0.0001)]. Total excretion of citrate in 24-h urine during fasting (U1+2) was more than non-fasting (U3) but without a statistically significant difference (cit1+2: 897.876 mg/d ± 533.98, cit3: 627.76 mg/d ± 533.98). Total excretion of magnesium in 24-h urine during fasting (U1+2) was significantly lower than non-fasting [U3; mg1+2: 86.17 mg/d ± 40.49, mg3: 104.67 ± 42.44 mg/d, 95% CI of diff. (1.45 to 35.55; P = 0.034)]. Total excretions of phosphate, potassium, oxalate, uric acid, and sodium in 24-h urine during fasting were not significantly different from non-fasting. The 24-h urine volume during fasting was significantly lower than non-fasting (V1+2: 1584 ml ± 576, V3: 1737 ml ± 465; P < 0.0001). In comparison of fasting concentrated urine (U2) and non-fasting urine (U3), concentration of calcium was significantly lower and concentration of uric acid, phosphate, citrate, and potassium were significantly higher than non-fasting. Conclusion. During Ramadan fasting, total excretion and concentration of urinary calcium was significantly lower than non-fasting and concentration of uric acid, potassium, and perhaps concentration and excretion of citrate were higher than non-fasting. The Ramadan fasting has some confusing and conflicting effects on stone formation risks that needs more studies.

O507 Leptin Levels and Lipid Profile in Lovastatin Administered Patients with Nephropathy Due to Diabetes Mellitus Type II

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Introduction. Nephrologic disorders are one of the current implications in diabetes type II. Control of metabolic disorders -lipid profile- is very vital in these patients. There is some controversy regarding the effect of statin groups on leptin as a biomarker for body fat.

Methods. A single blind clinical trial study was carried out from April 2008 to April 2009. In this study 30 patients (mean age of 54.47±6.11 range 25-60) with diabetic nephropathy (type II Diabetes mellitus) were assessed for the effect of lovastatin on leptin, transferrin, albumin and serum lipid profile (LDL, HDL, total...
Results. The 3 months application of lovastatin significantly lowered the levels of total cholesterol \([199.00±43.33 \text{ mg/dl to } 164.67±35.19 \text{ mg/dl (P < 0.001)}]\), LDL \([116.16±46.54 \text{ mg/dl to } 84.48 ±29.23 \text{ mg/dl (P < 0.001)}]\), and leptin \([10.78±8.30 \text{ mg/dl to } 7.80±5.41 \text{ mg/dl (P < 0.001)}]\). It also increased the mean serum level of HDL \([40.00±4.31 \text{ mg/dl to } 42.80±5.15 \text{ mg/dl (P < 0.005)}]\]. Lovastatin did not impact on the level of transferrin, albumin, 24 hr urine protein, BUN and clearance of creatinine in the patients with diabetic nephropathy.

Conclusion. Lovastin can decrease serum levels of LDL, total cholesterol and leptin. It increases the HDL level without any efficacy on the other markers of diabetic nephropathy.

O601

Time Boxing- A New Technique to Cure Missing Data of Chronic Studies, While Minimizing Information Lost and Perturbation: Implementation in Iran Peritoneal Dialysis Registry (IPDR), Shafa CAPD Research Center

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Introduction. Dealing with medico-health data usually culminates in applying the statistical analysis to data that is aligned onward a temporal dimension. Usually, due to a number of inevitable causes, missing data appears in final data sets. This missed information can either hinder the confidence and validity of the statistical analysis or put it completely out of the box. In Iran Peritoneal Dialysis Registry (IPDR), the number and scattered pattern of unavoidable missing data was disabling for statistical analysis methods, especially in survival analysis.

Methods. Different methods (e.g. imputation, list wise deletion, and substitution) are introduced to cure the data who embodies Missing Completely At Random (MCAR); but, they have problems such as lack of biological rationality, reduction of the power of study, and trading off the available information to preserve computability. “Time Boxing” is a new computational technique that can produce better results. The logic is to consider the time of the measurement as a box (or frame) instead of a point on the time vector. If we expand the box, the boxes of two measurements overlap eventually. Combining these overlapping boxes to form new boxes and using appropriate functions (e.g. mean, first, max) to pickup one of the measurements in combined boxes, fills the data holes while preserves real values and the trend of changes along the time and simultaneously minimizes information loss.

Conclusion. The Electronic Health Record (EHR) application that IPDR is based on (called Hakim), is enhanced to apply this technique to the data before exporting data to statistical analysis applications. In this article, we show how Time Boxing leads to significant improvement of the data quality without sacrificing other factors. Also, some interesting phenomena of IPDR data are discussed which seem prevalent across disease registries. The fact that most of the chronic follow-ups (especially in CKD) suffer from the same problem of incurable missing data, reveals importance of the new techniques such as Time Boxing.

O602

The Centers Response Rate to Questionnaire and its Relation to Patient and Technique Survival in Iranian PD Registry

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Introduction. The essential objective of the registry systems is not only establishment of a comprehensive database, but also facilitating and improvement of the quality of patient management through reminding the medical staff of the time of certain evaluations (Questionnaires). Therefore, the response rate of centers to registries could possibly reflect this quality of the patient care. In this article, we are going to evaluate if centers’ response rate has any correlation with patients’ outcome.
Methods. Between January 1995 and December 2006, from 26 PD centers, data on 1472 patients including demographic, clinical and laboratory characteristics, which were monthly collected through questionnaires were entered in “Hakim” (a Farsi database) and analyzed using STATA (9.0). The Pediatric centers and centers with less than 20 patients were excluded. In 14 remaining centers, the response rate to 108 questions were computed and the centers’ response rate were categorized as high, low, and average. Cox regression analysis was used to compare patient and technique survival in groups with different percentage of response rate. A P value < 0.05 was considered statistically significant.

Results. The highest mean response rate for the 14 centers was 70%, the lowest was 19%, and the average for all centers was 47%. Cox regression analysis showed that patient survival was significantly higher in the center with the highest response rates (HR = 2.65; P = 0.007); similar result was found for technique survival (HR = 3.09; P = 0.004). It was also shown that, patient and technique survival for the centers with average response rate of less than 60% was significantly lower (HR = 1.48, P = 0.002 and HR = 1.98, P = 0.001, respectively). The analyses also showed that the higher patient and technique survival in the center with higher response rate was not due to higher hemoglobin or albumin level negative selection resulted in higher catheter loss (P = 0.05), whereas gender and age ≥ 65 did not (P > 0.05). Cox proportional hazard model analysis revealed that age ≥ 65, low serum albumin levels, low appetite, heart failure, low ultrafiltration rate, low educational status, low HGB, and negative selection resulted in higher mortality rates (P < 0.05). Low educational status and negative selection resulted in higher catheter loss (P < 0.05), whereas gender and age ≥ 65 did not (P > 0.05).

Conclusion. In the elderly patients, CAPD is a good modality for renal replacement therapy with a suitable technique survival. However, patient survival is lower than younger patients. The most common cause of death is cardiovascular disease in elderly CAPD patients.

O604
Outcome in Primary Peritoneal Dialysis Patients Versus Those Transferred from Hemodialysis and Transplantation Centers

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Introduction. According to the concept of integrated care, transplantation (TX), peritoneal dialysis (PD), and hemodialysis (HD) should be considered three complementary methods of renal replacement therapy. There is evidence that patients who have experienced more than one therapy have a survival advantage. This study tried to ascertain patient outcome in 3 different groups of PD patients comprising primary PD therapy patients, those transferred with failing kidney transplantation, and patients transferred from hemodialysis.

Methods. Between January 1995 and 2006, from 26 PD centers, data of 1355 patients including demographic,
clinical and laboratory characteristics, which were monthly collected through questionnaires, were entered into “Hakim” (a Farsi database) and analyzed using STATA (9.0). We compared patients’ characteristics, factors affecting patient survival and patient outcome between PD first patients (group 1, n = 1067), TX transferred patients (group 2, n = 43), and HD transferred patients (group 3, n = 245) who were on HD at least three month before starting PD. The Kaplan-Meier method and Cox proportional hazards model were used to compare the technique and patient survival.

Results. There was no difference in number of the patients with diabetes in the 3 groups. Patients in TX group were significantly younger (P = 0.01) with more prominent male patients (P = 0.004) and less illiteracy (P = 0.02). HD group patients had a significantly more co-morbidity (P < 0.0001) and negative selection (P = 0.001), higher basal serum creatinine level (P < 0.0001), lower basal total creatinine clearance (P < 0.0001), lower total KT/V (P = 0.004), and less serum albumin level (P = 0.01). Peritonitis rate was 0.52, 1.36, and 0.53 episode/year in groups 1, 2, and 3, respectively. A total of 238 (17.5%) patients transferred to HD and there was no significant difference in technique survival between the 3 groups. The most common cause of PD exit was re-transplantation (35 patients, 81.5%) in TX group and death in PD and HD group. Death rate was 7%, 24%, and 26.5% in TX, PD and HD groups, respectively. Although Hazard ratio of unadjusted patient survival was 0.29 in TX group, there was no significant difference in patient survival between the 3 groups. In the Cox multiple regression model, age, serum albumin level, serum ferritin level, and appetite significantly influenced patient survival.

Conclusion. Our data suggests that outcome of the patients transferred from transplantation and hemodialysis to peritoneal dialysis does not differ from patients with primary peritoneal dialysis therapy. Thus, peritoneal dialysis could be considered in the patients experiencing complications on HD and in the patients with failing renal transplantation.

O605 The Role of Residual Renal Function and Net Fluid Removal on Patient Survival in Iranian CAPD Patients

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Introduction. Residual renal function (RRF) at the initiation of peritoneal dialysis is an important prognostic factor and rate of RRF decline can predict patients’ mortality. In this study, associations between patient survival and baseline urine volume (UV), ultrafiltration volume (UF), and combined UV and UF were evaluated in Iranian CAPD patients.

Methods. Between January 1995 and December 2006, from 26 PD centers, data on 1472 patients including demographic, clinical, and laboratory characteristics, which were monthly collected through questionnaires were entered in “Hakim” (a Farsi database). In this historical cohort study, the data was extracted from Iran PD registry and analyzed using STATA (9.0). Baseline UV was considered as an indicator of RRF and change in UV was observed over time. Mean of UF, within 3 months after starting CAPD, was also recorded.

Results. A total number of 1472 patients’ data through Iran PD registry were studied. We assessed multiple cutoffs and found significant correlation between baseline UV and patient survival when we categorized UV to < 250cc/d and ≥ 1000/d. We found that patients with higher baseline UV were more married and educated and were candidates for CAPD based on positive selection criteria. Mean of serum creatinine was lower and mean of serum albumin was higher in the patients with UV ≥ 1000cc/d. Multiple UV records were checked during follow-up and we categorized them into stable and decreased UV over time. Patients with stable UV had better survival compared to the patients with decreasing UV over time (P = 0.04). There was no correlation between UF and patient survival. We looked for the role of combination UV and UF (net positive fluid removal) and after assessing multiple cut offs, just in categorizing them into two groups ≥ 2000cc/d and < 500cc/d, we found a significant correlation between UV + UF and patient and technique survival. Multiple Cox regression analysis also showed correlation between this categorization (P = 0.01, HR = 13.2), higher serum albumin (P = 0.01, HR = 0.02), negative selection type (P = 0.09, HR = 11.8), and patient survival.

Conclusion. This study is consistent with the studies which confirm the role of RRF in patient survival. Also, it has been shown that loss of UV over time and lower net positive fluid removal increases mortality of these patients. As a result, all efforts should be applied to prevent loss of RRF and proper fluid balance.

O606 The Outcome of Peritoneal Dialysis Catheters in Patients with Previous Abdominal Operations and Intraperitoneal Adhesions
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Introduction. Previous abdominal surgery with the concern of intraperitoneal adhesions is often used to judge patient eligibility for peritoneal dialysis (PD). The purpose of the present study is to investigate how the use of a laparoscopic modality for catheter placement may affect the differences in catheter outcomes in patients with and without intra-abdominal adhesions.

Methods. All data in this report was recorded prospectively in a database of patients who underwent laparoscopic implantation of PD catheters between March 2004 and February 2008. Catheter implantation was performed using a two-port laparoscopic approach under local anesthesia. Overall, catheter survival probability was estimated using the method of Kaplan and Meier.

Results. Laparoscopic implantation of 217 catheters was reviewed. There was a history of previous abdominal surgery in 93 of 217 procedures (42.9%). Only 25 (26.9%) patients with previous surgery were noted to have intraperitoneal adhesions. Previous abdominal surgery in patients with adhesions included cesarean section, hysterectomy, cholecystectomy, renal transplantation, nephrectomy, abdominal wall hernia, and laparotomy for bowel obstruction and trauma. The results of the comparative analysis between the 31 patients with adhesions and the remaining 186 patients without intraperitoneal adhesions showed that there were no significant differences between the two groups for 1- and 2-year overall catheter survivals (89% versus 91%), mechanical complications (19.4% versus 22.6%), and infectious complications (51.6% versus 44.6%).

Conclusion. There is no significant difference between the outcome of PD catheters in patients with and without intraperitoneal adhesions. Patients should not be deprived from the opportunity to pursue PD because of a history of abdominal operations. Currently, laparoscopy is the only practical way to reliably investigate the suitability of the peritoneal cavity for PD and permits insertion of the catheter into the position of the most favorable function and enables adhesiolysis, when needed.