



ISPD Asian Chapter Newsletter

International Society for Peritoneal Dialysis (ISPD)

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From the Editorial Office

Dear All,

Welcome back from the 2008 ISPD congress held in Istanbul, Turkey. I think it was a great success.

In this issue, we are delighted to have Dr. C.Y. Chou from Taiwan to discuss his experience in treating chronic hepatitis carriers with peritoneal dialysis. You are most welcome to distribute this newsletter electronically, or in printed form, to your colleagues or other people who may be interested. If you or your colleagues would like to receive this newsletter directly from our editorial office, please send your e-mail address to: administration@multi-med.com

Sincerely,

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To our industry partners:

The editorial office welcomes your assistance in distributing this newsletter in electronic or printed form to the dialysis community. If you are interested in sending scientific messages through the newsletter, please contact the editor at: ccszeto@cuhk.edu.hk

Upcoming PD Meetings

29th Annual Dialysis Conference

March 8-10, 2009

George R. Brown Convention Center, Houston, Texas

Abstract Deadline: October 6, 2008

Website: <http://som.missouri.edu/CME/2009ADC.shtml>

Contact: Ms. Elaine Rogers. Email: dialysis@health.missouri.edu

Phone: 573-882-4105; Fax: 573-882-4106

World Congress of Nephrology 2009

May 22-26, 2009 Milan, Italy

The WCN 2009 is a joint meeting between ERA-EDTA and ISN.

Website: <http://www.wcn2009.org/sites/0/IT/default.tpl>

4th Asian Chapter Meeting

October 2009 Beijing, China

Mark your diary!

Research Update in PD

Update on Peritoneal Transport Model

The three-pore model of peritoneal fluid transport predicts that once the osmotic gradient has dissipated, fluid reabsorption will be due to a combination of small-pore reabsorption and lymphatic drainage. A recent study by Asghar and Davies measured fluid transport by these pathways by using radio-iodinated serum albumin as an intraperitoneal volume marker and changes in intraperitoneal sodium mass to determine small-pore versus transcellular fluid transport. In the absence of an osmotic gradient, fluid reabsorption occurred via the small-pore pathway, the rate being proportional to the small-solute transport characteristics of the membrane. In most cases, fluid removal from the peritoneal cavity by this pathway was faster than by lymphatic drainage. This study shows that in the presence of high solute transport, poor transcellular ultrafiltration was due to loss of the osmotic gradient and an enhanced small-pore reabsorption rate after this gradient dissipated.

Comments: This study, in essence, confirms the traditional three-pore model of peritoneal transport. The next step is to examine how reliable the model is in predicting fluid removal in real life practice.

- Asghar RB, Davies SJ. Pathways of fluid transport and reabsorption across the peritoneal membrane. *Kidney Int* 2008; 73: 1048-53.
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Cystatin C level and Residual Renal function

Cystatin C is a low-molecular-weight protein often used as a glomerular filtration rate marker. A recent cross-sectional study on 119 PD patients investigated whether serum cystatin C concentration is related to peritoneal and renal clearances. It was found that serum cystatin C concentration was related inversely to the residual GFR – defined as the average of urinary urea and creatinine clearance. In a multiple regression model, weight, normalized protein catabolic rate, and residual GFR had independent effects

on serum cystatin C concentrations. It was concluded that serum cystatin C concentrations reflect predominantly renal, not peritoneal, clearance.

Comments: For most practicing nephrologists who are not familiar with the unit and reference range of serum cystatin C level, the difficulty is how to interpret the result. Some would even argue that quantifying the volume of urine output per se is as important as measuring the clearance.

- Delaney MP, et al. Relationship of serum cystatin C to peritoneal and renal clearance measures in peritoneal dialysis: a cross-sectional study. *Am J Kidney Dis* 2008; 51: 278-84.
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Quality of Life of Caregivers

As PD patients become more elderly, with more co-morbidity, their dependence on caregivers to provide physical, emotional, and logistical support increases. Fan et al studied new PD patients and their caregivers over a 1-year period. They found that the baseline quality of life score correlated with co-morbidity and functional capacity. Scores of all domains improved after 1 year with some reaching statistical significance. When caregivers of highly dependent patients (required to perform daily dialysis) were compared to those of less dependent patients, the former had a significant worsening of their mental health. In other words, despite increasing the burden, with careful selection, education, and support, PD does not adversely affect the quality of life of caregivers whilst there was some evidence of worsening, especially in social functioning.

Comments: This study gives reassurance that establishing dependent patients on PD at least does no harm to their families or caregivers. Since ethnicity has a strong influence on the perception of the quality of life, similar studies would be necessary in Asian patients.

- Fan SL, et al. Quality of life of caregivers and patients on peritoneal dialysis. *Nephrol Dial Transplant* 2008; 23: 1713-1719.



Interview with Dr. Che-Yi Chou

Dr. Che-Yi Chou

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1. We are impressed by your recent paper “Mortality in hepatitis C-positive patients treated with peritoneal dialysis” in *Peritoneal Dialysis International*. Can you highlight your key findings to our readers ?

HCV-positive PD patients had higher mortality than the HCV-negative PD patients. The association between HCV infection and mortality was independent of diabetes. PD patients with HCV infection were more at risk for chronic infection, inflammation, and malnutrition. Cardiovascular mortality and infection were the leading causes of death among HCV-positive patients treated with PD.

2. What is the policy and practice of screening for hepatitis B and C in your unit ? Is there any vaccination program for patients without immunity to hepatitis B ?

We checked anti-HCV antibody and HBsAg using the 3rd generation ELISA test when patients started PD or HD, followed by a regular 6-month check for anti-HCV Ab and

HBsAg. We measured anti-HBsAb every year and treated patients with Anti-HBsAb titer less than 20 IU/L using hepatitis B vaccine. Patients who had never accepted hepatitis B vaccine were treated with double dose hepatitis B vaccine subcutaneously for 4 times (0, 1, 2, and 6 months) and patients who had been vaccinated before were treated with a double-dose of hepatitis B subcutaneously. We rechecked anti-HBs Ab in the following month to monitor the response to hepatitis B vaccine.

3. What specific problem do you encounter in cirrhotic patients undergoing PD? Is excessive ultrafiltration common? What is your experience in managing this problem?

The result of PET test, the prevalence of H/HA (about 20%), was not different in patients with liver cirrhosis to patients without. Adequate fluid removal with 1.5% and 2.5% PD solution can be achieved in most liver cirrhosis patients. Acute exacerbation of hepatitis C, decompensated liver cirrhosis, or fulminate hepatitis in PD patients are rare events in our experience. The hepatitis C in chronic PD patients seems to be a chronic stable disease, however, persisting chronic inflammation may explain the higher mortality rate in HCV-positive PD patients than in HCV-negative PD patients. Most liver cirrhosis patients had low body weight and serum albumin levels. It is possible that protein loss in dialysate may be higher in patients with liver cirrhosis.

4. What dietary advice do you give to cirrhotic PD patients? What is your practice of giving nutritional and vitamin supplements? Is there any collaboration with dietitian on this aspect?

It is difficult to suggest whether cirrhosis patients should take high protein diet, 1.2 to 1.5g/kg, or which kind of protein should suit them. Some patients developed grade 1 encephalopathy after taking 1.2 g/kg of protein. We have collaboration with a dietitian, however we can provide little help in preventing cirrhosis related encephalopathy.

5. Does the presence of cirrhosis affect your choice of PD fluid (e.g. lactate-free solution)?

As the use of Icodextrin and Nutrineal has been covered by national health insurance since 2001 (patients needed



to pay for the dialysate before 2001), the prevalence of using Nutrineal and Icodextrin has increased. About 60% of patients obtain adequate fluid removal using regular dialysate and 40% of patients do benefit from the use of Icodextran. About 20% patients have an increase of albumin levels after the use of Nutrineal.

6. Did some of your patients undergo combined liver-kidney transplant? When do you consider putting a patient on such a waiting list?

None of our HCV-positive patients received kidney transplantation because it was not recommended for patients with HCV infection in the past. Furthermore, the presence of HCV infection is a minus when a patient registers in our organ sharing system, resulting in low priority on the organ recipients list.

NEWS from the ISPD

ISPD has a new website

The ISPD launched a new website on June 20, 2008. It is more user-friendly, contains several new features, and lots of information about the ISPD and its regional chapters. The website address remains the same: www.ispd.org

'Ask the Experts'

Have you ever wanted to seek an expert's opinion to help you in managing your patients? In order to answer your questions, the ISPD is now providing an "Ask the Experts" service to doctors and nurses on the ISPD website. Simply visit www.ispd.org and you will find the "Ask the Experts" section on the main page. You can submit a question and a member of the ISPD will provide an answer. In less than a month from the launch of the new service, we had already received ten questions. Past questions and answers can also be found on the website in the archives and contain valuable information from which to learn about PD.

Asian Chapter Scholarship

This is a scholarship to support up to 3 months of training in clinical PD for doctors and nurses from Asia. There are two rounds and deadlines for application occur twice a year, either June 30th, or December 31st. **The next deadline is December 31, 2008.** Details and application procedures can be found under the Regional Chapters – Asian Chapter section, on the ISPD website.

As of June 2008, two applications have been received and are now undergoing processing.

Open bidding for the 5th Asian Chapter Meeting 2011

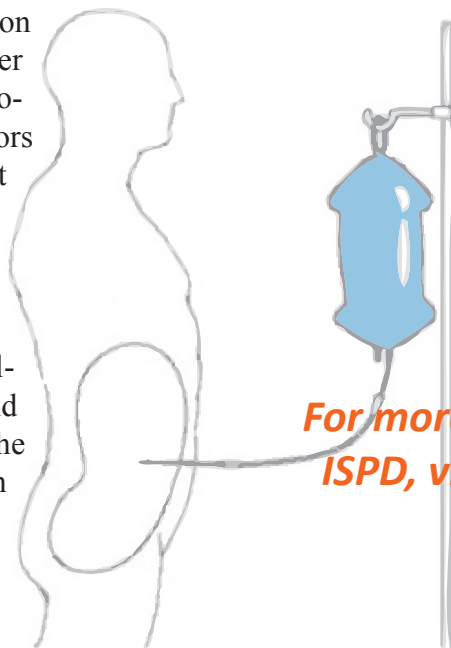
The 4th Asian Chapter Meeting will be held from October 15 – 17, 2009, in Beijing, China. The 5th Asian Chapter Meeting, scheduled for 2011, is now open for bidding. Interested parties please contact Prof. Tao Wang at wangt@bjmu.edu.cn

The 12th Congress of the ISPD

The 12th Congress was held on June 21-24, 2008 in Istanbul, Turkey. Over 2200 delegates attended the meeting. Delegates learned a great deal from the scientific content and were thrilled by the exotic cultural events. The next Congress will be held in July of 2010 in Mexico City, Mexico.



Galata Tower, Istanbul



For more information about the ISPD, visit the ISPD website at www.ispd.org

From the PD industry

Understanding Survival Data in Dialysis: A Statistician's Perspective

Edward F. Vonesh, Ph.D.

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Introduction

According to the 2006 and 2007 USRDS annual data reports as well as recent publications, clinical outcomes among peritoneal dialysis (PD) patients, including patient and technique survival, have shown significant improvements over the past 10-15 years as compared with little or no improvements in outcomes among hemodialysis (HD) patients. [1-4] Danish and Canadian registry data have likewise shown that PD patients have a survival advantage relative to HD patients particularly in the first 2 years. [5-7] Actually, there have been a number of large-scale registry and prospective cohort studies published in the past 10-15 years comparing patient survival among ESRD patients undergoing PD and HD, but unfortunately, results from these studies are both controversial and conflicting in nature (Table 1). In order to reach a consensus regarding the effectiveness of PD as a therapy of choice for ESRD patients, one must carefully weigh the strengths and weaknesses of each of these studies. The publications in Table 1 were assessed by examining the various methodological approaches used in survival comparisons.

Using incident patients

To avoid confusion due to vintage effects, and the fact that mortality rates between PD and HD are not proportional to one another over time, one should always use incident

patients when comparing patient survival. This effectively eliminates the paper by Bloembergen *et al.* [8] from serious consideration: by using prevalent-only patients, their analysis fails to fully account for the survival advantage shown for PD during the first year of dialysis. [6-7,9]

Adjusting for key confounding variables

One should make every attempt to adjust for all known risk factors when comparing survival. Ignoring important confounding variables may lead to considerable bias when estimating the relative risk of death. This explains, in part, the discrepancy in results between the paper by Collins *et al.*, [9] the papers by Ganesh *et al.*, [10] and Stack *et al.* [11] Because confounding risk factors like baseline co-morbidity, GFR, albumin, etc. were not available to Collins *et al.* [9] at the time of their analysis, their results were mostly favorable for PD as compared to the Ganesh and Stack papers which did adjust for confounding factors. Because it was only able to adjust for demographic characteristics (age, gender, race) and diabetes, the paper by Collins *et al.* [9] should also be removed from serious consideration.

Considering important interaction effects

Likewise, one should make every attempt to include important factors (like age and diabetes) that significantly interact with treatment modality in one's analysis as such interactions reflect important subgroup differences in the relative risk of death between PD and HD. This effectively removes the papers by Ganesh [10] and Stack [11] from serious consideration because both papers ignore the previously well-established and important finding of an interaction between age and modality, especially in diabetics. As demonstrated by Vonesh *et al.* [12], ignoring such an interaction leads to a survival model that fits the data poorly and thus can give very misleading results

Table 1 Summary finding of 14 recent publications showing conflicting results

HD has better outcomes	PD has better Outcomes	HD and PD have equal/mixed outcomes
Bloembergen (JASN 1995) [8]	Fenton (AJKD 1997) [6]	Vonesh (JASN 1999) [14]
Ganesh (JASN 2003) [10]	Schaubel (PDI 1998) [7]	Termorshuizen (JASN 2003) [15]
Stack (KI 2003) [11]	Collins (AJKD 1999) [9]	Xue (KI 2002) [16]
Jaar (Ann Int Med 2005) [13]	Heaf (NDT 2002) [5]	Vonesh (KI 2004 ; 2006) [12, 4]
		Liem et al. (KI 2007) [17]
		Van Manen et al. (NDT 2007) [18]

Table 2. Average relative risks (HD: PD) by method of analysis

Patient stratum			ITT analysis Adjusted RR (HD:PD) (95% CI)	As-treated analysis Adjusted RR (HD:PD) (95% CI)
Comorbid conditions	Cause of ESRD	Age		
None	Non-DM	18–44	1.24 (1.07, 1.44) ^a	1.55 (1.30, 1.84) ^a
		45–64	1.13 (1.02, 1.25) ^b	1.23 (1.10, 1.38) ^a
		≥65	1.13 (1.05, 1.21) ^a	1.18 (1.09, 1.28) ^a
	DM	18–44	1.22 (1.05, 1.42) ^b	1.45 (1.21, 1.74) ^a
		45–64	0.92 (0.85, 1.00) ^c	0.98 (0.89, 1.07) ^{NS}
		65+	0.86 (0.79, 0.93) ^a	0.86 (0.79, 0.94) ^a
	Non-DM	18–44	1.19 (0.94, 1.50) ^{NS}	1.34 (1.03, 1.76) ^c
		45–64	1.01 (0.92, 1.11) ^{NS}	1.10 (0.98, 1.22) ^{NS}
		≥65	0.96 (0.91, 1.01) ^{NS}	0.98 (0.93, 1.04) ^{NS}
One or more	DM	18–44	1.10 (0.92, 1.32) ^{NS}	1.35 (1.09, 1.68) ^b
		45–64	0.82 (0.77, 0.87) ^a	0.84 (0.78, 0.91) ^a
		≥65	0.80 (0.76, 0.85) ^a	0.82 (0.77, 0.87) ^a

Adapted from Vonesh E, KI 2004;66 (6):2389-2401 [12]

Considering impact of time-dependent covariates

Finally, one should be very careful when examining the impact of time-dependent covariates on the relative risk of death. Common mistakes include: one, adjusting for a time-dependent variable that is itself affected by one or both of the treatment groups being compared; and two, using future time-dependent measurements to predict past survival. This calls the paper by Jaar *et al* [7] into serious question. In addition to issues related to center-selection bias, this paper adjusts for C-reactive protein values that were, on average, measured 5 months after the start of dialysis thereby adjusting for a variable that is affected by 5 months on dialysis and which cannot logically be used to compare survival in the time preceding its measurement.

Conclusion

In summary, when we rule out some of the studies shown in Table 1 due to methodological flaws and consider results from the remaining publications, data from these large-scale registries suggest that, on average, overall patient survival is similar for PD and HD as indeed suggested by Vonesh *et al*. [4]. However, as shown in the paper by Vonesh, [12] important differences do exist within select subgroups of patients, particularly those subgroups defined by age and the presence or absence of diabetes and co-morbidity (Table 2).

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