Implementing a Successful PD Program in a Developing Country

Xueqing Yu  MD, PhD

Department of Nephrology, The First Affiliated Hospital Sun Yat-sen University, Guangzhou
CKD is a big public health problem in China

- Prevalence of CKD in Guangzhou: 12.1%
- Prevalence of CKD in Beijing: 11.3%
- Prevalence of CKD in Shanghai: 11.8%
- Prevalence of CKD in Zhengzhou: 13.5%

The Prevalence of CKD in China: 10.8%


- Prevalence of CKD in Zhengzhou: 13.5%

- Chen W, ...Yu XQ. et al. NDT 2009;24:1205-12
- Zhang L, ...Wang H.et al. AJKD, 2008 ;51(3):373-84
- Chen N, ...Fan Q. et al. NDT 2009;24:2117-23
Number of ESRD patients is rapidly increasing in China

In 2010

<table>
<thead>
<tr>
<th>Condition</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>30 million</td>
</tr>
<tr>
<td>High blood pressure/chronic renal disease</td>
<td>80 million</td>
</tr>
<tr>
<td>Need of dialysis</td>
<td>1 million</td>
</tr>
</tbody>
</table>

≈150,000 dialysis patients in China
Increasing Demand for PD in China

• Increasing population, especially the elderly age group
• High prevalence of CKD, more ESRD patients
• As the economy develops, Medical Insurance covers more dialysis patients
• Limited resource & infrastructure capacity (space, equipments and professional staff)
• Home dialysis becoming more popular
The advantage of PD in China

- Safe, convenient and easy to learn
- Good for patients living far away from dialysis centers
- Most Chinese people live in the countryside
- Most county hospitals lack of HD machines
- Suitable for patients with transmittable infectious diseases
Center Government Promote PD Therapy in China
How to Run a Successful PD Program
- Guangzhou’s experiences
PD Program Development at SYSU

• 1964: Commencing peritoneal dialysis
• 1978: First case using CAPD in China
• 2005: Set a New PD model in SYSU
• 2012: More than 1,000 PD patients
The PD team at Sun Yat-sen University

<table>
<thead>
<tr>
<th></th>
<th>2006</th>
<th>2009</th>
<th>2012</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Doctors</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In patient</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Follow up</td>
<td>2</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td><strong>Nurses</strong></td>
<td>5</td>
<td>6</td>
<td>13</td>
</tr>
<tr>
<td>Assistant</td>
<td>1</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Secretary</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

Nurses/patients ratio, Canada 1:25,  China 1:50,  SYSU 1:80
Nephrologists Roles & Responsibilities

• **In-patient ward**
  - Pre-dialysis counseling
  - Catheter insertion
  - PD Initiation

• **For follow-up unit**
  - Follow-up of PD patients
  - In charge of PD round
  - Quality control continuously
Nurse’s Role & Responsibility

• Training and retraining: reinforce the technique
• Follow-up: clinic, home visit and telephone call
• Compliance monitor and supportive counseling
• Continuous data collection: peritonitis rates drop-out; mortality; hospitalization etc.
• Identify problems and immediate feedback
PD team’s Role & Responsibility

• Insert catheter successfully and follow up
• Endorse patients’ self-management
• Enhance patient’s compliance to PD
• Promote patients’ confidence and self esteem
• Continuous quality improvement
• Achieve better patients clinic outcome
Excellent PD Team in SYSU
Complete Patients Record and CQI
Medical Document and Records

- Hard copies of patients file
- Electronic documents
- Monthly reports for PD patients
- Problem discussion and management meeting monthly
The registered PD patients in SYSU

Registration patients for follow-up

2006yr: 297
2007yr: 409
2008yr: 547
2009yr: 695
2010yr: 867
2011yr: 968

N=1040

2012. 8
Patient Survival for Prevalent Patients

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>12mo</th>
<th>36mo</th>
<th>60mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &lt; 64 ys</td>
<td>377</td>
<td>96 ± 0.01%</td>
<td>86 ± 0.02%</td>
<td>79 ± 0.03%</td>
</tr>
<tr>
<td>Age ≥ 65 ys</td>
<td>131</td>
<td>88 ± 0.03%</td>
<td>62 ± 0.05%</td>
<td>38 ± 0.06%</td>
</tr>
<tr>
<td>Total</td>
<td>508</td>
<td>94 ± 0.01%</td>
<td>79 ± 0.02%</td>
<td>66 ± 0.03%</td>
</tr>
</tbody>
</table>

Yang X, ... Yu XQ. CMJ 2011; 124:2696-2700
Technique Survival for Prevalent Patients

<table>
<thead>
<tr>
<th></th>
<th>12mo</th>
<th>36mo</th>
<th>60mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &lt; 64ys</td>
<td>99 ± 0.00%</td>
<td>96 ± 0.01%</td>
<td>86 ± 0.03%</td>
</tr>
<tr>
<td>Age ≥65 ys</td>
<td>97 ± 0.03%</td>
<td>88 ± 0.05%</td>
<td>80 ± 0.03%</td>
</tr>
<tr>
<td>Total</td>
<td>99 ± 0.02%</td>
<td>94 ± 0.03%</td>
<td>85 ± 0.06%</td>
</tr>
</tbody>
</table>

Yang X, ... Yu XQ. CMJ 2011; 124:2696-2700
Time on therapy (TOT) of CAPD patients

![Bar chart showing time on therapy (TOT) for CAPD patients from 2006 to 2011. Values are as follows:

- 2006: 30.5
- 2007: 29.8
- 2008: 33.6
- 2009: 30.3
- 2010: 30.1
- 2011: 33.1

The chart indicates an increase in TOT over the years.]
Drop-out rate of CAPD patients

Drop rate (including TX)

Drop rate (excluding TX)
The rate of peritonitis

(One episode / patient months)
## KPI Approach in SYSU 2011

<table>
<thead>
<tr>
<th>Indicators</th>
<th>KPI</th>
<th>Approach %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin (110-130g)</td>
<td>≥70%</td>
<td>65%</td>
</tr>
<tr>
<td>Serum Phosphate (≤1.78mmol/L)</td>
<td>≥70%</td>
<td>66%</td>
</tr>
<tr>
<td>Weekly Kt/V ≥1.7</td>
<td>≥90%</td>
<td>91%</td>
</tr>
<tr>
<td>SBP 105-140mmHg</td>
<td>≥70%</td>
<td>73%</td>
</tr>
<tr>
<td>Peritonitis Rate</td>
<td>≥1:30</td>
<td>1:86</td>
</tr>
<tr>
<td>Exit Infection Rate</td>
<td>≥1:50</td>
<td>1:87</td>
</tr>
<tr>
<td>Technical Survival (1 year)</td>
<td>≥ 85%</td>
<td>98%</td>
</tr>
<tr>
<td>Catheter Survival (1 year)</td>
<td>≥ 80%</td>
<td>94%</td>
</tr>
</tbody>
</table>

Johnson, DW, et al. ISPD ACM 2010, 8:2-3
Yang X, ... Yu XQ. CMJ 2011; 124:2696-2700
How to maintain PD patients in the PD therapy
Patient’s education - Issues and limitations

• Limited pre-operation education time
  - very limited time (1~3 days)

• Immediate start of PD after catheter insertion

• Post-operation training program
  - an average of 5 days

• Training not only patients, also related person
# Current PD Follow-up Program

<table>
<thead>
<tr>
<th>Time</th>
<th>Mode</th>
<th>Items</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monday (am)</td>
<td>Clinic Visit</td>
<td>• Evaluation</td>
</tr>
<tr>
<td>Thursday (am)</td>
<td></td>
<td>• Physical and blood examination</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Prescription assessment?</td>
</tr>
<tr>
<td>Tuesday (pm)</td>
<td>Prescription</td>
<td>• PD Solution</td>
</tr>
<tr>
<td>Friday (pm)</td>
<td></td>
<td>• Drugs</td>
</tr>
<tr>
<td>Monday (pm)</td>
<td>Data review management</td>
<td>• Reviewing biochemistry test results</td>
</tr>
<tr>
<td>Thursday (pm)</td>
<td></td>
<td>• Prescription change</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Informing patients</td>
</tr>
</tbody>
</table>
Purpose of PD Satellite Program

• To establish advanced PD satellite centers in Guangdong province with adequate education and training system

• Using standard PD program in patient’s training, education, procedures, and follow-up

• To set up a good model to improve PD outcome (i.e. patient and technical survival) and QOI
Some Indices have shown improving quality of PD

<table>
<thead>
<tr>
<th>Time</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
</tr>
</thead>
<tbody>
<tr>
<td>Annual dropout rate %</td>
<td>28.2±2.8</td>
<td>23.3±3.6</td>
<td>17.6±1.7a</td>
</tr>
<tr>
<td>Death</td>
<td>51.3</td>
<td>48.2</td>
<td>39.2</td>
</tr>
<tr>
<td>Kidney transplantation</td>
<td>26.2</td>
<td>22.7</td>
<td>18.2</td>
</tr>
<tr>
<td>Transfer to hemodialysis</td>
<td>12.5</td>
<td>14.8</td>
<td>16.9</td>
</tr>
<tr>
<td>Other</td>
<td>10.0</td>
<td>14.3</td>
<td>25.7</td>
</tr>
<tr>
<td>Incidence of peritonitis</td>
<td>39.4±2.7</td>
<td>41.3±4.2</td>
<td>46.2±3.9b</td>
</tr>
<tr>
<td>(patient-months/episode)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Technique survival (%)</td>
<td>88.7±1.5</td>
<td>89.1±1.9</td>
<td>93.0±0.8c</td>
</tr>
<tr>
<td>Patient Survival (%)</td>
<td>82.0±1.1</td>
<td>81.3±1.6</td>
<td>84.2±0.9</td>
</tr>
<tr>
<td>Time on PD (months)</td>
<td>16.3±1.8</td>
<td>17.5±1.6</td>
<td>18.3±2.4</td>
</tr>
</tbody>
</table>

Jiang ZP, Yu XQ, PDI 2011:3:121-126
PD Satellite Program in Southern China

29 PD centers in 11 provinces

Randomization to two group

Training groups

Control groups

Training program

3-5 years follow up

Data collection and analysis
Optimization of peritoneal dialysis through research activities
PD Research Program In SYSU

• Clinical problem or evidences driven research
• Basic research: mechanism explore
• Clinical practice: improving clinical outcome

Bed side ➔ Bench side ➔ Bed side
Basic Research Current and Future

Peritonitis and Peritoneal fibrosis

- TGF-/smad and EMT
- Signaling cross-talk
- cell to cell Junction in EMT
The role of TGF-β/smads in the mechanism of peritoneal fibrosis


**EMT and Fibrosis**
The Regulating Mechanism of TGF-β/Smads on EMT


Clinical Research Program

• Preservation of Peritoneal function
• Preservation of residual renal function
• Prevention of CVD in PD patients
• Bio-maker for the early diagnosis
• PD Satellite training Center in Guangdong
The Ongoing Program in SYSU

• ACEI, ARB and combination in the preservation of peritoneal and RRF.
• Low diet protein plus keto-acid in the preservation of peritoneal and RRF.
• The molecular mechanism of pathogen in PD related peritonitis and preventive strategy for the relapse peritonitis.
Preservation of RRF in PD patients: the role of RAS inhibitors

ClinicalTrials.gov ID: NCT00721773
Objectives

- To investigate the effects of RAS inhibitors on RRF in PD patients.
- To compare the effects of ACEI, ARB or combination of both therapy on RRF in PD patients.
Study Protocol

Patients enrolled (200)

Randomization

Control  Benazepril  Valsartan  Combination

Follow up every 3 months

RRF  Peritoneum function  Dialysis adequacy  Cardiovascular events
ACEI delay the rate of decline in RRF in CAPD patients.

However, the study need to be further investigated.
The Effect of RPD + KA on Preserving Peritoneal And RRF in CAPD Patients
Aim of This Study

The effects of LPD plus Keto Acid on CAPD Patients, including:

- Residual Renal Function
- Peritoneal Function
- The nutritional status
- Metabolic Acidosis
- Calcium, Phosphate, and C/P products
Clinical trial Design

Patients (n=240)

Randomization

- RPD
  N=80
- LPD
  N=80
- LPD+KA
  N=80

Follow up: 0, 3, 6, 12, 18, 24, 30 and 36 months
Summary of Pilot Study

• The dietary protein in both HD and PD patients recommended by NKF-KDOQI guidelines (1.2-1.3g/kg/day) seems little higher.

• Currently available researches shown that 0.8g/kg/day protein in diet is safe.

• Keto acids supplements are recommended for
  – RRF protection
  – Better nutritional status

• More RCT clinical trials are needed in the future.
Pathogenesis of peritoneal dialysis-related Escherichia coli peritonitis

• To explore the serotypes, genotypes, and virulence factors of *E. coli*

• To determine the innate immunity ability in peritoneum for long term PD

• To determine the adaptive immune responses in long term PD patients

This program was granted by Baxter EGP 2009
Genetic relationship among 29 *E. coli* strains.
The positive rates of virulence factors in *E. coli* stains

<table>
<thead>
<tr>
<th>VF</th>
<th>PD effluents</th>
<th>Blood</th>
</tr>
</thead>
<tbody>
<tr>
<td>fimH</td>
<td>19 / 28</td>
<td>1 / 1</td>
</tr>
<tr>
<td>sfaS</td>
<td>2 / 28</td>
<td>0 / 1</td>
</tr>
<tr>
<td>fyuA</td>
<td>17 / 28</td>
<td>1 / 1</td>
</tr>
<tr>
<td>kpsMT</td>
<td>0 / 28</td>
<td>0 / 1</td>
</tr>
<tr>
<td>cdtB</td>
<td>0 / 28</td>
<td>0 / 1</td>
</tr>
<tr>
<td>cnf1</td>
<td>0 / 28</td>
<td>0 / 1</td>
</tr>
</tbody>
</table>
Can We Explore Predictive Biomarkers in The Negative Culture Bacteria Peritonitis?
### Demographic and clinical characteristics of the patients with peritonitis

<table>
<thead>
<tr>
<th></th>
<th>control</th>
<th>E-coli</th>
<th>Streptococcus</th>
<th>CoNS</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>case</td>
<td>41</td>
<td>51</td>
<td>37</td>
<td>35</td>
<td>NA</td>
</tr>
<tr>
<td>Age (years/old)</td>
<td>47 ± 13</td>
<td>49 ± 13</td>
<td>54 ± 14</td>
<td>51 ± 17</td>
<td>0.28</td>
</tr>
<tr>
<td>Sex (male/female)</td>
<td>21/20</td>
<td>28/23</td>
<td>20/17</td>
<td>17/18</td>
<td>NA</td>
</tr>
<tr>
<td>DM</td>
<td>1/41</td>
<td>2/51</td>
<td>0/37</td>
<td>1/35</td>
<td>NA</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>31 ± 6</td>
<td>29 ± 6</td>
<td>30 ± 7</td>
<td>30 ± 6</td>
<td>0.86</td>
</tr>
<tr>
<td>Triglyceride (mmol/L)</td>
<td>1.9 ± 0.6</td>
<td>1.0 ± 0.4</td>
<td>1.4 ± 0.6</td>
<td>1.5 ± 0.7</td>
<td>0.08</td>
</tr>
<tr>
<td>Cholesterol (mmol/L)</td>
<td>5.1 ± 1.1</td>
<td>4.5 ± 1.1</td>
<td>5.0 ± 1.2</td>
<td>4.5 ± 1.0</td>
<td>0.11</td>
</tr>
<tr>
<td>Albumin (g/L)</td>
<td>38 ± 5</td>
<td>31 ± 6</td>
<td>34 ± 5</td>
<td>32 ± 6</td>
<td>0.25</td>
</tr>
<tr>
<td>Uric acid (umol/L)</td>
<td>377 ± 82</td>
<td>331 ± 99</td>
<td>364 ± 101</td>
<td>334 ± 89</td>
<td>0.06</td>
</tr>
<tr>
<td>GPT (U/L)</td>
<td>16 ± 9</td>
<td>15 ± 9</td>
<td>18 ± 6</td>
<td>17 ± 8</td>
<td>0.07</td>
</tr>
<tr>
<td>Creatinine (umol/L)</td>
<td>860 ± 260</td>
<td>790 ± 261</td>
<td>835 ± 291</td>
<td>893 ± 277</td>
<td>0.43</td>
</tr>
</tbody>
</table>
control E.coli CoNS streptococcus
## Validation of Model

### control

<table>
<thead>
<tr>
<th>Model Type</th>
<th>control</th>
<th>Non-control</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>control</td>
<td>46</td>
<td>7</td>
<td>53</td>
</tr>
<tr>
<td>Non-control</td>
<td>9</td>
<td>142</td>
<td>151</td>
</tr>
<tr>
<td>Total</td>
<td>55</td>
<td>149</td>
<td>204</td>
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</tbody>
</table>

### E.coli

<table>
<thead>
<tr>
<th>Model Type</th>
<th>E.coli</th>
<th>Non-E.coli</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>control</td>
<td>55</td>
<td>12</td>
<td>67</td>
</tr>
<tr>
<td>Non-control</td>
<td>4</td>
<td>133</td>
<td>137</td>
</tr>
<tr>
<td>Total</td>
<td>59</td>
<td>145</td>
<td>204</td>
</tr>
</tbody>
</table>

### CoNS

<table>
<thead>
<tr>
<th>Model Type</th>
<th>CoNS</th>
<th>Non-CoNS</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>control</td>
<td>30</td>
<td>7</td>
<td>37</td>
</tr>
<tr>
<td>Non-control</td>
<td>8</td>
<td>159</td>
<td>167</td>
</tr>
<tr>
<td>Total</td>
<td>38</td>
<td>166</td>
<td>204</td>
</tr>
</tbody>
</table>

### Streptococcus

<table>
<thead>
<tr>
<th>Model Type</th>
<th>strept</th>
<th>Non-strept</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>control</td>
<td>41</td>
<td>6</td>
<td>47</td>
</tr>
<tr>
<td>Non-strept</td>
<td>11</td>
<td>146</td>
<td>157</td>
</tr>
<tr>
<td>Total</td>
<td>52</td>
<td>152</td>
<td>204</td>
</tr>
</tbody>
</table>
Predictive Value With Peptome Profile Model

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity(%)</th>
<th>Specificity(%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>86.9 (46/53)</td>
<td>94.0 (142/151)</td>
<td>83.6 (46/55)</td>
<td>95.3 (142/149)</td>
</tr>
<tr>
<td>E.coli</td>
<td>82.1 (55/67)</td>
<td>97.1 (133/137)</td>
<td>93.2 (55/59)</td>
<td>91.7 (133/145)</td>
</tr>
<tr>
<td>CoNS</td>
<td>81.1 (30/37)</td>
<td>95.2 (159/167)</td>
<td>78.9 (30/38)</td>
<td>95.8 (159/166)</td>
</tr>
<tr>
<td>Streptococcus</td>
<td>87.2 (41/47)</td>
<td>93.0 (146/157)</td>
<td>78.8 (41/52)</td>
<td>96.1 (146/152)</td>
</tr>
</tbody>
</table>

PPV: positive predictive value
NPV: negative predictive value
A Prospective, Randomized, Multicenter Study Comparing Survival in Subjects Receiving Peritoneal Dialysis or Hemodialysis (SURinD): Feasibility and Preliminary Enrollment Data

On behalf of SURinD study group
Study Objectives

Primary Objective:  
To prospectively assess & compare survival in ESRD patients randomized to either PD or HD treatment.

Secondary Objectives:  To compare:
- Technique failure  
- Cause of death  
- Changes in comorbidity status throughout the study  
- Change in residual renal function (RRF)  
- 24-hour urine volume  
- Dialysis adequacy  
- Transplantation rate  
- Change in erythropoiesis-stimulating agent (ESA) dose  
- Change in blood pressure, hemoglobin, and S-phosphate  
- Change in nutritional status  
- Occurrence of bacterial and other infections  
- Hospitalization, including number, duration, and underlying reason(s)  
- Systemic inflammation as assessed by high-sensitivity C reactive protein (hs-CRP)  
- Quality of life (QOL)
Sample Size & Study Duration

• Prospective, randomized, multicenter, open-label, non-inferiority study

• Approximately 1,370 subjects, randomized to either peritoneal dialysis or hemodialysis in a 1:1 ratio

• The assessment period will be 260 weeks (5 yrs) after the first subject has been randomized. Assuming the recruitment period is 156 weeks (3 yrs), the follow-up period for the last subject is 104 weeks (2 yrs).
Study Timeline

- **Dec. 2010**: Finalize protocol
- **Feb. 2011**: Investigator Meeting
- **Sep. 2011**: Site Initiate FPFV
- **Sep. 2014**: LPFV
- **Sep. 2016**: LPLV
- **Dec. 2016**: Database lock
- **Feb. 2017**: Statistical report
- **Mar. 2017**: CSR finalized & approved
Recruitment Status Overview- 1st year

As of 31 May 2012

*Planned number is based on end of each month
Current Progress in Surind Study

- Recruitment began in September 2011
- 238 subjects had been enrolled at 33 study sites by July 30th, 2012.
- Study completion is expected in 2016.
ISPD Meeting in Mexico (2010)

- 9 abstracts were selected as the oral presentation
- 4 travel grant had been awarded in this meeting
SUMMARY

• A excellent PD team and team work
• Excellent program for patients follow-up
• Continuous quality improvement
• A fair PD reimbursement policy
• Satellite center maybe a good model
• Clinical questions or evidence driven study
Thank you!