

## PEER REVIEW HISTORY

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### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Complications and outcomes of urgent-start peritoneal dialysis in elderly patients with end-stage renal disease in China: A retrospective cohort study
<b>AUTHORS</b>	Zang, Xiujuan; Du, Xiu; Li, Lin; Mei, Changlin

### VERSION 1 – REVIEW

<b>REVIEWER</b>	Patrik Finne Helsinki University Hospital, Finland
<b>REVIEW RETURNED</b>	13-Sep-2019

<b>GENERAL COMMENTS</b>	<p>Zang et al present results from a retrospective cohort study on 542 elderly urgent-start dialysis patients who entered either peritoneal dialysis (USPD) or hemodialysis (USHD). Although peritoneal dialysis is an available option in most nephrological units, in many places the only available option for urgent-start of dialysis is HD. According to this study from Shanghai, USPD is more common than USHD, which is unusual, but appears to be associated with somewhat better results. Maybe one conclusion could be that USPD is underused in many places.</p> <p>The paper is very clearly written, and concise. I have a few questions and comments:</p> <ol style="list-style-type: none"> <li>1) The USPD and USHD groups are surprisingly similar, and looks like a randomized study. I would like the authors to extend the text a bit on the selection of patients into the treatment modalities. Usually PD is selected by patients who have the capability to do dialysis at home, and they are younger (although over 65 in this study) and have less comorbidities.</li> <li>2) Mortality was higher among USPD than USHD. Was there any difference in the causes of death? Were the causes of death in any way related to dialysis modality?</li> <li>3) Some earlier studies have shown that outcome of PD (compared to HD) is worse among elderly diabetes patients. I suggest that the authors do a separate analysis for patients with diabetes and those without? Is there a difference in relative risks of complications and mortality?</li> <li>4) What was the typical PD prescription for the urgent-start patients?</li> <li>5) The need for PD-re-cahterization of 1.6 % within 30 days appears very low. How does that compare to earlier research?</li> <li>6) As the authors point out, the study is retrospective with potential sources of bias. The dialysis modality cannot be causally linked to the outcome.</li> </ol> <p>Minor comment:</p>
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	1) In Table 4 it should be spelled out what unit of measure of serum potassium the relative risk refers to.
<b>REVIEWER</b>	Siribha Changsirikulchai Faculty of Medicine, Srinakharinwirot University, Thailand
<b>REVIEW RETURNED</b>	22-Sep-2019
<b>GENERAL COMMENTS</b>	<p>Thank you for giving me the opportunity to review the manuscript title "Urgent-start peritoneal dialysis in elderly patients with ESRD". I have some comments as the following:</p> <ol style="list-style-type: none"> <li>1. The authors should perform literature review and choose the variables for analysis to compare with previous studies.</li> <li>2. The authors should explain what the reasons choosing those variables for analysis.</li> <li>3. Primary diseases and serum phosphate levels were different between USPD and USHD.</li> <li>4. The authors should exclude patients with CRRT because these group had high mortality rate.</li> <li>5. Table 4; the authors should report in adjusted multivariate analysis.</li> <li>6. The authors should have native English person to help in writing manuscript.</li> <li>7. The authors should discuss more and find reason why their outcomes were different from previous studies.</li> </ol>

### VERSION 1 – AUTHOR RESPONSE

#### Reviewer #1

The paper is very clearly written, and concise. I have a few questions and comments:

1) The USPD and USHD groups are surprisingly similar, and looks like a randomized study. I would like the authors to extend the text a bit on the selection of patients into the treatment modalities. Usually PD is selected by patients who have the capability to do dialysis at home, and they are younger (although over 65 in this study) and have less comorbidities.

Response: We thank the Reviewer for the comment. Indeed, this was not a randomized trial, and some differences might be expected between the two groups. The population of Shanghai is now considered as aging. The elderly people of each community are offered physical examinations every year by the State. The community physicians provide treatments for patients in CKD stages 1-3 and even for some uncomplicated CKD stage 4 patients. So the patients in the general secondary or a tertiary hospital are both serious than the average level. This might be part of an explanation of why the baseline characteristics of the patients are similar. Otherwise, the strict application of the inclusion/exclusion criteria might also be a part of the explanation. And for the selection of USPD or USHD, it was carried out according to the willingness of the patients and the decision of the physicians at the Nephrology Department according to the condition of the patients (vital signs, cardiac functions, and biochemical indexes). This was clarified in methods.

2) Mortality was higher among USPD than USHD. Was there any difference in the causes of death? Were the causes of death in any way related to dialysis modality?

Response: We thank the Reviewer for the comment. Because of the retrospective nature of the study, and the regulations in China, the exact cause of death can be known only if written in the patient chart. Otherwise, such data might be available upon request to the central State database, but access to those data requires special authorization. As of now, the exact cause of death is missing for most

patients. Nevertheless, the difference between the two groups was not very large. This was noted as a limitation and added to the discussion.

3) Some earlier studies have shown that outcome of PD (compared to HD) is worse among elderly diabetes patients. I suggest that the authors do a separate analysis for patients with diabetes and those without? Is there a difference in relative risks of complications and mortality?

Response: We thank the Reviewer for the comment. We carried out the suggested analysis, and we found that USHD had a worse prognosis than USPD in elderly diabetic patients (HR=2.81, 95%CI: 1.09-7.33, P=0.03). Please see the table below. More complications within 30 days after catheter implantation in HD than PD might be a part of explanation. Previous studies reported conflicting results concerning the mortality of HD vs. PD. Indeed, a study showed that mortality was lower for PD in than for HD in non-diabetics, men <55 years of age, and in diabetics <55 years of age, but higher in diabetic women >55 years of age [1]. Lukowsky et al. [2] reported that PD led to better survival than HD in diabetic patients, while a number of studies reported no significant survival difference between HD and PD [3-9]. On the other hand, a meta-analysis suggested that elderly diabetic patients might benefit more from HD than PD [10]. There is still controversy in this area. Additional studies are necessary to examine this issue, especially since the present study specifically examined USPD and USHD, while those previous studies examined all patients. We hope our results will provide a new basis for this question.

Table. Multivariable Cox analysis of the independent factors for survival in elderly patients with diabetes.

Factor	HR	95%CI	P
Serum albumin (every 1 g/L increase)	0.926	0.861-1.00	0.049
Serum potassium (every 1 mmol/L increase)	0.258	0.126-0.538	<0.001
USHD (comparing with USPD)	2.813	1.092-7.330	0.033

4) What was the typical PD prescription for the urgent-start patients?

Response: We thank the Reviewer. For the patients in the USPD group, a PD catheter was used as access. All catheters were implanted by trained physicians after local anesthesia (5-10 ml of 1% lidocaine hydrochloride was applied layer by layer). After the catheter was implanted, the time of the dialysis initiation was decided by the physicians according to the clinical manifestations (vital signs, cardiac functions, and biochemical indexes). For all patients on PD, a swan-neck straight catheter was implanted, and glucose-based dialysate was used in all patients.

For the patients in the HD group, CVC was used as access. All CVCs were implanted into the internal jugular vein or femoral vein by trained physicians. The patients in the USHD group received HD (4 h/time, volume of blood flow was 250-300 ml/min) or continuous renal replacement treatment (CRRT; 6-8 h/time, volume of blood flow was 180-300 ml/min).

5) The need for PD-re-catheterization of 1.6 % within 30 days appears very low. How does that compare to earlier research?

Response: We thank the Reviewer for the comment. The usual rate of catheter dysfunction depends upon the method of implantation and is usually around 5%-8% [11]. We agree that this rate is low, but not so far than that of a study that reported a rate of 5.9% before a continuous quality improvement program and 1.5% after the program [12]. In our hospitals, even there is no official continuous quality improvement program, a strict protocol is followed, which could explain the low rate. Nevertheless, this was noted as a limitation.

6) As the authors point out, the study is retrospective with potential sources of bias. The dialysis modality cannot be causally linked to the outcome.

Response: We agree with the Reviewer. Indeed, no causality analysis is possible, and only associations can be observed. This was emphasized in the manuscript.

Minor comment:

1) In Table 4 it should be spelled out what unit of measure of serum potassium the relative risk refers to.

Response: We thank the reviewer for the suggestion. The units were added.

Reviewer #2

1. The authors should perform literature review and choose the variables for analysis to compare with previous studies.

Response: We thank the Reviewer for the comment. We performed a literature review and added some comparison with previous studies according to your suggestion. You can refer to the revised Discussion.

2. The authors should explain what the reasons choosing those variables for analysis.

Response: We thank the Reviewer for the comment. We performed a literature review prior to the study. We selected the variables that we thought were clinically relevant, as well as those that could be found in the patient charts. And for multivariable analysis, the factors that have been widely acknowledged to affect the survival of the patients, as well as the factors that were significantly different between the two groups at baseline were included. This was clarified in methods.

3. Primary diseases and serum phosphate levels were different between USPD and USHD.

Response: We agree with the Reviewer. The indications for USPD and USHD are not exactly the same, and the selection of USPD or USHD, was based on the physicians' experience. In addition, this was a retrospective study. So some variables may be different.

4. The authors should exclude patients with CRRT because these group had high mortality rate.

Response: We thank the Reviewer for the comment. In fact, we prefer to include those patients because they still have received USPD or USHD. Nevertheless, this was noted in the limitations according to your suggestion.

5. Table 4; the authors should report in adjusted multivariate analysis.

Response: We fear that we do not understand the Reviewer's comment. Table 4 already presents a multivariable analysis, in which all parameters are already adjusted according to the other parameters included in the model. And we only presented the parameters that were statistical significant ( $P < 0.05$ ). If we misunderstood your comment, please no hesitate to tell us.

6. The authors should have native English person to help in writing manuscript.

Response: We thank the Reviewer for the comment. The manuscript was proofread.

7. The authors should discuss more and find reason why their outcomes were different from previous studies.

Response: We thank the Reviewer for the comment. This could be due to the limitations highlighted by the above comments. Please see the revised Discussion.

References

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#### VERSION 2 – REVIEW

<b>REVIEWER</b>	Patrik Finne Helsinki University Hospital, Finland
<b>REVIEW RETURNED</b>	09-Jan-2020

<b>GENERAL COMMENTS</b>	I am satisfied with most of the response of the authors. In point 4) I asked for the PD prescription, and by this I would like to know the following: APD or CAPD? How many rounds/bag exchanges? What is the filling volume of PD fluid?
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## VERSION 2 – AUTHOR RESPONSE

Reviewer #1

I am satisfied with most of the response of the authors.

Response: We thank the Reviewer for taking the time to review our manuscript and for the constructive comments.

In point 4) I asked for the PD prescription, and by this I would like to know the following: APD or CAPD? How many rounds/bag exchanges? What is the filling volume of PD fluid?

Response: We thank the Reviewer. All patients in the USPD group received continuous ambulatory PD (CAPD), four bags/day, 2 L/bag. This was clarified in the manuscript.