Risk of first peritonitis episode in continuous ambulatory peritoneal dialysis and automated peritoneal dialysis: a population-based study

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To the Editor,

In Hong Kong, peritoneal dialysis (PD)-first policy has been adopted for all patients with kidney failure requiring dialysis unless medically contraindicated.¹ PD was generally well-tolerated with better quality of life, better preserved residual kidney function, increased hemodynamic stability, and a lower rate of blood-borne infections than HD.² Nonetheless, peritonitis is one major PD complication which could undermine dialysis, reduce quality of life, and is a major cause of morbidity and mortality.³,⁴ In addition, severe or repeated peritonitis can result in peritoneal membrane failure, leading to technique failure and conversion to chronic HD.⁵

The International Society for Peritonitis Dialysis (ISPD) published several recommendations to minimize peritonitis, but the adoption rate varies.⁶ A much-debated question is whether the use of automated peritoneal dialysis (APD) could lower the incidence of peritonitis compared to continuous ambulatory peritoneal dialysis (CAPD), on account of a lesser frequency of manual exchanges that could theoretically reduce the risk of contamination and hence the incidence of peritonitis.⁷ In particular, even though APD usually requires fewer manual exchanges, multiple line connections are required for each exchange, theoretically increasing the risk of contamination. However, data regarding the impact of PD modalities on the risk of peritonitis remains contradicting.⁸ We, therefore, conducted this study to evaluate the risk of first peritonitis episode among different PD systems.

Our study was a population-based, observational, retrospective cohort study using electronic medical records in the Hong Kong Hospital Authority. Adult patients who newly started PD
between 2007 and 2019 were included. The exposure was PD modality, classified as APD, Disc System (Andy Disc® and Stay Safe Disc®, Fresenius), Stay Safe Balance® (Fresenius) and UltraBag® (Baxter Healthcare). The primary outcome of interest was peritonitis, defined by diagnostic codes using the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM: 014.0, 032.83, 095.2, 098.86, 567.0, 567.1, 567.2, 567.89, 567.9, 996.68), with secondary outcomes of interest including all-cause mortality, cardiovascular death, all-cause accident and emergency department (AED) attendance and technique failure. Patients were followed from the date of the first outpatient or discharge prescription containing PD fluids until the date of outcome occurrence, changes in PD modality, conversion to HD or having been transplanted, discontinuation of PD, 3 years from the first prescription of PD fluid, or the end of the study period, whichever came first. We applied multi-group Inverse Probability of Treatment Weighting (IPTW) Cox proportional-hazards models and Kaplan–Meier curve to evaluate the hazard ratios and to illustrate the cumulative incidence of the outcomes over time respectively. Subgroup analyses and sensitivity analyses were also performed. Detailed methodology is described in Supplementary Material 1.

A total of 14,693 patients with a prescription of PD fluid were identified. After excluding patients without a discharge or outpatient prescription of PD fluid, initiated PD at age <18 or with a PD regimen containing either icodextrin, Spike or Twin-Bag, a record of 11,021 patients was retained and analysed (Supplementary Material 2).

More than 68.6% of the included patients were prescribed the Ultrabag® system, while 9.7%, 12.0%, and 9.6% of patients used the APD, Disc System, and Stay Safe Balance® systems,
respectively (Supplementary material 3). The adoption of different PD modalities evolved over the study period. The proportion of patients using the UltraBag® system gradually reduced from 71.9% in 2007 to 53.2% in 2019 while APD increased from 6.2% in 2013 to 18.7% in 2019. The use of the Disc system reduced gradually with the increase of use of the newer Stay Safe Balance® system over the study period (Supplementary Material 4). Age, sex, and proportion of different comorbidities were similar in each group after matching.

Compared to APD, the other three systems showed increased risks of peritonitis [Disc System: HR 1.88 (95% CI 1.51-2.33); Stay Safe Balance®: HR 2.22 (95% CI 1.76-2.80); UltraBag®: HR 1.93 (95% CI 1.61-2.33)] but not all-cause mortality and technique failure. APD also showed a reduced risk of AED attendance compared with Disc System [HR 1.30 (95% CI 1.10-1.55)] and Ultrabag® [HR 1.45 (95% CI 1.26-1.66)] systems, but not Stay Safe Balance® [HR 0.87 (95% CI 0.70-1.07)] system. (Table 1, Figure 1)

The subgroup analyses and sensitivity analyses are largely consistent with the main analysis, except for an increased risk of all-cause mortality [HR 1.72 (95% CI 1.10-2.68)] and cardiovascular death [HR 3.05 (95% CI 1.08-8.59)] observed in male patients using UltraBag® system. A reduction in risk of cardiovascular death in female patients [Disc System: HR 0.28 (95% CI 0.11-0.68); Stay Safe Balance®: HR 0.45 (95% CI 0.11-1.83); UltraBag®: HR 0.46 (95% CI 0.23-0.92)] was also observed. (Supplemental Materials 5 & 6).

The current study found that patients undergoing APD have a lower risk of peritonitis compared with the other three CAPD systems. We also observed a lower risk of AED attendance using
APD when compared to UltraBag® and Disc System. However, no difference in all-cause mortality, cardiovascular death and technique failure was observed among different PD systems. Compared with APD, the risks of all-cause mortality and cardiovascular death are higher in male patients using the UltraBag® system.

The reduction of risk of peritonitis can be explained by the fewer manual exchanges necessary for APD than CAPD. Our finding is consistent with previous studies from Taiwan and Mexico, both showing a reduced risk of peritonitis in APD compared with CAPD. On the other hand, a cohort study in Brazil found no difference in time till the first peritonitis episode between APD and CAPD modalities.

Compared to HD, PD is associated with increased rates of hospital admission and in-hospital morbidities, mainly due to peritonitis and cardiovascular complications. Hence, lowering the incidence of peritonitis may also decrease the frequency of AED attendance among patients using APD as illustrated in our study.

Studies in the US and Brazil have found better survival in patients undergoing APD. However, our study could not find a clear association between PD modalities and mortality. The relatively short follow-up period may have limited our finding of this association the potential long-term survival benefits of APD. Another contributing factor could arise from the PD-first policy in Hong Kong which selects younger and fitter patients with better preserved residual kidney function and hence a lower mortality rate at baseline.
In subgroup analyses, we found that the mortality was significantly higher in male patients using the UltraBag® system compared with APD, where the association was not found in female patients. The risk of cardiovascular death was also significantly higher in male patients using the UltraBag® system compared with APD, while the opposite was found in female patients. These unexpected results demonstrate the possibility that sex has an impact on the relationship between PD modalities and mortality. Further research investigating the impact of sex in the relationship between PD modalities and mortality would be necessary.

This study stands out as being the largest investigation into the relationship between different PD modalities and common PD outcomes, covering from 2007 to 2019 and encompasses over 10,000 patients. There are several limitations in the study. Firstly, although propensity score weighting was performed to reduce confounding factors, residual confounders (e.g. improving education and patient technique during manual exchanges) may still exist. Secondly, the severity of peritonitis could not be assessed and analysed with the use of electronic data. Thirdly, a recent study showed that the number of daily manual exchanges in CAPD was associated with the risk of peritonitis but this data could not be incorporated into the current analysis. A different study design is warranted to further explore the effect of the incremental approach in CAPD compared to APD. Fourthly, patients may switch to other PD modalities during the study period, but they would be censored once they changed the PD modalities. This limited the study's power to detect differences in outcomes. Lastly, there is a significant discrepancy in the number of patients in different groups since the cost of APD cyclers is not reimbursed in Hong Kong. Further studies are required to illustrate the cost-effectiveness of APD.
In conclusion, the current study found that among incident PD patients, APD was associated with a lower risk of first peritonitis compared with other CAPD modalities. Further studies are warranted to elucidate the association between PD modalities and the risk of mortality.

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AUTHORS’ CONTRIBUTIONS

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Formal analysis: Franco Wing Tak Cheng.

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**Writing – review & editing:** Franco Wing Tak Cheng, Xue Li, Sydney Chi Wai Tang, Ian Chi Kei Wong.

**CONFLICT OF INTEREST STATEMENT**

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REFERENCES


Table 1. Comparison of hazard ratio of peritonitis, all-cause mortality, cardiovascular mortality, AED attendance and technique failure among patients with APD and other CAPD modalities

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<th>Hazard Ratio</th>
<th>95% CI</th>
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<td>APD</td>
<td>142/1071</td>
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<tr>
<td>Disc System</td>
<td>420/1319</td>
<td>1.88</td>
<td>(1.51 - 2.33)</td>
<td>&lt; 0.001</td>
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<tr>
<td>Stay Safe Balance®</td>
<td>334/1061</td>
<td>2.22</td>
<td>(1.76 - 2.80)</td>
<td>&lt; 0.001</td>
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<td>UltraBag®</td>
<td>1877/7570</td>
<td>1.93</td>
<td>(1.61 - 2.33)</td>
<td>&lt; 0.001</td>
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<td><strong>All-cause mortality</strong></td>
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<tr>
<td>APD</td>
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<tr>
<td>Disc System</td>
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<td>1.01</td>
<td>(0.70 - 1.46)</td>
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<td>Stay Safe Balance®</td>
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<td>0.91</td>
<td>(0.57 - 1.45)</td>
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<td>1.35</td>
<td>(1.00 - 1.84)</td>
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<td>(0.59 - 1.73)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Disc System</td>
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<td>1.30</td>
<td>(1.10 - 1.55)</td>
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<td>Stay Safe Balance®</td>
<td>268/1061</td>
<td>0.87</td>
<td>(0.70 - 1.07)</td>
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<tr>
<td>UltraBag®</td>
<td>2513/7570</td>
<td>1.45</td>
<td>(1.26 - 1.66)</td>
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<td><strong>Technique failure</strong></td>
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<tr>
<td>Disc System</td>
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<td>0.72</td>
<td>(0.47 - 1.09)</td>
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<td>Stay Safe Balance®</td>
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<td>0.82</td>
<td>(0.51 - 1.32)</td>
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<td>346/7570</td>
<td>0.80</td>
<td>(0.58 - 1.10)</td>
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AED, accident and emergency department; APD, automated peritoneal dialysis; CI, confidence interval.
Figure 1a. Kaplan-Meier curve showing cumulative incidence of peritonitis in different groups

APD, automated peritoneal dialysis.
Figure 1b. Kaplan-Meier curve showing cumulative incidence of all-cause death in different groups

APD, automated peritoneal dialysis.
Figure 1c. Kaplan-Meier curve showing cumulative incidence of cardiovascular death in different groups

APD, automated peritoneal dialysis.
Figure 1d. Kaplan-Meier curve showing cumulative incidence of AED attendance in different groups

APD, automated peritoneal dialysis.
Figure 1e. Kaplan-Meier curve showing cumulative incidence of technique failure in different groups.

APD, automated peritoneal dialysis.