

# Ischaemic stroke in patients with atrial fibrillation with chronic kidney disease undergoing peritoneal dialysis

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## Aims

Little is known about the ischaemic stroke risk and benefit of warfarin therapy for stroke prevention in chronic kidney disease (CKD) patients on peritoneal dialysis (PD) with concomitant atrial fibrillation (AF). Our objective was to determine the risk of ischaemic stroke in a 'real-world' cohort of PD patients with AF, and clinical benefit or harm of aspirin and warfarin.

## Methods and results

This is a single-centred observational study of Chinese patients with non-valvular AF. Hospitalizations with ischaemic stroke and intracranial haemorrhage (ICH) were recorded. Of 9810 patients from a hospital-based AF registry, 271 CKD patients on PD with AF ( $76.8 \pm 12.5$  years, CHA<sub>2</sub>DS<sub>2</sub>-VASc:  $3.69 \pm 1.83$ , and HAS-BLED:  $2.07 \pm 0.97$ ) were identified. Amongst these PD patients, 24.7% received warfarin; 31.7% received aspirin; and 43.5% received no antithrombotic therapy. Amongst patients with no antithrombotic therapy, annual incidence of ischaemic stroke in PD patients was comparable with those non-CKD counterparts (9.32 vs. 9.30%/year). Similar to non-CKD patients, annual incidence of ischaemic stroke increased with increasing CHA<sub>2</sub>DS<sub>2</sub>-VASc score (CHA<sub>2</sub>DS<sub>2</sub>-VASc = 0–1: 5.76 vs. 5.70%/year,  $P = 1.00$ ; and CHA<sub>2</sub>DS<sub>2</sub>-VASc  $\geq 2$ : 10.80 vs. 9.94%/year,  $P = 0.78$ ). Amongst PD patients, warfarin therapy was associated with lower risk of ischaemic stroke compared with aspirin [Hazard ratio (HR): 0.16, 95% confidence interval (CI): 0.04–0.66,  $P = 0.01$ ] and no therapy (HR: 0.19, 95% CI: 0.06–0.65,  $P = 0.01$ ), but not associated with a higher risk of ICH.

## Conclusion

In CKD patients on PD with AF, who had similar ischaemic stroke risk as non-CKD counterparts, warfarin therapy is associated with reduction in risk of ischaemic stroke without a higher risk of ICH.

## Keywords

Peritoneal dialysis • Chronic kidney disease • Atrial fibrillation • Ischaemic stroke

## Introduction

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia encountered in clinical practice with the prevalence in general population around 1%.<sup>1</sup> The prevalence of AF increases with decreasing glomerular filtration rate,<sup>2–5</sup> and amongst patients with chronic kidney disease (CKD) on dialysis therapy, the prevalence of AF is high, between 7 and 27%.<sup>6–9</sup> On the other hand, CKD patients with AF may have a higher risk of ischaemic stroke

compared with non-CKD AF patients,<sup>10</sup> but risk factors predisposing ischaemic stroke are more prevalent amongst AF patients with CKD than non-CKD counterparts. While long-term anticoagulation therapy can effectively reduce ischaemic stroke risk in general AF patients, the generalizability to CKD patients remains inconclusive. Specifically, previous observational studies in haemodialysis patients have produced conflicting results concerning the net clinical benefits<sup>11</sup> and harms<sup>12–15</sup> of warfarin therapy. This could be at least partially related to the exceedingly high bleeding complications

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## What's new?

- Chronic kidney disease patients on PD with AF have comparable ischaemic stroke risk compared with those not on dialysis.
- Warfarin, as in patient not on dialysis, can reduce ischaemic stroke risk in AF patient on PD without increasing the risk of ICH.

amongst haemodialysis patients on warfarin due to the use of parental heparin and repeated arterial punctures during haemodialysis.

In contrast to Caucasian countries, the predominant mode of dialysis in Asian countries is peritoneal dialysis (PD) instead of haemodialysis, whereby the bleeding risk might be lower than that of haemodialysis patients. Unlike haemodialysis patients, there is a dearth of published data in the PD population concerning the risk of ischaemic stroke related to AF, and more importantly the net clinical benefits or harms of long-term anticoagulation therapy. The aim of this study was to determine the risk of ischaemic stroke in a 'real-world' cohort of PD patients with AF with detailed long-term follow-up, and the clinical benefit or harm of aspirin and warfarin use.

## Methods

### Patients

Between July 1997 and December 2011, 10 195 Chinese patients with a diagnosis of AF at Queen Mary Hospital, Hong Kong were identified from the computer-based clinical management system.<sup>16</sup> Patients were excluded if they had significant valvular heart disease or any degree of mitral stenosis, CKD stage 5 on haemodialysis, or CKD stage 5 not for renal replacement therapy or incomplete clinical and/or follow-up data. In addition, 83 CKD patients on maintenance PD with non-valvular AF from Tung Wah Hospital were also included. As a result, the final analysis included 9810 patients with non-valvular AF. Of these, 271 patients (2.76%) had CKD on long-term maintenance PD.

### Study design

This was an observational study. The study protocol was approved by the local Institutional Review Board. Demographic data, cardiovascular risk factors, and medications were recorded at the diagnosis of AF. The primary and secondary endpoints were hospital admission with stroke and intracranial haemorrhage (ICH) during the first 18 months of follow-up, respectively. The data were retrieved from the medical records and discharge summaries from the territory-wide information network of all public hospitals in Hong Kong. The index date was defined as the date of the first occurrence of AF. For the registration of outcome(s) during follow-up, a blanking period of 14 days after the index date was applied as the occurrence of an ischaemic stroke or ICH within the first few days of the diagnosis of AF was most likely related to initial presentation of AF rather than a new event.<sup>17</sup>

### Definitions

Hypertension was defined as resting systolic or diastolic blood pressure  $\geq 140/90$  mmHg on two occasions or prescription of anti-hypertensive drugs. Diabetes mellitus was defined as plasma fasting glucose

$\geq 7.0$  mmol/L or prescription of anti-diabetic medication. Heart failure was defined according to the Framingham Heart Study. Smoking status was recorded as smoker (past and current) or non-smoker. Ischaemic stroke was defined as a neurological deficit of sudden onset that persisted for more than 24 h corresponding to a vascular territory in the absence of primary haemorrhage or other cause (trauma, infection, and vasculitis) and confirmed by CT scan or magnetic resonance imaging of the brain.<sup>18–20</sup> Intracranial haemorrhage was diagnosed in the presence of new onset neurological symptoms with radiological confirmation, and classified as intra-cerebral haemorrhage, subarachnoid haemorrhage, or subdural haemorrhage.<sup>16,21–24</sup>

## Statistical analysis

Continuous and discrete variables are expressed as mean  $\pm$  standard derivation and percentages, respectively. Statistical comparisons of the baseline clinical characteristics were performed using Student's *t*-test, one-way ANOVA or Fisher's exact test as appropriate. Kaplan–Meier survival analyses with the log-rank test were carried out. Hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated by univariate and multivariate Cox proportional hazard regression models. Multivariate analyses were performed with an enter regression model in which each variable with a *P*-value of  $\leq 0.1$  (based on univariate analysis) was entered into the model. Calculations were performed using a statistical software package (IBM SPSS, version 19.0). A *P*-value  $< 0.05$  was considered to be statistically significant.

## Results

We studied 9810 patients with non-valvular AF. Table 1 summarizes the clinical characteristics of the study cohort. The mean age was  $76.8 \pm 12.5$  years, and 52.0% were female. The mean CHA<sub>2</sub>DS<sub>2</sub>-VASc and HAS-BLED scores were  $3.69 \pm 1.83$  and  $2.08 \pm 0.97$ , respectively. Amongst these, 271 patients (2.76%) had CKD and were on long-term PD. Compared with non-CKD counterparts, PD patients were younger ( $71.6 \pm 11.2$  vs.  $76.9 \pm 12.5$  years,  $P < 0.001$ ), with a higher proportion of male (59.8 vs. 47.7%,  $P < 0.001$ ), hypertension (70.8 vs. 54.2%,  $P < 0.001$ ), diabetes mellitus (41.3 vs. 21.6%  $P < 0.001$ ) and coronary artery disease (29.9 vs. 18.0%,  $P < 0.001$ ), but a lower prevalence of prior ischaemic stroke (17.0 vs. 23.7%,  $P = 0.01$ ).

## Ischaemic stroke risk in peritoneal dialysis patients on no antithrombotic therapy

Of the 3932 patients prescribed no antithrombotic therapy, 118 patients had CKD and were on PD (Table 1). Peritoneal dialysis patients were younger ( $69.4 \pm 12.7$  vs.  $77.3 \pm 13.3$  years,  $P < 0.001$ ), had a higher proportion of females (38.1 vs. 53.7%,  $P = 0.001$ ), hypertension (63.6 vs. 47.0%,  $P = 0.001$ ), diabetes mellitus (39.0 vs. 17.6%,  $P < 0.001$ ), and coronary artery disease (20.3 vs. 8.2%,  $P < 0.001$ ), but a lower prevalence of smokers and history of ischaemic stroke/transient ischaemic attack. The mean CHA<sub>2</sub>DS<sub>2</sub>-VASc and HAS-BLED scores were  $2.97 \pm 2.01$  and  $2.56 \pm 0.97$  amongst PD patients, and were  $3.34 \pm 1.70$  and  $1.94 \pm 0.94$  amongst non-CKD patients, respectively. The overall annual ischaemic stroke risk of PD patients was comparable with that of non-CKD patients (9.32 vs. 9.30%). In fact, the risk of ischaemic stroke stratified with CHA<sub>2</sub>DS<sub>2</sub>-VASc score amongst PD patients was likewise comparable with those non-CKD patients (Figure 1).

**Table 1** Baseline characteristics of study cohort

	Peritoneal dialysis				P-Value <sup>#</sup>	P-Value <sup>§</sup>
	No	Yes				
	No antithrombotic (n = 3814)	No antithrombotic (n = 118)	Aspirin (n = 86)	Warfarin (n = 67)		
Mean age (years)	77.3 ± 13.3	69.4 ± 12.7	73.0 ± 10.0	69.5 ± 9.5	<0.001*	0.05
Female, n (%)	2048 (53.7)	45 (38.1)	36 (41.9)	28 (41.8)	0.001*	0.83
HT, n (%)	1794 (47.0)	75 (63.6)	75 (87.2)	42 (62.7)	0.001*	<0.001*
DM, n (%)	673 (17.6)	46 (39.0)	40 (46.5)	26 (38.8)	<0.001*	0.50
Smoker, n (%)	1341 (35.2)	27 (22.9)	26 (30.2)	29 (43.4)	0.006*	0.02*
Heart failure, n (%)	718 (18.3)	24 (20.3)	18 (20.9)	20 (29.9)	0.679	0.29
CAD, n (%)	312 (8.2)	24 (20.3)	33 (38.4)	24 (35.8)	<0.001*	0.01*
Prior stroke/TIA, n (%)	672 (17.6)	12 (10.2)	22 (25.6)	12 (17.9)	0.036*	0.02*
Prior ICH, n (%)	113 (3.0)	1 (0.8)	4 (4.7)	1 (1.5)	0.177	0.17
Mean CHA <sub>2</sub> DS <sub>2</sub> -VASc	3.34 ± 1.70	2.97 ± 2.01	4.16 ± 1.73	3.46 ± 1.91	0.02*	<0.001*
CHA <sub>2</sub> DS <sub>2</sub> -VASc					<0.001*	0.002*
0, n (%)	188 (4.9)	19 (16.1)	2 (2.3)	3 (4.5)		
1, n (%)	347 (9.1)	12 (3.3)	4 (4.7)	8 (11.9)		
2, n (%)	669 (17.5)	17 (14.4)	11 (12.8)	7 (10.4)		
3, n (%)	880 (23.1)	23 (19.5)	10 (11.6)	13 (19.4)		
4, n (%)	797 (20.9)	17 (14.4)	21 (24.4)	15 (22.4)		
5, n (%)	541 (14.2)	19 (16.1)	16 (18.6)	14 (20.9)		
6–9, n (%)	392 (10.3)	11 (9.3)	22 (25.6)	7 (10.4)		
Mean HAS-BLED	1.94 ± 0.94	2.56 ± 0.97	3.22 ± 0.87	2.55 ± 0.82	<0.001*	<0.001*

CAD, coronary artery disease; CHA<sub>2</sub>DS<sub>2</sub>-VASC score, Congestive heart failure, Hypertension, Age ≥ 75 = 2 marks, diabetes mellitus, Stroke/TIA history = 2 marks; Vascular disease, Age 65–74 years, Sex category; DM, diabetes mellitus; HAS-BLED, Hypertension, Abnormal Renal/Liver Function, Stroke, Bleeding History or Predisposition, Labile INR, Elderly (Age > 65 years), Drugs/Alcohol concomitantly; HT, hypertension; ICH, intracranial haemorrhage; TIA, transient ischaemic attack.

\*P < 0.05.

<sup>#</sup>P-Value for comparison between patients with no antithrombotic therapy on and not on PD.

<sup>§</sup>P-Value for comparison amongst the three groups of patients on PD.

Kaplan–Meier analyses revealed similar ischaemic stroke-free survival between PD patients and non-CKD patients, in both CHA<sub>2</sub>DS<sub>2</sub>-VASC score 0–1 and ≥ 2 categories (Figure 2A and B).

Table 2 summarizes individual risk factors with the corresponding HRs and 95% CIs based on Cox proportional hazard model. Increasing age ( $P < 0.01$ ), hypertension (HR: 1.58, 95% CI: 1.38–1.80,  $P < 0.01$ ), diabetes mellitus (HR: 1.39, 95% CI: 1.18–1.64,  $P < 0.01$ ), and prior ischaemic stroke (HR: 1.52, 95% CI: 1.27–1.81,  $P < 0.01$ ) were associated with development of ischaemic stroke in both univariate and multivariate CKD on analysis. Peritoneal dialysis was not independently associated with a higher stroke risk.

## Efficacy and safety of warfarin and aspirin in chronic kidney disease patients on peritoneal dialysis

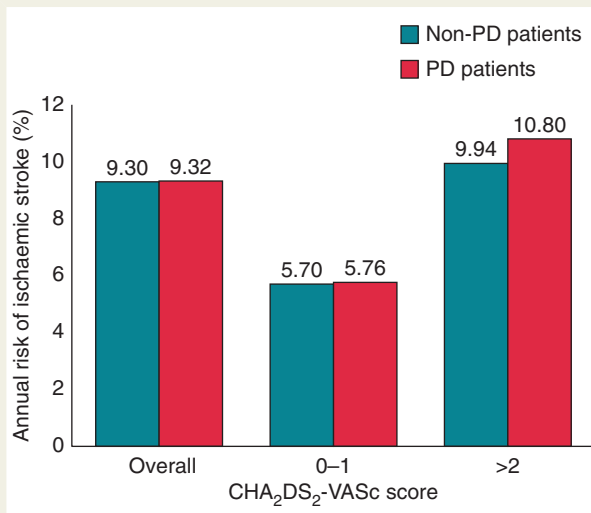
Amongst 271 patients with CKD and on PD, 118 patients (43.5%) received no antithrombotic therapy, 86 patients (31.7%) received aspirin and only 67 patients (24.6%) on warfarin. Table 1 summarizes the clinical characteristics of patients receiving no antithrombotic therapy, aspirin, or warfarin. Of notes, patients on aspirin had the highest CHA<sub>2</sub>DS<sub>2</sub>-VASC score compared with patients on warfarin and on no therapy (4.16 ± 1.73 vs. 3.46 ± 1.91 vs. 2.97 ± 2.01,

$P < 0.001$ ). Likewise, patients on aspirin also had the highest HAS-BLED score amongst the three groups. There were altogether 19 ischaemic strokes: 11 in PD patients no receiving any antithrombotic therapy, 8 in those on aspirin, and none in patients receiving warfarin.

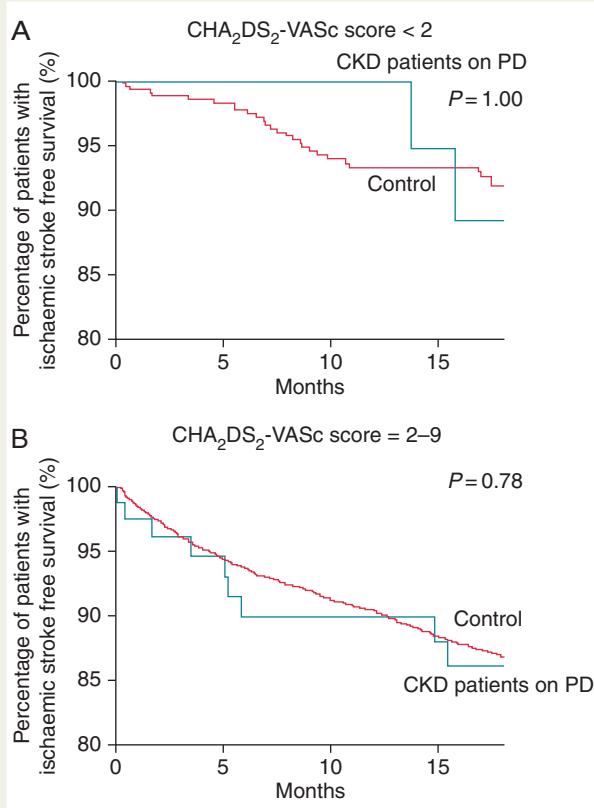
Figure 3 depicts the Kaplan–Meier analysis of ischaemic stroke amongst patients on warfarin, aspirin, and no therapy. Patients receiving warfarin had the lowest ischaemic stroke, compared with those on aspirin (HR: 0.16, 95% CI: 0.04–0.66,  $P = 0.01$ ) and no antithrombotic therapy (HR: 0.19, 95% CI: 0.06–0.65,  $P = 0.01$ ). There were only two ICHs amongst PD patients during the follow-up period, both occurring in patients on aspirin.

## Discussion

To the best of our knowledge, this is the largest ‘real-world’ cohort of CKD patients on long-term maintenance PD and concomitant AF, in which we studied the risk of ischaemic stroke and the clinical benefit of warfarin therapy for stroke prevention. First, we showed that resembling general AF population, the risk of ischaemic stroke amongst PD patients with AF was substantial and increased with CHA<sub>2</sub>DS<sub>2</sub>-VASC score. More importantly, warfarin therapy was



**Figure 1** Annual risk of ischaemic stroke in PD patients compared with those patients with CKD not on dialysis or without CKD, categorized according to CHA<sub>2</sub>DS<sub>2</sub>-VASc score. No statistical significance in ischaemic stroke risk in between the two categories of patients.



**Figure 2** Kaplan-Meier curve of ischaemic stroke-free survival in PD patients compared with those patients with CKD not on dialysis or without CKD (A) in patients with CHA<sub>2</sub>DS<sub>2</sub>-VASc score < 2; (B) in patients with CHA<sub>2</sub>DS<sub>2</sub>-VASc score 2-9.

associated with lower risk ischaemic stroke, but not with an increased risk of ICH in this PD patient cohort.

A striking feature of our cohort is the overall high ischaemic stroke risk (both PD patients and non-PD patients) compared with previously published primarily Caucasian cohorts.<sup>25-29</sup> While the high ischaemic stroke risk in our cohort would be the result of the nature of the hospital-based registry, which typical includes sicker patients, and the possible under-recognition of comorbidities such as hypertension, metabolic syndrome, and diabetes, emerging evidences suggest that Chinese may have a higher ischaemic stroke risk than Caucasian, particularly amongst those with low CHA<sub>2</sub>DS<sub>2</sub>-VASc score.<sup>16,30,31</sup> In fact, in recent randomized control trials for non-vitamin K oral anticoagulants for stroke prevention in AF, the ischaemic stroke risk amongst Asian patients are likewise higher than that of non-Asian counterparts for as high as 2.5-fold, despite comparable CHA<sub>2</sub>DS<sub>2</sub>-VASc scores.<sup>32</sup> These findings are in accordance with the fact that globally, China as well as other Asian countries is amongst the countries with the highest stroke,<sup>33</sup> albeit the underlying mechanisms for such high ischaemic stroke risk remain elusive.<sup>34,35</sup>

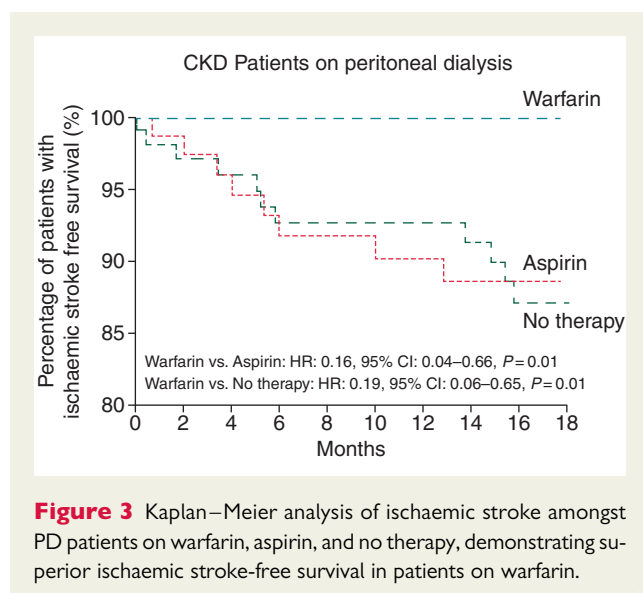
Atrial fibrillation and CKD commonly co-exist. In contemporary population-based studies, the prevalence of AF increases with decreasing glomerular filtration rate.<sup>2-5</sup> The prevalence of AF in patients on dialysis has been reported to be as high as 7-27%,<sup>6-9</sup> compared with a prevalence of 1-2% in the general population. In addition, CKD increases ischaemic stroke risk in AF population.<sup>10,36-38</sup> However, risk factors predisposing ischaemic stroke such as hypertension, diabetes mellitus, and heart failure are more prevalent in patients with CKD, thereby the additive contributory role of CKD *per se* is often difficult to ascertain. In the present study, for similar mean CHA<sub>2</sub>DS<sub>2</sub>-VASc scores, the risk of ischaemic stroke amongst PD patients not receiving any antithrombotic therapy did not differ significantly from the non-CKD patients, despite the differences in individual risk factors contributory to CHA<sub>2</sub>DS<sub>2</sub>-VASc score.

Long-term warfarin therapy has been established as the standard therapy for stroke prevention in AF in general population.<sup>39</sup> However, the decision to initiate long-term anticoagulation therapy in CKD patients remains challenging. Evidence justifying the benefit of warfarin therapy in AF is mainly from randomized controlled trials, in which CKD patients particularly those on long-term maintenance dialysis were grossly under-represented or even excluded. While warfarin therapy markedly reduces ischaemic stroke in AF patients with mild to moderate renal impairment (stage 3 CKD),<sup>40</sup> large observational studies<sup>12,40</sup> have repeatedly demonstrated that warfarin therapy was associated with a higher risk of ischaemic stroke in stage 4/5 CKD patients maintained on haemodialysis. For example, in the Dialysis Outcomes and Practice Patterns Study, an international, observational study of haemodialysis practices and outcomes, those haemodialysis patients with pre-existing AF receiving warfarin had elevated risks of stroke compared with non-warfarin users, which progressively increased with age.<sup>41</sup> Likewise, in a cohort of 1671 haemodialysis patients with AF from North America, warfarin therapy was associated with nearly two-fold increase in stroke.<sup>12</sup> On the other hand, the risk of haemorrhagic stroke amongst haemodialysis patients with AF receiving also increases substantially.<sup>13,27</sup> Indeed, the latest clinical guidelines from Kidney Disease: Improving Global Outcomes no longer recommend

**Table 2** Associations between baseline factors and ischaemic stroke (no therapy)

	Number of ischaemic strokes	Univariate analysis		Multivariate analysis	
		HR (95% CI)	P-Value	HR (95% CI)	P-Value
Age					
<65	71	Reference		Reference	
65–75	234	2.40 (1.83–3.13)	<0.01*	2.14 (1.63–2.81)	<0.01*
>75	546	2.67 (2.07–3.43)	<0.01*	2.32 (1.78–3.00)	<0.01*
Female	507	1.37 (1.04–1.37)	0.01*	1.03 (0.89–1.20)	0.70
Hypertension	430	1.58 (1.38–1.80)	<0.01*	1.35 (1.17–1.55)	<0.01*
Diabetes mellitus	173	1.39 (1.18–1.64)	<0.01*	1.20 (1.00–1.43)	0.04*
Smoker	274	0.88 (0.76–1.01)	0.08	0.91 (0.78–1.07)	0.24
CKD on PD	20	0.66 (0.42–1.02)	0.06	0.76 (0.48–1.19)	0.224
Heart failure	130	1.12 (0.99–1.44)	0.06	1.05 (0.87–1.27)	0.22
Coronary artery disease	77	1.14 (0.90–1.44)	0.29		
Prior ischaemic stroke	151	1.52 (1.27–1.81)	<0.01*	1.30 (1.09–1.56)	<0.01*
Prior intracranial haemorrhage	24	0.88 (0.58–1.32)	0.53		

Abbreviations as in Table 1.

\* $P < 0.05$ .**Figure 3** Kaplan–Meier analysis of ischaemic stroke amongst PD patients on warfarin, aspirin, and no therapy, demonstrating superior ischaemic stroke-free survival in patients on warfarin.

warfarin therapy for stroke prevention in AF amongst dialysis patients.<sup>42</sup> In contrast to Western countries, the predominant mode of long-term maintenance dialysis in many Asian countries is PD instead of haemodialysis. While it seems inappropriate to directly extrapolate data from haemodialysis to PD patients, there is a dearth of clinical evidence about the stroke prevention strategy for PD patients with AF. To date, there have only been two published studies involving PD patients with AF. The first one from Quebec and Ontario, Canada<sup>27</sup> studied a cohort of 1626 patients on dialysis (both haemodialysis and PD) in which warfarin has not been shown to have any beneficial effect in reducing ischaemic stroke but a higher risk of bleeding.<sup>27</sup> Unfortunately, the proportion of PD patients has not been specified in the study, it would be expected around 10% according

to previously published data.<sup>43</sup> In a more recent study from Denmark involving 1728 AF patients on dialysis with a much higher proportion of PD (28.0%),<sup>28</sup> warfarin is associated with reduction in all-cause mortality. In a stark contrast to these cohorts of predominantly haemodialysis AF patients, our results in a pure PD cohort have demonstrated that warfarin therapy was associated with a reduction of >70% in ischaemic stroke risk when compared with aspirin therapy or no therapy. Of note, the small number of PD patients receiving warfarin in our cohort and the lower baseline ischaemic stroke risk amongst patients on warfarin may introduce bias that favouring warfarin therapy. Nonetheless, this finding is qualitatively consistent with the randomized control trials<sup>44</sup> and registry data that warfarin therapy significantly reduces ischaemic stroke risk in our cohort of PD AF patients. Quantitatively, the magnitude of stroke risk reduction of warfarin is also consistent with general AF patients (~64%)<sup>44</sup> and AF patients with CKD.<sup>40</sup> For example, in patients with stage 3 CKD participating in the Stroke Prevention in Atrial Fibrillation III trials, patients randomized to receive adjusted-dose warfarin with target international normalized ratio (INR) 2–3 had a 76% ischaemic stroke risk reduction compared with those on aspirin.<sup>40</sup> Plausible explanations for such discrepancy in benefits (and harm) of warfarin therapy between haemodialysis patients and PD patients may be related to the frequent heparinization during haemodialysis with a possible rebound pro-thrombotic state and fluctuations in blood pressure during and in between haemodialysis that may offset the benefit of warfarin therapy. In fact, there are evidences that the plasma levels naturally occurring anticoagulants such as protein C, protein S, and antithrombin III were substantially lower in haemodialysis patients than PD patients,<sup>45–49</sup> which might account for the difference in thrombotic and bleeding risk between PD and haemodialysis patients. Also, the quality of anticoagulation control, as reflected by average time in therapeutic range, may be a factor associated with the higher risk of thromboembolism and bleeding in CKD patients.



## Limitations

Our study is limited by its cohort-based and single-centre observational design in primarily hospital-based patients. Secondly, the number of PD patients receiving warfarin therapy is small and the follow-up period is relatively short. This is probably the most important limitation of the present study. Thirdly, despite our patients with concomitant CKD on PD and AF treated with warfarin having a substantially reduced risk of ischaemic stroke compared with patients on aspirin or no therapy, the decision and selection of antithrombotic strategies was non-randomized. As such, patients prescribed warfarin might be in many ways different from those on aspirin or no therapy, as decided by the attending physicians, thus imposing a selection bias in our cohort. Amongst those on warfarin, the quality of anticoagulation is of paramount importance to the clinical outcomes. Unfortunately, we lack full access to the INR results for all patients. In addition, while we carefully ascertained all strokes and ICH by careful examination of hospitalization records, laboratory and imaging results, patients with a milder stroke, TIAs and/or ICH who were not hospitalized were not included. Notwithstanding with all these limitations, our data at least demonstrate the intermediate term efficacy and safety of warfarin therapy in PD patients with AF. Randomized placebo-control trials, the golden standard to demonstrate treatment effects, are definitely needed in this population.

## Conclusions

In CKD patients on PD with AF, warfarin therapy is associated with lower risk of ischaemic stroke, without a higher risk of ICH. Peritoneal dialysis patients with AF had similar risk of ischaemic stroke compared with non-CKD counterparts.

**Conflict of interest:** G.Y.L. has served as a consultant for Bayer, Astellas, Merck, AstraZeneca, Sanofi, BMS/Pfizer, Daiichi-Sankyo, Medtronic, Biotronik, Portola, and Boehringer Ingelheim and has been on the speakers bureau for Bayer, BMS/Pfizer, Boehringer Ingelheim, Medtronic, Daiichi-Sankyo, and Sanofi Aventis.

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# Management of a previously unreported implantable cardioverter-defibrillator lead complication

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A 68-year-old male with a right pectoral implantable cardioverter-defibrillator (ICD) *in situ* underwent a technically challenging extraction/replacement of a Sprint Fidelis lead at the time of elective replacement of the generator. During implantation of the new model 6935M 55 cm defibrillator lead, the suture sleeve migrated along the lead into the superior vena cava (Figure).

Six months later the patient was referred for management of a right pectoral pocket erosion. There was concern over potential embolism of the intravascular suture sleeve during defibrillator lead removal. In order to stabilize the lead distal to the suture sleeve and to prevent its migration toward the lead tip during attempts at retrieval, the lead was snared from a right femoral venous approach by a second operator. A 16 F laser sheath and outer sheath were advanced over the lead until the entire suture sleeve was within the lumen of the outer sheath. The sheaths, the lead, and the suture sleeve were then removed as a unit. A left pectoral dual-chamber ICD was later implanted.

Operators engaging in lead management should remain vigilant, particularly when implanting new leads after creating large openings into the subclavian veins during complex lead extraction cases. In the present case, the lead and suture sleeve were successfully removed using a two operator technique.



The full-length version of this report can be viewed at: <http://www.escardio.org/Guidelines-&Education/E%E2%80%933learning/Clinical-cases/Electrophysiology/EP-Case-Reports>

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