Risk Factors for Out-of-Clinic Sudden Cardiac Death in Hemodialysis Patients

Patrick H. Pun, MD, MHS; Ruediger W. Lehrich, MD; John P. Middleton, MD

Department of Medicine, Division of Nephrology, Duke University Medical Center - Durham, North Carolina, USA

DaVita. Clinical Research

Introduction:

▪ Although sudden death is the most common cause of death in hemodialysis patients, the primary causes are uncertain.

▪We recently reported that modifiable dialysis factors such as exposure to low potassium and calcium dialysate, as well as predialysis serum potassium and creatinine and are strong predictors of peridialytic in-clinic sudden cardiac arrest (SCA)[1].

▪Whether or not these factors are also predictive of sudden deaths occuring outside the dialysis clinic is unknown.

Study objective: To compare risk factors for in-clinic SCA and out-of-clinic sudden cardiac death (SCD).

Methods:

◆ *Patient Population:* 43,200 prevalent hemodialysis patients dializing in 565 clinics of DaVita Inc. (formerly Gambro) in the United States between 2002-2005.

◆ *Study Design*: Nested Case-Control. We previously identified 502 patients who had a witnessed in-clinic SCA. Each SCA case patient with 3 random control patients matched by age, dialysis vintage, and year of event. The method employed by the USRDS CVSCC[2] was used to identify control patients who experienced sudden cardiac death outside of dialysis clinics.

◆ *Data Source:* Clinical Event Reporting database (ERMS) to adjudicate in-clinic SCA events. Laboratory data, comorbid conditions extracted from clinical database and linkage to USRDS.

◆ *Study Design/Statistical Analysis:*
  ◆ Data from 64,400 dialysis treatments compared between cohorts
  ◆ Repeated measures summarized over 90 day period leading up to event
  ◆ Multivariate logistic regression models used in adjusted analysis.

Results

Table 1: Baseline Characteristics of the Study Cohorts

Case-Mix and Reported Co-morbid Factors

Variable	In-Clinic SCA	Out of Clinic SCD	No SCD	P value
Median Age (years)	65	69	66	<0.001
Median Dialysis Vintage (years)	2.9	2.9	2.7	0.3
% Male	53%	55%	52%	0.7
% White	47%	47%	42%	0.2
% Coronary Artery Disease	36%	47%	31%	<0.0001
% Congestive Heart Failure	40%	43%	34%	<0.0001
% History of Arrhythmia	14%	14%	13%	<0.001
% Diabetes	57%	59%	53%	0.1
% Hypertension	87%	91%	87%	0.3
% Hyperlipidemia	8%	7%	6%	0.4
% Peripheral Vascular Disease	21%	30%	18%	0.4
% Cerebrovascular Disease	13%	12%	9%	0.3
% Tobacco Use	3%	2%	4%	0.4

Dialysis Characteristics and Predialysis Lab Data

Variable	In-Clinic SCA	Out of Clinic SCD	No SCD	P value
Dialysis dose (urea reduction ratio)	0.72	0.71	0.71	0.8
Serum Potassium (meq/L)	4.72	4.66	4.78	0.07
% Last Treatment using Dialysate [K] < 2 meq/L	17.7%	10.1%	9.2%	<0.0001
Serum Calcium (mg/dL)	9.26	9.20	9.17	0.4
% Last Treatment using Dialysate [Ca] < 2.5 meq/L	11.8%	6.6%	6.1%	<0.001
Ultrafiltration rate (cc/kg/min) (median over 90days)	10.4	10.0	10.1	0.5
Mean Arterial BP (mmHg) (predialysis, mean over 90 days)	98	96	102	<0.0001
Serum Creatinine (mg/dL)	7.4	7.2	8.3	<0.0001
Dialysis catheter access (%)	33%	33%	33%	0.9
Serum Albumin (mg/dL)	3.57	3.56	3.65	<0.0001
Serum Bicarbonate (meq/L)	21.3	22.2	21.5	<0.01

Prescribed Medications and Related Laboratory Data

Variable	In-Clinic SCA	Out of Clinic SCD	No SCD	P value
% Beta-Blocker	58%	48%	49%	0.003
% ACEI/ARB	57%	46%	44%	<0.0001
% Statin	36%	23%	29%	0.001
% Aspirin	42%	48%	33%	<0.0001
% Anti-arrhythmic	13%	20%	13%	<0.0001
Serum Phosphorus (mg/dL)	5.26	5.21	5.26	0.5
PTH (pg/mL)	218	216	225	0.2
% Vitamin D	78%	64%	72%	<0.001
Hemoglobin (g/dL)	11.5	11.6	11.7	<0.0001
EPO dose (U/treatment)	10543	7609	8752	<0.0001

Figure 1: Study Design

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DaVita Prevalent Dialysis
Population 2002-2005 n=43,200
          |
   Matching by age and
   dialysis vintage
     |            |
In-Clinic SCA   No In-Clinic Events
N=502           N=1632
                     |
           |                   |
   Out-of-clinic SCD      No Sudden Death
   N=172                  N=1460
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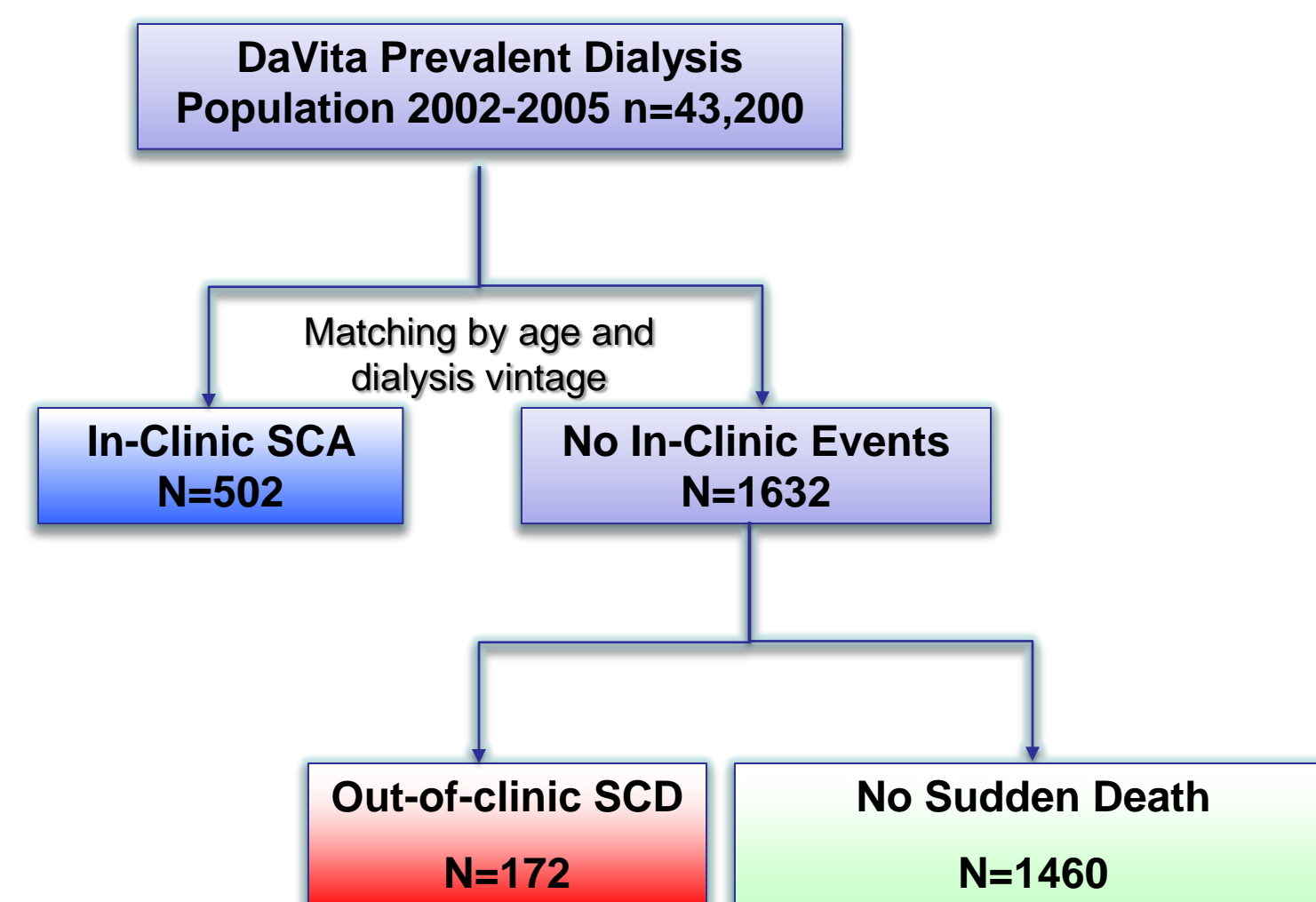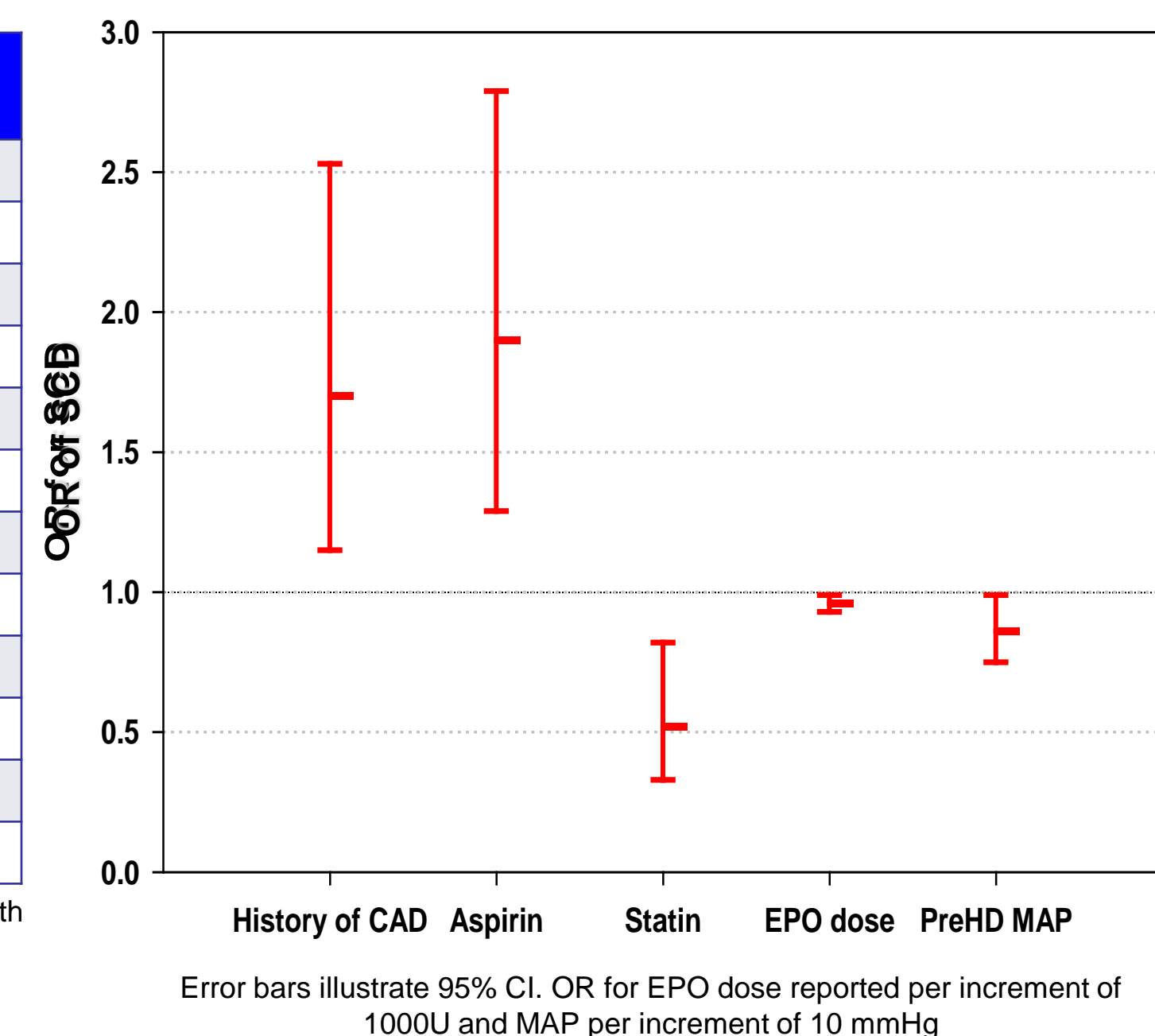
Table 2: Comparison of independent Risk Factors determined from multivariable logistic regression[*]

Independent Risk Factors for In-Clinic SCA[1]	Independent Risk Factors for Out-of-clinic SCD
Serum Creatinine	Statin prescription
Dialysate K < 2	Aspirin prescription
Serum potassium	EPO dose
Antiarrhythmic prescription	Mean Arterial BP
Dialysate Ca < 2.5	CAD
EPO dose	
Ultrafiltration Rate	
ACEI/ARB prescription	
Hemoglobin	
Vitamin D prescription	
Serum bicarbonate	
Mean Arterial BP	

[*]Variables entered into the model included all variables significantly associated with outcome in unadjusted analyses. Independent variables were confirmed by modeling using forward selection.

Figure 2: Adjusted OR of Out-of-clinic SCD

Error bars illustrate 95% CI. OR for EPO dose reported per increment of 1000U and MAP per increment of 10 mmHg

Summary:

1. Rate of in-clinic SCA was 7 per 1000 pt yrs.

2. Rate of out-of-clinic SCD was 41 per 1000 pt yrs.

3. Risk of both in-clinic and out-of-clinic SCA was elevated in elderly patients, those with prior history of heart disease and those with lower blood pressure and biomarkers of poor nutrition.

4. In-clinic SCA was associated with hemodialysis-related exposures such as low dialysate potassium and calcium.

5. In contrast, out of clinic SCD was higher among those with pre-existing CAD and those prescribed ASA, but lower in those treated with statin.

Conclusion:

Changes to the hemodialysis prescription may reduce the rate of in-clinic SCA, but more conventional management of cardiovascular risk may be needed to reduce the greater risk of out-of-clinic SCA.

References:
1. Pun, PH et. al. Kidney Int. 2010 Sep 1.
2. USRDS Annual Data Report, 2006.

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Correspondence:
Patrick.Pun@duke.edu

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