

Interdialytic Weight Gain and Cardiovascular Disease Outcomes

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Introduction

- In patients with end-stage renal disease (ESRD), the critical and immediate need for renal replacement therapy can overshadow the persistent risk of cardiovascular events and death. However, cardiovascular disease-related morbidity and mortality is greater in ESRD patients compared to the general population; published estimates suggest the risk is many times greater.^{1,2} This is probably related to the vast constellation of underlying conditions that contribute to the deterioration of the circulatory system, including high blood pressure and dialysis-related episodes of intravascular hypovolemia with attendant tissue hypoxia, all superimposed on a background of vascular disease, diabetes, and autonomic nervous system dysfunction.
- Chronic hypervolemia through excessive fluid accumulation between dialysis treatments is yet another physical insult upon the cardiovascular system of vulnerable dialysis patients. Thus, the potential associations between interdialytic weight gain (IDWG) and cardiovascular events and death were studied.

Objective

The primary goal of the current study was to estimate the association between fluid accumulation (IDWG) and specific cardiovascular episodes, hospitalization events, and death in patients with ESRD.

Methods

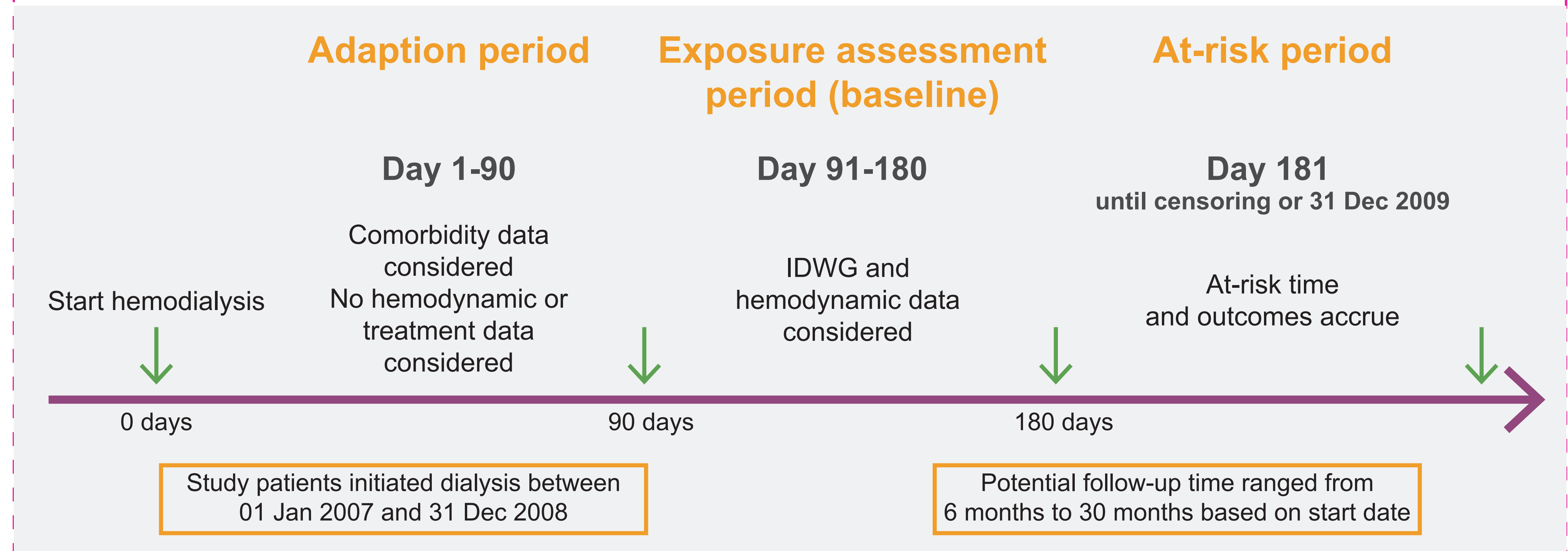
Patients

- The current study analyzed electronic medical records of US patients incident to in-center hemodialysis (01 Jan 2007–31 Dec 2008) who remained on this modality for ≥ 181 days and had Medicare or Medicaid as their primary insurer (Figure 1).
- Patients included in the analysis were treated at dialysis facilities located across the US within a large dialysis organization.

Analytics

- Relative (rel) and absolute (abs) IDWG were assessed over dialysis days 91-180 (to provide opportunity for initial equilibration to dialysis).
 - Cross-sectional associations with covariates estimated using contingency tables and chi-square testing.
- Outcomes were identified through US Renal Data System claims data and were considered as those occurring on/after dialysis day 181 until death, care transfer, modality change, or end of study period (31 Dec 2009).
 - Longitudinal associations were estimated using proportional hazards regression.

Figure 1. Study Design



Exposure

- IDWG (exposure) was defined as the amount of fluid gained between dialysis sessions, from the end of one dialysis session to the beginning of the next.
 - Relative IDWG describes the amount of fluid accumulation as a percentage of patient's post-dialysis weight
 - Absolute IDWG is calculated as the pre-dialysis weight from one treatment minus the post-dialysis weight from the previous dialysis treatment

Outcomes

- The patient outcomes studied during the at-risk period were:
 - Hospitalization for heart failure/fluid overload
 - Composite hospitalization for heart failure/fluid overload or cardiovascular mortality
 - Cardiovascular mortality (death attributed to myocardial infarction, atherosclerotic heart disease, cardiac arrhythmia, congestive heart failure, cardiomyopathy, cardiac arrest, valvular heart disease, pulmonary edema, cerebrovascular accident including intracranial hemorrhage, or ischemic brain damage/anoxic encephalopathy)
 - All-cause mortality
 - Myocardial infarction
- The association between intradialytic hypotension (IDH) and IDWG was also examined.

Results

Figure 2. Association of IDWG and Cardiovascular Events

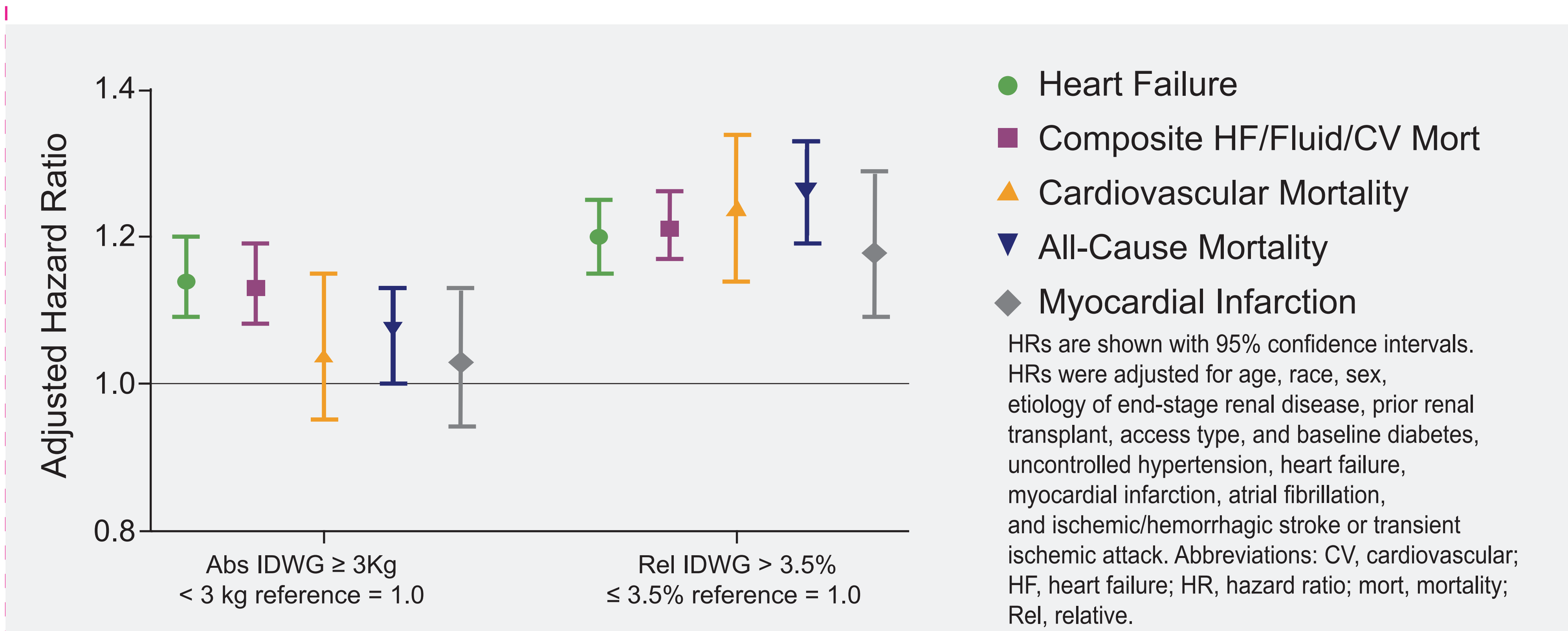
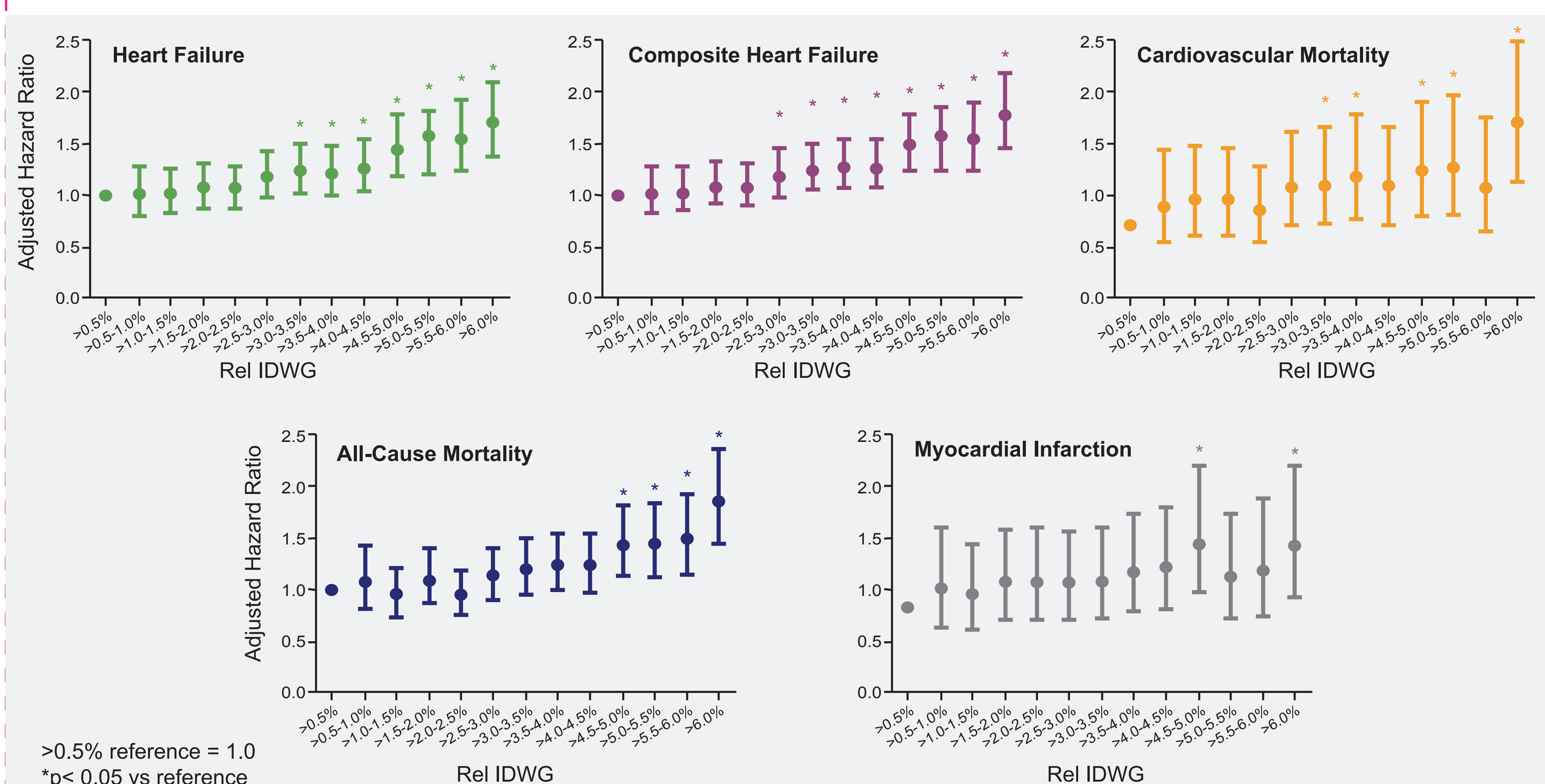
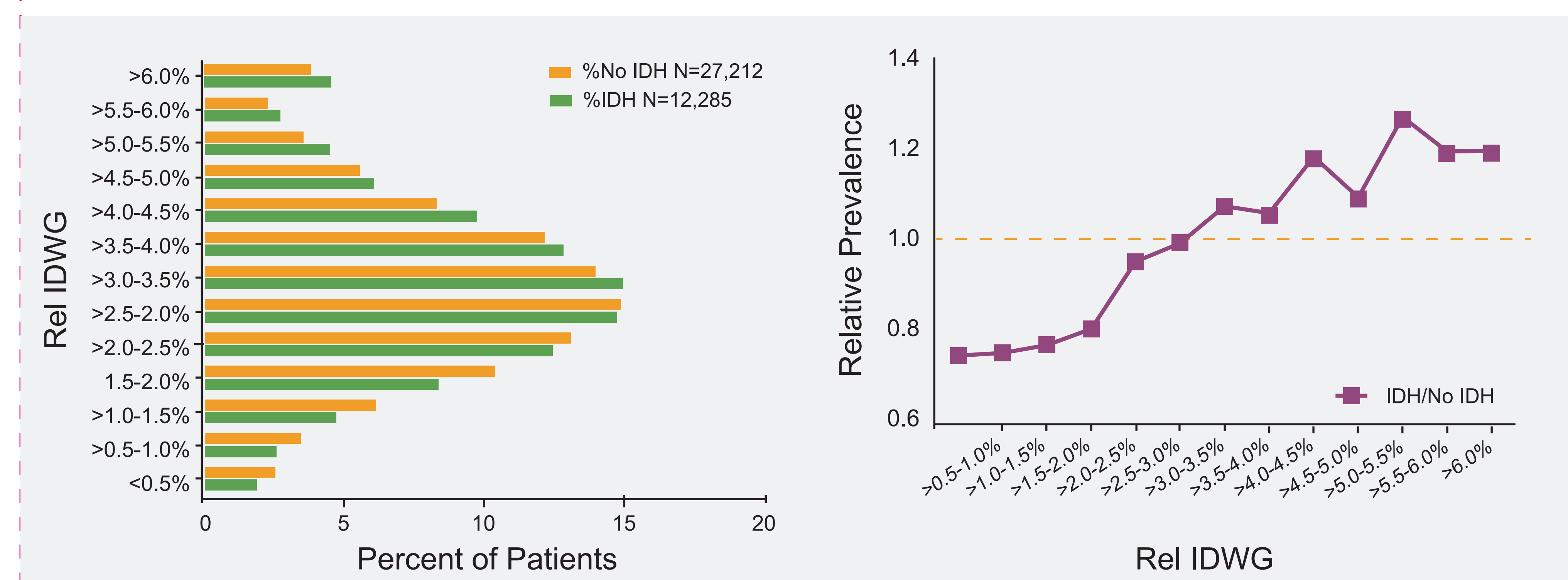


Figure 3. Relative IDWG and Events During At-Risk Period



Abbreviations: IDWG, interdialytic weight gain; Rel, relative.

Figure 4. Association Between IDWG and IDH



Left panel shows 2 overlaid histograms of Rel IDWG: (orange bars) among patients who experience IDH and (green bars) among patients who did not. Right panel is an alternative presentation of these same data showing the relative prevalence of IDH according to Rel IDWG (p<0.001). Abbreviations: IDH, intradialytic hypotension; IDWG, interdialytic weight gain; Rel, relative.

Table 1. Cohort Characteristics and Cardiovascular Comorbidities at Study Baseline

Categorical Variables ^a		N		Proportion (%)		
N = 39,864						
Female sex		17,493		43.9		
Race/Ethnicity						
White		18,381		46.1		
Black		12,623		31.7		
Hispanic		5,832		14.6		
Asian		1,274		3.2		
Other		1,735		4.4		
Etiology of ESRD						
Diabetes		18,735		47.0		
Hypertension		12,110		30.4		
Glomerular disease		2,880		7.2		
Other		6,139		15.4		
Continuous Variables ^b	N	Mean	SD	Median	Lower quartile	Upper quartile
Age (at dialysis initiation, years)	39,864	62.2	15.3	63	52	74
Number of prevalent CV comorbidities		N		%		
0		7,204		18.1		
1		14,905		37.4		
2		10,764		27.0		
3		5,531		13.9		
4		1,359		3.4		
5		101		0.3		
Prior renal transplant		704		1.8		
Prevalent diabetes ^c		27,152		68.1		
Prevalent heart failure ^c		15,903		39.9		
Prevalent myocardial infarction ^c		10,067		25.3		
Prevalent atrial fibrillation ^c		2,381		6.0		
Prevalent ischemic stroke ^d		344		0.9		
Prevalent hemorrhagic stroke ^d		65		0.2		
Prevalent cerebrovascular disease ^e		3,464		8.71		
Uncontrolled hypertension ^f		37,829		94.9		

Abbreviations: CV, cardiovascular; ESRD, end-stage renal disease; SD, standard deviation.

^aDefined based on CMS Medical Evidence Form 2728 data, or claims (1 inpatient, or 2 outpatient), or DaVita EMR records prior to dialysis day

^bDuring exposure assessment period (dialysis days 91-180) except for age, which is considered as of dialysis initiation.

^cDefined as the number of prevalent diabetes, heart failure, myocardial infarction, atrial fibrillation, cerebrovascular disease present as of dialysis day 180 (each as defined above).

^dDefined based on claims (1 inpatient, or 2 outpatient) or DaVita EHR record prior to dialysis day 180. Data from CMS Medical Evidence Form 2728 not included because they do not distinguish among ischemic stroke, hemorrhagic stroke, or transient ischemic attack.

^eDefined based on CMS Medical Evidence Form 2728, claims (1 inpatient, or 2 outpatient), DaVita EHR record prior to dialysis day 180. Includes ischemic stroke, hemorrhagic stroke, and transient ischemic attack.

^fDefined as mean pre-dialysis blood pressure > 140/90 mm Hg or post-dialysis blood pressure > 130/85 mm Hg during the exposure assessment period (dialysis days 91-180).

Table 2. Incidence Rates and Cumulative Incidence of Outcomes

Variable ^a	Number patients affected	% patients affected	Incidence rate 100 patient-years (95% CI)
Hospitalization for HF/volume overload	8,896	22.4	24.4 (23.9-24.9)
Composite hospitalization for HF/volume overload/CV mortality	10,805	27.2	27.8 (27.3-28.4)
Cardiovascular mortality	2,976	7.5	5.6 (5.4-5.8)
All-cause mortality	7,646	19.2	14.2 (13.8-14.6)
Myocardial infarction	2,396	6.0	6.0 (5.7-6.2)

Abbreviations: CI, confidence interval; CV, cardiovascular; HF, heart failure

^aAt-risk period began on dialysis day 181 and continued until death or censoring.

Discussion

- Compared to measures of absolute IDWG, relative IDWG measures demonstrated more potent associations with the outcomes studied (Figure 2).
- There was a strong incremental dose-response association between relative IDWG and the patient outcomes considered (Figure 3).
- IDWG—in absolute or relative terms—was associated with poorer outcomes, and relative IDWG may be the more clinically relevant parameter for future studies and in clinical practice.
- Greater fluid accumulation was associated with greater prevalence of IDH (Figure 4). In a related analysis, Cabrera et al³ have shown that IDH was independently associated with greater risk of death and cardiovascular events.
- These findings may be due in part to hypertension and the cardiovascular strain associated with fluid overload. An alternative mechanism might include myocardial stunning associated with high ultrafiltration rates during dialysis.

Conclusions

- These study results demonstrate an increased risk of myocardial infarction and heart failure/fluid overload for patients undergoing hemodialysis with greater fluid accumulation (IDWG).
- All-cause death and cardiovascular death were also highly associated with fluid accumulation.

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