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

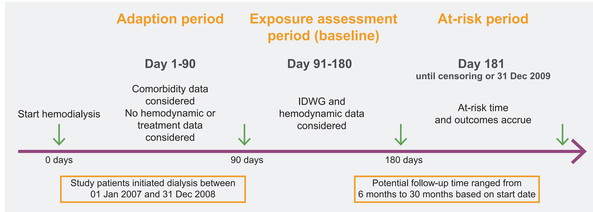
Patients

- 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

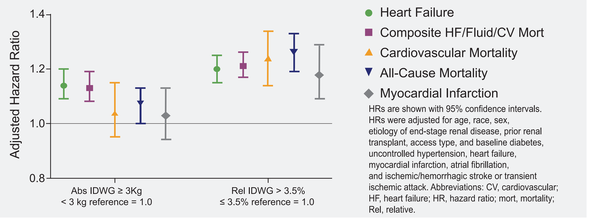
- IDWG (exposure) was defined as the amount of fluid gained between dialysis sessions, from the end of one dialysis session to the beginning of the next.
  - Relative IDWG describes the amount of fluid accumulation as a percentage of patient's post-dialysis weight
  - Absolute IDWG is calculated as the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

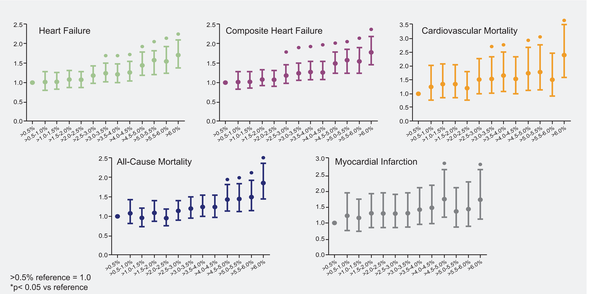
Results

Figure 2. Association of IDWG and Cardiovascular Events



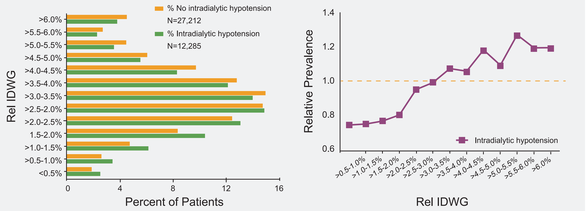
HRs are shown with 95% confidence intervals. HRs were adjusted for age, race, sex, etiology of end-stage renal disease, prior renal transplant, access type, and baseline diabetes, uncontrolled hypertension, heart failure, myocardial infarction, atrial fibrillation, and ischemic/hemorrhagic stroke or transient ischemic attack. Abbreviations: CV, cardiovascular; HF, heart failure; HR, hazard ratio; mort, mortality; Rel, relative.

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



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

Figure 4. Association Between IDWG and Intradialytic Hypotension



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

Table 1. Cohort Characteristics and Cardiovascular Comorbidities at Study Baseline

Categorical Variables[a] N = 39,864	N	Proportion (%)
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	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[b]	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[c]	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.
[a]During exposure assessment period (dialysis days 91-180) except for age, which is considered as of dialysis initiation; defined based on CMS Medical Evidence Form 2728 data, or claims (1 inpatient, or 2 outpatient), or DaVita EMR records prior to dialysis day. [b]Defined as the number of prevalent diabetes, heart failure, myocardial infarction, atrial fibrillation, cerebrovascular disease present as of dialysis day 180 (each as defined above).[c]Defined based on CMS Medical Evidence Form 2728 data, or claims (1 inpatient, or 2 outpatient), or DaVita EMR records prior to dialysis day 180. [d]Defined 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.[e]Defined 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. [f]Defined 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] N = 39,782	Number patients affected	% patients affected	Incidence rate per 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
[a]At-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 intradialytic hypotension (Figure 4). In a related analysis, Cabrera et al[3] have shown that intradialytic hypotension 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.

References

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