Long-Term Survival of Incident Hemodialysis Patients Who Are Hospitalized for Congestive Heart Failure, Pulmonary Edema, or Fluid Overload

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Background and objectives: Mortality in patients who are on maintenance hemodialysis and have congestive heart failure is high in small cohort studies. The aim of this study was to determine long-term survival in a large cohort of dialysis patients with congestive heart failure and suspected fluid overload or pulmonary edema.

Design, setting, participants, & measurements: Data were analyzed, retrospectively, on 1,119,808 patients who started hemodialysis between January 1977 and December 1999. Survival was estimated from the first (index) hospital admission with congestive heart failure, fluid overload, or pulmonary edema, after 60 d of successful hemodialysis using the life-table method. The impact of patient characteristics on outcome was assessed by the Cox proportional hazards model.

Results: Of the 310,456 patients included in the study, 233,454 were admitted with congestive heart failure, 63,886 with fluid overload, and 13,116 with pulmonary edema. The patients with congestive heart failure were older and often white and had diabetes or hypertension as the cause of renal failure. Deaths during the index hospital admission were 8.7% for congestive heart failure, 4.0% for fluid overload, and 6.6% for pulmonary edema. Five-year survival was 12.5, 20.2, and 21.3%, respectively. The independent positive predictors for mortality in these patients were age, male gender, diabetes, hypertension, history of cardiovascular disease, and congestive heart failure.

Conclusions: This study demonstrates very poor survival in dialysis patients who present with congestive heart failure, pulmonary edema, or fluid overload compared with patients who present with congestive heart failure without renal failure. Meticulous management of cardiovascular risk should improve survival.

study. The first (index) hospital admission with heart failure, fluid overload, or pulmonary edema at least 60 d after dialysis initiation was considered for analysis. The data for index hospitalization were obtained from Medicare Part A hospital claims, as validated in a previous study (9).

The patient cohorts were identified from the International Classification of Diseases, Ninth Revision, Clinical Modification codes for CHF (428.3), fluid overload (276.6), or pulmonary edema (518.4). Initial assumption in the study was that the diagnosis of “pulmonary edema” without heart failure was similar to the diagnosis of “fluid overload.” The clinical hypothesis was that both fluid overload and pulmonary edema without heart failure, in a dialysis patient, were the result of inability to comply with fluid restriction. The cohorts were followed from the index hospitalization until death, transplantation, or end of study. Long-term survival was estimated with the life-table method. Further adjusted analyses were performed using the Cox proportional hazards model to assess the impact of independent predictors, including age, gender, race, ethnicity, primary cause of renal failure, and comorbidities before study. The comorbidities included diseases of the cardiovascular, neurologic, respiratory, and gastrointestinal systems. The diagnosis of CHF, fluid overload, or pulmonary edema was made from Part A of Medicare claims data at the first presentation 60 d after starting dialysis, whereas the data on comorbidities were obtained from both Part A (inpatient) and Part B (outpatient) of Medicare claims, at any time, using a previously developed method and validated in patients (10,11). Thus, there were no previous hospitalizations for CHF, fluid overload, or pulmonary edema before the index hospitalization and 60 d after the start of hemodialysis. The study was approved by the institutional review board of Hennepin County Medical Center (Minneapolis, MN).

Survival was estimated for CHF, fluid overload, and pulmonary edema. Survivals of subgroups were compared using the log-rank test. It was further adjusted in the Cox proportional hazards model for age, gender, race, ethnicity, primary cause of renal failure, and comorbid medical conditions. SAS 8 (SAS Institute, Cary, NC) was used for statistical analysis.

### Results

Data were analyzed on 1,119,808 incident hemodialysis patients. During the study period and after the first 60 d of successful hemodialysis, 310,456 patients were identified as being admitted to the hospital with the diagnosis of CHF, fluid overload, or pulmonary edema. A cohort of 233,454 patients were admitted with a sole diagnosis of CHF. The rest of the patients were admitted with either fluid overload \((n = 63,886)\) or pulmonary edema \((n = 13,116)\). The patients with CHF were older. They were more often white and had diabetes and diabetic nephropathy compared with patients with fluid overload or pulmonary edema (Table 1).

Deaths during the index hospital admission were higher in CHF (8.7%) compared with fluid overload (4.0%) or pulmonary edema (6.6%). The 1- and 2-yr survivals were 54.1 and 36.4% with CHF, 65.8 and 48.3% with fluid overload, and 64.9 and 46.8% for pulmonary edema. On further follow-up, the 5-yr survival of the patients with fluid overload and pulmonary edema was poor: 20.2 and 21.3%, respectively. The 5-yr survival in CHF was even worse: 12.5% (Figure 1). In the Cox proportional hazards model, the independent positive predictors of mortality were older age, male gender, white race, diabetes and hypertension as the cause of renal failure, previous cardiovascular comorbidities, and CHF (Table 2).

### Discussion

The study reinforces the poor outcome in patients with CHF in a large cohort of maintenance hemodialysis patients. This phenomenon has been described previously but in a small cohort of patients (7). The strength of this study relates to the large size of the cohort, with all demographic subgroups followed for a long period until a firm end point (all-cause death).

### Table 1. Demographics \((n = 310,456)\) of patients at initiation of hemodialysis*

<table>
<thead>
<tr>
<th>Variables</th>
<th>Pulmonary Edema ((n = 13,116))</th>
<th>Fluid Overload ((n = 63,886))</th>
<th>CHF ((n = 233,454))</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;45</td>
<td>2808 (21.4)</td>
<td>15,436 (24.2)</td>
<td>21,713 (9.3)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>45 to 64</td>
<td>4774 (36.4)</td>
<td>23,395 (36.6)</td>
<td>71,361 (30.6)</td>
<td></td>
</tr>
<tr>
<td>65 to 74</td>
<td>3579 (27.3)</td>
<td>15,956 (25.0)</td>
<td>79,455 (34.0)</td>
<td></td>
</tr>
<tr>
<td>≥75</td>
<td>1955 (14.9)</td>
<td>9099 (20.6)</td>
<td>60,952 (26.1)</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td>0.2713</td>
</tr>
<tr>
<td>male</td>
<td>6590 (50.2)</td>
<td>32,156 (50.3)</td>
<td>118,248 (50.7)</td>
<td></td>
</tr>
<tr>
<td>female</td>
<td>6526 (49.8)</td>
<td>31,730 (49.7)</td>
<td>115,206 (49.3)</td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Caucasian</td>
<td>7574 (57.8)</td>
<td>35,775 (56.0)</td>
<td>152,980 (65.5)</td>
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<tr>
<td>African American</td>
<td>4924 (37.5)</td>
<td>25,097 (39.3)</td>
<td>70,254 (30.1)</td>
<td></td>
</tr>
<tr>
<td>Native American</td>
<td>194 (1.5)</td>
<td>1089 (1.7)</td>
<td>3019 (1.3)</td>
<td></td>
</tr>
<tr>
<td>other</td>
<td>424 (3.2)</td>
<td>1924 (3.0)</td>
<td>7202 (3.1)</td>
<td></td>
</tr>
<tr>
<td>ESRD cause</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>diabetes</td>
<td>3990 (30.4)</td>
<td>22,236 (34.8)</td>
<td>91,400 (39.2)</td>
<td></td>
</tr>
<tr>
<td>hypertension</td>
<td>3929 (29.9)</td>
<td>17,890 (28.0)</td>
<td>69,995 (30.0)</td>
<td></td>
</tr>
<tr>
<td>other</td>
<td>5199 (39.6)</td>
<td>23,760 (37.2)</td>
<td>72,099 (30.9)</td>
<td></td>
</tr>
</tbody>
</table>

*Data are \(n\)%.

CHF, congestive heart failure.
In comparison with the previous cohort study (7) of 432 hemodialysis patients including 133 patients with CHF, this study describes a poorer survival. The median survival was 18 mo compared with 36 mo in the other study. It could be explained by the larger proportion of patients with diabetes and elderly patients in this study. Moreover, it is an unselected population with large variability of care. Perhaps the extremely poor survival in this study is in agreement with previous evidence of poor cardiovascular outcomes in patients with asymptomatic systolic dysfunction (3,12). These findings collectively suggest that cardiac abnormalities in hemodialysis patients form a spectrum, ranging from left ventricular hypertrophy and left ventricular dilation to asymptomatic systolic dysfunction and symptomatic heart failure. The mortality increases along the spectrum and with higher risk patients, such as those with diabetes and the elderly. This phenomenon is well established in the general population (13,14).

It must be noted that the survival of patients who have heart failure and are on hemodialysis is worse compared with the general population. In the Framingham population in 1990 to 1999, the 5-yr survival in patients with heart failure was 60% in women and 46% in men, compared with 12.5% in our hemodialysis population (13). The survival of patients with CHF in the general population has also improved over the years. In the previously mentioned study, the 5-yr survival in men has improved from 34 to 46% (53 to 60% in women) between the 1950s and the 1990s (13). Similar trends have been demonstrated in the United Kingdom and Europe (15,16). This is certainly the result of better management of the condition in the general population. In a previous study in a similar population of 286,623 patients who were on maintenance hemodialysis between 1977 and 2000, there was no improvement in survival over the years. The 2-yr survival after CHF admission was 37.5% in 1977 to 1990, 35.9% in 1991 to 1994, 36.6% in 1995 to 1997, and 36.5% in 1998 to 2000; however, the time-dependent analysis was not adjusted for comorbidities (17). This study also demonstrates that the incidence of heart failure is much higher in patients who are on maintenance hemodialysis compared with the general population; therefore, it could be suggested that diagnosis and proper management of CHF might improve long-term survival in patients who are on maintenance hemodialysis.

This study attempted to distinguish between CHF and fluid overload (or pulmonary edema without heart failure) as separate risk factors for adverse outcomes. Patients with CHF in this study had very poor survival (12.5% at 5 yr), worse than patients with fluid overload or pulmonary edema without heart failure (20.2 and 21.3% at 5 yr, respectively); however, the survival of patients with diagnosis of fluid overload or pulmonary edema was also alarming. Hypothetically, the distinction

![Figure 1. All-cause survival (composite groups). Event-free survival of patients who were on maintenance hemodialysis from first hospitalization after initiation of renal replacement therapy with congestive heart failure (CHF), pulmonary edema, and fluid overload.](image-url)
between the two might have some added benefits. It perhaps raises the possibility of identifying patients who have left ventricular dysfunction hidden in the fluid overload group and might need extra care; however, as demonstrated in the study, the practical significance of such distinction is minimal.

More important, these results prompt further attention toward management of CHF in hemodialysis patients. The available evidence is limited but suggests that survival can be improved. For patients with pulmonary edema or fluid overload, heart failure is always in the differential diagnosis and so should be managed along a similar pathway. All such patients with heart failure, fluid overload, and pulmonary edema should have an echocardiogram at presentation. An echocardiogram, if not already done, might assist in estimation of ejection fraction and subtle volume overload after ultrafiltration (12,18). In all acute presentation, acute coronary syndrome should be excluded with electrocardiogram and biomarkers. As an example, in a patient who presents with unusual shortness of breath on a Monday morning, an electrocardiogram might be helpful in identifying an acute coronary event. The prognosis after myocardial infarction is poor, the management of which would be more than ultrafiltration for associated pulmonary edema (19). A stress echocardiogram with or without coronary angiogram might be able to identify and treat reversible, chronic ischemia-induced myocardial dysfunction (20,21). There is evidence to suggest the benefit of using β blockers to improve outcomes from randomized, controlled trials, a treatment that is underused (22–26). In patients with chronic kidney disease and acute myocardial infarction, the use of aspirin and angiotensin-converting enzyme inhibitors in addition to β blockers is associated with improved survival (27,28).

Another management strategy, which is potentially beneficial in patients who start hemodialysis, is performing an echocardiogram (12,29,30). As highlighted in the study, once patients develop congestive cardiac failure or even fluid overload without clinically overt heart failure, the prognosis is poor. Identification of left ventricular dysfunction, with an echocardiogram, before development of clinically overt heart failure might be of assistance (3,12,18). On identification of left ventricular hypertrophy, systolic or diastolic dysfunction, management should include aggressive treatment of hypertension with drugs and volume control together with treatment of myocardial ischemia (including coronary revascularization). Such strategies might prevent subsequent heart failure and attending mortality (4).

In the study that compared different subgroups, the patients with diabetes and the elderly had worse outcome. This is probably related increased burden of ischemic heart disease in these patients. The ischemic burden could explain why diabetes, age, and male gender are significant risk factors of subsequent mortality during follow-up. The poor survival in white patients is a previously well-documented phenomenon. Several hypotheses could be proposed. It could be due to increased death in sicker black patients before starting dialysis with limited access to medical care. It could also be due to the different nature of cardiomyopathy in black patients, being more hypertensive than ischemic. The improved survival in patients who were on hemodialysis after 1 yr of starting hemodialysis could be related to the increased early deaths of sicker patients who started on dialysis.

There are several limitations of the study, mostly related to the nature of the data set. It is a retrospective study from an administrative data set and lacks important clinical information on physical examination, electrocardiogram, and echocardiogram. The groups with fluid overload and pulmonary edema without CHF were considered similar and had similar prognosis. This is only a presumption and cannot be verified without additional clinical data. The inferences on diagnosis depend entirely on coding of hospital admissions, which is less reliable compared with data collected in prospective studies. Several other management issues that could have altered the prognosis of these patients with CHF were not available for consideration during analysis, including use of medications. The cardiovascular deaths were not analyzed separately because of the potentially unreliable nature of the data on cause of death in the available data set.

Conclusions
This study demonstrates an extremely poor survival with patients who have CHF and are on hemodialysis compared with the general population. Patients with fluid overload and pulmonary edema have a poor prognosis as well. These results prompt further investigations into the possible prevention and proper management of CHF in patients who are on maintenance hemodialysis.

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Disclosures
None.

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