

Subdural Hematomas in Chronic Dialysis Patients: Significant and Increasing

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Background and Objectives: Subdural hematoma is a known complication of long-term hemodialysis.

Design, Setting, Participants, and Measurements: The US Renal Data System was used to determine the occurrence rate of nontraumatic subdural hematoma in long-term dialysis patients and to evaluate time trends.

Results: The occurrence rate of subdural hematoma in long-term dialysis patients is 10 times higher than that of the general population. From 1991 to 2002, the occurrence rate of subdural hematoma in hemodialysis patients doubled, whereas it did not change in peritoneal dialysis patients.

Conclusions: This high occurrence rate of subdural hematoma and its recent increase may be related to increased use of anticoagulants in long-term hemodialysis patients.

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Although cardiovascular disease is the major complication of renal failure, other organ systems are at risk. Cognitive impairment may result from uremia itself, and patients who have ESRD and are on dialysis are liable to develop neuropsychiatric adverse effects from commonly used medications. The differential diagnosis of declining mental status in these patients also includes stroke and, more specifically, subdural hematoma (SDH). Our recent clinical experience suggested to us that SDH has continued to occur in long-term dialysis patients and that it is now perhaps even more common than in past years. On review of the literature, we found only one study that evaluated SDH in dialysis patients, and it reported a cumulative incidence of 3.3% during an 8-year period (1). This study is now more than 30 years old. In addition, it is a single-center report and did not report comparative data. Using the US Renal Data System, we evaluated the epidemiology of SDH in long-term dialysis patients and studied the demographics of long-term dialysis patients who develop SDH.

Materials and Methods

The US Renal Data System database contains data that have been collected prospectively since 1988 and contains the essential medical information on >93% of the long-term dialysis patients in the United States. We used the database to identify nontraumatic SDH in 1991 to 2002. The *International Classifications of Diseases, Ninth Revision*, code 432.1 was used to identify patients with nontraumatic SDH. The Form 2728 data were used to obtain data on 14 comorbidities that routinely were recorded at the start of dialysis (available only from 1998 to 2002). The incidence rate of SDH in hemodialysis patients was calculated for

1991 to 2002. The Kendall-Rank correlation test was done to analyze the time trend. The association of comorbidities with SDH was calculated using a χ^2 test.

Results

A total of 2793 SDH were reported from 1991 to 2002. Detailed demographic information about these cases was available only from 1998 to 2002. A total of 53% of the patients were male; 58% were white; 68% were >65 yr of age; and 37% had diabetes as the cause of ESRD as compared with 32 and 31%, respectively, for hypertension and other as cause of their ESRD. The 30-day mortality of SDH in this population was 39%.

The incidence rate for SDH in dialysis patients was 191 per 100,000 dialysis patients per year in 2002 as compared with three to 58 cases per 100,000 general population per year, reported from other studies worldwide (2–5) (Figure 1).

The incidence rate of SDH has more than doubled from 90 per 100,000 dialysis patients per year in 1991 to almost 200 per 100,000 per year in 2002. The time trend analysis shows a very significant positive relationship ($r = 0.96$, 95% confidence interval 0.88 to 0.99; $r^2 = 0.94$, $P < 0.001$; Figure 2).

Furthermore, the relationship of each comorbidity with SDH was analyzed using a χ^2 test. Multiple regression could not be performed because these were aggregate rather than individual patient-level data. Seven of the 14 comorbidities, namely congestive heart failure, diabetes, hypertension, ischemic heart disease, myocardial infarction, peripheral vascular disease, and chronic obstructive pulmonary disease were significantly associated ($P < 0.05$) with SDH (Table 1). The other seven of the 14 comorbidities, namely cerebral vascular accident, cancer, pericarditis, AIDS, dysrhythmia, inability to ambulate, and inability to transfer, were not significantly associated with SDH ($P > 0.05$; Table 1).

A separate analysis in peritoneal dialysis patients found a stable incidence rate of SDH ranging from 57 per 100,000

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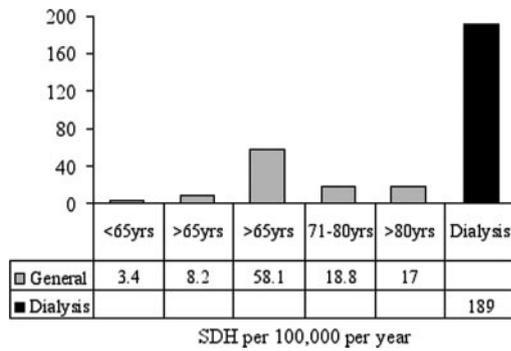


Figure 1. Incidence rate for subdural hematoma (SDH) per 100,000 patient-years. The incidence of SDH in long-term dialysis patients as of 2002 is higher than that of the general population for all age groups reported in the literature (2-5).

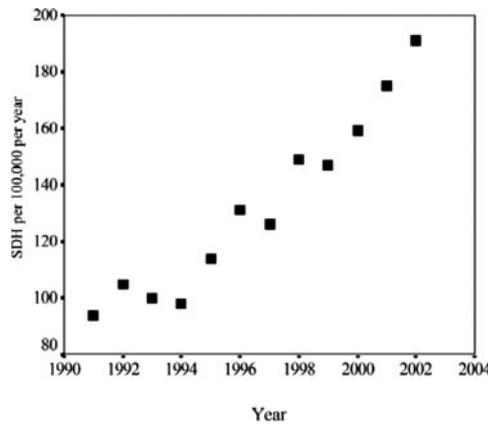


Figure 2. Incidence rate for SDH in long-term dialysis patients, from 1991 to 2002. The incidence rate of SDH in long-term dialysis patients has steadily increased since 1990 ($r = 0.96$, 95% confidence interval 0.88 to 0.99).

peritoneal dialysis patients per year in 1993 to 82 per 100,000 per year in 2002 with no clear time trend ($r = 0.48$, $P = 0.31$; Figure 3).

Discussion

These data confirm and quantify the much greater incidence rate of SDH in long-term dialysis patients compared with the general population. It is likely that volume overload and coagulation abnormalities contribute to this phenomenon. The volume-overloaded long-term dialysis patient is likely to have venous hypertension, and, if this patient's platelet function is deficient, then small venous tears of dural bridging veins are apt to expand and cause a SDH (6). To this is added the anticoagulant effect of systemic heparin during the dialysis procedure.

The 30-day mortality in this population was almost 40%, which further underlines the impact of SDH. The general population has a similar mortality rate from warfarin-associated intracranial hemorrhage (7).

In addition, there is a clear and very significant increase in the incidence rate of SDH from 1991 to 2002, the time period of

Table 1. Relationship of comorbidities at start of dialysis to the subsequent occurrence of nontraumatic subdural hematoma

Comorbidity	Associated P
Congestive heart failure	<0.001
Chronic obstructive pulmonary disease	<0.05
Diabetes	<0.001
Hypertension	<0.001
Ischemic heart disease	<0.001
Myocardial infarction	<0.05
Peripheral vascular disease	<0.001
Cancer	>0.1
Pericarditis	>0.1
Inability to ambulate	>0.1
Inability to transfer	>0.1
AIDS	>0.1
Dysrhythmia	>0.1
Cerebral vascular accident	>0.1

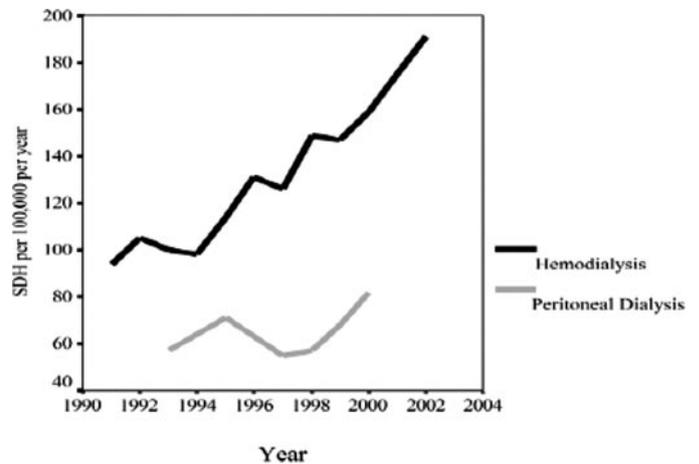


Figure 3. Incidence rates for SDH in hemodialysis and peritoneal dialysis patients. The rising incidence rates of SDH are confined to hemodialysis patients. The trend for peritoneal dialysis patients is not significant ($r = 0.48$, $P = 0.31$).

this study. It is not clear why this has occurred. The comorbidities that may be associated with SDH did not greatly change during the period of the study, and the dialysis population did not age to an extent that would explain a doubling of the occurrence of SDH. It is possible that there have been changes in dialysis practice such as increases in heparin dosing, but this is speculative. An additional influence may be the use of warfarin, used either for cardiac valvular disease or to maintain arteriovenous graft patency. The increase in incidence rate of SDH in the hemodialysis population without a corresponding increase in the peritoneal dialysis population suggests that use of warfarin to maintain arteriovenous graft patency may be relevant. Use of arteriovenous grafts using prosthetic material for hemodialysis access has become much more frequent in recent years (8). In contrast to native arteriovenous fistulas,

such grafts have lesser long-term patency and have frequent clotting (9). Warfarin is now commonly used to try to prevent such clotting and prolong the life of the graft. This should be carefully considered in view of the recent reports that showed no improvement in access patency for patients who were administered warfarin (10–12). Indeed, the major cause of arteriovenous graft clotting is anatomic, not functional. Graft stenosis, usually venous, is the major culprit in arteriovenous graft clotting (13). Therefore, use of warfarin may be ill-advised in such cases, because it has no clear benefit and may predispose to SDH or other bleeding complications (14).

There may be additional factors that lead to use of warfarin in patients with ESRD. Compared with the general population, these patients have an increased incidence and prevalence of aortic valve calcification and mitral annular calcification, which lead to aortic and mitral stenosis, respectively (15–18). Patients who develop mitral stenosis are often put on long-term anticoagulation because they have increased rates of atrial fibrillation and are at risk for stroke (19). These aspects would probably affect both hemodialysis and peritoneal dialysis patients, however. In addition, it is unlikely that cardiac valvular disease in ESRD has doubled from 1992 to 2002. Even considering these issues, data are lacking to quantify changes in warfarin use during the period of this study. In the general population, increasing warfarin use does seem to have increased the occurrence of intracranial hemorrhage (20), but it remains speculative that warfarin caused the rising occurrence of SDH in dialysis patients.

Other factors that explain the increasing incidence of SDH with time are the increasing mean incident and prevalent age of patients with ESRD. The prevalent average age of patients with ESRD increased from 53.4 years in 1995 to 58.2 in 2003. Age has been reported in previous studies to be an independent risk factor for SDH (2–6). The incidence rate of SDH has been reported to be 3.4 per 100,000 general population per year for <65 years and a varying rate ranging from 8 to 58 per 100,000 per year in those >65 years of age (2–4). Even if all new dialysis patients were older than 65 years, the incidence rate of 200 per 100,000 of SDH in the dialysis population would still be well over that reported for the general population.

Seven of the 14 comorbidities, namely congestive heart failure, diabetes, hypertension, ischemic heart disease, myocardial infarction, peripheral vascular disease, and chronic obstructive pulmonary disease were found to be significantly associated with SDH in the dialysis population ($P < 0.05$, χ^2). During the period of the study, there is only a slight increase in prevalence of these significant comorbidities in the dialysis population. These comorbidities, however, are not known to be associated with SDH in the general population. In dialysis patients, a significantly associated comorbidity could be interacting or having an effect modification with other comorbidities. Such interplay of factors could be playing a protective or contributing role toward current trends of SDH in dialysis patients. The direction of this effect cannot be gauged from an aggregate data study such as ours. A patient-level analysis of these comorbidities with multiple logistic regression is required to find the direction of this effect and the magnitude of it.

Conclusions

SDH is more frequent in long-term dialysis patients compared with the general population. SDH in long-term dialysis patients has doubled in frequency in recent years, possibly in association with use of warfarin. This anticoagulant should be used in long-term dialysis patients only when necessary and when justified by published evidence.

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Disclosures

None.

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