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CLINICAL STUDY

## Hemorrhagic Stroke in Chronic Dialysis Patients

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### ABSTRACT

**Aims:** This study was designed to retrospectively investigate the clinical profiles, disease course and management of hemorrhagic stroke in chronic dialysis patients. We emphasized on the factors affecting the prognosis. **Patients and Methods:** We retrospectively studied (January 1991–June 1999) the chronic dialysis patients who were admitted to our facility with a diagnosis of acute hemorrhagic stroke. The medical results were reviewed in detail and the clinical characteristics, laboratory data and management records of each individual were collected for analysis. **Results:** There were 16 patients analyzed in total, 9 males and 7 females. The average age was  $59.4 \pm 13.3$  years old. Before admission, 14 patients received chronic hemodialysis (HD) and two patients peritoneal dialysis (PD). The co-morbidities included hypertension (16/16), Diabetes Mellitus (DM) (9/16), previous cerebrovascular accidents (9/16) and hyperlipidemia (5/16). The locations of cerebral hemorrhage (CH) were: the putamen (6/16), brain stem (3/16), thalamus (3/16) and others (4/16). Among the 14 HD patients, 8 remained on HD after onset of CH, while 6 switched to PD. Those who received PD before their development of CH continued to perform PD. The overall mortality was 44% (7/16). One of the 8 patients who continued on HD died (mortality 12.5%). Among the 8 patients who received PD, 6 died (mortality 75%). Two patients who underwent surgical intervention also passed away. The major cause of death was neurological deterioration. The interval between the onset of CH and death was short ( $15 \pm 13$  days, range 2–39 days). **Conclusion:** The overall prognosis of CH in the chronic dialysis population is poor. Patients with lower

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hemoglobin levels upon presentation and those performing PD after CH may have even worse prognosis.

**Key Words:** Hemorrhagic stroke; Hemodialysis-peritoneal dialysis; Hemoglobin.

## INTRODUCTION

Cardiovascular diseases and cerebrovascular diseases are important causes of death in chronic dialysis patients.<sup>[1–5]</sup> The risk of stroke is five times higher in dialysis patients than in the general population.<sup>[6,7]</sup> Co-morbid conditions, such as hypertension, diabetes and hyperlipidemia, which are risk factors of cerebrovascular disease, are common in chronic dialysis patients. According to previous reports, the incidence of cerebral hemorrhage (CH) may be higher than cerebral infarct (CI) in patients under chronic dialysis.<sup>[6,8–10]</sup> CH could result in significant mortality and morbidity of the patients.<sup>[7,11–14]</sup> However, the optimal modality of dialysis after CH is still controversial, although, there is a preference towards slow continuous dialysis, such as peritoneal dialysis (PD) and continuous renal replacement therapy.<sup>[15–21]</sup>

This study was designed to retrospectively investigate the clinical profiles, disease course and management of CH in chronic dialysis patients.

## PATIENTS AND METHODS

We retrospectively studied chronic dialysis patients who were admitted to our hospital (January 1991–June 1999) with the diagnosis of acute hemorrhagic stroke. All patients had been dialyzed for more than one month. Qualified neurologists under classical neurological findings made the diagnosis of hemorrhagic stroke. Brain computed tomography scans were available for every patient. The medical results were reviewed in detail and the clinical characteristics, laboratory data and management records of each individual were collected for analysis.

### Statistical Analysis

All data was recorded as Mean  $\pm$  SEM, except where otherwise indicated. For comparisons of age, duration of dialysis and biochemical parameters between survivor and non-survivor groups, the Student's unpaired t-test was used. To compare the

proportions of male and female patients and the mode of dialysis between the groups, the Chi-square method was used. Statistical significance for intergroup comparison was defined as  $p < 0.05$ .

## RESULTS

Clinical characteristics are shown in Table 1. There were 16 patients analyzed in total (9 males, 7 females). The average age was  $59.4 \pm 13.3$  (range: 32–80) year-old. Fourteen patients had HD and 2 patients had PD. The average duration of dialysis was  $31.3 \pm 35.5$  (range, 1–108) months. Co-morbidities included: hypertension (16/16), diabetes (9/16), previous cerebrovascular accidents (9/16) and hyperlipidemia (5/16). The locations of CH included: the putamen (6/16), brain stem (3/16), thalamus (3/16), massive (2/16) and others (2/16) (Table 2). CH involving more than one lobe was defined as “massive.”

When they arrived at our emergency station, 6 patients were unconsciousness and 3 were intubated immediately. The blood pressure and heart rate at presentation of each victim are shown in Table 3. Among the 14 patients who had chronic HD before CH, 8 patients continued HD and the other 6 patients switched to PD for the sake of reducing the risk of increased intracranial pressure. Three of these 6 patients who switched to PD returned to receive HD later due to ultrafiltration failure of the PD technique. The 2 patients who were under chronic PD continued

**Table 1.** Clinical characteristics of the patients (n=16).

|                                   |                         |
|-----------------------------------|-------------------------|
| Age, years (range)                | 59.4 $\pm$ 13.3 (32–80) |
| Sex (M:F)                         | 9:7                     |
| Hypertension                      | 16/16 (100%)            |
| Diabetes                          | 9/16 (56.3%)            |
| Hyperlipidemia                    | 5/16 (31.3%)            |
| Previous CVA                      | 9/16 (56.3%)            |
| Duration of dialysis, mon.(range) | 31.3 $\pm$ 35.5 (1–108) |
| Hemodialysis                      | 14/16 (87.5%)           |
| Peritoneal dialysis               | 2/16 (12.5%)            |

CVA, cerebrovascular accident.



**Table 2.** Locations of intracerebral hemorrhage.

|            | No. of patients |
|------------|-----------------|
| Putamen    | 6/16 (37.5%)    |
| Thalamus   | 3/16 (18.8%)    |
| Brain stem | 3/16 (18.8%)    |
| Massive    | 2/16 (12.5%)    |
| Others     | 2/16 (12.5%)    |

to perform PD after the onset of CH (Table 4). In our patients, no one received continuous renal replacement therapy, defined as continuous venovenous hemofiltration (CVVH).

The overall mortality was 44% (7/16). Among the 8 patients who continued HD, one died (making mortality rate of 12.5%). Among the 8 patients who had PD after CH, 6 patients died (a mortality rate of 75%). Two patients underwent surgical intervention, but unfortunately, both of them died. The major cause of death after surgery was neurological deterioration. The interval between the onset of CH and death was short ( $15.0 \pm 13.0$  days, 2–39 days). When we compared the clinical parameters of patients between the survival group and the non-survival group, only the hemoglobin concentrations and the mode of dialysis after the episode were found to be statistically significant (Table 5). The patients with lower hemoglobin concentrations at presentation and those who underwent PD after CH had worse prognoses. Although not statistically significant, tendencies were found in the non-survival group towards older age, longer

duration of dialysis, and worse neurological status at the onset of CH.

## DISCUSSION

Stroke remains the second leading cause of death in the general population in Taiwan,<sup>[22]</sup> and the risk of this disorder is significantly greater in the end stage renal disease (ESRD) population.<sup>[6–10]</sup> Indeed, it accounts for 5.6–11% of death in the ESRD population<sup>[23,24]</sup> and results in significant morbidity of the patients. The incidence of stroke in chronic dialysis patients is reported to be 11.5 to 17.2 per 1,000 patient year.<sup>[6,8]</sup> The relative risk to dialysis patients, compared to the general population, is 5 times higher for stroke, 10 times higher for CH, and twice as high for CI.<sup>[6]</sup> Interestingly, the incidence of CH is higher than CI.<sup>[6,8–10]</sup> Furthermore, CH in a chronic dialysis population occurs 10 years earlier than in the general population,<sup>[6]</sup> and has an especially poor prognosis.<sup>[11–14]</sup> From the literature review, it has been suggested that hypertension,<sup>[6,9,10]</sup> left ventricular hypertrophy,<sup>[9]</sup> low Kt/V,<sup>[9]</sup> low albumin and cholesterol levels<sup>[6]</sup> should be recognized as risk factors for CH in the ESRD population. Not all these risk factors were available in our work, except that all of our patients had hypertension and were under antihypertensive treatment before CH. The prevalence of hypertension in the general dialysis population in Taiwan is 50%.<sup>[25]</sup> Most of our patients had hematoma located at the putamen and thalamus, which are traditionally thought to be the sites of hypertensive hemorrhage.<sup>[26,27]</sup>

**Table 3.** Initial manifestations.

| Patient | Location of ICH | Consciousness | BP (mmHg) | HR/min | Outcome  |
|---------|-----------------|---------------|-----------|--------|----------|
| 1       | Putamen         | E4M6V5        | 130/60    | 80     | Survived |
| 2       | Occipital lobe  | E4M6V5        | 150/100   | 80     | Survived |
| 3       | Putamen         | E4M6V5        | 190/110   | 92     | Survived |
| 4       | Cortex          | E4M5V5        | 139/51    | 72     | Survived |
| 5       | Putamen         | Lethargic     | 200/100   | –      | Survived |
| 6       | Thalamus        | E4M6V5        | 138/88    | 131    | Survived |
| 7       | Pontine         | Arousable     | 194/113   | 103    | Survived |
| 8       | Thalamus        | E1M3V1        | 152/58    | 92     | Survived |
| 9       | Putamen         | E4M6Va        | 171/104   | 68     | Survived |
| 10      | Pontine         | E1M2Vt        | 99/52     | 79     | Died     |
| 11      | Pontine         | E3M5Va        | 166/80    | 81     | Died     |
| 12      | Massive         | E1M1Vt        | 200/80    | 64     | Died     |
| 13      | Putamen         | E1M4V2        | 201/114   | 83     | Died     |
| 14      | Massive         | E1M1Vt        | 140/70    | 103    | Died     |
| 15      | Putamen         | E4M6V1        | 207/119   | 88     | Died     |
| 16      | Thalamus        | E1M1V2        | 254/100   | 78     | Died     |



**Table 4.** Selection of dialysis mode.

| Before ICH          | After ICH           | No. of patients | Survived | Non-survived |
|---------------------|---------------------|-----------------|----------|--------------|
| Hemodialysis        | Hemodialysis        | 8/16 (50%)      | 7/8      | 1/8 (12.5%)  |
| Hemodialysis        | Peritoneal dialysis | 6/16 (27.5%)    | 2/6      | 4/6 (66.7%)  |
| Peritoneal dialysis | Peritoneal dialysis | 2/16 (12.5%)    | 0/2      | 2/2 (100%)   |

**Table 5.** Comparison of clinical parameters between survived and non-survived groups.

|                                    | Survived  | Non-survived | P value       |
|------------------------------------|-----------|--------------|---------------|
| Age, years                         | 57±14.2   | 62.6±12.3    | 0.415         |
| Sex (female)                       | 4/9       | 4/7          | 1.00          |
| Duration of dialysis, months       | 22.1±12.5 | 43±51.5      | 0.331         |
| DM                                 | 6/9       | 3/7          | 0.615         |
| Hb conc. at presentation, gm/dL    | 10.6±1.4  | 8.7±1.42     | 0.018 (<0.05) |
| Glasgow coma scale at presentation | 12.9±3.76 | 5.86±3.19    | 0.334         |
| Peritoneal dialysis after ICH      | 2/9       | 6/7          | 0.041 (<0.05) |

These observations imply that hypertension might play an important role in the development of CH in our patients.

In patients with CH, dialysis itself may entail specific problems, chief of which is increased intracranial pressure and progressive brain edema as a result of rapid changes in serum osmolality and pH values.<sup>[15,18,21,28]</sup> Other major problems of dialysis are a tendency to hemorrhage in response to systemic anticoagulation and insufficient dialysis.<sup>[20]</sup> Gonda, et al.<sup>[17]</sup> reported 17 neurosurgical patients who were assigned to either continuous dialysis [continuous arteriovenous hemofiltration (CAVH), continuous ambulatory PD (CAPD), and cyclic PD] or intermittent dialysis [intermittent HD (IHD) and intermittent PD]. They found that continuous dialysis appeared to be superior to intermittent dialysis for survival; in this the former produced less brain edema. Yorioka, et al.<sup>[16]</sup> also observed that patients having CAPD after CH had better prognosis than those undergoing IHD after CH. However, in this work, we did not observe any advantage in prognosis of PD in our patients. To the contrary, the patients having PD had significantly worse prognosis. In a recent review by Davenport, PD<sup>[18]</sup> in patients with acute brain injury is said to have disadvantages like cardiovascular and intracranial instability caused by rapid changes in intraperitoneal volume, and poor dialysis efficacy. They recommended continuous renal replacement therapy like CAVH or CVVH. Joseph, et al.<sup>[29]</sup> also report that the risk of fatal stroke is higher in patients on PD, although the reason was unclear. The patient number of this work was limited; therefore the result might not have important clinical significance.

The prognosis of CH in chronic dialysis patients is poor.<sup>[7,12–14]</sup> The short-term mortality rate is reported to be as high as 70%. The long-term survival rate is also poor. CH in chronic dialysis patients is clinically more severe and the patients tend to have larger hematoma at presentation.<sup>[11,12]</sup> Large hematoma volume,<sup>[11,12]</sup> poor admission Glasgow coma scale, age >65 years, sugar >200 mg/dL<sup>[13]</sup> and DM<sup>[8]</sup> are reported to be poor prognostic factors. The mortality of our patient group was 44%. The duration between the onset of CH and death was short, 15.0±13.0 days (2–39 days). Poor prognostic factors showing statistical significance include: lower hemoglobin levels at presentation and selection of PD after CH (Table 5). Low hemoglobin levels in chronic dialysis population are associated with inadequate dialysis, chronic illness,<sup>[30]</sup> poor nutritional status<sup>[31]</sup> and bleeding tendency.<sup>[32]</sup> These conditions may contribute to a poor prognosis in the non-survivor group.

In conclusion, CH in patients under maintenance dialysis had a high rate of acute death. Control of hypertension may help to reduce the risk of this dreadful complication. Further investigation is required to define the optimal method of dialysis in patients with CH.

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