International Journal of Cardiology 224 (2016) 267–270

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Correspondence

End-stage renal disease patients on chronic maintenance hemodialysis in a hospitalized acute heart failure cohort: Prevalence, clinical characteristics, therapeutic options, and mortality☆

Yuichiro Minami [a,*], Katsuya Kajimoto [b], Naoki Sato [c], Nobuhisa Hagiwara [a], Teruo Takano [d], on behalf of the ATTEND study investigators

[a] Department of Cardiology, Tokyo Women's Medical University, Tokyo, Japan
[b] Division of Cardiology, Sekikawa Hospital, Tokyo, Japan
[c] Internal Medicine, Cardiology, and Intensive Care Unit, Nippon Medical School Musashi-Kosugi Hospital, Kawasaki, Japan
[d] Department of Internal Medicine, Nippon Medical School, Tokyo, Japan

ARTICLE INFO

Article history:
Received 17 June 2016
Received in revised form 5 September 2016
Accepted 15 September 2016
Available online 17 September 2016

Keywords:
Epidemiology
Heart failure
Hemodialysis
Kidney
Prognosis

Heart failure is present in more than one-third of new hemodialysis patients with end-stage renal disease (ESRD), and more than half of ESRD patients treated by chronic maintenance hemodialysis die of cardiovascular diseases including heart failure [1,2]. Although ESRD patients on hemodialysis might thus be included in an acute heart failure (AHF) population, this subgroup of patients has remained underappreciated, and the clinical profiles of AHF patients on hemodialysis remain largely undefined. Therefore, this study was undertaken to investigate the prevalence, clinical characteristics, management, and mortality of ESRD patients on hemodialysis prior to admission in a hospitalized AHF cohort.

The AcuTe decompensaTEd heart failure syNDromes (ATTEND) study is a nationwide, multicenter, hospital-based, observational, prospective cohort study that focuses on AHF in Japan, the details of which have been reported previously [3]. Among 4842 patients registered in the ATTEND study, 7 patients with missing information about hemodialysis were excluded, and the remaining 4835 patients (99.9%) were included in the analysis. At the time of admission, the investigators confirmed whether or not the registered patient underwent chronic maintenance hemodialysis for ESRD (mostly undergoing a 4-hour hemodialysis session 3 times per week) before admission as part of the patient's medical history. Student's t-tests were used to compare normally-distributed continuous variables. Chi-square tests were used to compare nominal variables. Mann–Whitney U tests were used for the variables with skewed-distributions. The probabilities of all-cause death and sudden cardiac death were estimated by the Kaplan–Meier method, after which log-rank tests were used to compare survival curves. Cox proportional hazards models were used to evaluate the impact of hemodialysis on the all-cause death and sudden death. Two-tailed P values of <0.05 were considered statistically significant.

Among the 4835 patients, 79 (1.6%) were undergoing chronic maintenance hemodialysis for ESRD before admission. A statistically significant difference was observed in the distribution of the day of admission between AHF patents with and without hemodialysis, and more than half of the patients on hemodialysis (42 of 79 patients; 53.2%) were admitted on Monday and Tuesday (Fig. 1A). The baseline characteristics and in-hospital managements of the AHF patients with and without hemodialysis are presented in Table 1. Among the 79 patients undergoing hemodialysis on admission, 26 (32.9%) died during the median follow-up period of 458 (interquartile range 239–677) days, including 17 (21.5%) with cardiac etiology (9 heart failure, 7 sudden cardiac death, and 1 other cardiac cause), 8 (10.1%) from a non-cardiac cause, and 1 from an unknown cause. Regarding the causes of death after admission, the probability of sudden death among patients with hemodialysis was significantly higher than that among patients without hemodialysis (Fig. 1B). Hemodialysis patients who died suddenly were more likely to have ischemic etiology than those without sudden death, but the difference was not statistically significant (71.4% vs 45.8%; $P = 0.196$). Patients with hemodialysis had a significantly greater risk of all-cause death and sudden death than those without hemodialysis after hospitalization (32.9% vs 24.3% and 8.9% vs 2.8%) (Fig. 1C, D). In age and sex adjusted Cox proportional hazards models, hemodialysis on admission were associated with higher risks of all-cause death (hazard ratio 1.78, 95% confidence interval 1.21–2.63; $P = 0.004$) and sudden death (hazard ratio 3.85, 95% confidence

☆ These authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

* Corresponding author: Department of Cardiology, Tokyo Women's Medical University, 8-1 Kawada-cho, Shinjuku-ku, Tokyo 162-8666, Japan.
E-mail address: yuichiro24@celery.ocn.ne.jp (Y. Minami).

http://dx.doi.org/10.1016/j.ijcard.2016.09.038

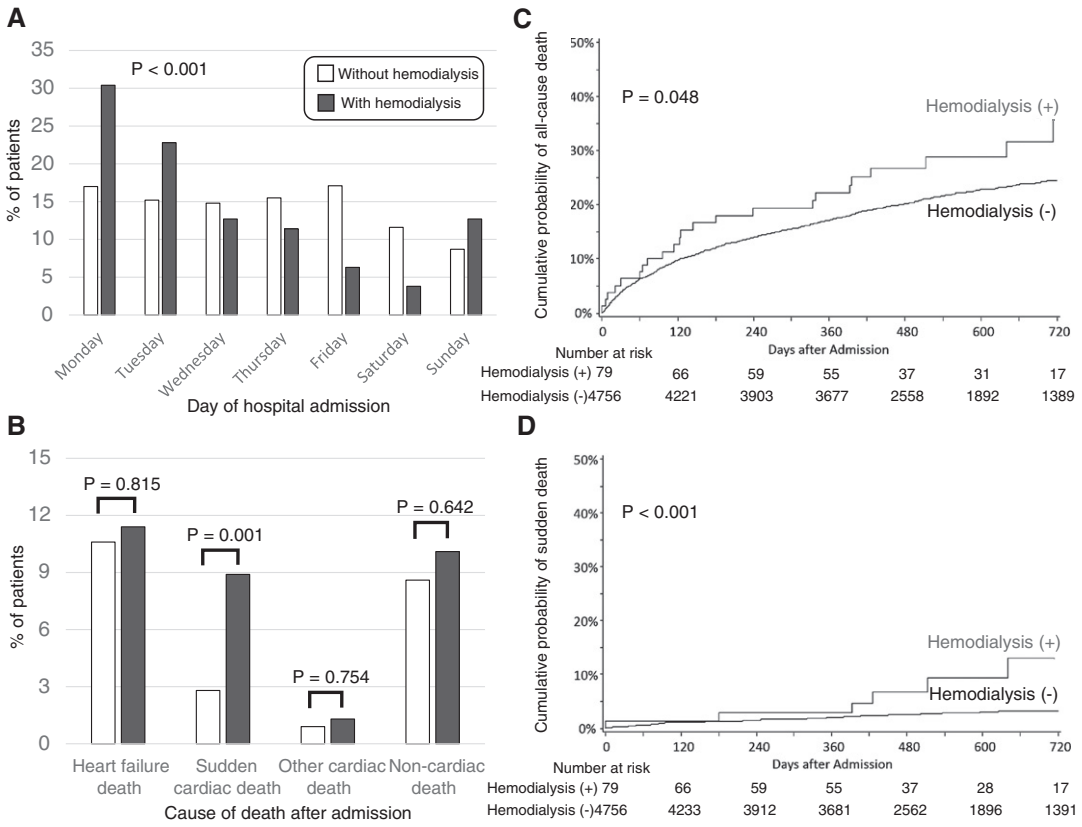

Fig. 1. (A) Distribution of hospitalizations for AHF by day of the week of admission, according to whether the patients underwent chronic maintenance hemodialysis to treat ESRD (with hemodialysis, shaded bars) or not (without hemodialysis, open bars). (B) Comparison of cause of death during the follow-up period in patients hospitalized for AHF, according to whether the patients underwent chronic maintenance hemodialysis to treat ESRD (with hemodialysis, shaded bars) or not (without hemodialysis, open bars). Kaplan–Meier survival curves for cumulative (C) all-cause death and (D) sudden cardiac death after hospitalization for AHF in patients with chronic maintenance hemodialysis versus those without chronic maintenance hemodialysis. AHF, acute heart failure; ESRD, end-stage renal disease.

interval 1.80–8.25; $P < 0.001$). One-fourth of hemodialysis patients needed continuous hemodiafiltration during AHF hospitalization, and hemodialysis patients who underwent continuous hemodiafiltration had a significantly greater risk of death than those without continuous hemodiafiltration (52.6% vs 26.7%; $P = 0.036$).

Interestingly, more than half of the study AHF patients on hemodialysis for ESRD were admitted at the beginning of the week. Hemodialysis is typically performed on Mondays, Wednesdays, and Fridays or Tuesdays, Thursdays, and Saturdays for the vast majority of patients on chronic maintenance hemodialysis [4]. This timing results in two 48-h and one 72-h interval (weekend interval) between the start of hemodialysis treatments. Increasing volume overload and worsening hypertension occur before hemodialysis, especially at the end of the weekend interval, and both volume overload and hypertension might be associated with an increased incidence of AHF episodes.

In this study, patients on hemodialysis were more likely to have ischemic etiology and were treated more often with coronary revascularization therapy than non-hemodialysis patients. The risk of coronary artery disease (CAD) in ESRD patients on hemodialysis appears to be far greater than in the general population [5]. The excess risk of CAD in hemodialysis patients is caused, in part, by a higher prevalence of conditions that are recognized as conventional risk factors for CAD [5]. Other potential CAD risk factors also operate in the context of hemodialysis, including endothelial dysfunction, oxidant stress, vascular calcifications, and inflammation [5].

In this analysis, the probability of sudden death among patients with hemodialysis was significantly higher than that among those without hemodialysis. Sudden death was the major cause of death, accounting for about one-quarter of all-cause death among AHF patients with hemodialysis, a result almost identical to that of a previous report from the United States Renal Data System cohort [2,6]. The high rate of sudden death in hemodialysis patients may be related not only to the high prevalence of underlying cardiac disease such as CAD but also to the stress of the hemodialysis procedure itself, such as rapid electrolyte shifts, QT dispersion, volume overload during the interdialytic period, increased sympathetic tone, calcium phosphate deposition, inflammation, and iron toxicity [4,6]. Although data regarding the use and benefit of implantable cardioverter-defibrillators for hemodialysis patients are not satisfactory, this does not mean that hemodialysis patients will not benefit from defibrillators. Furthermore, randomized trials of the β-blocker and angiotensin-receptor blocker showed survival advantage in hemodialysis patients with heart failure [7]. Additional studies are required to determine whether dual-acting angiotensin-receptor-neprilysin inhibitor decreases mortality in heart failure patients receiving hemodialysis [8,9].

As our data were derived only from Japanese patients, the results may not reflect international patterns of AHF patients and/or ESRD patients on hemodialysis. Therefore, caution must be exercised when applying our findings to different ethnic cohorts of AHF patients [10]. Despite above limitation, our results revealed novel epidemiological information regarding hemodialysis patients in a relatively large AHF patient cohort.

Funding

The ATTEND study was supported by the Japan Heart Foundation, which had no role in the conduct of this study, but provided funding for statistical support and administration. This funding organization