International Medicine

https://www.theinternationalmedicine.com

Editorial

Some topics on cardiovascular events related to public health, statistic, and renal hemodynamics aspects

Hiroshi Bando[1,2], Yoshikane Kato[2]

[1]Medical Research/Tokushima University, Tokushima, Japan

[2]Kanaiso Hospital, Tokushima, Japan

Received:8 August 2020 / Accepted: 10 September 2020

Our clinical research group has managed many patients involved in diabetes, nephropathy, and dialysis [1,2]. Among them, we reported cases of diabetes, chronic kidney disease (CKD), and hemodialysis associated with various complications and medical problems [3]. Furthermore, we have shown current topics including diabetes, renal/ cardiovascular diseases, and recent effective medicines [4]. In this article, some topics on blood pressure and cardiovascular events (CVEs) would be described from following some perspectives. They are from the viewpoints of public health, statistic, CVEs, blood pressure, and renal/cardiovascular hemodynamics.

From a statistic point of view, the population of Japan is 120 million, of which about 20 million people seem to have diabetes and pre-diabetes together [5]. Among them, the proportion of people strongly suspected of having diabetes is 16.3% for men and 9.3% for women as a whole, depending on a different age. Next, the number of CKD patients in Japan is estimated to be about 13.3 million, which is 13% of the adult population. Among them, 340 thousand patients are on the dialysis treatment of hemodialysis (HD) and peritoneal dialysis (PD). In recent years, approximately 40 thousand patients started dialysis each year, and 33 thousand patients died each year.

There are summarized recent data from the Japanese Society of Dialysis Therapy and others [6-8]. Subjects were divided into two groups, where general people and patients with dialysis. Differences in the causes of death between them were compared. In the former general population, there are 1.34 million deaths per year, and the top five causes of death are as follows: 1) malignant tumor 27.9%, 2) heart disease 15.3%, 3) cerebrovascular disease 8.2%, 4) senility 7.6%, 5) pneumonia 7.2%. Among them, CVEs includes 2 and 3 (23.5%) [6-8].

On the other hand, the latter dialysis group has 33,000 deaths per year. The causes of death were 1) heart failure 23.5%, 2) infectious disease 21.3%, 3) malignant tumor 8.4%, 4) cerebrovascular disorder 6.0%, 5) uremia 5.7%, 6) myocardial infarction 3.6%. From these data, CVEs are 33.1% including 1,5,6. Thus, dialysis patients have many causes of CVEs death. However, the mortality rate of CVEs was 54.8% 30 years ago. Consequently, a remarkable decrease was observed with probable better medical management for CVEs for long years.

In the light of hypertension, two groups of the general population and patients with dialysis are compared. As to the former, there are about 43 million hypertensive people in Japan, which is equivalent to about 33% of people according to the Hypertension Treatment Guidelines 2019 [9]. It is expected that the number of hypertensive patients will continue to increase with the westernization of eating habits and the aging of the population.

Address for Correspondence: Hiroshi Bando, Medical Research/Tokushima University, Tokushima, Japan.
E-mail: pianomed@bronze.ocn.ne.jp

DOI: 10.5455/im.134433

In contrast, the latter has the general status of keeping water and sodium excessively stored in the blood vessels, and the sympathetic nerve is in rather stimulated status. Therefore, the prevalence of hypertension has been as high as 70-85%, and the CVEs have been also high. Hypervolemia increased sympathetic activity and hypertension are all independent risk factors for CVEs.

In dialysis patients, the correlation between systolic blood pressure and the hazard ratio of all deaths showed U-shaped [10]. On the other hand, the correlation between systolic blood pressure and the hazard ratio of stroke death was linear [11]. A 20 mmHg increase in systolic blood pressure resulted in a significantly higher hazard ratio for stroke death. Therefore, systolic blood pressure of less than 130 mmHg is recommended to reduce stroke death, which has been common in Japanese people.

Several antihypertensive targets have been proposed to reduce CVEs based on prospective trials. Three representative examples for BP guidelines are shown in the following: I) home BP is less than 120-130 mmHg by Agarwal et al.[12], II) BP before dialysis is less than 140/90 by Japan Dialysis Society [13], III) home blood pressure is less than 120-135/60-80 mmHg by Turner [14]. Among these, home blood pressure is more correlated with CVEs than blood pressure in dialysis facilities, then it is more rational to set home BP as the guideline of BP reduction target.

Myocardial infarction also differs between the two groups. Symptoms of myocardial infarction are typical and easily found in the former. On the other hand, it is atypical and difficult to detect in the latter dialysis patients. As a matter of fact, dialysis patients are limited to treating myocardial infarction. In other words, it is difficult to administer percutaneous coronary intervention (PCI) because an anticoagulant has been already used [15]. Furthermore, statins or warfarin have no effect on the preventive measure in the latter. Warfarin administration in dialysis patients has promoted arterial calcification [16]. Ablation of atrial fibrillation has characteristics such as life prognosis not improving in dialysis patients.

Generally, angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) would reduce the risk of CVEs and preserve renal function in CKD patients. A recent study [17] showed that I) both therapies can decrease the loss of residual renal function, mainly for patients with peritoneal dialysis (PD), II) both medicines do not reduce CVEs in dialysis patients, III) however, treatment with ARBs seems to reduce CVEs including heart failure. Among them, a meta-analysis of overall 1115 individuals for 4 RCTs revealed a relative risk RR of 0.67 and a 95% confidence interval of 0.47-0.93.

As to the prognosis of CKD, a community-based prospective cohort study was conducted for 15 years in Okinawa, Japan [18]). Subjects were 69,238 cases (mean 55.6±14.7 years; eGFR, 80.2±21.2 ml/min/1.73 m^2) and the endpoint was end-stage renal disease (ESRD). As a result, 15.8% had a low eGFR (less than 60 ml/min/ 1.73 m^2) and 36.1/100,000 person-years developed ESRD.

There was a nationwide prospective cohort study of CKD in Japan [19]. The protocol included 2400 subjects from 30 representative hospitals for 5 years. For the detail follow up the renal function, they used the international CKD Outcomes and Practice Patterns Study (CKDopps) and questionnaires for patients by nephrologist-practice surveys. It will become a possibly fundamental platform for the international comparison data for CKD.

In summary, this article showed recent clinical problems about renal and CVEs in patients with hemodialysis and CKD. Compared with three decades ago, the rate of CVEs decreased. For their improved prognosis, the reduction target of home BP would be lower. This report will be hopefully a reference for future clinical practice and research.

Conflict of interest

The authors declare no conflict of interest.

Funding

There was no funding received for this paper.

References

1. Kato Y, Bando H, Yamashita H, Yada S, Tokuhara S, Tokuhara H, et al. Seasonal changes in HbA1c values from young to elderly diabetic patients. J Diabetes Metab Disord Control 2019;6:89-92.
2. Kakutani H, Kato Y, Fujikawa T, Kawata T, Yamamoto M, et al. Carnitine for body composition in hemodialysis patients. Edel J Biomed Res Rev 2019;2:6-9.
3. Kato Y, Bando H, Yamashita H, Yada S, Tokuhara S, Tokuhara H, et al. Impressive clinical course of diabetic patient with various medical problems and remarkable improvement by insulin degludec and liraglutide (Xultophy). MOJ Clin Med Case Rep 2020;10:48-51.
4. Bando H. Recommended management of hypertensive patients with diabetes for renin-angiotensin system (RAS) inhibitors. Diab Res Open Access 2020;16;2:4-8.
5. Katakami N, Mita T, Takahara M, Hashigami K, Kawashima M, Shimomura I, et al. Rationale and design for the J-DISCOVER Study: DISCOVERing the treatment reality of type 2 diabetes in a real-world setting in Japan-A protocol. Diabetes Ther 2018;9:165-75.

6. Tsuruya K, Kanda E, Nomura T, Iseki K, Hirakata H. Postdialysis blood pressure is a better predictor of mortality than predialysis blood pressure in Japanese hemodialysis patients: the Japan Dialysis Outcomes and Practice Patterns Study. Hypertens Res 2020;43:791–7.
7. Nishiwaki H, Hasegawa T, Koiwa F, Hamano T, Masakane I. The association of the difference in hemoglobin levels before and after hemodialysis with the risk of 1-year mortality in patients undergoing hemodialysis. Results from a nationwide cohort study of the Japanese Renal Data Registry. PLoS ONE 2019;14:e0210533.
8. Wakasugi M, Narita I. Lifetime and age-conditional risk estimates of end-stage kidney disease requiring maintenance dialysis in Japan. Clin Exp Nephrol 2020;24:518–25.
9. Japanese Society of Hypertension (JSH). Hypertension Treatment Guidelines Development Committee: Hypertension Treatment Guidelines 2019. Life Science Publishing; 2019.
10. Bansal N, McCulloch CE, Lin F, Arnold A, Anderson A, Cuevas M, et al. Blood pressure and risk of cardiovascular events in patients on chronic hemodialysis: The CRIC Study (Chronic Renal Insufficiency Cohort). Hypertension 2017;70:435-43.
11. Inaba M, Karaboyas A, Akiba T, Akizawa T, Saito A, et al. Association of blood pressure with all-cause mortality and stroke in Japanese hemodialysis patients: the Japan Dialysis Outcomes and Practice Pattern Study. Hemodial Int 2014;18:607-15.
12. Sinha AD, Agarwal R. BP components in advanced CKD and the competing risks of death, ESRD, and cardiovascular events. Clin J Am Soc Nephrol 2015;10:911-3.
13. Iseki K. Control of hypertension and survival in haemodialysis patients. Nephrology 2015;20:49-54.
14. Turner JM, Peixoto AJ. Blood pressure targets for hemodialysis patients. Kidney Int 2017;92:816-23.
15. Numasawa Y, Inohara T, Ishii H, Yamaji K, Hirano K. An overview of percutaneous coronary intervention in dialysis patients: Insights from a Japanese nationwide registry. Catheter Cardiovasc Interv 2019;94:1-8.
16. Nigwekar SU, Kroshinsky D, Nazarian RM, Goverman J, Malhotra R, Jackson VA, et al. Calciphylaxis: risk factors, diagnosis, and treatment. Am J Kidney Dis 2015;66:133-46.
17. Liu Y, Ma X, Zheng J, Jia J, Yan T. Effects of angiotensin-converting enzyme inhibitors and angiotensin receptor blockers on cardiovascular events and residual renal function in dialysis patients: a meta-analysis of randomised controlled trials. BMC Nephrol 2017;18:206.
18. Kanda E, Usui T, Kashihara N, Iseki C, Iseki K, Nangaku M. Importance of glomerular filtration rate change as surrogate endpoint for the future incidence of end-stage renal disease in general Japanese population: community-based cohort study. Clin Exp Nephrol 2017;22:318–27.
19. Hoshino J, Nagai K, Kai H, Saito C, Ito Y, Asahi K, Yamagata K. A nationwide prospective cohort study of patients with advanced chronic kidney disease in Japan: The Reach-J CKD cohort study. Clin Exp Nephrol 2018;22:309–17.