What Is the Appropriate Strategy for Coronary Revascularization in Hemodialysis Patient in Japan?

Shigemasa Tani, MD; Ken Nagao, MD; Atsushi Hirayama, MD

No large-scale randomized studies have been conducted yet to verify the efficacy of invasive coronary revascularization (percutaneous coronary intervention [PCI] vs. coronary artery bypass grafting [CABG]) in hemodialysis (HD) patients with coronary artery disease (CAD). This may be primarily attributable to impairment of the activities of daily living (ADL) and poor general condition of HD patients seen frequently as a result of cerebro-/cardiovascular disease, dysdialysis syndrome, and/or malnutrition, as well as the mental, psychological, familial and social problems of these patients. It is unclear whether evidence from retrospective studies carried out in Europe and the United States to examine the relative superiority of coronary revascularization procedures in HD patients would be applicable to Japanese patients or not, because there are obvious differences between Western countries and Japan in the percentages of cases treated by these procedures, in the medical care systems, including the hemodialysis therapy system, the morbidity rate of CAD, etc.

Article p 986

In this issue of the Journal, Kumada and colleagues report on a comparative study, although it was retrospective, to assess the 10-year long-term prognostic outcomes, based on propensity scores calculated from the therapeutic responses, to coronary revascularization procedures in a large series of maintenance HD patients (997 cases),¹ as the first step toward resolution of this problem.

Characteristic Features of CAD in HD Patients

Coronary artery lesions are reported to be detectable in approximately 40% of HD patients; intricate involvement of calcium and phosphorus metabolism and particular body fluid factors, as well as the usual progression process are implicated in the progression of arteriosclerosis in patients on maintenance HD. Complicated atherosclerotic lesions with pronounced arterial calcification are common in HD patients (Figure 1). The prognosis in HD patients with concurrent CAD is unfavorable inasmuch as complex multivessel coronary artery lesions, cerebrovascular disorders, arteriosclerosis obliterans, and HD being extracorporeal circulation per se, place a substantial burden on cardiac function in these patients. The patient population on HD has been steadily increasing from year to year, as shown in Figure 2, and in patients with diabetes mellitus, in particular,

Figure 1. The patient, a 53-year-old man with a 5-year history of being under maintenance hemodialysis therapy, had coronary artery disease with concurrent arteriosclerosis obliterans of the lower limbs. Marked calcification of the arteries of the lower extremities can be seen on plain computed tomography images.

which is the most frequent underlying disorder in patients started on hemodialysis therapy, the prognosis of CAD is especially poor.² The number of patients with diabetes mellitus has been continuously increasing and this trend is serious, not only in the field of cardiovascular medicine but in other related fields as well.

The opinions expressed in this article are not necessarily those of the editors or of the Japanese Circulation Society.

Received February 2, 2014; accepted February 3, 2014; released online February 21, 2014

Department of Cardiology, Surugadai Nihon University Hospital (S.T., K.N.); Division of Cardiology, Department of Medicine, Nihon University School of Medicine (S.T., K.N., A.H.), Tokyo, Japan

Mailing address: Shigemasa Tani, MD, Department of Cardiology, Surugadai Nihon University Hospital, 1-8-13 Kanda-Surugadai, Chiyoda-ku, Tokyo 101-8309, Japan. E-mail: tanishigem@yahoo.co.jp

ISSN-1346-9843 doi:10.1253/circj.CJ-14-0128

All rights are reserved to the Japanese Circulation Society. For permissions, please e-mail: cj@j-circ.or.jp

Figure 2. (Upper) Clinical progress chart of the chronic dialysis patient. (Lower) Annual changes in the percentages of major primary diseases in patients started on hemodialysis therapy. RPGN, rapidly progressive glomerulonephritis; SLE, systemic lupus erythematosus. The Japanese Society for Dialysis Therapy (JSDT). Modified from the JSDT Statistical Survey Committee: Illustration - Present Status of Chronic Dialysis Therapy in Japan as of December 31, 2012.

Currently Available Evidence From Europe and the United States Regarding Coronary Revascularization in HD Patients

Many reports have indicated that the therapeutic outcomes of CABG, which effects complete revascularization and protects the left anterior descending vessel, is more gratifying than PCI in terms of the prognosis following coronary revascularization procedures in HD patients.^{2,3} Most of these reports, however, are derived from studies conducted in small numbers of patients at single centers, so that the evidence level is low. A meta-analysis by Nevis and colleagues has shown that the mortality rate within 30 days after intervention was significantly higher in patients treated by CABG as compared with that for patients treated by PCI, although there was no significant difference in the long-term mortality rate.⁴ However, it is stated in that paper that the results of the meta-analysis are lacking in ubiquity, because there were few applicable studies that could be included in

the meta-analysis.

In recent years, however, Chang et al⁵ have comparatively assessed the pertinent data of 14,098 patients with multivessel coronary artery lesions, corrected using the propensity score, out of 21,981 registered cases of dialysis patients in the United States Renal Data System database, who underwent PCI or CABG (median follow-up duration: CABG, 1.9 years; and PCI, 1.4 years). The mortality rate (hazard ratio [HR] = 0.87, 95% confidence interval [CI] = 0.84–0.90) and overall mortality/myocardial infarction rate (HR = 0.88, 95% CI = 0.86–0.91) during follow-up were lower, with a more favorable long-term prognosis, in the CABG group as compared with the PCI group. Consistent with the report by Nevis et al, the results showed a significantly higher mortality rate in the CABG group within 6 months of coronary revascularization (HR = 1.08, 95% CI = 1.01–1.16).⁵

Now Is the Time to Reconsider the HD Patient Selection Criteria for Coronary Revascularization in Japan

Kumada et al demonstrate that the long-term prognostic outcome of patients treated by CABG was more favorable than that of patients treated by PCI, this trend being more conspicuous in patients with multivessel lesions. This is consistent with the evidence published from Europe and the United States; that is, the reported superiority of CABG over PCI in terms of the incidence of cardiovascular events, such as the need for coronary re-revascularization over the long term, although the complication rates in the intraoperative and immediate postoperative periods were higher in the CABG group. It is noteworthy, however, that although the percentage of patients requiring coronary re-revascularization was higher among the patients treated by PCI with drug-eluting stents (DES) than among the patients treated by CABG, there was no significant difference in the occurrence of major adverse cardiac events (MACE) between the 2 groups. This reflects a reduction in the incidence of restenosis as a result of DES placement, because the propensity-adjusted HR for revascularization increased from 0.25 to 0.38. It is thus suggested that the therapeutic outcome of PCI is approximately equal to that of CABG with increasing accumulation of cases with DES placement, especially new-generation DES,⁶ among the patients enrolled in this study, necessitating revision of the HD patient selection criteria for coronary revascularization.

Although the analysis using the propensity score in the present study might not completely exclude baseline bias of the 2 treatment modalities assessed, the results are expected to create a stir over the selection of coronary revascularization procedures for the management of CAD in HD patients at the present time, when no large-scale randomized prospective studies have yet been carried out. The authors earnestly hope that a large-scale randomized prospective study will be conducted soon, and that a guideline will be established by the concerned scientific society for diagnosis and treatment based on the registry concern-

ing coronary revascularization in HD patients.

However, it should also be borne in mind that treatment suited to individual patients be selected without adhering too strictly to evidence inasmuch as the conditions may vary among patients in the clinical practice setting.

Acknowledgments

We are greatly indebted to Dr Hirofumi Kawamata, Chief of the Hemodialysis Division of our Institution, for providing [Figure 1](#).

Disclosures

Conflict of interest: none.

References

1. Kumada Y, Ishii H, Aoyama T, Kamoi D, Kawamura Y, Sakakibara T, et al. Long-term clinical outcome after surgical or percutaneous coronary revascularization in hemodialysis patients. *Circ J* 2014; **78**: 986–992.
2. Herzog CA, Ma JZ, Collins AJ. Comparative survival of dialysis patients in the United States after coronary angioplasty, coronary artery stenting, and coronary artery bypass surgery and impact of diabetes. *Circulation* 2002; **106**: 2207–2211.
3. Hemmelgarn BR, Southern D, Culleton BF, Mitchell LB, Knudtson ML, Ghali WA; Alberta provincial project for outcomes assessment in coronary heart disease (APPROACH) investigators. Survival after coronary revascularization among patients with kidney disease. *Circulation* 2004; **110**: 1890–1895.
4. Nevis IF, Mathew A, Novick RJ, Parikh CR, Devereaux PJ, Natarajan MK, et al. Optimal method of coronary revascularization in patients receiving dialysis: Systematic review. *Clin J Am Soc Nephrol* 2009; **4**: 369–378.
5. Chang TI, Shilane D, Kazi DS, Montez-Rath ME, Hlatky MA, Winkelmayer WC. Multivessel coronary artery bypass grafting versus percutaneous coronary intervention in ESRD. *J Am Soc Nephrol* 2012; **23**: 2042–2049.
6. Sakakibara T, Ishii H, Toriyama T, Aoyama T, Takahashi H, Kamoi D, et al. Sirolimus-eluting stent vs. everolimus-eluting stent for coronary intervention in patients on chronic hemodialysis. *Circ J* 2012; **76**: 351–355.