In the middle of the last century, Lev and Unger and Lenègre enthusiastically carried out microscopic examination of the cardiac conduction system of autopsy cases showing bundle branch block and complete atrioventricular block as a standpoint of electrocardiographic vs. pathologic correlation. They commonly demonstrated pathological abnormalities in the conduction system, showing fibrous deposition in patients who developed cardiac conduction disturbances. These pathologists were certainly pioneers who postulated the concept of progressive cardiac conduction disease (PCCD) prior to the molecular genomic era. Thereafter, thanks to the marked advances in genetic research, PCCD was unveiled as an inherited cardiac conduction disorder caused by a high degree of genetic heterogeneity, which includes the mutation of genes encoding cardiac ion channels responsible for electrical conduction or associated cytoskeletal proteins.\textsuperscript{3-5}

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In this issue of the Journal, Kawaguchi et al expand the concept of PCCD, and enrolled 458 patients with PCCD characterized by temporal increases in the PR interval and QRS duration from numerous hospital-based populations.\textsuperscript{6} The incidence of PCCD according to their definition is 0.4% (458/114,334). It is noteworthy that approximately one-quarter of enrolled patients were hospitalized because of heart failure during a mean follow-up period of 13.3±6.4 years. Moreover, they demonstrated that temporal incremental rates of the PR interval and QRS duration are associated with not only heart-failure-related hospitalization, but also cardiovascular mortality.

Acute-onset advanced conduction block is associated with serious complications such as syncope and sudden cardiac death. Using their hospital-based cohort, Kawaguchi et al focus on the late-onset and slowly progressive supra- and intraventricular conduction disorder. This type of electrical disease does not usually show syncope and sudden cardiac death. On the contrary, most of the affected patients show a progressive decline in left ventricular (LV) contractile function according to the QRS widening and subsequent loss of synchronous LV wall motion. Both the PR interval and QRS duration are strictly dependent on the basal heart rate.\textsuperscript{7,8} In the study by Kawaguchi et al, the heart rate on follow-up ECG (66.1±13.1 beats/min) was significantly slower than that of the baseline ECG (68.6±14.1 beats/min); that is, the average RR interval prolongation in the long-term follow-up period was 33.1 ms. On the other hand, PR lengthening during this follow-up period was 13.9±20.2 ms, whereas QRS widening in the same period was 24.0±22.5 ms. It seems unlikely that a reduced heart rate induced natural prolongations of the PR and QRS intervals in the enrolled patients with PCCD, because temporal increases in the PR and QRS intervals are greater in patients with heart-failure-related hospitalization than in these intervals in patients without such hospitalization. This implies that the intrinsic pathologic effect is contained in patients showing PR lengthening and QRS widening to an extent greater than the unknown tolerance level. Moreover, a clear increase in right bundle branch block, a marginal increase of left bundle branch block, and second- or third-degree atrioventricular block were observed in the enrolled patients with PCCD during this follow-up period.\textsuperscript{6} Taken together, these findings suggest that progressive electrical disorder affecting the His bundle and bundle branch conduction system leads to heart failure requiring hospitalization.

However, the study by Kawaguchi et al contains several limitations, as they mention in their report. First of all, this study is a retrospective, single-center study. Second, they assessed the prognostic significance of increments in the PR interval and QRS duration independently. Readers’ interest must lie in whether the mutual conduction delays are additive or synergistic. Finally, gene analysis is desired for risk stratification of PCCD in their cohort.

Besides the concept of specialized cardiac conduction system disorder as an inherited electrical disease, it is evident in modern electrocardiology that such a simple ECG measure as the QRS interval has a marked clinical effect on an adverse prognosis in a variety of cardiac patients with heart failure, cardiac device implantation, and so on.\textsuperscript{9-12} When we consider such prognostic implications, strict identification of the onset and termination of the QRS complex is essential in digitally processed ECG. Recently, ECG became retrievable in a computer-assisted database, and serial measurements of stored ECG are feasible in the central ECG laboratory. The present investigation by Kawaguchi et al is naïve but important, and this type of ECG study benefits from such electrocardiographic sophistication. Finally, another more important issue relating to this study is cardiac resynchronization therapy (CRT). Although controversy exists, the indication of CRT implantation relies mostly on the QRS interval and subsequent LV mechanical dyssynchrony.\textsuperscript{13,14} State-of-the-art CRT adapts to the individual patient’s native heart rhythm and intrinsic conduction
system by dynamic controls of atrioventricular and biventricular delays without echocardiographic optimization under the best minimization of inappropriate right ventricular pacing.15 The study by Kawaguchi et al may contribute to adaptive CRT algorithm updating.

**Disclosure**

No author has a real or perceived conflict of interest.

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