Coronary angioplasty was first introduced in 1977 by Andreas Roland Grüntzig and since then various devices for percutaneous coronary intervention (PCI) have been developed over many years. After the procedure of PCI shifted from balloon dilation to stent implantation, stents themselves gradually developed from bare metal (BMS) to drug-eluting (DES). To date, dozens of stents have come onto the market and disappeared, the sirolimus-eluting stent (SES) being one with the most conspicuous and memorable existence. At the time of its initial appearance, because of a very low target lesion revascularization ratio, it was welcomed and utilized by all catheter interventionists as the perfect stent. The SES was characterized by its overwhelming reduction of late loss by sirolimus, which suppresses the proliferation of vascular endothelial cells, and the strong radial force applied by a relatively rigid stent platform. It was a report of stent thrombosis (ST) after SES implantation, which was a fatal complication, that shadowed its majesty. The number of reports gradually increased and finally SES became a synonym of very late ST (VLST).

A variety of mechanisms have been proposed as the cause of VLST, such as insufficient endothelialization, stent fracture, off-label use and neoatherosclerosis and so on.

Nakazawa et al reported that insufficient endothelialization of stent struts was a cause of ST based on autopsy cases of 1st-generation DES including SES and the paclitaxel-eluting stent, and they also found less endothelialization of stent struts of 1st-generation DES compared with BMS. There is also a report that hypersensitivity to the polymer is more noticeable in SES lesions than with other types of stent.

Furthermore, angiographic evidence of exudation of the contrast agent surrounding the stent (peri-stent contrast staining: PSS) was observed especially after SES deployment and considered as one of the causes of ST.

Another major concern of SES was impairment of the endothelial function of the coronary arteries. Fuke et al showed that abnormal endothelial reaction to intracoronary acetylcholine infusion was significantly greater after implantation of SES compared with BMS and they suggested that SES deployment causes coronary endothelial dysfunction (Figures 1, 2).

As Beltrame et al have stated that the primary pathophysiology of coronary artery spasm is vascular smooth muscle cell hyper-reactivity, SES-induced coronary endothelial...
dysfunction could be responsible for vasospastic angina (VSA).

In this issue of the Journal, Hata et al. report that the different types of stents could have different clinical effects on late-term prognosis in patients with VSA. They classified 304 patients undergoing stent implantation for organic stenosis according to stent type (BMS, SES and newer DES) and clinical entity (VSA and non-VSA). In their results, the 2-year cumulative incidence of the primary outcome was significantly higher in the VSA group than in the non-VSA group after SES implantation; on the other hand, there were no differences between the groups after either BMS or newer-DES implantation. This result is in agreement with a previously reported study that suggested SES implantation causes abnormal coronary endothelial function. In other words, it indicates that 1 or more of the components of SES, which is sirolimus, the stent polymer, and stent platform, may contribute to unnatural spasm of the coronary artery. There was also a significant difference between the VSA and non-VSA groups only in the SES group, in accordance with the %diameter stenosis in the chronic phase. This phenomenon also seems to be related to substances not in the newer DES but in the SES (i.e., the drug itself, polymer etc.).

Although not directly the purpose of this study, it is still noteworthy that the %diameter stenosis in the chronic phase in the BMS group improved, especially in the non-VSA group. This phenomenon was not observed even in the newer-DES group and may suggest the existence of something that interferes with late lumen gain even in the latest DES. In any case, it is notable that SES has some undesirable effects in VSA patients, although the cause of the reaction in stented lesions is still unclear.

Currently, more than 20 years have passed and the SES is no longer used, but the risk of developing unfavorable events in the chronic phase will remain forever. We clinicians, who are not passive observers but parties concerned, have an obligation to keep watching carefully this negative history. Last year 2017, was the milestone of 40 years since Andreas Grüntzig started coronary intervention. It was probably difficult for Dr. Grüntzig to foresee this unexpected turn of events. In order not to repeat this negative legacy of SES, it is reasonable to examine all new devices and therapeutic guidelines objectively and fairly.

Turning to the topic of this report, there are some points to be considered. First, the SES was compared with other newer DES, but it is somewhat illogical to segregate only SES from other DES, because even among newer DES there are several differences in the drug, polymer composition, stent platform and so on. Second, there was a lack of detail about the PCI procedure, such as the location of the lesion, stent length or stent diameter and stent inflation pressure, especially during SES implantation. Furthermore, the technology of PCI has been continually changing and so there are some points that have to be considered other than differences in the stent itself over the long observation period. Nonetheless, this research on SES implantation in VSA patients should be respected, and certainly contains valuable data for the future development of coronary intervention.

References