Progress in Percutaneous Coronary Intervention—Prevention of restenosis using IVUS—

Masato NAKAMURA

Assistant Professor, The Third Department of Internal Medicine,
Toho University School of Medicine

Abstract: Intravascular ultrasound (IVUS) appeared at the same time as the induction of new technology in the field of coronary intervention, and both have supplemented each other in their development. IVUS, which can directly observe a cross section of the coronary artery, has contributed to the elucidation of the dilatation mechanism and restenosis mechanism related to the device, and the findings obtained have been reflected in new clinical techniques. In a comparison with the coronary angiography guide, it was found that a large lumen can be secured with a big balloon with the IVUS guide without increasing the risk of complications. The observation of the luminal area makes provisional stenting possible. In this regard, a technique called “spot stenting,” involving the insertion of a stent to an insufficiently dilated site, has been devised. Though there is no special definition of optimal stenting, “bigger is better” when it comes to the stent area measurement, which is useful for the prevention of restenosis. It is essential for the DCA technique to grasp the volume and direction of the atheroma. The technique involving ablation of the plaque with the use of the IVUS guide to find its direction as accurately as possible is now a standard DCA technique. In view of the correlation of residual plaque to intimal proliferation, a debulking stent has been developed for insertion of a stent after ablation of the atheroma. As to the eluting stent that has recently been attracting attention, good apposition to the vessel wall is essential for the stent to demonstrate its effect. In this regard, the role played by IVUS is expected to become more important.

Key words: IVUS; Percutaneous coronary intervention; Restenosis

This article is a revised English version of a paper originally published in the Journal of the Japan Medical Association (Vol. 128, No. 1, 2002, pages 33–37).
Introduction

Observation of coronary arteries was made possible in 1988 with intravascular ultrasound (IVUS). This was about ten years after the introduction of percutaneous coronary intervention (PCI), a time that corresponds with the appearance of the new devices in the field of interventional cardiology. The elucidation of dilatation form and the restenosis mechanism is essential for the development of PCI. IVUS, which allows direct observation of vascular short axis images, is ideal for this purpose. In fact, feedback from the findings obtained by IVUS was used in developing the technique and indications of PCI. PCI, and IVUS have supplemented each other in their development. The accumulation of findings related to restenosis in particular has had a great impact on the PCI technique.

Current use of IVUS in PCI

While the coronary angiography is a method to capture the silhouette of the vascular lumen, IVUS directly observes the vascular cross section. With IVUS, quantitative evaluation including the vessel size, the amount and local presence of the plaque, and the luminal size as well as qualitative evaluation including the plaque characteristics is possible. The information obtained is used for such reasons as to select a device, to determine the size and length of device, to grasp the direction of ablation and to determine the endpoint.

Mechanism of restenosis

The long-term outcomes achieved by PCI are determined by net gain (subtracting late loss from acute gain). This late stage lumen loss corresponds to the mechanism of restenosis. The loss has been considered to be attributable to the proliferation of neointima. However, investigations using IVUS clarified that the reduction of coronary vessel size (negative remodeling) is a big factor causing the late stage lumen loss (Fig. 1). The stent is a device that can prevent this negative remodeling and consequently prevent restenosis.

1. Bigger is better

As described above, the restenosis is determined by net gain. Accordingly, it is important to obtain a bigger acute gain in the initial stage. This concept, expressed as “bigger is better,” is commonly applied to all devices. In fact, the follow-up results after stent treatment correlates to the stent area observed by IVUS (Fig. 2). The final stent area and diameter are also used as factors to predict restenosis in multivariate analysis. On the other hand, neointimal...
IVUS guided balloon dilatation

As observation by IVUS can accurately assess vessel size, an appropriate balloon size can be selected, thereby improving the long-term outcomes. The CLOUT pilot trial investigated the effect of balloon dilatation using the IVUS guide. According to the results, the observation by IVUS disclosed that a larger balloon was necessary in 73% of the lesions even though optimal results were indicated by the coronary angiography. After the size upgrade, the residual stenosis improved from $28 \pm 15\%$ to $18 \pm 14\%$ and the minimum lumen area was increased from $3.16 \pm 1.04 \text{mm}^2$ to $4.52 \pm 1.14 \text{mm}^2$.5)

2. Stent

Though the stent plays a central role in PCI, it cannot completely solve the problem of restenosis. Rather, treatment against stent restenosis is causing a new clinical problem. Various stenting techniques have been investigated to prevent restenosis.

(1) Provisional stenting, spot stenting

The strategy to additionally insert a stent only when the results of balloon dilatation is suboptimal is called “provisional stenting”. The IVUS guide is used in this strategy in order to select the optimal balloon size and to check for suboptimal angiographic results. The revascularization rate in provisional stenting using the IVUS guide was favorable at 8% and was reported to reduce the need for stent insertion by half. According to SIPS, provisional stenting using the IVUS guide contributed better to long-term outcomes in comparison with the coronary angiography guide.6)

Spot stenting is an extrapolation of provisional stenting. Columbo et al. proposed the usefulness of a therapeutic technique to treat diffuse lesions using the IVUS guide and to conduct spot stenting in insufficiently dilatated sites.7)

(2) Optimal stenting using the IVUS guide

The concept of optimal stenting was generated to prevent thrombotic occlusion of the stent. However, favorable stent expansion, attributable to high pressure, and administration of a strong anti-platelet drug have solved this problem. Accordingly, the investigation is focused on optimal stenting from the viewpoint of restenosis prevention.

However, there is no definite criteria for the

proliferation after stent deployment is unrelated to the stent size, indicating a limit to the efficacy of stent against small vessel disease.

2. Residual plaque volume and restenosis

A report by Mintz attracted attention to the residual plaque volume as a factor to predict restenosis.3) When the restenosis rate and residual plaque volume were investigated in the clinical studies CAVEAT, OARS, and ABACUS using DCA (directional coronary atherectomy), there was a correlation. Subsequently, Prati et al. reported that the degree of intimal proliferation in the stenting cases was also related to the amount of plaque outside the stent (Fig. 3).4) Accordingly, the PCI technique to reduce the residual plaque volume is considered to decrease the restenosis rate.

Current strategies for the prevention of restenosis

1. IVUS guided balloon dilatation

As observation by IVUS can accurately assess vessel size, an appropriate balloon size can be selected, thereby improving the long-term outcomes. The CLOUT pilot trial investigated the effect of balloon dilatation using the IVUS guide. According to the results, the observation by IVUS disclosed that a larger balloon was necessary in 73% of the lesions even though optimal results were indicated by the coronary angiography. After the size upgrade, the residual stenosis improved from $28 \pm 15\%$ to $18 \pm 14\%$ and the minimum lumen area was increased from $3.16 \pm 1.04 \text{mm}^2$ to $4.52 \pm 1.14 \text{mm}^2$.5)

2. Stent

Though the stent plays a central role in PCI, it cannot completely solve the problem of restenosis. Rather, treatment against stent restenosis is causing a new clinical problem. Various stenting techniques have been investigated to prevent restenosis.

(1) Provisional stenting, spot stenting

The strategy to additionally insert a stent only when the results of balloon dilatation is suboptimal is called “provisional stenting”. The IVUS guide is used in this strategy in order to select the optimal balloon size and to check for suboptimal angiographic results. The revascularization rate in provisional stenting using the IVUS guide was favorable at 8% and was reported to reduce the need for stent insertion by half. According to SIPS, provisional stenting using the IVUS guide contributed better to long-term outcomes in comparison with the coronary angiography guide.6)

Spot stenting is an extrapolation of provisional stenting. Columbo et al. proposed the usefulness of a therapeutic technique to treat diffuse lesions using the IVUS guide and to conduct spot stenting in insufficiently dilatated sites.7)

(2) Optimal stenting using the IVUS guide

The concept of optimal stenting was generated to prevent thrombotic occlusion of the stent. However, favorable stent expansion, attributable to high pressure, and administration of a strong anti-platelet drug have solved this problem. Accordingly, the investigation is focused on optimal stenting from the viewpoint of restenosis prevention.

However, there is no definite criteria for the
endpoint of IVUS in stent insertion. In this regard, no definite conclusion was obtained as to the usefulness of IVUS in restenosis prevention in multicenter comparative studies (CRUISE, OPTICUS, AVID) that compared the stent insertion using the coronary angiography guide with that using the IVUS guide.8,9) Accordingly, in the case of simple lesions indicated for a clinical study, the stent implantation to reduce the residual stenosis to 10% or less by high pressure stent expansion without the IVUS guide is expected to achieve a result comparable to that obtained by stent insertion using the IVUS guide.

On the other hand, the superiority of the IVUS guide was demonstrated in each clinical study involving various factors such as the minimum lumen diameter and residual stenosis. Accordingly, the stent insertion using the IVUS guide is considered valid against complicated lesions and high risk lesions.

It is noteworthy that about 30% of the cases did not clear the endpoint in OPTICUS.8) The result reflected that insufficient expansion of stent is a big factor in causing stent restenosis.

3. DCA

According to the results of clinical studies CAVEAT and CCAT of DCA conducted in the initial stage, there was no difference in the restenosis rate between the balloon dilatation cases and DCA cases. Rather than that, the increase in creatine kinase was observed more frequently in the cases treated with DCA.
However, the high restenosis rate in the DCA group in these studies was assumed to be attributable to a problem in the technique of DCA. As a result, the optimal DCA to reduce the residual plaque volume is now considered ideal. In fact, the BOAT study conducted to verify the therapeutic effect of DCA to more aggressively ablate the plaque indicated that the restenosis rate could be decreased by DCA.

At present, the technique to ablate plaque as much as possible while grasping the direction of plaque using the IVUS guide is accepted as a standard technique (Fig. 5).

**Conclusion**

Current IVUS usage is described above from the viewpoint of restenosis prevention. As to the eluting stent that has recently been attracting attention, good apposition to the vessel wall is essential for the stent to demonstrate its effect. In this regard, the role played by IVUS is expected to become more important.

**REFERENCES**

1) Moussa, I. et al.: Does the specific intravascular ultrasound criterion used to optimize stent expansion have an impact on the probability of stent restenosis? *Am J Cardiol* 1999; 83: 1012–1017.


