Coronary bifurcation model created using a novel directional heat injury catheter

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Objective: The present study aimed to develop a swine coronary bifurcation model.

Background: In human coronary bifurcation lesion, atherosclerotic plaques are usually observed in the lateral wall, whereas the flow divider regions are spared. There is currently no suitable coronary bifurcation animal model, on which a new stent can be tested.

Methods: We developed a novel directional heat injury catheter, which comprised of a non-compliant balloon catheter (diameter: 3.0 mm, length: 15 mm), and two electrode cables, that were attached to either side of the balloon catheter. The technique was performed on 4 healthy pigs, and assessed in 7 lesions. We inflated the balloon at the main bifurcation branch, following which a high frequency generator was used to transmit heat to the opposite side of the bifurcation (duration: 5 min, frequency: 2 times). We performed a post-angiography 28 days after the pre-angiography, to observe the distribution of neointima. The neointimal area was divided into the carina side and the opposite side of carina, and the 2 sides were compared.

Results: The neointimal area at the opposite side of the carina was significantly larger than the carina side (1.51 ± 0.40 mm² vs. 0.95 ± 0.27 mm², p < 0.0001). The percentage of area of stenosis on the opposite side of carina was also higher than that on the carina side (55.4 ± 7.0% vs. 34.9 ± 4.2%, p < 0.0001).

Conclusions: We successfully developed a novel swine coronary bifurcation model using directional heat injury catheter.

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1. Background

Coronary artery bifurcation lesions have several anatomical features. One of the main features is the localized plaque on the side opposite to the coronary bifurcation carina [1–3]. The non-homogeneous distribution of plaque often causes a carina shift and side branch narrowing following bifurcation stenting [4–6]. Therefore, specialized stents for bifurcation lesions, such as the Tryton Side Branch Stent, were recently introduced [7]. However, the Tryton Side Branch Stent failed to meet the non-inferiority endpoint compared to provisional stenting, in patients with non-left main true coronary bifurcation lesions. One of the challenges for development of new bifurcation stents is that, no suitable coronary bifurcation animal model is available for testing them. The purpose of our study was to develop a swine coronary bifurcation model, having stenosis distributions similar to those observed in humans, using a novel directional heat injury catheter.

2. Method

2.1. Heat injury catheter

The directional heat injury catheter used in this experiment was originally prepared from a non-compliant balloon catheter (diameter: 3.0 mm, length: 15 mm, Cyclone HP, Fukuda Denshi Co. Ltd., Tokyo, Japan), and 2 electrode cables (diameter: 0.3 mm), were attached to either side of the balloon catheter. We also attached radiopaque markers on each electrode cable, to enable identification under X-ray fluoroscopy. Following this, the electrode cables attached on the opposite side of the carina were connected to a high-frequency bipolar electrosurgical unit (KN-301-B, Natsume Co. Ltd., Tokyo, Japan). The design drawing and photograph of the heat injury catheter are shown in Fig. 1. Chicken meat was deployed to measure the temperature, to decide the optimal frequency (Fig. 2). The frequency was set at a temperature of 80 degrees.
Celsius for a period of 3 min as was done in a previous study [8,9]. We conducted the animal coronary artery experiments with this setting.

2.2. Animal experiment

The experiments were performed in 4 healthy mini pigs, with a body weight of 40 kg. Under general anesthesia, a 7-F sheath was inserted into the right femoral artery, and left coronary artery angiography was performed (Fig. 3A). If a suitable coronary bifurcation lesion, potentially likely to lead to development of stenosis, was observed, the balloon was inflated at the main bifurcation branch. Following this, heat was transmitted using the high frequency generator, to the opposite side electrode facing the bifurcation carina, guided by the marker attached to the balloon catheter (duration: 5 min, frequency: 2 times) (Fig. 3B). We performed a post-angiography 28 days after pre-angiography, to observe the distribution of neointima (Fig. 3C). Subsequently, intravascular ultrasound (IVUS) (Eagle Eye, Volcano, CA, USA) was also performed at a pullback speed of 1 mm/s (Fig. 4). The study protocol was approved by Kyoto University Animal Care and Use Committee and performed in accordance with the Guide for the Care and Use of Laboratory Animals.

2.3. IVUS analysis

We classified the neointimal area of the IVUS image as the carina side and the opposite side of the carina, and measured each area. The IVUS analyses were performed using Zaio Term 2009 (Ziosoft Inc., Tokyo, Japan) and Adobe Photoshop CS2 (Adobe systems Inc., CA, USA) (Fig. 4).

2.4. Histologic evaluation

One pig was euthanized 28 days after the initial procedure and the target coronary artery was perfusion-fixed with lactated Ringer’s solution, followed by 10% buffered formalin and placed in the same solution. The main branch of the target bifurcation lesion was cross-sectioned and stained with stained with hematoxylin and eosin (H&E).

2.5. Statistical analysis

All data are expressed as mean ± standard deviation. We compared the neointima areas of the carina side and the opposite side of the carina, using a paired-t test. A p-value < 0.05 was considered statistically significant.

3. Results

We conducted the analysis in 4 pigs with 7 bifurcation lesions. The degree of narrowing in the main branch was 53.7 ± 13.7% by quantitative coronary angiography and 45.0 ± 4.7% by IVUS 28 days after procedure. On distribution analysis, the neointimal area on the opposite side of the carina was significantly larger than that on the carina side (1.51 ± 0.40 mm² vs. 0.95 ± 0.27 mm², p < 0.0001). The percentage area of stenosis on the opposite side of the carina was also higher than that on the carina side (55.4 ± 7.0% vs. 34.9 ± 4.2%, p < 0.0001) (Fig. 5). Histological analysis showed that concentric neointimal formation was observed and the neointimal area on the opposite side of the carina was larger in the main branch (Fig. 6).

4. Discussion

We successfully developed a swine coronary bifurcation model using a directional novel heat injury catheter. The model localized the neointima on the opposite side of the carina. Our swine model is extremely similar to clinical bifurcation lesions.

Coronary bifurcation lesions are considered as complex and their treatment is still the subject of substantial debate. Several classification schemes have been proposed to characterize coronary bifurcation lesions. The Medina classification has been widely adopted because of its simplicity [10]. The Medina classification is made based on...
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