Optical coherence tomography imaging of denervated renal arteries

Wewnątrznaczyniowa optyczna tomografia koherentna w ocenie tętnic nerkowych poddanych przezskórnej denerwacji

**INTRODUCTION**

The catheter-based radiofrequency renal denervation (RF-RDN) is of a broad interest as a tool to treat patients with resistant hypertension. It is still under debate whether RF-RND application brings benefit to such patients. The initial enthusiasm derived from the

**Keywords**

optical coherence tomography, catheter-based renal denervation, renal arteries

**Słowa kluczowe**
optyczna tomografia koheretna, tętnice nerkowe, przeskórna denerwacja tętnic nerkowych

**Conflict of interest**

Konflikt interesów

None
Brak konfliktu interesów

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promising results of Simplicity HTN-1 and Simplicity HTN-2 trials was somewhat tempered by poor outcomes of Simplicity HTN-3 trial (1-3). However, main limitations of Simplicity HTN-3 study were a small number of procedures performed per operator and the lack of appropriate monitoring of RF energy application (3). Data from histology suggested that RF-RND might modify a vessel wall structure but such small edemas and fibrosis within the vessel wall might have been omitted by the relatively low-resolution angio-CT imaging (1, 2, 4). The detection of morphological markers of RF-RND application within the vessel wall in vivo could help to monitor the effectiveness of the procedure, but there was no imaging of renal arteries performed using novel imaging techniques post RND at follow-up.

Intravascular optical coherence tomography (OCT) is an imaging tool that provides high-resolution imaging (10-20 µm), which presents the morphology of the vessel wall with a very high precision (5, 6). It is broadly applied in the coronary imaging to assess the effects of stenting. In the present study we tested whether OCT may be feasible to assess renal artery healing after RF RND.

AIM

The aim of the study was to test whether OCT may be feasible to assess renal artery healing after RF RND.

MATERIAL AND METHODS

The study was performed at the Upper Silesian Medical Center of the Medical University of Silesia in Katowice. The Ethics Committee of the Medical University of Silesia approved the study. All of the patients gave written informed consent.

Inclusion criteria

Patients with resistant primary hypertension and more than 18 years old were enrolled into the study. Resistant hypertension was diagnosed in patients when office systolic blood pressure (SBP) was ≥ 160 mmHg (or ≥ 150 mmHg in patients with type 2 diabetes) lasted ≥ 5 weeks despite adherence to at least three antihypertensive drugs. Patients with renal insufficiency (glomerular filtration rate (GFR) < 45 ml/min/1.73 m² estimated by MDRD formula), significant renal artery stenosis and severe peripheral atherosclerosis leading to the loss of arterial access via femoral arteries were excluded from the study.

Renal denervation procedure

The renal denervation procedure was performed using Symplicity® system (Medtronic, Minneapolis, MN, USA). All patients received unfractionated heparin in doses to achieve activated clotting time (ACT) of > 300 s. Femoral artery closure devices were used in every patient.

OCT imaging

Intravascular OCT imaging of renal arteries was performed after the angiography using commercially available St. Jude iLumien OPTIS system at the follow-up only. Using 6F femoral access, the OCT Dragonfly Duo catheter was introduced into the renal artery through the guiding catheter, and over 0.014” coronary guidewire. The OCT probe (a mid marker at the OCT catheter) was positioned in the distal segment of the renal artery. The OCT imaging was intended to image the entire length of the renal artery. At the time of OCT imaging, the renal artery was flushed by the injection of 30 ml Ultravist contrast with a flow rate 8 ml/s and pressure of 700 psi. This triggered the automated OCT pullback with a speed of 20 mm/s.

OCT image analysis

The off-line analysis (St. Jude OPTIS LightLab off-line review station) was performed every 1 mm of the renal artery length to evaluate lumen area and the minimal and maximal diameter of the lumen at vessel cross-sections. Due to OCT imaging limitations, not every OCT cross-section was able to visualize the full circumference of the renal artery. Therefore, the area beyond imaging coverage was assessed and expressed as an angle (fig. 1). All OCT pullbacks were evaluated for presence of changes of renal artery morphology (calcifications, focal intimal thickening, thrombus, vasospasm, intimal tear and dissections). Also, the area of focal intimal thickening was measured and expressed in mm².

Statistical analysis

The Kolmogorov-Smirnov test was used to analyze the continuous data distribution. Normally distributed values were presented as mean with standard deviation. Non-normally distributed values were presented as median with 25th and 75th percentile (interquartile range – IQR). Paired t-test was used to compare normally distributed data, and the Wilcoxon test was used to compare non-normally distributed data. Chi-square test was used to compare categorical data. P < 0.05 was considered as statistically significant (MedCalc software, version 14.10)

RESULTS

The study group

Out of the 86 patients prescreened, 18 were ultimately treated with RDN. Among these 18 patients, 12 patients agreed to undergo renal angiography and OCT imaging at follow-up. Finally, OCT imaging analy-

![Fig. 1. Representative OCT image of a left renal artery. A) A cross-sectional OCT image of a left renal artery. B) Angiography of the left renal artery. The cylinder corresponds to OCT image](image-url)
sis was performed in 22 arteries at 18.41 ± 5.83 months after renal denervation. Two arteries were excluded from analysis because of poor imaging quality. The study group consisted of 8 females (66%) and 4 males with mean age of 61.66 ± 11.97 years. The mean body mass index was 29.77 ± 4.01, 3 patients (25%) had a prior PCI, 1 (8%) patient underwent CABG, 9 (92%) had hyperlipidemia, 6 (50%) suffered from diabetes mellitus 6 (50%), 2 (17%) were smokers. The mean LV ejection fraction was 59.2 ± 4.0%. The mean number of drugs per patient at follow-up was 4.50 ± 1.08; 11 (92%) used beta-blockers, 11 (92%) calcium channel blockers, 5 (42%) used ACE inhibitors, 8 (66%) used ARBs, and 11 (92%) – diuretics. Their mean creatinine concentration was 0.87 ± 0.24 mg/dl, and glomerular filtration rate was 79.33 ± 15.87 ml/min/1.73 m².

Clinical follow-up

The office systolic blood pressure decreased significantly from 195 ± 23 to 157 ± 6 mmHg (p < 0.001) and diastolic blood pressure from 104 ± 9 to 85 ± 4 mmHg (p < 0.001) at follow-up. There were two (17%) non-responders to RF-RND.

OCT analysis

The full cross-sectional image of renal arteries was successfully visualized in 487 mm (80%) of all analyzed pullbacks (from a total of 608 mm) (fig. 1). In segments where full cross-section of the artery was not presented (20%), 265 (IQR 243, 290) degrees of the arterial wall circumference was visible. The OCT analysis showed that 2 (9%) treated arteries contained calcifications. There were 26 areas of focal intimal thickening found in 11 (92%) patients and in 14 (64%) arteries. We identified a median of one (IQR 1, 2.5) area of focal intimal thickening per patient. These areas of focal intimal thickening were visualized in both arteries in 4 patients, and in one of the two treated renal arteries in the other 6 patients. The mean area of focal intimal thickening was 0.054 ± 0.033 mm². There were no vessel dissections, thrombi or intimal tears observed on the OCT analysis.

DISCUSSION

Our study showed that OCT imaging is a feasible method to present renal arteries healing post RF-RND at late follow-up. However due to technological limitation, a full perimeter of the vessel wall was not visible in 20% of total length of analyzed arteries. Nevertheless, OCT enabled to present vessel wall structure and small focal intimal thickenings, whose size was beyond the resolution of other available imaging modalities.

Pre-clinical histological findings at time of RDN have shown that this procedure causes endothelial denudation, internal elastic lamina disruption, edema of media, and coagulation of connective tissue in the adventitia (7). Although the endothelium heals ten days after intervention, intimal thickening and medial and adventitial fibrosis may persist at 6 months post procedure (4).

To accurately assess this healing process in humans, CTA and angiography may not be adequate but intravascular ultrasound (IVUS) seems to be an alternative (8). IVUS, due to high signal penetration, provides a comprehensive topography of the analyzed tissue and enables to present plaque burden within the analyzed vessel. Its properties were well explored in the coronary vessel imaging, but there still scant data about its application in renal artery imaging (9). One of the previous studies suggested that IVUS is feasible to detect lesions and calcifications within renal arteries and help to guide renal artery stenting (8, 10). Furthermore, IVUS was suggested to be effective to detect early transplant renal vasculopathy (11). However, the resolution of IVUS is 10 times lower than that of OCT (100-200 µm), and its grey-scale does not allow for a precise assessment of chemical composition of the analyzed tissue. It has high accuracy to detect calcification, but adequate recognition of soft plaques is still a challenge. The introduction of radiofrequency IVUS-based analysis (Virtual Histology IVUS) seemed to enhance the IVUS analysis by detecting necrotic core or fibrotic, calcium, and fibro-fatty tissue (12). However, the results of VH-IVUS analysis poorly correlated with the histological tissue characteristics (13). Recently, combined imaging using near-infrared spectroscopy and IVUS was employed in the intravascular imaging in vivo to enhance IVUS analysis (14). Although the detection of lipid is very accurate, the resolution of IVUS is still relatively low (15). The introduction of high resolution IVUS (50 um) might potentially improve ultrasound imaging of the vessels (16).

OCT imaging may be an alternative to IVUS. Previous OCT observations at the time of RDN have suggested that it easily detects thrombus, dissections, calcifications and intimal edema (17). Moreover, it enables a relatively precise analysis of tissue chemical composition. However, OCT has never been applied in the assessment of renal artery healing at follow-up. Studies looking at longer-term healing were performed only in animal experiments, or with CT or angiographic follow-up. Our data show that OCT can be successfully applied for the imaging of denervated renal arteries. Since OCT imaging permits to accurately evaluate vessel injury and vessel healing post RDN, it is possible that OCT could also be used to confirm appropriate RF-RDN treatment.

Study limitations

The lack of IVUS examination and its comparison with OCT results is the main limitation of our study, as it does not clarify which modality is best for renal artery assessment. The assessment of media and adventitial healing after renal denervation was not possible due to limited penetration of OCT imaging, and since the blood must be flushed out at the time of imaging, OCT did not allow for the assessment of renal artery ostia.
CONCLUSIONS

OCT is a feasible tool to assess vessel healing post intervention performed within the renal arteries, but in large renal arteries it does not permit to image the full circumference of vessel wall.

BIBLIOGRAPHY


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