



Case Report: Combination of Pressure Guidewire and Optical Coherence Tomography-Guided Drug-Coated Balloon Revascularization for Renal Artery Fibromuscular Dysplasia

Yuxi Li^{1,2,3†}, Xinyan Wen^{1,2,3†}, Bo Zheng^{1,2,3}, Ming Chen^{1,2,3}, Wei Ma^{1,2,3} and Jianping Li^{1,2,3*}

¹ Department of Cardiology, Peking University First Hospital, Beijing, China, ² Institute of Cardiovascular Disease, Peking University First Hospital, Beijing, China, ³ Hypertension Precision Diagnosis and Treatment Research Center, Peking University First Hospital, Beijing, China

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*Correspondence:

Jianping Li
lijianping03455@pkufh.com

†These authors have contributed
equally to this work

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Fibromuscular dysplasia (FMD) is the second common cause of renovascular hypertension. With the advent of endovascular therapy, angiography has become a diagnostic gold standard for FMD. Optical coherence tomography (OCT) by reflecting *in vivo* histology may improve diagnostic and classification accuracy. Renal fractional flow reserve (rFFR), measured by pressure guidewire, may distinguish the patients who may benefit from revascularization by identifying physiologically significant stenoses. However, the role of usage of both OCT and rFFR is not well-studied. We herein report a 17-year-old male with renovascular hypertension due to FMD. Angioplasty of drug-coated balloon (DCB) guided by OCT and FFR favorably achieved blood pressure (BP) control. In conclusion, the utility of both OCT and FFR may be useful for the appropriate selection of patients with renal FMD.

Keywords: fibromuscular dysplasia, pressure guidewire, optical coherence tomography, secondary hypertension, drug-coated balloon

INTRODUCTION

Fibromuscular dysplasia (FMD) is a non-atherosclerotic arterial disease, which is characterized by abnormal cellular proliferation and distorted architecture of the arterial wall (1). FMD most commonly affects the renal artery and is the second-most common etiology of renal artery stenosis (RAS) and renovascular hypertension, especially in young patients (2–4). Based on previous studies, the prevalence of FMD was underestimated and has been drawing attention recently.

The diagnosis and classification of renal FMD were mainly based on angiographic characteristics, among which the “string of beads” appearance was the most striking feature (5). However, FMD had been divided into several subtypes according to histopathological characteristics in early studies, which was no longer available since the advent of endovascular therapy (6). Optical coherence tomography (OCT), which can clearly visualize the medial thickening and wavy intimal lining of FMD, demonstrated to be a good tool for FMD diagnosis and evaluation based on the previous reports (7, 8). Furthermore, stenting is generally not indicated in renal FMD, while angioplasty or drug-coated balloon (DCB) revascularization requires precise evaluation and is guided by intravascular imaging such as OCT and intravascular ultrasound (IVUS).

On the other hand, the revascularization criteria of RAS remain debatable. Based on the latest consensus, the pressure gradient could provide further information to identify with hemodynamically significant stenosis, even though, which was validated on studies of atherosclerotic RAS (5). However, the most common methods to measure pressure gradient were based on catheters rather than by pressure guidewire, which was suitable for distal lesions and could provide much more accuracy and detailed information than catheter (9). We report a case of the combination of pressure guidewire and OCT-guided DCB treatment in a young hypertensive patient with renal FMD.

A 17-year-old male who presented with hypertension for 1 month was admitted to the cardiology department, whose ambulatory blood pressure (ABPM) showed an average blood pressure (BP) of 160/98 mm Hg despite anti-hypertensive therapy consisting of bisoprolol and nifedipine. A smoking history for 7 years was noticed. Physical examination was unremarkable, and abdominal bruit and peripheral edema were absent. ABPM showed elevated mean BP of 154/93 mmHg (daytime: 165/105 mmHg, nighttime: 135/72 mmHg). An ECG showed sinus rhythm with left ventricular hypertrophy, and echocardiography revealed a left ventricular ejection fraction (LVEF) of 71.6%. Laboratory examination revealed a normal result of a full blood cell count, renal, and liver function. Since the young age of the patient, without a family history or risk factors for hypertension, investigation for secondary hypertension was first considered. Initial workup noted elevated aldosterone level and plasma renin activity both beyond the upper limit of reference, which posed a strong suspicion of renovascular hypertension. The stenosis of the main branch of the right renal artery was finally revealed after repeated ultrasound examinations. CT angiography was also performed, which demonstrated the stenosis in the initial segment of the anterior segmental artery of the right kidney. Possible involvement of other vascular beds was ruled out with Doppler ultrasound and enhanced CT. The kidney ultrasound and urinalysis of the patient were normal. A radionuclide renal scintigraphy showed mild impairment of the function of the right kidney and normal function of the left kidney. Thyroid-stimulating hormone, the circadian rhythm of cortisol, level of serum catecholamines, and metanephrines were all normal, and other causes for secondary hypertension were ruled out. Autoimmunity screening was negative, which ruled out underlying vasculitis diseases. The lipid profile was normal with low-density lipoprotein cholesterol (LDL-C) of 2.25 mmol/L. Based on these findings, we tentatively diagnosed the patient with renovascular hypertension secondary to RAS, and FMD was highly suspected due to his young age, smoking history, and no further atherosclerosis evidence.

To confirm the diagnosis, renal angiography was performed (Figure 1). After insertion of a 6F guiding catheter through the femoral artery, selected angiography showed focal stenosis in the mid-segment of the right renal artery, accompanied by post-stenotic dilatation. A 0.014-inch pressure guidewire (Pressure Guidewire, MN, USA, Abbott), which was advanced across the lesion after equalization, was used to measure the pressure gradient. The value of rFFR (defined as the ratio of

mean arterial pressure distal to the stenosis (Pd) to the mean aortic pressure measured from the guiding catheter (Pa), as follows: $rFFR = Pd/Pa$) was 0.49, and the mean artery pressure gradient at resting was 40 mmHg before the revascularization. A significant increase of Pd was found after the pullback of the guidewire when across the lesions (Figure 2). OCT (C7 XR, MA, USA, Abbott) showed that the minimal lumen area of the renal artery was 1.92 mm² and the wavy endothelium of the right renal artery in longitudinal reconstruction and luminal stenosis due to intimal hyperplasia in cross-sectional imaging, which was compatible with pathognomonic for FMD (Figure 3). In view of difficult-to-control hypertension of short duration with the goal of a cure of hypertension, OCT-guided right renal artery angioplasty with DCB was performed, which resulted in good blood flow across the lesion and no residual trans-lesion pressure gradient (rFFR 0.93, pressure gradient 5 mmHg after revascularization). After the procedure, the BP of the patient decreased to 130–140/80–90 mm Hg with candesartan 4 mg one time a day and was normalized with candesartan 2 mg daily during the next 6 months of follow-up. A smoking cessation education was also provided for the patient.

DISCUSSION

To the best of our knowledge, this is the first published case combining the pressure guidewire and OCT to guide the endovascular therapy of DCB in renal FMD. FMD is the second common cause of renovascular hypertension, and balloon angioplasty is the revascularization approach of choice for renal artery FMD. With the advancement of intravascular imaging, it has been inaccessible to histological specimens and catheter-based angiography becomes the gold standard modality for the diagnosis of renal artery FMD nowadays (3). Several recently published cases showed that OCT can clearly visualize three layers of renal arteries. Therefore, the utility of OCT in confirming the diagnosis in the angiographically ambiguous lesions, properly classifying FMD, and guiding and optimizing the intervention has been reported (8, 10, 11).

Revascularization for the renal artery FMD is predicated on clinical indicators beyond the simple presence of FMD (3). However, several studies suggested that medial fibroplasia may progress with time (12). The pressure gradient is mandated to evaluate the degree of stenoses, which can predict the BP response after revascularization (13, 14). In addition, a pressure gradient of 10% mean pressure is proposed as a threshold to perform balloon angioplasty, based upon the study of atherosclerotic RAS (5). However, the pressure gradient is affected by multiple factors, such as systemic BP, the state of renal blood flow, and renal microvasculature. There is a lack of evidence from the study of FMD.

Fractional flow reserve is a lesion-specific indicator, which is recommended by guidelines to determine lesion significance and appropriateness for revascularization in coronary artery disease.

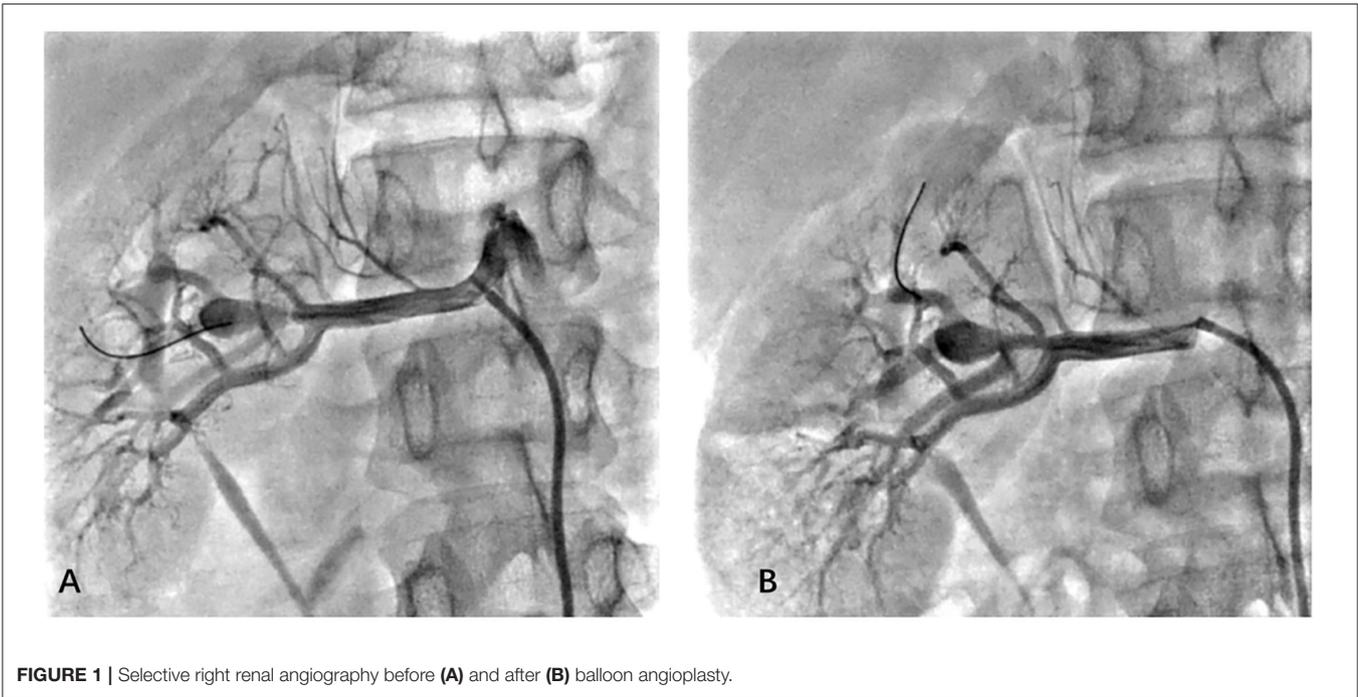


FIGURE 1 | Selective right renal angiography before (A) and after (B) balloon angioplasty.

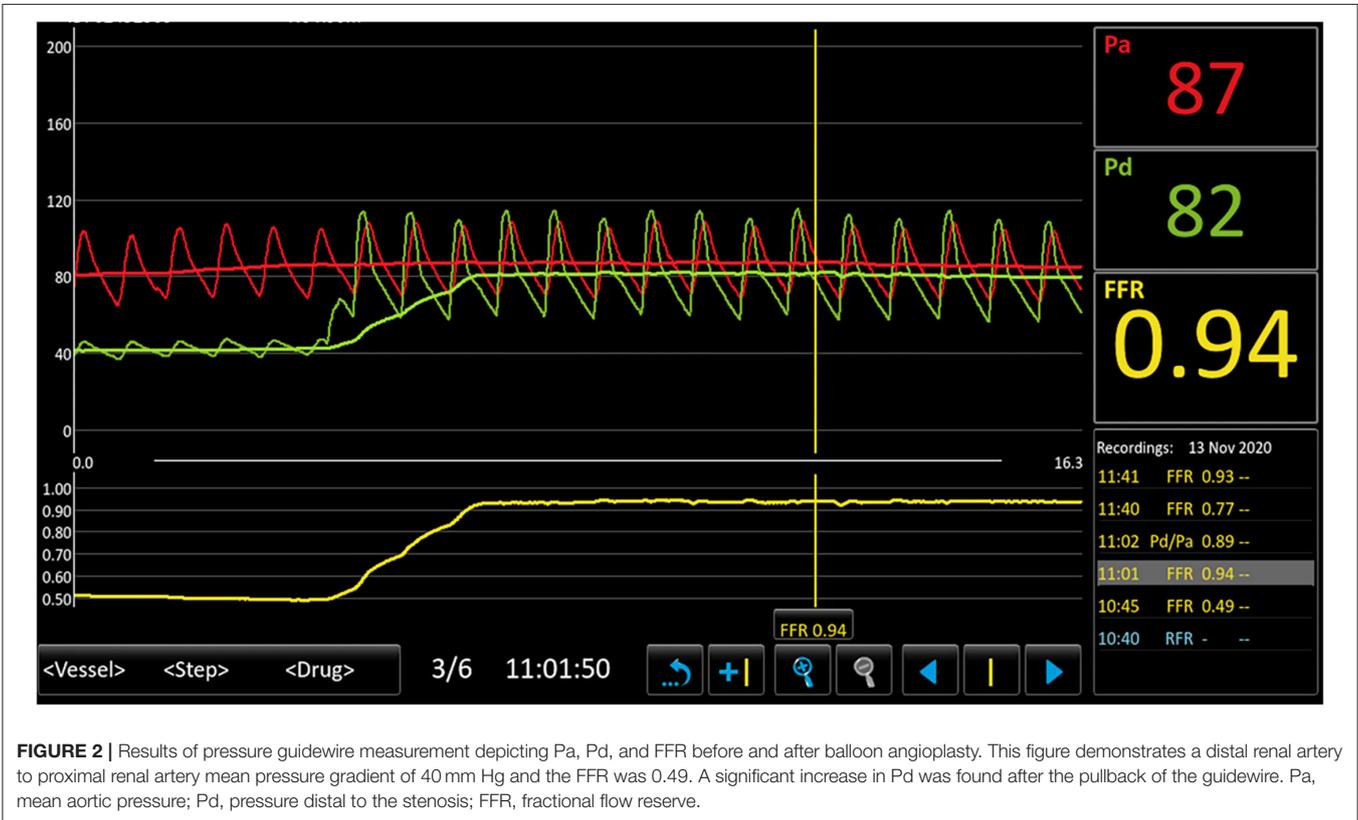
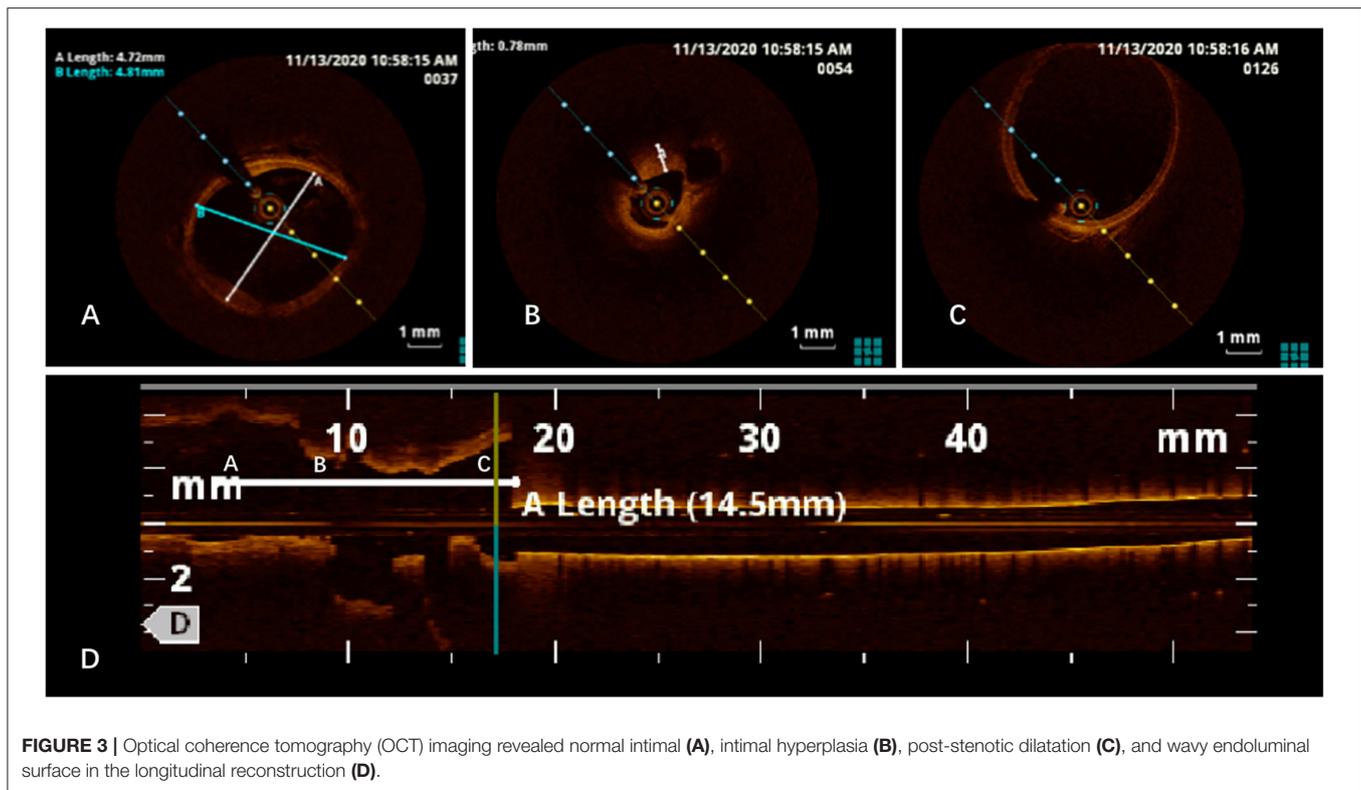


FIGURE 2 | Results of pressure guidewire measurement depicting Pa, Pd, and FFR before and after balloon angioplasty. This figure demonstrates a distal renal artery to proximal renal artery mean pressure gradient of 40 mm Hg and the FFR was 0.49. A significant increase in Pd was found after the pullback of the guidewire. Pa, mean aortic pressure; Pd, pressure distal to the stenosis; FFR, fractional flow reserve.

Subramanian et al. (15) demonstrated that rFFR correlated well with pressure gradient and was a good predictor of lesion severity in the setting of RAS. Mitchell et al. (16) found that rFFR could

identify people who are likely to benefit from percutaneous renal revascularization in terms of BP. In contrast, Leesar et al. (14) reported that FFR was not a predictive indicator for BP



improvement and Kadziela et al. (17, 18) showed that FFR did not predict BP response and kidney function improvement after renal revascularization. These results are quite opposite to the observations by the investigators mentioned above. The reason for this difference in the observations is not clear; one possible reason may be the method of measuring trans-lesion pressure gradient was based on catheters rather than pressure guidewire. The FFR result could be more precise when measured by a pressure guidewire than a 4f catheter, furthermore, the hyperemic pressure gradient by dopamine could only be measured by a pressure guidewire, and the pressure guidewire was the only method when facing significant stenosis lesions like this case. Moreover, these studies were conducted among patients with atherosclerotic RAS and have not been validated in patients with FMD. The success rate of revascularization among non-medial types of FMD (65%) was lower than those observed in the medial type of FMD (79–100%) (1, 19). These data suggest that the FMD subtype may determine the success rate of the procedure. The combination of OCT and renal FFR may be useful for the appropriate selection of patients with renal hypertension.

In conclusion, the combination of OCT and rFFR may improve the accuracy of diagnosis and classification, gauge the severity of stenosis, identify a patient who may respond to revascularization, and guide the procedure. Further research confirming the efficacy of OCT in the diagnosis and classification of FMD, and the prognostic value of FFR in a different type of renovascular FMD is warranted.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author/s.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Ethics Committee of Peking University First Hospital. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin. Written informed consent was obtained from the minor(s)' legal guardian/next of kin for the publication of any potentially identifiable images or data included in this article.

AUTHOR CONTRIBUTIONS

YL, BZ, MC, and JL contributed to the clinical treatment of this case. YL and XW contributed to manuscript writing. WM contributed to the review of the manuscript. All authors listed have contributed sufficiently to the project in order to be included as authors and approved the final version of the manuscript for publication.

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