To the Editor: Drug-coated balloon (DCB) has become more and more clinically used as a new interventional treatment technology in recent years. Especially in the treatment of in-stent restenosis (ISR), DCB has demonstrated an unparalleled advantage. However, the related adverse events after DCB treatment are rarely reported. Here, we report two cases of coronary artery aneurysm formation after DCB treatment.

A 62-year-old man suffered from unstable angina received coronary angiography (CAG) in November 2011 which demonstrated that there were diffuse lesions in the proximal segment of the left anterior descending artery (LAD) with complete occlusion of the middle segment. Cypher 2.5 mm × 33 mm and Cypher 2.75 mm × 23 mm stents were implanted sequentially from the middle to the proximal segment of the LAD. These two stents were connected and partially overlapped. Six years later, coronary artery computed tomography (CT) showed a diffuse severe ISR in the LAD with local occlusion and distal stent fracture without artery aneurysm formation [Figure 1a]. Subsequently, CAG confirmed the CT findings, and percutaneous transluminal coronary angioplasty (PTCA) was performed on the LAD. After predilation and postdilation, SeQuent Please (B. Braun Melsungen, Germany) 2.0 mm × 20 mm, 2.5 mm × 30 mm, and 3.0 mm × 30 mm DCBs were sequentially used from the distal to the proximal segment of the LAD dilating for 60 s at 6–10 atm. Retrospective angiography showed a residual stenosis of 30–40% of the middle segment of the LAD. One month after discharge, the patient received a CT myocardial perfusion scintigraphy, which showed that blood perfusion of the left ventricular lateral wall was significantly decreased after adenosine triphosphate load and that the value of myocardial blood flow (MBF) was 52.74 ml/100 ml per minute [Figure 1g and 1h]. One year later, we repeated the CT myocardial perfusion scintigraphy. The result was unexpected and showed that the proximal segment of the LAD presented a stenosis of approximately 70% with aneurysm formation and intra-aneurysmal thrombosis following the stenosis. However, blood perfusion of the left ventricular lateral wall improved [Figure 1i and 1j]. The value of the MBF was 68.23 ml/100 ml/min. Hence, we chose to continue the conservative medical treatment and closely follow-up the patient.

The DCB has been increasingly used as a new clinical interventional treatment technology in recent years. Especially in the treatment of ISR, the DCB has demonstrated an unparalleled advantage. However, the related adverse events after DCB treatment are rarely reported. Vassilev et al.[1] first reported the formation of aneurysm two months after DCB treatment for the ISR of the LAD.

Previous perspectives suggested that the possible mechanisms of interventional treatment-related aneurysms include the toxic effects of the drug coatings and local inflammatory and hypersensitivity reactions.[2] Both of the cases we reported used the SeQuent Please DCB. This DCB adopts a patented coating technology called PACCOCATH, wherein the paclitaxel and iopromide mixed matrix is evenly coated on the distal balloon of the traditional PTCA catheter so that the bioavailability of the drug is significantly increased.

Coronary Artery Aneurysm Formation after Drug-Coated Balloon Treatment

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paclitaxel is greatly improved, the contact area of the drug and the arterial wall is increased, the attraction between the drug molecules is weakened, and the cell proliferation and vascular intimal hyperplasia are effectively suppressed. However, in the process of efficiently inhibiting the repair, proliferation, migration, and intimal hyperplasia of vascular smooth muscle and endothelial cells, it will inevitably affect the repair of the intima at the interventional site and delay the healing of blood vessels, which causes thinning of the arterial wall and enlargement of the damaged area in the intima and middle layer, while the pressure in the blood vessel increases, and it will eventually lead to the formation of aneurysms. It is worth noting that DCB has a rapid onset and has a high drug load ($3 \mu g/mm^2$) than the dosage drug-eluting stent (DES) released (300–600 $\mu g$) which undoubtedly amplifies the local toxic effects of paclitaxel. In the first case, multiple DCBs are used in combination which led to higher drug concentration in the overlapping sites and is more likely to cause aneurysm formation. In the second case, we also speculate that the greater local concentrations of the drug are the main reason of aneurysm formation. On the other hand, the operation itself may also lead to aneurysm formation. Too large of the balloon diameter and overexpansion may be the important reason of DCB-related aneurysms, both of which can make the local artery wall teared and thus lead to the formation of coronary aneurysm or even pseudoaneurysms.

There is still much controversy over the treatment of postoperative aneurysm formation and there is also no uniform treatment protocol. The formulation of specific treatment strategies mainly depends on the extent, degree, risk, characteristics of the lesions, and the surgeon’s personal experience. Even if aneurysm formation or stent fracture occurred in the two cases we reported, the forward blood flow of the coronary artery was not affected. Hence, no ischemic chest pain and acute coronary events occurred. This may be because DCBs release antiproliferative drugs locally to the coronary arterial wall, which inhibits intimal hyperplasia and reduces inflammatory responses, and as a result, the risk of thrombosis is greatly reduced.

According to the above reasons, we only chose dual antiplatelet therapy and followed the patient closely long term.

In summary, we propose the potential risk of aneurysm formation after DCB treatment through these two cases, which might be associated with the high dose, high concentration, and rapid onset of cytotoxic drugs coated on DCB. The safety of DCB should be further consideration and discussion.
Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identities, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

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