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CASE SERIES
Structural intervention

Use of cangrelor for complex percutaneous coronary intervention in the context of concomitant severe aortic stenosis: a case series

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Background There is a growing need for percutaneous coronary intervention (PCI) to be performed within the same transcatheter aortic valve implantation (TAVI) procedure. In such cases, cangrelor, a fast-acting intravenous P2Y12-inhibitor with a short offset, is potential clinical utility to minimize bleeding and vascular complications during large-bore arterial access (LBAA) as well as the thrombotic risk associated with concomitant PCI.

Case summary We report two cases of TAVI with an indication to concomitant, high-risk PCI. In the first one, cangrelor was started only after LBAA was secured and TAVI completed, just before the initiation of complex PCI. In the second case, due to predicted complex coronary cannulation after TAVI, complex PCI was performed before TAVI and cangrelor started just after LBAA. In both cases, use of cangrelor (vs. pre-treatment with oral P2Y12-i) allowed for a tailored minimization of the risk of bleeding and vascular complications during LBAA while offering full platelet inhibition during a complex/high-risk PCI.

Discussion In this case series, we illustrate a possible approach to the use of cangrelor for patients undergoing TAVI and complex/high-risk PCI. In such complex cases, thorough pre-procedural planning might include a cangrelor to minimize vascular, bleeding, and ischaemic complications.

Keywords TAVI • PCI • CHIP • Aortic stenosis • Case report

ESC curriculum 3.1 Coronary artery disease • 3.4 Coronary angiography • 4.2 Aortic stenosis

Learning points

- Patients with indications to concomitant transcatheter aortic valve interventions and complex/high-risk percutaneous coronary intervention require a thorough pre-procedural planning.
- The use of cangrelor after large-bore arterial access minimizes the risk of peri-procedural bleeding and vascular complications (vs. pre-loading with oral $P2Y_{12}$-i).
- The risk of ischaemic complications (including peri-procedural myocardial infarction and stent thrombosis) is minimized with cangrelor (vs. post-loading with oral $P2Y_{12}$-i).
- A tailored antiplatelet approach including *cangrelor* might improve procedural outcomes.

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Introduction

As the use of transcatheter aortic valve implantation (TAVI) to treat symptomatic severe aortic stenosis (AS) increases, there is also a growing need for percutaneous coronary intervention (PCI) to be performed within the same TAVI procedure.[1] In such cases, pre-loading with a $P2Y_{12}$-inhibitor exposes the patient at higher risk of bleeding because of the use of large-bore arterial access (LBAA),[2] while administering the drug at the end of the procedure might increase thrombotic complication during PCI. In light of these considerations, cangrelor, a fast-acting intravenous $P2Y_{12}$-inhibitor with a short offset, has a potential clinical utility.[3] In this case series, we will present two real-world clinical scenarios where it was strategized to use cangrelor in order to minimize the bleeding and thrombotic risk associated with the procedure of TAVI and concomitant PCI.

Summary figure

Proposal for a therapeutic algorithm for the use of cangrelor in cases of same-stage TAVI and complex/high-risk PCI. ASCoP, aortic stenosis

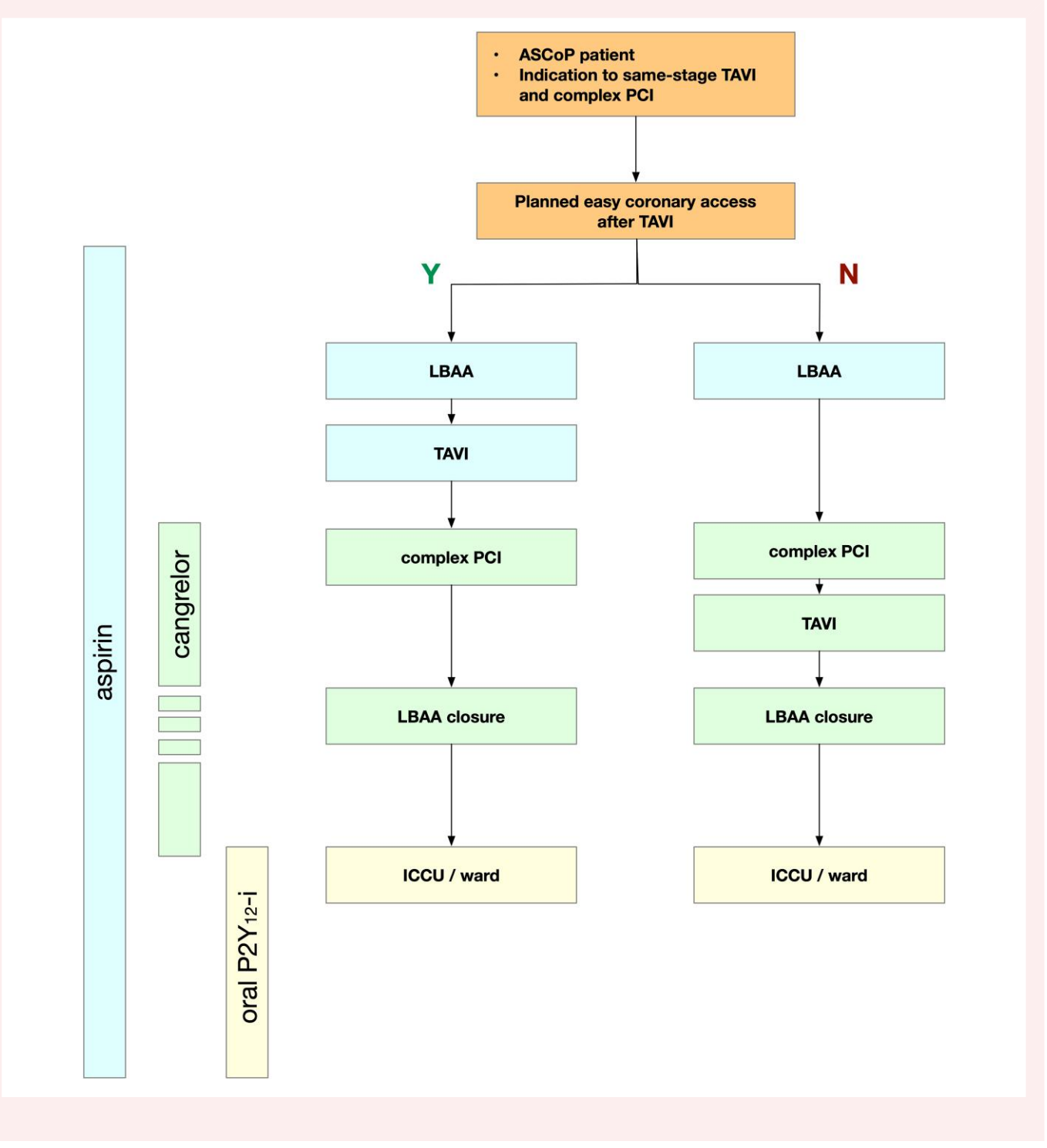

Table 1 Timeline

Day	Case 1	Case 2
0	ER: presenting with worsening angina and dyspnoea Echo: severe AS	ER: presenting with NSTE-ACS and worsening dyspnoea Echo: severe AS
1	Angiogram: calcific stenosis in LAD and subocclusive LCx	Angiogram: subocclusive, calcific stenosis of the ostium of the LCx and severe ISR of LAD
2	Heart team discussion: indication to TAVI plus complex PCI Pre-procedural CT scan: severe vasculopathy; predicted easy coronary access after TAVI	Heart Team Discussion: indication to TAVI plus complex PCI Pre-procedural CT scan: severe vasculopathy; predicted difficult coronary access after TAVI
5	Concomitant TAVI procedure + complex PCI; peri-procedural cangrelor Overnight stay in ICCU	Concomitant complex PCI + TAVI; peri-procedural cangrelor Overnight stay in ICCU
6	Transferred to cardio ward	Transferred to cardio ward
8	Discharged home	
9		Discharged home

AS, aortic stenosis; CT, computed tomography; ER, emergency room; ICCU, intensive cardiac care unit; ISR, in-stent restenosis; LAD, left anterior descending; LCx, left circumflex; NSTE-ACS, non-ST elevation acute coronary syndrome; PCI, percutaneous coronary intervention; TAVI, transcatheter aortic valve intervention.

with complex PCI features; ICCU, intensive cardiac care unit; LBAA, large-bore arterial access; P2Y12-i, P2Y12-inhibitor; PCI, percutaneous coronary intervention; TAVI, transcatheter aortic valve intervention.

Case 1

An 81-year-old man hospitalized for worsening chest discomfort and shortness of breath was found to have severe, calcific AS (aortic valve area; AVA, 0.8 cm^2, G med/max 37/62 mmHg) (*Table 1*). Cardiac enzymes and ECG excluded an acute coronary syndrome. Comorbidities included chronic obstructive pulmonary disease, kidney disease in chronic dialysis, and diabetes mellitus with multiple end-organ complications including severe lower limb vasculopathy with a history of bilateral femoral percutaneous angioplasty. Before hospital admission, the patient was managing well at home with all conditions well controlled with medical therapy and with some degree of routine exercise (Rockwood Frailty Scale 3). His left ventricular ejection fraction (LVEF) was mildly impaired (40%). Coronary angiography revealed a significant, long, calcific lesion in the proximal left anterior descending (LAD) and focal, subocclusive stenosis of the left circumflex (LCx); a severely calcific and long lesion of the right coronary artery (RCA) was also present (*Figure 1*; Supplementary material online, *Video S1*). Heart team discussion was in favour of fully percutaneous treatment, due to high surgical risk (STS 37.2%, EuroScore II 16.7%) and severe comorbidities, including severe peripheral vasculopathy.

Considering the need for complex PCI, the team opted for the use of a Acurate Neo2 (Boston Scientific, Marlborough, MA, USA) that allows for commissural alignment and facilitated access to coronary ostia due to tall stabilizing arches.[4] The patient was also perceived to be at both higher ischaemic and bleeding risk, due to the planned high-risk PCI (multivessel PCI with ongoing severe AS) and need for LBAA for TAVI in the context of severe vasculopathy, which mandated a specific strategy. Thus, firstly, femoral access was obtained with echo guidance and with no antiplatelet therapy in order to minimize LBAA-related bleeding risk. Secondly, TAVI procedure was performed with the implantation of an Acurate Neo2 (27 mm) valve and commissural alignment. Thirdly, intravenous aspirin and cangrelor infusion were administered and high-risk, complex PCI was performed with full platelet inhibition ongoing through the iSleeve 14 Fr sheet (Boston Scientific, Marlborough, MA, USA) used for TAVI. Complex PCI consisted of lesion preparation with multiple runs of orbital atherectomy with coronary DiamondBack 360 (CSI, Minneapolis, MN, USA) on both the proximal LAD and LCx and subsequent implantation of a drug-eluting stent in both vessels. Optimal final angiographic result was confirmed by intravascular ultrasound. Finally, haemostasis was achieved with the aid of two ProGlide that were pre-positioned. Cangrelor was then shifted to clopidogrel on the clinical ward. At 6-month follow-up, the patient was free from anginal symptoms and exertional dyspnoea, therefore the RCA was not staged for treatment.

Case 2

An 80-year-old gentleman with a history of previous three-vessel PCI presented to our emergency department with recent-onset angina and worsening dyspnoea. Diagnostic workup was suggestive of non-ST elevation acute coronary syndrome (peak cardiac Troponin T = 436 ng/L, mild dynamic ST-T changes) in the context of a newly diagnosed severely impaired LVEF (25%) with low-flow low-gradient AS (AVA 0.9 cm^2, G med/max 15/30 mmHg). Coronary angiography revealed subocclusive, calcific stenosis of the ostium of the LCx and severe in-stent restenosis of LAD. After heart discussion, surgical options were excluded due to prohibitive risk (STS 4.28, EuroScore II 13.37) and a full percutaneous approach was favoured. In addition, pre-TAVI computed tomography showed a very large annulus (25 mm × 31 mm) and bilateral severely calcified stenosis of the iliac and femoral axes, and therefore the patient was also perceived at high risk of vascular and bleeding complications during LBAA (*Figure 2*; Supplementary material online, *Video S2*). The multidisciplinary team opted for a strategy of complex PCI with LV support with Impella (Abiomed, Danvers, MA, USA) upfront, followed by TAVI, in order minimize any jeopardy to the newly implanted valve by the axial-flow pump. Considering the ongoing severe AS, a balloon aortic valvuloplasty (BAV) prior to LV unloading with Impella was also needed.

In brief, femoral access was obtained with echo guidance and without $P2Y_{12}$-i ongoing, in order to minimize the risk of access-related bleeding. The 14 Fr iSleeve sheath was advanced, and gentle BAV was performed with relatively undersized (18 mm) balloon. Then, the 14 Fr Impella sheath was advanced in the expandable iSleeve sheath and Impella support was commenced. Only at this point, cangrelor infusion was initiated to achieve optimal platelet inhibition in order to minimize

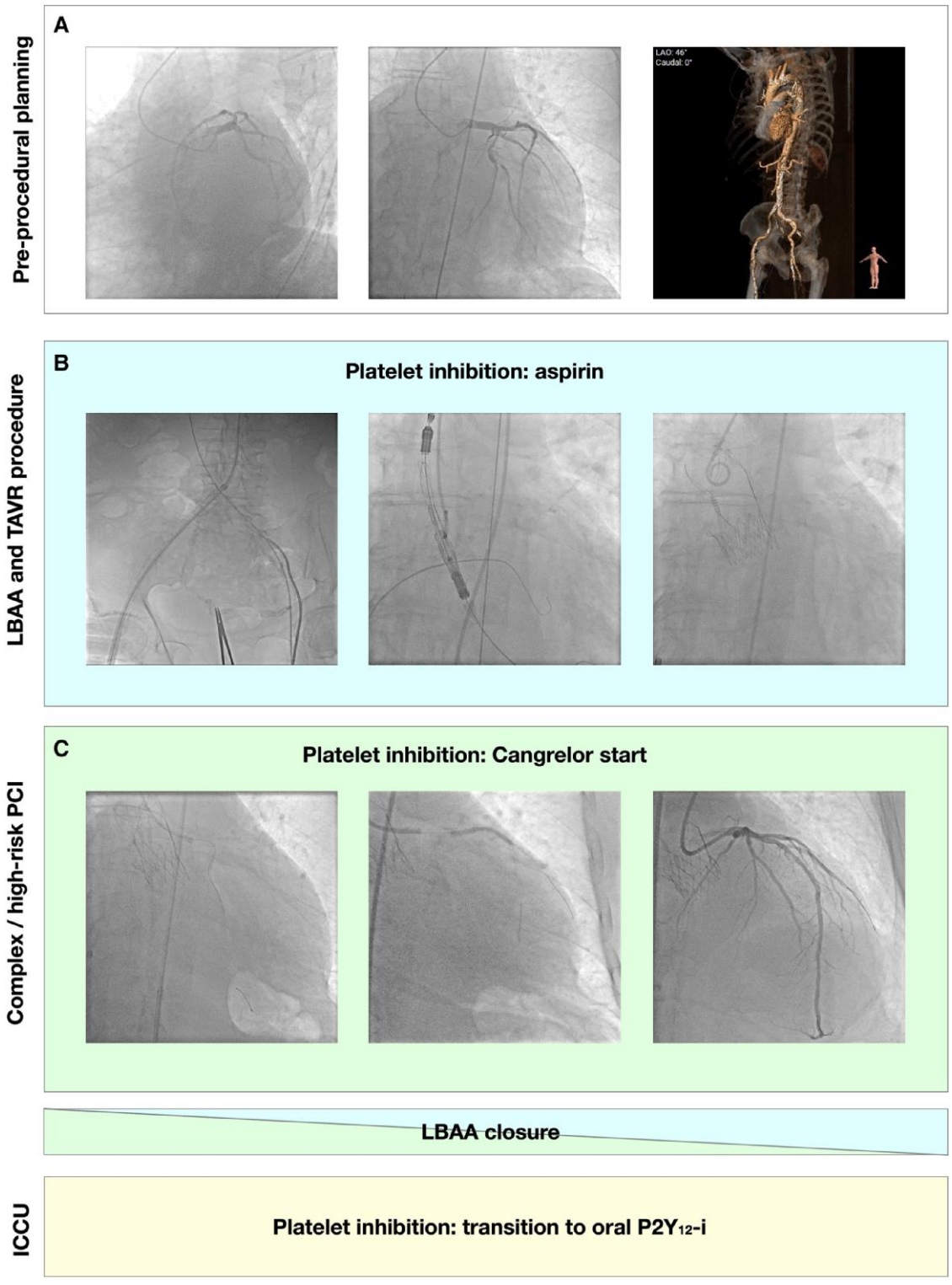

Figure 1 Patient 1. Case summary. (*A*) Pre-procedural planning, with coronary angiography showing severe calcific stenosis of the ostio-proximal LCx artery and proximal LAD and severe femoro-iliac calcification. (*B*) Large-bore access and transcatheter aortic valve implantation with commissural alignment of a Acurate Neo2 valve; (*C*) complex/high-risk PCI with orbital atherectomy and stenting of both LAD and LCx. LAD, left anterior descending; LCx, left circumflex; other abbreviations as in *Summary figure*.

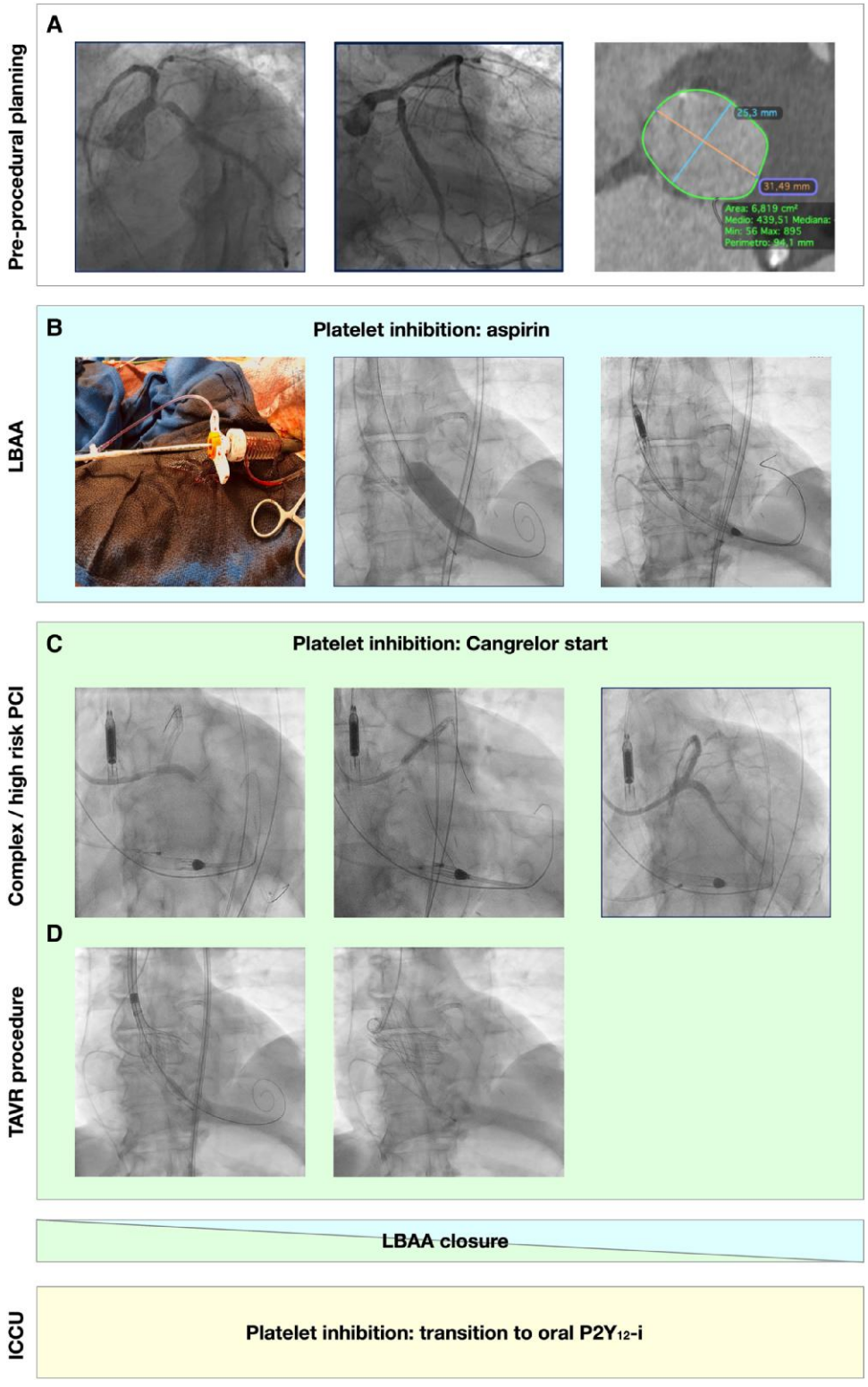

Figure 2 Patient 2. (*A*) Pre-procedural planning, with coronary angiography showing severe calcific stenosis of ostial LCx artery and severe calcific in-stent restenosis of the proximal LAD; the large aortic annulus is also shown. (*B*) Large-bore access with Impella placement after balloon aortic valvuloplasty; (*C*) complex/high-risk PCI with stenting of the left-main-LCx axis and cutting balloon for proximal LAD; (*D*) transcatheter aortic valve implantation with commissural alignment of an Evolut Pro+ 34. Abbreviations: as in *Summary figure* and *Figure 1*.

procedural risk during PCI. After pre-dilation with a scoring-balloon, a single everolimus-eluting stent was implanted in the LM-LCx, while the LAD lesion was treated with drug-eluting balloon. After optimal angiographic result was confirmed by intravascular ultrasound, the Impella catheter and sheath were removed and an Evolut Pro+ 34 (Medtronic, Minneapolis, MN, USA) was implanted using commissural alignment. A mild-to-moderate paravalvular leak was observed at final angiography; considering the older age of the patient with a relatively reduced exertion capacity at home, the clinical decision in this case was to avoid aggressive post-dilation. Finally, haemostasis was completed with two pre-implanted ProGlide and cangrelor was shifted to ticagrelor on the clinical ward. At 6-month follow-up, the patient had no residual dyspnoea at clinical follow-up.

Discussion

Cangrelor is an intravenous drug that acts as a direct, reversible $P2Y_{12}$ antagonist and that has a fast onset of action reaching maximum serum concentration within 2 min. Moreover, this peculiar drug also has a very rapid offset, with a half-life of 3–6 min and complete platelet function restoration within 60 min. In the CHAMPION-PHOENIX trial, it has been shown to significantly reduce peri-procedural events compared to clopidogrel, including a composite of death, myocardial infarction, and stent thrombosis (ST) and ST alone (odds ratio, 0.62; 95% CI, 0.43–0.90; $P = 0.01$), with similar rates of bleedings. The European Society of Cardiology guidelines recommend to consider cangrelor in $P2Y_{12}$-i naïve patients undergoing PCI, both in the acute and chronic setting (class IIb-A).[5,6] Albeit the use of cangrelor *tout-court* in PCI might be questionable, it appears compelling in cases of complex coronary lesions and whenever an acute ST is particularly feared. When concomitant severe AS is present, such threshold might be even lower as any coronary complications in this setting might be catastrophic.

The peculiar pharmacodynamic properties of cangrelor (rapid onset and offset) allow some specific procedural strategy in the setting of concomitant TAVI and PCI (*Summary figure*). In fact, TAVI is burdened by a significant rate of procedural bleeding, which are often related to the LBAA.[2] For this reason, upfront $P2Y_{12}$ inhibition (which requires up to several hours if given orally) is often avoided in this context in order to minimize bleeding risk at the moment of LBAA before or after TAVI. Cangrelor, on the other hand, can be switched-on only after LBAA is secured, therefore allowing for a safe femoral access with minimal procedural bleeding risk.

In the first case presented, concomitant treatment of severe AS and severe coronary artery disease was mainly driven by the need to minimize the risk of vascular complications in a patient with severe vasculopathy and when femoral approach could also facilitate a complex coronary revascularization.[7] In order to minimize bleeding and vascular complications related to LBAA and ischaemic risk due to PCI, $P2Y_{12}$-i with cangrelor was commenced only after securing the vascular access. Similarly, in the second case presented, the use of cangrelor allowed for selective protection of the very complex and high-risk PCI only after safe LBAA was obtained.

While recent data suggested that performing staged PCI after TAVI is associated with improved clinical outcomes,[8] only a minority of cases in that registry presented with such high-risk/complex PCI features that might jeopardize TAVI procedure, as in the first case presented here. Moreover, patient's anatomy might favour the use of a valve model with anticipated difficult coronary reaccess, thus augmenting further procedural complexity. In summary, while we do not advocate that same-stage TAVI and PCI should be applied to every case, we believe that there is a minor, but numerically relevant, proportion of patients that could benefit from such a strategy.

Finally, despite not presented in this case series, it is reasonable that when deemed appropriate for very complex vascular access and higher risk of bleeding during haemostasis, cangrelor could be stopped momentarily as a bailout, with a partial recovery of platelet function within minutes.

In conclusion, cangrelor has a niche for use also in complex cases when TAVI and PCI are planned to be performed in the same procedure. Despite not ordinary, we anticipate that such cases will increase in number over time considering the wide expansion of TAVI and ever-growing age of the population.

Lead author biography

Dr Montalto is an interventional cardiologist at Niguarda Hospital (Milan) and a PhD student at University of Milan-Bicocca. He has extensive experience in clinical research in coronary and valve interventions with a focus on antiplatelet therapy and elderly subjects.

Supplementary material

Supplementary material is available at *European Heart Journal – Case Reports* online.

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In memory of Ugo Luigi Montalto (Tripoli, 1933–Rome, 2024).

Consent: Written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

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Data availability

No new data were created or analysed in this article.

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