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The Choice of Antithrombotic Therapy in a Patient with New-Onset Atrial Fibrillation and High Coronary Thrombotic Risk.

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Abstract

Current guidelines are mandatory in the choice of anticoagulant and/or antiplatelet therapy in patients with atrial fibrillation undergoing percutaneous transluminal coronary angioplasty and in patients with coronary artery disease and previous percutaneous transluminal coronary angioplasty that develop atrial fibrillation. However, in the real world there are crossroads with multiple choices, especially taking into account patient's peculiar characteristics and risk factors, which sometimes are not well represented in the guidelines.

The reported clinical case focuses on the choice of anticoagulation therapy in a patient with chronic and severe coronary artery disease and new diagnosis of atrial fibrillation who,considering his specifically high coronary thrombotic risk, probably should continue antiplatelet therapy.

Case Report

A 51 years old man with a severe coronary artery disease was admitted to emergency department (ED) with a history of 3-days of palpitation and dyspnoea and a new onset of chest pain.

The patient was smoker and was affected by symptomatic heart failure with mid-range ejection fraction (45%) and NYHA class II-III, type 2 diabetes, dyslipidaemia and hypertension.He had normal renal and hepatic function and had no history of clinically relevant bleeding.

One year earlier, in a different hospital, the patient underwent coronary artery bypass graft with left internal mammary artery (LIMA) graft for intermediate coronary artery (ICA),great saphenous vein (GSV) for left descending coronary artery (LDCA) and GSV for posterior descending coronary artery (PDCA) [Figure 1A]. During hospitalization,due to recurrent angina, the patient underwent coronary angiography and percutaneous transluminal coronary intervention (PCI) with stent placement in left main coronary artery (LMCA) [Figure 1B]. At discharge, an echocardiography showed heart failure with midrange ejection fraction of 40-45% and akinesia of septum and apex.

Six months after discharge, due to recurrent low threshold angina (Canadian Cardiovascular Society Angina Grade = III-IV), an additional coronary angiography was performed and showed:LMCA completely occluded by in-stent restenosis; LDCA and circumflex coronary artery were not viewable from anterograde flow; the right coronary artery (RCA) was severely atheromatous with diffuse plaques and critical stenosis in the middle and distal pre-crux tract; GVS for RCA was patent and functional as well as GVS for septal LDCA, although the downstream vessel appeared thin and widely atheromatous swith sub-critical stenosis; diagonal LDCA filled up with flow coming from collateral vessels of septal LDCA; the LIMA for ICA was hypoplastic with markedly reduced flow and the downstream vessel was thin and diffusely atheromatous [Figure 1C]. No additional PCI was performed; on the other hand, medical therapy was optimized.

Thus, the patient was on dual antiplatelet therapy (DAPT) with ticagrelor 90 mg bid and aspirin; bisoprolol 2,5 mg/day, ranolazine 500 mg bid, zofenopril 7,5 mg/day, furosemide 25 mg/day, pantoprazole 20 mg/day, atorvastatin 40 mg/day and metformin 500 mg tid. At the admission to ED, the electrocardiogram (ECG) showed atrial fibrillation with mean heart rate of 120 bpm [Figure 2] and diffuses but non specific alterations of ST segment and T wave. Since the symptoms had been starting 3 days earlier, the first therapeutic strategy was heart rate control in order to target amean heart rate < 110 bpm.

In order to set up a strategy for the prevention of cardioembolic stroke in atrial fibrillation, CHA_2DS_2-VASc was calculated and resulted 4 (1 congestive heart failure, hypertension, diabetes and vascular disease each) with an estimated annual stroke risk of 5,9%. The HASBLED score was 1.

Key Words

Atrial Fibrillation, Oral Anticoagulant, Antiplatelet Therapy, Coronary Artery Disease, Percutaneous Transluminal Coronary Angioplasty, Guidelines.

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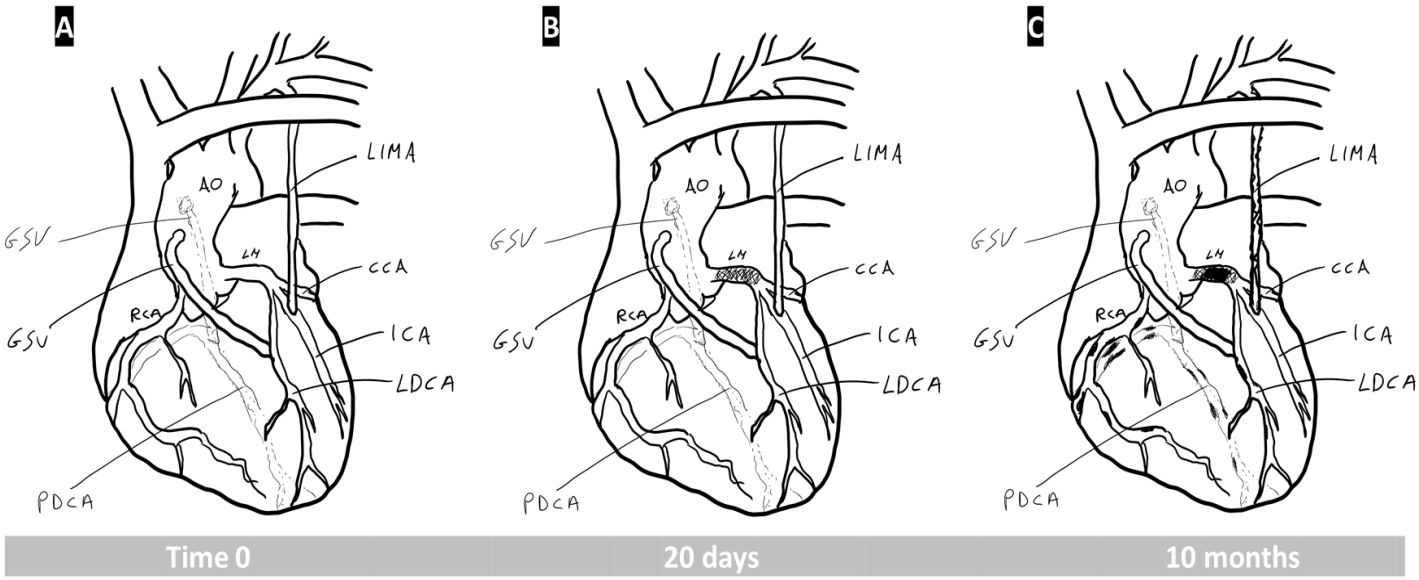

Figure 1: Schematic representation of coronary anatomy and intervention during the time (time 0 refers to time of surgery). A: undergone coronary artery bypass graft with left internal mammary artery (LIMA) graft for intermediate coronary artery (ICA), great saphenous vein (GSV) for left descending coronary artery (LDCA) and GSV for posterior descending coronary artery (PDCA); B: stenting of left main coronary artery (LMCA) C: LMCA completely occluded by instent restenosis; LDCA and circumflex coronary artery were not viewable from anterograde flow; the right coronary artery (RCA) was severely atheromatous in the middle and distal pre-crux tract; GVS for RCA was patent and functional as well as GVS for septal LDCA, although the downstream vessel appeared thin and widely atheromatous with sub-critical stenosis; diagonal LDCA filled up with flow coming from collateral vessels of septal LDCA; the LIMA for ICA was hypoplastic with markedly reduced flow and the downstream vessel was thin and diffusely atheromatous

Discussion

According to CHA_2DS_2-VASc score, the anticoagulant therapy was mandatory. However, considering the progressive worsening of CAD, the choice whether to maintain or not DAPT represented a therapeutic challenge.

The opportunity of long term DAPT was determinate from DAPT score (www.daptstudy.org) and PRECISE-DAPT 5-item bleeding risk score (age, creatinine clearance, Hemoglobin, white blood cell count, and prior spontaneous bleeding) is used for the prediction of out-of-hospital bleeding hazard as a complementary tool to the DAPT score (Capodanno D, 2018) (Costa F & Inves, 2017).DAPT score indicates the opportunity of long term DAPT (30 months) in case of a score ≥ 2 (Marco Valgimigli, 2018). In the present case, the DAPT score was 3 (smoking, diabetes, prior PCI), suggesting the need of long term DAPT. Nevertheless, the DAPT score does not take into account additional potential risk factors for ischemic coronary events suchinstent re-stenosis or site of stenting (left main) or the rapid progression of CAD, all conditions found in the present case.

In the current guidelines on DAPT, for patients with an indication for oral anticoagulation (OA) undergoing PCI there are only class IIaB or IIaA recommendations. While these recommendations

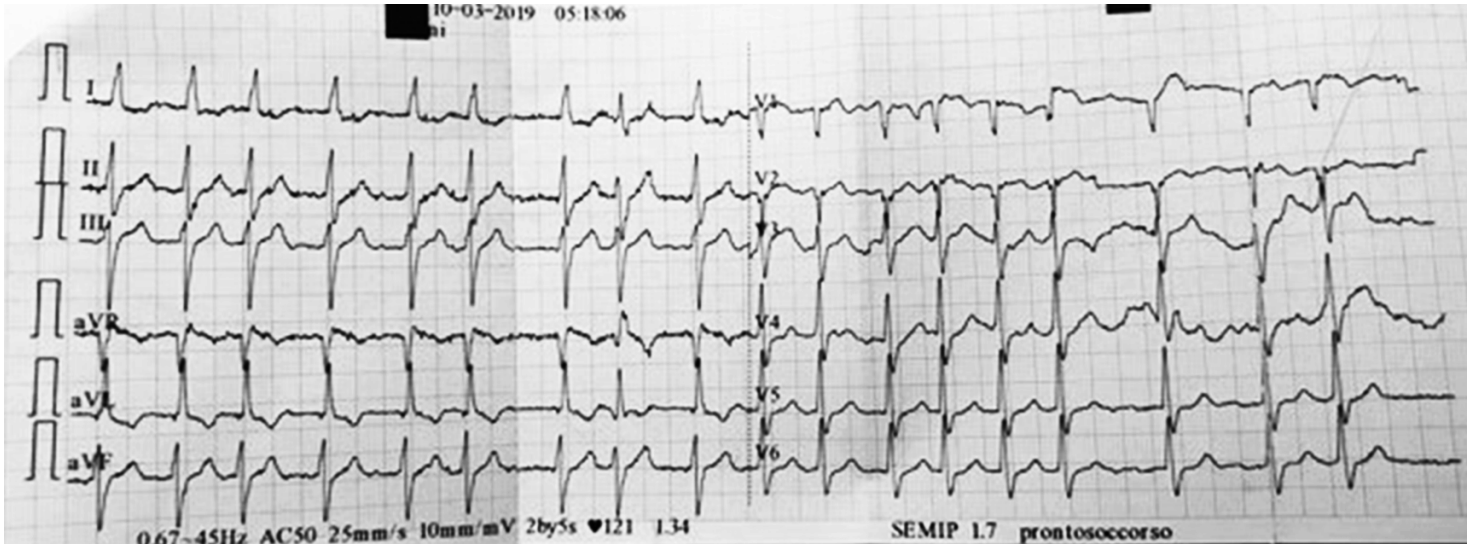

Figure 2: The ECG at admission to emergency department showed atrial fibrillation with an average ventricular rate of 120 bpm and with diffuses but non specific alterations of ST segment and T wave.

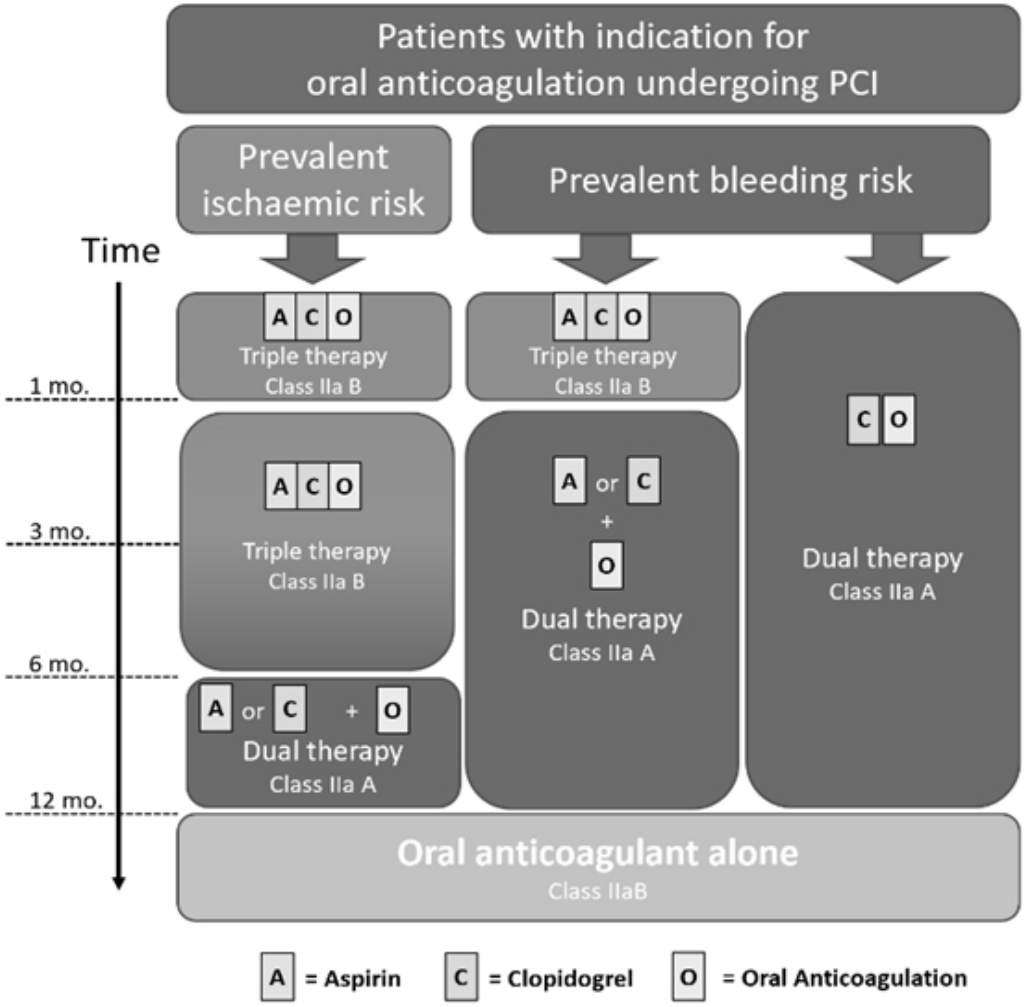

Figure 3: **Adapted from Esc Guidelines 2017. Algorithm for dual antiplatelet therapy (DAPT) in patients with an indication for oral anticoagulation undergoing percutaneous coronary intervention (PCI). Triple therapy denotes treatment with DAPT plus oral anticoagulant (OAC). Dual therapy denotes treatment witha single antiplatelet agent (aspirin or clopidogrel) plus OAC. ABC = age, biomarkers, clinical history; ACS = acute coronary syndrome; mo. = month(s); PCI = percutaneous coronary intervention.**

take into account the prevalence of ischemic risk and bleeding risk in the first 12 months from PCI [Figure 3], they do not consider the "coronary history" and the severity of CAD. However, the same guidelines recommend to use only anticoagulant therapy after 12 month from PCI.

In order to choose a double-therapy regimen, clopidogrel is indicated as preferred antiplatelet in accordance with the recent clinical trial regarding patients with atrial fibrillation treated with OA undergoing percutaneous coronary intervention(Gibson CM, 2016), (Renato D. Lopes, 2019)(Christopher P. Cannon, 2017); moreover, in the WOEST trial the use of clopidogrel without aspirin was associated with a significant reduction in bleeding complications and no increase in the rate of thrombotic events (Willem J M Dewilde, 2013).

In literature there are different opinions regarding dual and triple antithrombotic therapy, especially when it comes to long-term therapies. In a recently published position paper, Angiolillo et al. suggest that in patients undergoing PCI a double-therapy (DT: OA and antiplatelet) regimen by the time of hospital discharge should be considered for most patients, whereas triple therapy (TT) beyond hospital discharge should be considered only for selected patients at high ischemic/ thrombotic and low bleeding risks and for a limited period of time(Angiolillo DJ, 2018).

The duration of DT and TT in selected patients is controversy. Although Angiolillo et al. affirm that most patients need a DT by the time of hospital discharge, current guidelines indicates TT up to 1-6 months in according to bleeding/ischemic risk and recommended DT up to 12 months from PCI. Moreover, in some patients with high ischemic risk, the DAPTscore indicates the use of DAPT up to 30 months and it is considerable prolonged DAPT if CAD is not resolved or still ongoing. The progression of coronary heart disease as a new event, regardless of the execution of an angioplasty or a stent placement, should be taken into consideration and DT or TT has reason to be maintained over time, above all in relation to age and low risk of bleeding. Certainly, in these selected cases it may be necessary

to provide other therapeutic strategies as left atrial appendage closure or to evaluate the hypothesis of cardiac transplantation in order to severe coronary artery disease and heart failure.

Conclusion

In our clinical case, considering the severity and rapid progression of CAD and the low bleeding risk, we decidedtoadd OA to the DAPT regimen and to prolong the use of DAPT over 12 months (30 months long DAPT).Since continuing ticagrelor is not recommended as a part of the triple antithrombotic therapy, a switch to clopidogrel was decided. As for OA therapy, five possible scenarios were available: one of the four new oral anticoagulant (Apixaban, Edoxaban, Dabigratan, Rivaroxaban) at the lowest approved dose effective for stroke prevention (IIaC) or the use of rivaroxaban 15 mg o.d. instead of rivaroxaban 20 mg o.d. (IIbB). In the present case, rivaroxaban 15 mg o.d. was chosen and added to clopidogrel and aspirin for a total of 30 months, according to PIONEER AF-PCI (Gibson CM, 2016) demonstrating that 15 mg was as effective as 20 mg. After 30 months from the last "coronary event" the antithrombotic therapy will be re-evaluatedand other therapeutic hypotheses (left atrial appendage closure or the hypothesis of cardiac transplantation) will be take into account. At three months follow up, neither cerebral and cardiovascular ischemic events, nor major or clinically relevant non-major bleeding were observed; long term follow up is going on.

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