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DOACs in Patients With Giant Coronary Artery Aneurysms After Kawasaki Disease

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Direct oral anticoagulants in~~for~~ patients with giant coronary artery aneurysms after Kawasaki disease

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Introduction

Coronary artery aneurysms (CAA) ~~can~~ result from ~~the~~ intense ~~inflammatory response~~inflammation during acute Kawasaki disease (KD) with resultant destruction of the normal architecture of the vessel wall. The altered rheodynamics through this section of the artery with decreased wall shear stress and increased particle residence time is a major risk factor for ischemia and thrombosis.[1] Although there are no randomized clinical trials to guide management, there is consensus among international guidelines that patients with aneurysms measuring 8 mm or having a Z-score (internal diameter normalized for body surface area) of ≥10 SD units should be treated with systemic anti-coagulation and anti-platelet therapy.[2,3]Warfarin and low-molecular weight heparin (LMWH) are the standard anticoagulants ~~used~~ for these patients, but each have significant drawbacks. Limitations of warfarin include a narrow therapeutic range, ~~multiple~~ food and medication interactions, need for frequent monitoring with phlebotomy or fingerstick, bleeding complications, and vascular wall calcification due to inhibition of the enzyme matrix gamma-carboxyglutamate Gla protein (MGP) that scavenges calcium phosphate in the tissues.[4] Therapeutic LMWH requires twice daily subcutaneous injections that ~~can~~ cause discomfort and affect quality of life in children. Therefore, we offered direct oral anticoagulants (DOACs) to a ~~U.S. cohort of~~group of KD patients ~~in the United States~~ with giant coronary artery aneurysms as an option for systemic anticoagulation.

Methods

~~We reviewed the records of~~This is a case series of 24 KD patients who required systemic anticoagulation due to giant CAA or regional hypokinesis secondary to thrombotic sequelae of KD and~~who~~ opted to be treated with a DOAC. IRB approval

and consent/assent for longitudinal KD studies were obtained. Records from the adult and pediatric cardiologyKD clinics were reviewed (San Diego Cardiac Center, Rady Children's Hospital San Diego). Patients were followed for 1.9-30 years.

Results

Twenty-four KD patients were treated with DOACs for systemic anticoagulation. Nineteen were male. Eight received IVIG and/or aspirin at the time of acute presentation, six received delayed IVIG treatment, and ten were never recognized or treated until presentation in adulthood with myocardial infarction or symptoms requiring interventional catheterization. The median observation period on DOAC therapy was 4.9 years (IQR 4.2-8.0) with 138 total treatment-years observed (**Table 1**). Six of the 24 subjects started a DOAC at age less than 18 years. There were no major bleeding events during the observation period. MACE occurred in three subjects: one myocardial infarction with LAD occlusion on dabigatran while running a marathon (Table, Pt. 9), one ischemic event with a filling defect in both branches of the obtuse marginal off the circumflex that was due to distal thrombus while on rivaroxaban (Pt. 10), and one recurrent MI while on apixaban (Pt. 13).

Discussion

As a study small case series, the generalizability of our findings to a larger KD population is unknown. The three adult KD patients who suffered a MACE on three different DOACs demonstrate that these lesions are at substantial risk of thrombosis. In a multicenter, North American cohort of 80 KD patients treated with warfarin, the cumulative incidence of coronary artery thrombosis over 2.2 years (IQR 0.9-7.1) was 6.7 ± 3.7%.[5] In a Japanese study of 273 Japanese KD patients anticoagulated with warfarin for giant CAAs, the event-free survival was only 52% for males and 75% for females at 10 years.[6] Thus, the long-term outlook for those

patients with giant CAA due to KD includes significant morbidity and mortality, which is not fully mitigated with systemic anticoagulation.

~~There are known~~We recognize as limitations ~~to a~~the case series design~~,~~ ~~namely lack of a~~ with no control ~~population~~group and only a single center experience. In conclusion, it is reasonable to consider a DOAC as chronic management for adult and pediatric KD patients with giant CAAs. A large-scale, registry-based study of KD patients with giant aneurysms on systemic anticoagulation could help to provide further guidance for optimal patient management.

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