We believe that the extended therapy in patients with PAD and coronary disease might be much more beneficial than the conclusions derived from DAPT. Besides the differences in the inclusion criteria where DAPT focused on patients after stenting and PEGASUS on prior myocardial infarction, in DAPT, two-thirds received clopidogrel and the remaining one-third prasugrel, whereas in PEGASUS, the drug was ticagrelor. In this latter trial, none of the subgroups stratified by age, sex, race, weight, type of myocardial infarction, time from myocardial infarction to randomization, history of percutaneous coronary intervention, diabetes, multivessel disease, chronic kidney disease, aspirin dose, and geographic region showed heterogeneity in the efficacy of ticagrelor at either dose with respect to the primary composite endpoint (4). However, PAD was not included in that list and, concretely, is where prolonged therapy obtained remarkable benefits with an absolute risk reduction of 4.1% and a number needed to treat of 25 compared with the absolute risk reduction of 1% and a number needed to treat of 100 in patients without PAD. Moreover, the absolute excess of TIMI major bleeding was only 0.12% with a number needed to harm of 834 in patients with PAD, without significant differences with the shorter therapy, not only in major, but also in minor bleeding, with any of the 2 tested doses (5). The 60-mg dose had particularly favorable outcomes for cardiovascular and all-cause mortality.

In conclusion, in our opinion, the better profile of ticagrelor in comparison with clopidogrel and prasugrel may have played a relevant role in the differences between the substudies of PAD in DAPT and PEGASUS, and although the EUCLID study (A Study Comparing Cardiovascular Effects of Ticagrelor and Clopidogrel in Patients With Peripheral Artery Disease), which did not require a previous myocardial infarction for inclusion, was negative, the patients with PAD and coronary disease are the ones where the threshold of prolonged double therapy should be lower.

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REFERENCES

1. Secemsky E, Yeh R, Kereiakes D, et al. Extended duration dual antiplatelet therapy after coronary stenting among patients with peripheral arterial disease. J Am Coll Cardiol Intv 2017;65:942–54.

2. Eckstein H, Stadlbauer T. The DAPT trial and peripheral arterial disease from a vascular medicine perspective. J Am Coll Cardiol Intv 2017;10:955–7.

3. Fuster V. The proliferation of scoring systems: trying to keep our heads out of the clouds. J Am Coll Cardiol 2017;69:1640–1.

4. Bonaca MP, Bhatt DL, Cohen M, et al., PEGASUS-TIMI 54 Steering Committee and Investigators. Long-term use of ticagrelor in patients with prior myocardial infarction. N Engl J Med 2015;372:1791–800.

5. Bonaca MP, Bhatt DL, Storey RF, et al. Ticagrelor for prevention of ischemic events after myocardial infarction in patients with peripheral artery disease. J Am Coll Cardiol 2016;67:2719–28.

REPLY: Duration of the Double Antiplatelet Therapy in Patients With Coronary and Peripheral Arterial Disease

The Key Might Be in the Type of Drug

We thank Dr. Lozano and colleagues for their comments in regards to our recently published study in *JACC: Cardiovascular Interventions* (1). In our secondary analysis of the Dual Antiplatelet Therapy (DAPT) study (2), we found that extending thienopyridine therapy from 12 to 30 months post-coronary stenting with either clopidogrel or prasugrel on a background of aspirin resulted in consistent ischemic event reductions and consistent bleeding risk increases between those with and without a history of peripheral arterial disease (PAD). The authors of this letter correctly point out that the DAPT study did not evaluate the treatment effects of ticagrelor, which was not approved at the time of enrollment (2). The authors suggest that ticagrelor may confer benefits that outweigh risks among patients with PAD and coronary artery disease (CAD). From the available data, we believe that there is currently insufficient evidence to conclude that ticagrelor may offer a better risk-benefit profile than clopidogrel or prasugrel in patients with PAD and stable CAD.

The PEGASUS (Prevention of Cardiovascular Events in Patients with Prior Heart Attack Using Ticagrelor Compared to Placebo on a Background of Aspirin-Thrombolysis In Myocardial Infarction 54) trial compared ticagrelor to placebo in patients with a history of myocardial infarction 1 or more years before enrollment and reported an ischemic event reduction with ticagrelor without an increase in TIMI (Thrombolysis In Myocardial Infarction) major bleeding among those with PAD (3). However, the PEGASUS trial did not detect heterogeneous

treatment effects with ticagrelor for either the ischemic or bleeding endpoints between those with and without PAD (3). This suggests that there is unlikely a true lack of bleeding risk in such patients, given the known mechanism of action of the drug. Notably, as Lozano and colleagues acknowledge, recent results from the EUCLID (A Study Comparing Cardiovascular Effects of Ticagrelor and Clopidogrel in Patients With Peripheral Artery Disease) trial, where patients with symptomatic PAD, 29% with prior CAD, were randomized to monotherapy with either ticagrelor or clopidogrel, found no difference in ischemic outcomes between therapies (4).

Nonetheless, we agree with Dr. Lozano and colleagues that patients with PAD and concurrent CAD represent a high-risk patient population—for both ischemic and bleeding events—and are worthy of additional investigation into treatment strategies to optimize care, including more individualized assessment of risk and benefit (5).

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REFERENCES

1. Secemsky EA, Yeh RW, Kereiakes DJ, et al. Extended duration dual antiplatelet therapy after coronary stenting among patients with peripheral arterial disease: a subanalysis of the dual antiplatelet therapy study. J Am Coll Cardiol Intv 2017;10:942–54.

2. Mauri L, Kereiakes DJ, Yeh RW, et al. Twelve or 30 months of dual antiplatelet therapy after drug-eluting stents. N Engl J Med 2014:2155–66.

3. Bonaca MP, Bhatt DL, Storey RF, et al. Ticagrelor for prevention of ischemic events after myocardial infarction in patients with peripheral artery disease. J Am Coll Cardiol 2016;67:2719–28.

4. Hiatt WR, Fowkes FG, Heizer G, et al. Ticagrelor versus clopidogrel in symptomatic peripheral artery disease. N Engl J Med 2017;376:32–40.

5. Yeh RW, Secemsky EA, Kereiakes DJ, et al. Development and validation of a prediction rule for benefit and harm of dual antiplatelet therapy beyond 1 year after percutaneous coronary intervention. JAMA 2016;315:1735–49.

RESEARCH LETTER:

Pulse on Spontaneous Coronary Artery Dissections

Experience-Based Survey

Spontaneous coronary artery dissection (SCAD) mostly affects young adults (especially women), and clinical manifestations vary from chest pain to sudden cardiac death. It occurs in 0.1% to 1.1% of angiographic series and represents 0.1% to 4% of acute coronary syndromes (ACS) (1,2). However, this condition is underestimated, primarily because its classic angiographic hallmarks are lacking in >70% and may be discovered exclusively with intravascular imaging (3,4). Furthermore, its management remains challenging because of the lack of evidence supporting therapy, and the role of percutaneous or surgical revascularization is still debated.

In this contribution, a group of SCAD experts and the European Society of Cardiology SCAD Working Group developed 20 questions regarding diagnosis, therapy, and follow-up of SCAD (Online Table 1). Surveys were sent out electronically in November 2016 to all the first/corresponding authors (whose e-mail contact was available) of the 609 articles on the topic found on PubMed. These articles were selected with the keyword "Spontaneous coronary artery dissection" or by the acronym "SCAD." Two reminders were sent to nonresponders after 1 and 2 months. The survey was closed in February 2017.

We obtained 402 complete responses to the questionnaire from 609 surveys sent (66%). The responses were from interventional cardiologists in 81%, clinical cardiologists in 14%, cardiac surgeons in 3%, and other physicians in 2%. Fifty-five percent of the responders had seen 1 to 10 SCAD cases in their experience, and only 7% had seen over 50. According to their responses, the most relevant risk factors for SCAD were female sex, pregnancy, or the peripartum period, young age, absence of classical risks factors, heavy physical/psychic stress, and systemic connective tissue disorders, as well as noncoronary vasculopathies (e.g., fibromuscular dysplasia). Considered of minor importance were the use of oral contraceptives or chronic inflammatory diseases. The principal clinical presentation of SCAD was non-ST-segment elevation ACS (56%), followed