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Clinical Cardiovascular Care: Antiplatelet & Anticoagulation Strategies

Dr. Sorrentino:
Patients with clinical cardiovascular disease can be treated with a growing number of interventional strategies. Following an intervention or major cardiovascular event, a number of different regimens of antiplatelet agents and anticoagulants are recommended to prevent complications of cardiovascular disease.

This is *Heart Matters* on ReachMD. I'm Dr. Matthew Sorrentino and joining me to discuss antiplatelet and anticoagulation strategies for patients with cardiovascular disease is Dr. Michael Gibson, a Professor of Medicine and Cardiology and Interventional Cardiologist at the Beth Israel Deaconess Medical Center and CEO of the Combined Non-Profit BAIM and Profuse Research Institute at Harvard Medical School in Boston, Massachusetts. Dr. Gibson, welcome to the program.

Dr. Gibson:
Great. Thanks, Matt. Good to connect with you, again.

Dr. Sorrentino:
Dr. Gibson, I'd like to start by asking about dual antiplatelet therapy or "DAPT". This has become the standard management of patients following a myocardial infarction or the insertion of a drug-eluting stent. In patients who are at high risk of bleeding, patients we're all seeing more and more these days, what is the minimum amount of time that we should be using DAPT to reduce stent thrombosis or recurrent cardiovascular event?

Dr. Gibson:
Yeah, that's an excellent question and there have been a lot of studies looking at shortening DAPT. I'll give you a scenario: in the Cath Lab the other day, we had a patient just like you described, and the fellow said, "Oh, no, no, no, we don't need to give aspirin, Mike showed that in the TWILIGHT study." That's not what we showed. I want to make it absolutely clear that everyone getting a PCI should probably get aspirin. And if they are allergic to aspirin or have sensitivity, they should get desensitized before the procedure. So, everyone gets aspirin. I would say the shortest that I'm hearing about is people getting aspirin while in the hospital, perhaps at discharge. Many more people are shortening things if they can extended out to a month. But, these days, a central tendency is to give these high risk bleeding people perhaps three months of DAPT. All of this is an individualized decision, and you have to balance bleeding risk versus ischemic risks. Here, this patient had, let's say a STEMI or let's say a high risk of recurrent STEMI given the anatomy, the number of stents, the complexity of the intervention, if it's a sole remaining conduit or left main, those are high-risk for an ischemic outcome and that pushes you towards a longer duration. But the shortest would be at discharge or a week or month.

Dr. Sorrentino:
If you do stop the aspirin short term, how long would you continue the P2Y12 agent? Ahould we still go for a year with clopidogrel or ticagrelor in those patients?

Dr. Gibson:
You know, again, you have to make an individualized decision. If it is someone who had an ACS, an acute coronary syndrome, then the goal is to treat them longer, say for a year if you think they can tolerate it and if possible, use dual antiplatelet therapy, if you think you can tolerate it. But if it's a stable elective case, then you might be able to shorten that to, say, three months. I will say that even though we have outcomes data showing that shorter is better, with respect to bleeding, I'm still very concerned that we have not excluded an ischemic hazard by dramatically shortening the therapy. While it looks to be pretty good, I don't have as much confidence in the ischemic outcomes as I do have in the bleeding outcomes.

Dr. Sorrentino:
I remember years ago when the CAPRIE trial came out, one of the first trials with clopidogrel, a lot of cardiologists at that time said that we should be using aspirin and clopidogrel indefinitely in these higher-risk patients. Is there a cohort of patients where DAPT should be considered longer than one year for therapy and what type of patients would you consider for longer term DAPT?

Dr. Gibson:
There probably are; I would point out the fact that after a year, Deepak Bhatt did some analysis showing that if you haven't bled in the first year of DAPT with clopidogrel, you're probably not gonna bleed in the second year; you're not gonna have an increased risk of bleeding. So, in his analysis, if you made it through a year with no excess risk of bleeding, there was no excess risk of bleeding beyond that, so it's almost as though we're giving the person a bleeding stress test. And of course, you know the results of the DAPT study that extending out treatment longer in those people who did not have a bad bleeding outcome, did yield some bleeding in that randomized trial, but also reduced stent thrombosis and recurrent MI. The right patient is obviously going to be the patient who has a high-risk of recurrent ischemic events. Who is that? That patient is usually someone who has multi-vessel disease, someone who is older, someone who may not have actually had an intervention, or, you know, is still at risk of multi-vessel plaque rupture, someone with bad anatomy like left main disease, or a sole-remaining conduit. And again, someone with a lot of metal in their arteries or with complex lesions with a lot of overlapping metal, like a lot of bifurcation stenting. Those are really the center of the bullseye for prolonged DAPT.

Dr. Sorrentino:
For those just joining us, this is *Heart Matters* on ReachMD. I'm Dr. Matthew Sorrentino and I'm speaking with Dr. Michael Gibson about antiplatelet therapy and anticoagulant therapy in patients with cardiovascular disease. Mike, I'd like to make it a little bit more difficult now by adding patients with atrial fibrillation. So, now we've got a patient with atrial fibrillation, a recent MI or a recent insertion of a drug-eluting stent, we know they're at increased thrombo-embolic risk and stroke risk, what are the current recommendations regarding anticoagulation, plus DAPT; is there a current preferred regimen for these patients?

Dr. Gibson:
Yeah. I think we've converged in on the notion that these people should get very brief period of aspirin, you know just after the case or at discharge; probably most of them, I must say, are at very high risk of ischemic event should get their aspirin stopped early. And the best strategy appears to be a novel oral anticoagulant, like rivaroxaban, which I led in pioneer or apixaban, or edoxaban, dabigatran, those would be the right drugs to use with a thienopyridine. In 95% of patients in our studies, they received clopidogrel with a NOAC, not ticagrelor or prasugrel. Remember, those constitute an only, say, 4% ticagrelor or 1% prasugrel in these studies, so we don't have a lot of information about NOACs, plus ticagrelor, or prasugrel. In fact, the guidelines kind of push you away a bit from that choice. And it's always up to you, it's always up to physician discretion, but those are not preferred regimens. Then the duration, if it is someone who is at high risk of bleeding, well, you know, you may only go for a month to 3 months intermediate risk, go for 6 months and if they are in a lower risk of bleeding, you can go for the full 1 year. And then the person remains on a NOAC for their AFib.

Dr. Sorrentino:
Let's switch to the chronic stable patient now. So, we're outside of the drug-eluting stent and the acute coronary syndrome where a patient who has known clinical coronary artery disease now has atrial fibrillation and we started them on a anticoagulant, one of the NOACs, should we continue low-dose aspirin in this group or is it now contraindicated, and we should be stopping aspirin in all of our patients on anti-coagulants?

Dr. Gibson:
Well, I would offer up another solution: to think about continuing the thienopyridine, which does not have the GI distress and that's another thought. I have to say, none of these choices have been that well-studied. There was a Chinese study looking at this question; it's modest size, we don't have definitive data about the right choice, I think it's just like anything we've been talking about, you've gotta kind of look at the patient, if they've tolerated it well, if they are low risk of bleeding, but you're very worried because they have a lot of stents in or a lot metal or complexity or multi-vessel disease, then that's the kind of patient you might want to continue long-term antiplatelet therapy in. But if they've had a rocky course with some bleeds, some nose bleeds, if they're old and frail, then that would pull you back to just giving the NOAC alone. I will point out that in one of the trials I led, ATLAS, believe it or not, rivaroxaban was associated with a 31% reduction in stent thrombosis. So, the thing that makes your platelets the angriest is thrombin and if you're turning down thrombin-generation, you actually have some benefits there in stent thrombosis, so it's not as though you're offering no protection, but if you can get some antiplatelets on board, it wouldn't be bad.

Dr. Sorrentino:
I think that anticipates my, uh, next question. We know in some recent studies, low-dose anticoagulation therapy with aspirin has been shown to give benefit in clinical peripheral arterial disease. Can you let us know if there's any data on benefit of low-dose

anticoagulation with aspirin in patients who have more diffuse coronary artery disease, such as low dose rivaroxaban?

Dr. Gibson:
Yeah, so I led a trial called ATLAS2 where we tested that out, and in these folks, and in the COMPASS study, COMPASS was more stable patients, ATLAS was more acute coronary syndrome patients in the coronary bed, we found that it was very consistent, didn't matter if it was an acute syndrome or a chronic syndrome, that combination of Reva 2.5 plus aspirin or a thienopyridine really reduced events to the same magnitude. We were somewhat surprised that the event reduction was similar for both chronic and acute coronary syndrome, say, after about 30 days. So, in both those kinds of patients, this kind of combination looks quite promising.

Dr. Sorrentino:
Was there an increased bleeding risk that was a problem in ATLAS2?

Dr. Gibson:
There was increased bleeding, but, you know, I think it was misunderstood by many people. The increased bleeding was the same as what would be seen with, say, ticagrelor or prasugrel. Let me explain: both ticagrelor and prasugrel have a 0.6% increase in TIMI major bleeding, non-CABG, TIMI major bleeding compared to clopidogrel. So, you see about a 0.6% uptick over a year. We treated for 2 years and saw a 1.2% uptick, so on an annualized basis, it was, again, a 0.6% per year increase in major bleeding so, the bottom line is if you accept the bleeding associated with ticagrelor, you should find the bleeding associated with rivaroxaban also acceptable.

Dr. Sorrentino:
I have to ask one final question about aspirin. It seems to be one of the most common questions I'm asked, these days. As you know, the efficacy of aspirin as monotherapy has been questioned in a lot of several recent studies. Is aspirin, as monotherapy, still useful in patients with cardiovascular risk factors? I'm thinking of patients who have not had a clinical event, but patients who are at high risk of a clinical event, for example, sub-clinical atherosclerosis, coronary artery calcium score greater than 100. Is there a role for aspirin in this group, or has it pretty much been shown not to give benefit?

Dr. Gibson:
Yeah, you know, that's a really good question, because the person may not have had an event, yet, and so you're really kind of calling it primary prevention but on the other hand, Matt, you know they have the disease, right? So, it's in the spot where, yeah, you've got it, but you just haven't had an event and I don't know that that has been as well-characterized as a pure, kind of, primary prevention population who's a little younger. My gut instinct is if someone could tolerate it, I would go ahead and probably use it.

Dr. Sorrentino:
Well, this has been a great discussion, Mike, and thanks so much for your recommendations on how to approach, which is, still I think, an evolving area on how to use these anti-thrombotic therapies. I want to thank my guest, Dr. Michael Gibson for joining me to discuss antiplatelet and anticoagulant therapy for our patients with cardiovascular disease. Dr. Gibson, it was really great having you on our program today.

Dr. Gibson:
Great chatting with you.

Dr. Sorrentino:
I'm Dr. Matthew Sorrentino. To access this and other episodes in our series, visit ReachMD.com/HeartMatters, where you can Be Part of the Knowledge. Thanks for listening.