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Less Bleeding, Similar Outcomes With Dual vs Triple Therapy After PCI in Patients With A-fib

A new meta-analysis adds further support to concerns that triple therapy may not be the safest strategy in this situation and offers no added efficacy.

By **Todd Neale** *April 24, 2018*

Patients with A-fib who need to undergo PCI may end up receiving triple therapy—aspirin, a P2Y12 inhibitor, and an oral anticoagulant—but a new meta-analysis adds to accumulating evidence indicating that that might not be the best approach.

In pooled results from four randomized trials, use of dual instead of triple antithrombotic therapy was associated with a lower risk of TIMI major or minor bleeding (4.3% vs 9.0%; HR 0.53; 95% CI

0.36-0.85), with a similar but nonsignificant trend for intracranial hemorrhage (HR 0.58; 95% CI 0.23-1.49), according to researchers led by Harsh Golwala, MBBS (Brigham and Women's Hospital, Boston, MA).

That lower risk of bleeding was not accompanied by greater risks of trial-defined MACE (10.4% vs 10.0%; HR 0.85; 95% CI 0.48-1.29) or other clinical outcomes, including all-cause mortality, cardiac death, MI, stent thrombosis, and stroke, they report in a study published recently online ahead of print in the European Heart Journal.

Use of triple therapy in this setting is still relatively common, senior author Deepak Bhatt, MD (Brigham and Women's Hospital), told TCTMD. "I hope these data will provide further reassurance that, for . . . the vast majority of patients with atrial fibrillation undergoing PCI, discharging them on double therapy is likely sufficient and that going to triple therapy increases bleeding risk for sure, including bad bleeding, with no evidence that it actually reduces ischemic or thromboembolic complications."

Commenting for TCTMD, R. David Anderson, MD (University of Florida, Gainesville), said that this meta-analysis confirms that dual therapy reduces bleeding compared with triple therapy and that there is probably enough accumulated evidence at this point to modify guidelines to support that approach.

"The strength of this, I think, is probably enough that the guideline committees are going to have to take a look at changing the recommendations," he said.

"The bleeding risk is substantially reduced [with dual therapy], and I think it's getting to be pretty hard to argue with that," Anderson concluded. "I just don't see a role for triple therapy anymore."

It is estimated that 5% to 10% of patients with A-fib will undergo PCI, and the choice of antithrombotic therapy in this population is tricky because there are indications both for oral anticoagulation and dual antiplatelet therapy (DAPT). Triple therapy incorporating an oral anticoagulant, aspirin, and a P2Y12 inhibitor has been commonly used, but concerns about bleeding have led to the search for a better option.

One strategy that has been evaluated to mitigate the risk of bleeding is dropping one of the antiplatelet agents and using

dual therapy with an oral anticoagulant and either aspirin or a P2Y12 inhibitor. Prior studies have indicated that dual therapy reduces bleeding without increasing ischemic or thromboembolic events, but no individual trial has been large enough to provide a definitive answer.

To assess the totality of the evidence in this area, Golwala, Bhatt, and colleagues pooled trial-level data from four phase III randomized trials that explored the utility of dual versus triple therapy: WOEST, ISAR-TRIPLE, PIONEER AF-PCI, and RE-DUAL PCI. There were a total of 5,317 patients, most of whom (57%) received dual therapy.

The results of the meta-analysis indicated that use of dual therapy cuts bleeding risks without placing patients in harm's way in terms of ischemic or thromboembolic events.

Bhatt acknowledged that some people have criticized these trials for lacking adequate statistical power to look at rare events like stent thrombosis: "For sure, all these trials individually are underpowered for that, but taken together I think there's a reasonable degree of evidence and statistical power."

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> DEEPAK BHATT

But he pointed out that evidence supporting use of triple therapy as the standard in this setting is lacking. "It's just become a de facto gold standard, but it's not as though any large randomized clinical trial ever showed that using triple therapy in these patients is the right thing to do," Bhatt said. It's logical to think that DAPT is needed following stenting, anticoagulation is needed for stroke prevention in A-fib, and combining those regimens together is the best strategy for patients who require both, Bhatt said, adding that he practiced that way for many years.

Now, though, there's enough data to support dual therapy, he said, pointing out that the best combination remains to be seen

considering the large variety of antiplatelet agents and oral anticoagulants that are currently available.

Ongoing trials such as AUGUSTUS and ENTRUST-AF PCI will provide incremental information regarding the best cocktail and whether there are any high-risk subgroups that may benefit from triple therapy, Bhatt said.

"However, I wouldn't wait for those trials before changing practice," he said. "I think folks who are still using routine triple therapy in this population, it's a mistake, because if you do it in enough patients and if you do it for long enough, you'll see some bad bleeding."

He added that shortening the duration of triple therapy after PCI likely will not be sufficient to avoid the bleeding risks, because in the ISAR-TRIPLE trial about half of the "bad" bleeding occurred in the first 4 to 6 weeks.

In addition to questions about the best dual regimen, Anderson said another area of uncertainty is whether longer-term protection against stroke is impaired by using dual versus triple therapy. "I think we probably need longer studies to make sure that there's no loss of stroke risk reduction," he commented.

Sources

Golwala HB, Cannon CP, Steg PG, et al. Safety and efficacy of dual vs. triple antithrombotic therapy in patients with atrial fibrillation following percutaneous coronary intervention: a systematic review and meta-analysis of randomized clinical trials. Eur Heart J. 2018;Epub ahead of print.

Disclosures

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Bhatt reports serving on multiple advisory boards and receiving research funding and royalties from several drug and device manufacturers.

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