WHAT WILL CHANGE IN MY PRACTICE AFTER THE 2018 ESC CONGRESS?

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The ESC congress provides us with the most interesting and controversial data that may possibly change our daily practice. Primary prevention is one of the significant topics that needs lots of attention. During the 2018 ESC congress, in Hotline sessions, the anticipated data from the ARRIVE and ASCEND trials on primary prevention were presented.

ARRIVE TRIAL

The ARRIVE trial was a randomized, double-blind, placebo-controlled, multicenter clinical trial that was conducted to assess the efficacy and safety of aspirin in primary prevention in patients at a moderate risk of cardiovascular disease. The study included more than 12 000 patients without established cardiovascular disease or diabetes, but with multiple cardiovascular risk factors (men ≥55 years old with 2 or more cardiovascular risk factors or women ≥60 years old with 3 or more cardiovascular risk factors). Patients were randomized in a 1:1 ratio to receive either 100 mg aspirin or placebo. The primary efficacy end point was time to the first occurrence of the composite end point, which consisted of cardiovascular death, myocardial infarction, unstable angina, stroke, and transient ischemic attack. There was no overall reduction in major cardiovascular events between groups, even the event rates were lower than expected in both groups (4.29% in the aspirin group vs 4.48% in the placebo group; HR, 0.96; 95% CI, 0.81-1.13; *P*=0.60). In the aspirin group, higher rates of gastrointestinal bleeding were observed; however, the rate of bleeding was also lower than expected (0.97% vs 0.46% in the placebo group; HR, 2.11; 95% CI, 1.36-3.28; *P*=0.0007).

In the per-protocol analysis, there was a significant decrease in the first nonfatal myocardial infarction in the aspirin group (37% vs 72% in the placebo group; HR, 0.53; 95% CI, 0.36-0.79; *P*=0.0014). A subgroup analysis revealed that aspirin may be better in patients with a lower BMI (≤25 kg/m^2) (HR, 0.75; 95% CI, 0.52-1.09; *P*=0.0920). The totality of the study was negative; one of the main reasons

contributing to treatment failure was a dramatically high level of treatment non-adherence (≈40%). Finally, J. Michael Gaziano (US) concluded that "the use of aspirin remains a decision that should involve a thoughtful discussion between a clinician and a patient given the need to weigh the cardiovascular and cancer benefits against the bleeding risks, patient preferences, cost, and other factors."[1]

ASCEND TRIAL

The ASCEND trial was the largest and longest trial that was conducted to assess the efficacy and safety of aspirin and omega-3 fatty acids in primary prevention in patients with diabetes. More than 15 000 patients underwent 2x2 factorial randomization to receive aspirin 100 mg daily or placebo and to receive omega-3 fatty acid supplements (1-g capsules) daily or placebo. The primary efficacy outcome was the incidence of serious vascular events (nonfatal myocardial infarction, nonhemorrhagic stroke, transient ischemic attack, or cardiovascular death, excluding any confirmed intracranial hemorrhage). The mean follow-up was 7.4 years.

Jane Armitage (UK) presented the results from the aspirin arm. A significant reduction in serious vascular events was demonstrated in the aspirin group compared with the placebo group (8.5% vs 9.6%; rate ratio, 0.88; 95% CI, 0.79-0.97; *P*=0.01). Unfortunately, this benefit was accompanied by a significant increase in major bleeding risk (4.1% in the aspirin group vs 3.2% in the placebo group; rate ratio, 1.29; 95% CI, 1.09-1.52; *P*=0.003) with no reduction in the incidence of gastrointestinal cancer (2.0% vs 2.0%, rate ratio, 0.99; 95% CI, 0.80-1.24). She concluded that "the absolute benefits from avoiding serious vascular events were largely counterbalanced by the increased risk of bleeding," so once-daily aspirin should not be routinely prescribed in patients with diabetes for primary prevention.[2]

Louise Bowman (UK) presented the results from the omega-3 fatty acid arm. Daily supplements of omega-3 fatty acid did not result in a reduction in serious vascular events (8.9% vs 9.2%; rate ratio, 0.97; 95% CI, 0.87-1.08; *P*=0.55) or in a reduction in the composite outcome of serious vascular events or revascularization (11.4% vs 11.5%; rate ratio, 1.00; 95% CI, 0.91-1.09). There was no effect on total or cause-specific mortality. Death from any cause occurred in 9.7% of patients in the omega-3 fatty acid group compared with 10.2% in the placebo group (rate ratio, 0.95; 95% CI, 0.86-1.05). There was also a nonsignificant between-group difference in the incidence of cancer (both overall and site-specific cancer) (11.6% in omega-3 fatty acid group vs 11.5% in placebo group; rate ratio, 1.00; 95% CI, 0.99-1.10). Although taking a daily supplement of omega-3 fatty acid remains safe, there was no difference in the rates of nonfatal serious adverse events. Thus, the investigators suggested reconsidering the guideline recommendations.[3,4]

Once-daily aspirin failed in primary prevention in patients without established cardiovascular diseases and moderate cardiovascular risk, either in patients with

diabetes. A similar conclusion can be drawn about omega-3 fatty acid in primary prevention of cardiovascular events in patients with diabetes.

OPTIMIZE HF PROGRAM

Despite the negative results from the primary prevention trials, Yuri Lopatin (RU) presented substantial data from the international multicenter OPTIMIZE HF program about secondary prevention and the increase in physician and patient adherence. The main aim of this study was to evaluate the impact of physician and patient adherence to guideline-recommended therapy on all-cause mortality, death, and rehospitalization rates in patients with heart failure. All included patients (n=635; mean age, 62; 72% male; 75.6% in sinus rhythm) were hospitalized with decompensated heart failure, NYHA class II-IV, and an LVEF less than 40% (mean EF, 33.6%). The follow-up time was 12 months and, at every visit, a five-class guideline adherence score was collected. Adherence was classified as good, moderate, or poor. According to physician adherence, all patients were divided into three groups: good physician adherence (n=224), moderate (n=396), or poor (n=15). In the good and moderate groups of physician adherence, all patients were also divided into three groups depending on their adherence (good, moderate, or poor). In the poor physician adherence group (n=15), all patients also had poor adherence. The rate of all-cause mortality was significantly lower in the group with good physician and patient adherence (2.2%, $P<0.0001$) compared with the groups of moderate or poor physician adherence and poor patient adherence (19% and 21%, respectively). In addition, after the 12-month follow-up, the rates of all-cause mortality and heart failure rehospitalization were significantly higher in all three groups of physician adherence when patient adherence was poor (HR, 2.7; 95% CI, 1.8-3.4; $P=0.0001$).[5] Today, physician and patient adherence remains a cornerstone in the prognosis of patients with heart failure, so it is time to continue the current optimize program and establish new initiatives to optimize the management of patients with heart failure. ■

Declaration of interest: The authors have nothing to declare.

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