Angiotensin Receptor Blockers Not Effective Against COVID-19

A pragmatic randomized clinical trial demonstrated that angiotensin receptor blockers (ARBs), widely used as an antihypertensive and used to treat individuals with a high risk of heart disease, did not improve clinical outcomes among people hospitalized with COVID-19.

Because SARS-CoV-2 enters host cells by binding to angiotensin-converting enzyme 2 (ACE-2) receptors, the investigators evaluated whether modulation of the renin-angiotensin system with ARBs might reduce disease severity.

The trial was conducted at 17 hospitals in Australia and India from May 2020 through November 2021. It included 787 patients whose average age was 49 years and who were naïve to ARBs.

The 778 participants in India were randomly assigned to receive 40 mg/d of telmisartan or to receive placebo for 28 days. In Australia, the ARB type and dose were at the discretion of the treating physician; the control group received only standard of care because the placebo was not available there during the early stage of the pandemic. The primary end point was COVID-19 disease severity using a modified World Health Organization (WHO) Clinical Progression Scale.

After 14 days of treatment, there was no meaningful difference in illness severity between the 2 groups, so the trial was stopped for futility.

The trial cohort had milder disease than anticipated; nearly 75% of the participants returned home by day 7 and nearly all were home by day 14. ARBs may have a different effect among patients with more severe disease or at a higher dose, according to the investigators.

They concluded that although ARBs did not provide benefit in the treatment of COVID-19, the drugs are safe to use in patients with the infection. The results were reported in The BMJ.

Surgical Procedures for Ankle Osteoarthritis Produce Similar Results

Total ankle replacement and ankle fusion were equally effective for improving end-stage ankle osteoarthritis and had a similar number of harms, trialists reported in the Annals of Internal Medicine.

Ankle fusion fuses the bones and prevents ankle joint movement—allowing movement of the other joints in the foot—while total ankle replacement, a newer procedure, replaces the joint to retain ankle joint movement. Over the long term, repeat surgeries may be necessary to replace mechanical joints after total ankle replacement or to alleviate pain in nearby joints from stress and movement after ankle fusion. Patients are often unsure which of the 2 procedures to choose, and this is the first randomized clinical trial comparing them.

The trial’s 303 participants, aged 50 to 85 years, were recruited from 17 outpatient clinics in the UK and randomly assigned to 1 of the surgeries. The participants’ average age was 68 years and 71% of them were men. In the total ankle replacement group, 54% of participants received a fixed-bearing prosthesis and 46% received a mobile-bearing prosthesis. The primary outcome was the change in questionnaire-based walking and standing scores between baseline and 52 weeks after surgery.

The scores improved for both groups. Although the total ankle replacement group’s scores were better, the difference between groups was not clinically or statistically significant. Adverse events also were similar between the groups, but there were more wound-healing complications and nerve injuries in the replacement group and more thromboembolic events and nonunion of the bone in the fusion group. The symptomatic nonunion rate for ankle fusion was 7%.

A post hoc analysis found that fixed-bearing total ankle replacement was superior to ankle fusion when patients had osteoarthritis in adjacent joints. This finding is important given that the investigators also discovered that many patients—43%—had osteoarthritis in adjacent joints before surgery, often without symptoms.

A limitation of the study is that patients were followed up for only 52 weeks.

The authors noted that more time is needed to compare the procedures’ long-term effectiveness.

Intensive Therapy Reduces Risks for Patients With Acute Heart Failure

Patients who were hospitalized for acute heart failure had a lower risk of all-cause death and heart failure readmission when they received early and rapid high-intensity medical therapy after discharge. The international STRONG-HF (Safety, Tolerability and Efficacy of Rapid Optimization, Helped by NT-proBNP Testing, of Heart Failure Therapies) trial is the first randomized clinical trial to compare the safety and efficacy of an intensified protocol of oral heart medications with usual care during the vulnerable early period after discharge.

The study, published in The Lancet, randomly assigned 1078 patients to receive either usual care or high-intensity care prior to discharge from the hospital. High-intensity care involved the up titration of oral heart failure medications to 100% of recommended doses within 2 weeks of discharge and 4 scheduled outpatient visits during the 2 months after discharge. The follow-up visits closely monitored clinical status, laboratory values, and N-terminal pro–brain natriuretic peptide (NT-proBNP) concentrations.

By day 90, blood pressure, pulse, body weight, and NT-proBNP concentration had decreased more in the high-intensity care...
group than in the usual care group. In addition, symptoms, signs of congestion, and quality of life were significantly improved among participants in the high-intensity care group. Heart failure readmission or all-cause death occurred among 15.2% of participants in the high-intensity group compared with 23.3% in the usual care group by day 180.

Adverse events were more common in the high-intensity group—41% vs 29% in the usual care group—but serious or fatal adverse events were similar between the groups. The investigators noted that the increased adverse events in the high-intensity group may have been due to greater opportunities for detection during multiple follow-up visits. The trial was terminated before the investigators enrolled the planned 1800 participants due to the greater-than-expected differences between groups.

**Moderna COVID-19 Vaccine Safe and Effective for Children 6 Months to 5 Years**

A trial found that two 25-μg doses of the mRNA-1273 (Moderna) vaccine were safe for children aged 6 months to 5 years and elicited immune responses consistent with those seen in older children, adolescents, and adults who had received higher doses of the vaccine.

The ongoing phase 2-3 KidCOVE trial was conducted in 2 parts. After the part 1 dose-escalation phase, the investigators chose a 25-μg dose of vaccine for evaluation among children in 2 age cohorts: 2 to 5 years and 6 to 23 months. Interim results were reported in the *New England Journal of Medicine*. The 4048 children aged 2 to 5 years and 2355 children aged 6 to 23 months were randomly assigned to receive two 25-μg injections of mRNA-1273 or placebo administered 28 days apart.

Adverse events were mainly low-grade and transient. At day 57, neutralizing antibody geometric mean concentrations were 1410 among 2- to 5-year-olds and 1781 among 6- to 23-month-olds, compared with 1391 among young adults, who had received 100-μg injections of mRNA-1273 in the COVE trial.

The estimated vaccine efficacy against COVID-19 was 36.8% among 2- to 5-year-olds and 50.6% among 6- to 23-month-olds at a time when the Omicron variant was the predominant circulating variant. Reduced vaccine effectiveness against the Omicron variant has also been observed among adults and adolescents. The long-term effectiveness of mRNA-1273 will continue to be assessed in the trial. — Anita Slomski

Note: Source references are available through embedded hyperlinks in the article text online.