The fight against heart failure remains an uphill battle: Too few effective treatments exist, even after Food and Drug Administration (FDA) approval of ivabradine (Corlanor, Amgen) and sacubitril/valsartan (Entresto, Novartis) in 2015. Researchers described efforts to improve outcomes at HFSA 2019, the 23rd annual scientific meeting of the Heart Failure Society of America, held September 13–16 in Philadelphia.

Clinical Effectiveness of Sacubitril/Valsartan Among Patients Hospitalized for Heart Failure With Reduced Ejection Fraction

• Stephen Greene, MD, fellow in the advanced heart failure and cardiac transplant clinic at Duke University Medical Center, Durham, North Carolina

Use of sacubitril/valsartan has grown little since its FDA approval in July 2015, and a linked-database follow-up study of the Get With The Guidelines–Heart Failure (GWTG-HF) registry of patients with heart failure with reduced ejection fraction showed mixed efficacy results for the drug. Alarmingly, a substantial minority of patients (37.6%) who did not receive sacubitril/valsartan in this study also did not receive either an angiotensin-converting enzyme inhibitor (ACEI) or an angiotensin receptor blocker (ARB).

“Unfortunately, this isn’t the first time these major gaps in quality of care have been identified. Patients who are eligible for therapy do not receive it,” Dr. Greene said. The drug received a class I recommendation in a guideline from the HFSA, American College of Cardiology, and American Heart Association in 2017, but utilization has not picked up. “There’s always a concern that the real-world population will have different results from the clinical trial population,” Dr. Greene explained.

An earlier study found that use of sacubitril/valsartan was 2.3% one year after the drug’s approval. That figure has grown only to 8.1%, according to the study, which merged data from the GWTG-HF registry with Medicare claims data.

Unadjusted data at 12 months showed a statistically significant benefit for sacubitril/valsartan, including an advantage in all-cause mortality (28.9% versus 39.6%), but the comparator group included patients who received neither sacubitril/valsartan nor an ACEI or an ARB. Adjusted all-cause mortality also showed a benefit in those who received sacubitril/valsartan compared with those who received an ACEI or an ARB (hazard ratio [HR], 0.83; \( P = 0.047 \)). Statistical adjustments were necessary because the baseline populations were dissimilar, according to Dr. Greene, who added that data concerning 24 potential confounders were not presented.

Unadjusted, the 12-month results did not show a statistically significant benefit for sacubitril/valsartan compared with an ACEI or an ARB in the rate of heart failure hospitalizations, and even after adjustment, any difference in the rate was not statistically significant (HR, 0.89; \( P = 0.14 \)).

Use of Low-Dose Dopamine in Heart Failure With Preserved Ejection Fraction Patients With Right Ventricular Dysfunction

• Joban Vaishnav, MD, advanced heart failure fellow, Johns Hopkins University Medical Center, Baltimore, Maryland

Effective treatment for heart failure with preserved ejection fraction (HFPEF) remains elusive, but use of dopamine in decompensated patients with right ventricle dysfunction (RVD) may at least reduce hospital length of stay. “The length of stay in patients with RVD who received dopamine was only about seven to eight days, but close to 19 days in those who did not,” explained Dr. Vaishnav, lead author of the poster presentation.

While the characterization of HFPEF remains controversial since its description some five years ago, researchers wanted to revisit the ROPA-DOP study conducted between 2013 and 2016 to explore a hypothesized role of RVD. The original cohort consisted entirely of patients with decompensation, or excessive fluid build-up. Dopamine was not shown to be beneficial, but researchers did not initially explore whether it had utility in patients with RVD.

HFPEF, which usually occurs in women, is defined in part by left ventricular dysfunction, but RVD also occurs in some patients.

Neither the initial study nor the post-hoc analysis presented this year found any statistically significant benefit from dopamine, in patients with or without RVD, but this year’s poster suggested that its use did result in shorter hospitalization for those with RVD (\( P = 0.01 \)). Other researchers have shown that overall outcomes in patients with RVD are worse, although in the post-hoc analysis the comparison just missed statistical significance at \( P = 0.06 \).

“If you look at the absolute rates, one-year mortality was more than double in those patients with RVD. You can’t ignore the fact that 33% of them were not alive after one year,” Dr. Vaishnav observed.

Routine Surveillance for Rejection Greater Than Two Years After Heart Transplant is Not Cost-Effective

• Jessica Golbus, MD, cardiology fellow at the University of Michigan Health System, Ann Arbor, Michigan

Two common methods of monitoring heart transplant patients for organ rejection are cost-ineffective and had an incremental cost-effectiveness ratio of $1.57 million per quality-adjusted life year, researchers found.

The researchers analyzed data from 159 patients who sur-
MEETING HIGHLIGHTS: Digestive Disease Week 2019

Prescription of Less Important Drugs May Lead to Noncompliance With Heart Failure Medications

The higher the number of drugs a heart failure patient has been prescribed, the greater the likelihood of readmission within 90 days, according to a poster presented at the annual meeting of the HFSA.

“We need to be a little more careful in prescribing non–heart failure, non-essential medicines, so that patients are not so overwhelmed with costs and confusion that they’re not sure which are the important medicines, and which ones are not,” said Azam Hadi, MD, associate professor of medicine at Allegheny Health Network in Pittsburgh.

Sometimes these prescriptions are holdover medications that have been prescribed in the hospital. For example, pain medications are commonly part of order set,” added Hadi, an author on poster 61, “Number of prescribed non-heart failure medications predicts readmission following heart failure hospitalization.”

The researchers performed a retrospective cohort study of all patients discharged following heart failure from Allegheny General Hospital in Pittsburgh or Forbes Hospital in Monroeville, Pennsylvania, in 2017 and 2018. Only patients with 90-day follow-up were included; patients awaiting transplant or on inotropy were excluded.

Of 1,367 patients, the average age was 73, 55.23% were male, and 15.14% were African-American, according to the poster. The study included patients classified as having heart failure with preserved ejection fraction (about 40%), Hadi said. At discharge, the average patient was on 1.69 heart failure drugs, plus 11.84 drugs that were not for heart failure, for a total of 13.52 drugs.

“There was clearly a trend towards readmission the more drugs a patient was prescribed,” said Hadi.

For those patients prescribed no more than three non-heart failure medications, the 90-day readmission rate was 27.1%; but for those receiving 21 or more the rate was 48.2% (P = 0.0246). (The effect of polypharmacy on 30-day readmissions just missed statistical significance at $P = 0.0692$).

However, the curves crossed in places. For example, the rate of 90-day readmission for those patients prescribed 19 to 21 non-heart failure medications was 37.2%, actually lower than for those prescribed 16-18 other drugs (41.8%).

“Even seemingly benign medications like Motrin or ibuprofen would be detrimental. Patients feel worse, as the medications have the effect of causing the patient to retain more fluid, thereby affecting the kidneys,” Hadi explained.

Continuous Outpatient Intravenous Inotrope Therapy: Milrinone Is Associated With Improved Survival Compared to Dobutamine Irrespective of Indication

• Gregg Lanier, MD, assistant director of heart failure, Westchester Medical Center, Valhalla, New York

Survival rates for patients receiving milrinone may be significantly more favorable than previously thought, making outpatient inotrope therapy a potential option for heart failure patients awaiting a heart transplant or too sick for a ventricular assist device (VAD).

“VADs are in demand, because the supply of heart transplantations is very limited; the annual rate of 2,000 is very fixed, but the overall demand continues to go up,” said Dr. Lanier, one of the authors of the poster. “My experience locally was pretty favorable with intravenous medication. In this retrospective analysis, survival was much better than studies often referred to, such as the REMATCH trial of 2001.”

In REMATCH, one-year survival for patients receiving continuous outpatient intravenous inotrope therapy was 25%; at two years, survival was just 8%. In the poster at HFSA, by contrast, one-year survival was 70.7% for patients on milrinone; at two years, the figure was 46%, according to the poster. (For patients who received dobutamine instead of milrinone, one-year survival was only 46.2%, according to Dr. Lanier.)

“In that era before defibrillators they used to say that home inotropy was a death sentence,” he said. “I would imagine defibrillator use is close to 90%. The second answer as to why there are improved results is that beta blocker use is most likely higher.”

The retrospective study differentiated between patients who underwent routine rejection surveillance more than two years post-transplant, and those who whose surveillance was prompted by observed clinical change. “In only 1% of patients was rejection detected in a routine study,” said Dr. Golbus, lead author of the poster presentation.

Guidelines from the International Society for Heart and Lung Transplantation suggest surveillance for rejection for up to two years. “Many patients at lower risk undergo surveillance for shorter periods of time, and the guidelines say surveillance might be reasonable for even longer; after five years,” Dr. Golbus said.

In the poster, researchers looked at two methods of surveillance: gene expression profiling via a tool called the AlloMap (estimated 2015 cost, $2,750), and endomyocardial biopsy (about $3,000).

The AlloMap is easy to perform but has a high rate of false positives. Its positive predictive value was only 4.3% six months after transplant. Endomyocardial biopsy is an invasive procedure in which the provider samples heart tissue through the jugular vein.

The outcome was different for patients whose surveillance was triggered by clinical developments. “We had 169 triggered biopsies, and there were 27 that were positive,” Dr. Golbus noted.

“The literature has consistently demonstrated a change over the past 10 to 15 years, that with the newer immunosuppression regimens, the risk of rejection is lower than in the prior era of transplant medicine,” she explained.