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 Abstract

**Impact of the addition of sacubitril/valsartan on ejection fraction in patients with heart failure with reduced ejection fraction**

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**Purpose/Background:**

Heart failure (HF) affects 5.1 million Americans, with the lifetime risk of developing HF being 20% for those 40 years and older. Survival rate has improved over the recent years, however absolute mortality rates remain 50% within 5 years of diagnosis. Pharmacologic management of heart failure includes angiotensin-converting enzyme inhibitors (ACEI), angiotensin receptor blockers (ARB), beta-blockers, aldosterone antagonists, and hydralazine/isosorbide dinitrate.

One of the recent advancements in management is the use of an angiotensin-neprilsyn inhibitor (ARNI). All of these therapies have been shown to improve symptoms, reduce hospitalizations, and decrease mortality. In PARADIGM-HF, ARNI was shown to be superior to ACEI in reducing cardiovascular death and HF hospitalization, with a 20% risk reduction.

When evaluating patients with HF, an echocardiogram (ECHO) is recommended to assess

echocardiographic variables, such as left ventricular ejection fraction (LVEF), diastolic function,

chamber size, ventricular wall thickness, and hemodynamic parameters. After guideline-directed medical therapy is achieved for 3 to 6 months, a repeat ECHO may be done to assess whether device primary prevention of sudden cardiac death to reduce total mortality in selected patients at least 40 days post-MI with LVEF =35% with NYHA class II or III symptoms on chronic GDMT, who have an expectation of survival for at least 1 year.

Limited studies have been conducted to assess the effect of ARNI on these variables, specifically on LVEF as a meta-analysis by Kramer et al. showed that improvement in LVEF was associated with lower rates of mortality among patients with HFrEF. A study conducted by Almufleh et al. found that the addition of an ARNI to the HF regimen resulted in a significant increase in LVEF by an average of 5% over a median of 3 months. Similar improvements were seen in another trial by Ganesananthan et al, which showed a significant improvement in LVEF by an average of 7%.

The PROVE-HF trial examined the association of change in NT-proBNP after initiation of an ARNI with changes in cardiac remodeling. The study found a correlation between the two points as well as an increase in LVEF by 9.4% at 12 months. In the trial, about 75% of patients were on an

ACEI/ARB at baseline. The aim of this study is to evaluate the impact of transition from

ACEI/ARB therapy to ARNI therapy on LVEF in patients with HFrEF in patients, who are on

guideline-directed medical therapy (GDMT). GDMT is defined as ACEI/ARB, beta-blockers, sodium glucose transporter inhibitors, and aldosterone antagonist therapy.

**Objective:**

To determine the effect of sacubitril/valsartan on ejection fraction in patients with heart

failure with reduced ejection fraction.

**Methods:**

This study will be a retrospective cohort study. Evaluation of effect on ejection fraction will be based on ECHO data, dose of sacubitril/valsartan, and concomitant medications. Outcomes assessed will include first EF >35% and EF at 3-5 months, 6-9 months, and 10-14 months. Subjects will be followed for the occurrence of any safety or efficacy outcomes for 1 year after randomization. Outcomes will be statistically evaluated with the descriptive statistics and parametric rank tests.

**Results:**

There were no statistically significant differences in ejection fraction between any groups. In all analyses, mean change in ejection fraction was higher for patients taking sacubitril/valsartan than for patients taking an ACEI or ARB alone.

**Conclusion:**

This study was one of the first to our knowledge analyzing the impact of sacubitril/valsartan in patients with heart failure with reduced ejection fraction. The lack of significant difference between groups may indicate that sacubitril/valsartan’s known benefits may come from other mechanisms than ejection fraction improvement, or that this improvement may be more long-term in nature. It does appear that groups taking sacubitril/valsartan had a higher average of ejection fraction improvement. More studies are needed to identify exact effect of sacubitril/valsartan on ejection fraction.