Depression and Heart Failure? Put Down the SSRI

Put to rest the practice of starting SSRIs in patients with depression and heart failure in an attempt to affect CVD outcomes.

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PRACTICE CHANGER

Do not prescribe selective serotonin reuptake inhibitors (SSRIs) to improve depression and reduce cardiovascular risk in patients with congestive heart failure.

STRENGTH OF RECOMMENDATION

B: Based on one large randomized controlled trial (RCT).[1]

A 60-year-old man presents for a follow-up visit to talk about his congestive heart failure. He has New York Heart Association class 3 heart failure with a left ventricular ejection fraction of 30%. You notice that he is downcast, and based on his self-administered 9-item Patient Health Questionnaire (PHQ-9) score of 17, you determine that he is having a concomitant major depressive episode. Should you start him on an SSRI?

Depression is widely recognized as an independent risk factor for cardiovascular disease (CVD), as well as adverse outcomes in patients with known CVD.[2-5] Previous studies have identified poor health behaviors as the primary underlying link between depression and CVD risk.[2,6] Conversely, a recent systematic review found that positive constructs, mediated primarily through lifestyle behaviors, may have a protective effect on outcomes.[7]

Recently, researchers have focused on treating depression to simultaneously improve CVD outcomes. While some studies have shown SSRIs to be a safe and effective treatment for depression in patients with coronary disease, they have not demonstrated improvement in CVD outcomes.[8,9] However, a post hoc analysis of the ENRICHD trial did suggest that SSRI treatment may improve mortality and morbidity post-MI.[10]

The prevalence of depression among patients with heart failure ranges from 10% to 40%, depending on disease severity.[11] Depression is associated with lower quality of life (QoL), poorer treatment adherence, and higher rates of rehospitalization among patients with heart failure; it is an independent predictor of mortality in this patient population.[1] Until recently, only one RCT (the SADHART-CHF study) looked at SSRI treatment in patients with heart failure and depression.[12] In that 12-week trial, sertraline did not improve depression or CVD outcomes when compared with placebo—but the study period may have been too short to capture long-term outcomes.

STUDY SUMMARY

SADHART-CHF, but better

In the MOOD-HF study, investigators sought to determine whether SSRI treatment for depression in patients with heart failure could improve CVD outcomes over a longer study period (up to 24 mo).[1] Specifically, this RCT assessed whether treatment with escitalopram could reduce morbidity and mortality risk in patients with comorbid chronic systolic heart failure and depression.

This double-blind, placebo-controlled trial was conducted at 16 tertiary medical centers in Germany between 2009 and 2014. Adult patients with New York Heart Association class 2 to 4 heart failure and left ventricular ejection fractions < 45% were screened for depression using the PHQ-9. Patients with PHQ-9 scores ≥ 12 underwent a structured psychiatric interview with a psychiatrist or psychosomatic specialist, and those diagnosed with major depression were in-

vited to participate in the trial. Patients with recent SSRI use and/or psychotherapy were excluded.

Eligible participants were randomized to receive either escitalopram (10-20 mg/d) or placebo for up to 24 months, in addition to standard heart failure care. The starting dose of 5 mg was increased to 10 to 20 mg as tolerated until week 12 of the study; the dose at 12 weeks was considered the maintenance dose. Psychiatric and medical assessments were performed every six months during the study period. Depression severity was assessed using the 10-item Montgomery-Åsberg Depression Rating Scale (MADRS).

Outcomes. The study used a composite endpoint of all-cause death or hospitalization; the primary outcome was time to first event of this composite. Secondary outcomes included MADRS score at 12 weeks, anxiety as assessed by the Generalized Anxiety Disorder 7-item scale, and health-related QoL as assessed by the Kansas City Cardiomyopathy Questionnaire (KCCQ). The sample size was calculated to achieve 80% power for the primary outcome. Baseline characteristics between the intervention and placebo groups were balanced after randomization, and the modified intention-to-treat study population included participants who took at least one dose of the study medication.[1]

Results. Ultimately, 372 participants were included in the analysis (185 escitalopram, 187 placebo). A primary endpoint event occurred in 116 participants (63%) in the escitalopram group and in 119 participants (64%) in the placebo group (hazard ratio [HR], 0.99).[1] No differences were found between treatment groups for the primary endpoints in either adjusted or unadjusted analyses.

The mean MADRS score changed from 20.2 at baseline to 11.2 at 12 weeks with escitalopram, and from 21.4 to 12.5 in the placebo group (between-group difference, –0.9).[10] Overall, the two treatment groups had comparable daily medication doses and mean treatment duration (18 mo), and both groups demonstrated partial remission of depression symptoms, improved health status, and improved QoL over the study period.

Interestingly, the placebo group experienced significantly improved QoL at 12 months.[1] There were no between-group differences in adverse events or safety measures.[1] The trial was discontinued prematurely based on futility after a recommendation from the data and safety monitoring committee.

WHAT'S NEW

Longer study period/different SSRI

The MOOD-HF trial directly addresses the major criticism of the SADHART-CHF trial by conducting the study over a much longer duration (up to 24 mo vs 12 wk). Also, in contrast to SADHART-CHF, this trial studied escitalopram rather than sertraline, because some evidence indicates that escitalopram is superior at treating primary depression.[13] Despite these differences, the results of MOOD-HF are consistent with the findings of SADHART-CHF: SSRI treatment for patients with heart failure and depression did not reduce the elevated morbidity and mortality risk seen with these comorbid conditions.

Also consistent with SADHART-CHF findings, participants in both groups in the MOOD-HF trial had partial remission of depressive symptoms over the study period, with no significant difference between those treated with escitalopram versus placebo. Given that this high-quality trial replicated the findings of SADHART-CHF with a longer treatment period and a potentially more effective SSRI, the results of MOOD-HF should put to rest the practice of initiating SSRI treatment in depressed patients with heart failure in an attempt to affect CVD outcomes.

CAVEATS

There are other SSRI fish in the sea

There are other SSRIs, besides escitalopram and sertraline, available for use. However, it is likely that this is a class effect.

Additionally, none of the patients in this trial had severe depression, as their PHQ-9 scores were all below 19. Therefore, it remains to be determined if treating severe

depression has an impact on cardiovascular outcomes.

Lastly, and most importantly, this study only looked at initiating SSRIs for depression in the setting of heart failure. The trial did not include patients already taking SSRIs for pre-existing depression. Thus, the results do not imply evidence for discontinuing SSRIs in patients with heart failure.

Treating comorbid depression and CVD to mitigate the elevated risk for adverse clinical outcomes remains nuanced and elusive. The same can be said of non-CVD chronic conditions (eg, diabetes) based on recent systematic reviews.[13] In sum, these studies suggest that a traditional screen-and-treat approach using SSRIs for depression treatment to affect chronic disease outcomes (that are likely lifestyle-related) may not be cost-effective or patient-centered.

A recent study showing that cognitive behavioral therapy did improve depression—but not heart failure—among patients with both conditions reaffirms that teasing out the impact of depression on lifestyle behaviors and chronic disease outcomes among multimorbid patients is more complex than previously thought.[14] Nevertheless, this area of research should continue to be explored, given the worsened chronic disease outcomes in the presence of depression.

CHALLENGES TO IMPLEMENTATION

Changing the tide can be difficult

As with any behavior change, we expect that it will be a challenge to convince providers to stop initiating SSRI treatment to affect cardiovascular outcomes in patients with depression and heart failure—especially given the body of evidence denoting depression as a risk factor for increased morbidity and mortality in this population. **CR**

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