

Editor's Page

Increasing Complexity of Heart Failure Therapy Requires Earlier and More Frequent Referral

LARS H. LUND, MD PhD^{1,2}*Stockholm, Sweden*

Looking back over 50 years since the 1st heart transplantation in 1967, there have been remarkable advances in the therapy of heart failure with reduced ejection fraction. The neurohormonal hypothesis explained why HF did not heal but instead progressed spontaneously. This paved way for a remarkable series of randomized controlled trials (RCTs) establishing angiotensin-converting inhibitors (ACEi) and angiotensin receptor blockers (ARB), beta blockers and mineralocorticoid receptor antagonists as life-prolonging therapy in a broad range of patients with HFrEF.

But HFrEF therapy introduced thereafter has been indicated in only some patients with HFrEF – “one size fits some”¹; e.g. cardiac resynchronization therapy (CRT) only in the presence of prolonged QRS (approximately 1/3 of HFrEF patients²). Implantable cardioverter defibrillators (ICDs) may not be beneficial for all patients with HFrEF, as a recent trial suggested absence of benefit in elderly patients with non-ischemic cardiomyopathy.³ Intravenous iron requires functional iron deficiency and the sinus node inhibitor ivabradine requires sinus rhythm ≥ 70 beats per minute despite maximum tolerated beta blockade, which is rare.⁴

Angiotensin-receptor neprilysin inhibition (ARNi) was a major breakthrough not only because it reduced all-cause mortality on top of optimal baseline therapy, but also because it suggested that not all neurohormonal compensation is maladaptive; boosting the endogenous levels of compensatory natriuretic peptides turns out to be adaptive and beneficial for hemodynamics, symptoms and survival. This changed HF teaching from a focus on neurohormonal blockade to neurohormonal modulation. However, due to the fact that the PARADIGM-HF trial required a run-in demonstrating tolerance to target doses of both enalapril and sacubitril/valsartan,⁵ and registry data suggesting that only a minority of HFrEF patients

meet PARADIGM criteria,⁶ guidelines and payers generally do not support the use of ARNi in all patients with HFrEF. The recent PIONEER trial may justify broadening the use of ARNi to both hospitalized and ACEi/ARB naïve patients.⁷

Since ARNi was introduced, novel HFrEF interventions have continued to be tested in increasingly selected populations. In patients with HFrEF and symptomatic paroxysmal or persistent atrial fibrillation, catheter ablation reduced the composite of HF hospitalization or death from any cause.⁸ However, there were concerns regarding patient selection, screening failures and trial design that suggest that catheter ablation may be suitable only for a strictly selected minority of HFrEF patients with AF. Secondary mitral regurgitation has long been considered a marker of more severe left ventricular dilation and severity of HF rather than a direct cause of HF progression and morbidity. Therefore it is difficult to interpret 2 recent trials of percutaneous mitral-valve repair for secondary MR in HF. The French MITRA-FR was neutral,⁹ whereas the North American COAPT trial demonstrated reduction in the composite of HF hospitalization and all-cause death.¹⁰ It has been suggested that a greater MR in relation to ventricular dilatation (“disproportionate MR”),¹¹ more common in COAPT than in MITRA-FR, may identify candidates more likely to benefit. Yet a post-hoc analysis from COAPT could not identify and echocardiographic sub-groups more or less likely to benefit.¹²

Because recent HFrEF interventions appear suitable for increasingly selected patients, it is now more than ever critical that we encourage timely referral to multidisciplinary HF teams. These teams, rather than the general cardiologist or internist, can both determine indications and contraindications for particular interventions, and make complex choices among many different potential interventions as well as their optimal timing. Basic medical HFrEF therapy is indicated in a broad range of patients with HFrEF, is relatively low-risk, and is clearly cost effective; for these patients, treatment decisions are easy. In contrast, the decisions to proceed with advanced HF interventions in highly specific and targeted patient subgroups, are best performed by the advanced HF team.¹³ Given recent intriguing data, particularly with catheter based interventions, timely referral to comprehensive expertise is imperative.

From the ¹Karolinska Institutet, Department of Medicine, 17177 Stockholm, Sweden and ²Karolinska University Hospital, Heart and Vascular Theme, 17176 Stockholm, Sweden.

Correspondence: Lars H. Lund MD, PhD, Karolinska Institutet, Solna, 17176 Stockholm. Fax: +46-8- 311044, Phone: +46-8-51770000. E-mail: lars.lund@alumni.duke.edu

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