CASE REPORT

Hybrid Heart Failure Treatment

Antonis S. Manolis, MD,[1] *Antonis A. Manolis, MS, BSc[2]

[1]First Department of Cardiology, Athens University School of Medicine, Athens, Greece
[2]Patras University School of Medicine, Patras, Greece

* E-mail: asm@otenet.gr

Abstract

A case of refractory heart failure (HF) is presented in a 64-year-old gentleman with ischemic cardiomyopathy and severe left ventricular dysfunction, who availed himself of currently available hybrid HF treatment, like optimal medical treatment, electrical and interventional therapies comprising drugs, an implantable cardiac resynchronization therapy defibrillator (CRT-D) effected via alternate route (middle cardiac vein) for left ventricular lead placement combined with percutaneous mitral valve therapy (MitraClip) that prolonged his life to ~10 years. ***Rhythmos 2021; 16(1):99-101.***

Key Words: heart failure; cardiac resynchronization therapy; implantable cardioverter defibrillator; left bundle branch block; cardiac dyssynchrony; biventricular pacing

Abbreviations: ARB = angiotensin receptor blocker; ARNI = angiotensin receptor neprilysin inhibitor; AV = atrioventricular; BB = beta-blocker; CAD = coronary artery disease; CRT = cardiac resynchronization therapy; CRT-D = cardiac resynchronization therapy-defibrillator; CRT-P = cardiac resynchronization therapy-pacemaker; CS = coronary sinus; ECG = electrocardiogram; ICD = implantable cardioverter defibrillator; LBBB = left bundle branch block; LV = left ventric-le(-ular); LVEF = left ventricular ejection fraction; MCV = middle cardiac vein; MRA = mineralocorticoid receptor antagonist; NIPS = noninvasive programmed stimulation; NS = phrenic nerve stimulation; NYHA = New York Heart Association

Introduction

Cardiac resynchronization therapy (CRT) is standard therapy for patients with heart failure (NYHA class II-ambulatory IV), reduced left ventricular (LV) ejection fraction (LVEF <35%) and prolonged (>130-150 ms) QRS (cardiac dyssynchrony) usually in the form of a left bundle branch block (LBBB).[1, 2] It is effected via biventricular pacing with the LV lead inserted via the coronary sinus (CS) and placed at a posterolateral venous branch. It can be applied via a pacemaker (CRT-P) or implantable cardiac defibrillator (ICD) device (CRT-D). However, obtaining a stable and functional LV lead position remains a challenge.[3] Furthermore, this electrical therapy needs to be combined with optimal medical therapy, optimal device programming, and other percutaneous and/or surgical interventions (e.g., revascularization, correction of severe mitral regurgitation, conversion of arrhythmias, etc.).[4, 5] We herein present such a complex case of a patient with severe LV dysfunction and refractory heart failure who availed himself of these hybrid therapies as they were progressively becoming available during his lifetime.

Case Report

A 64-year-old gentleman with history of an old anterior myocardial infarction (MI) and s/p coronary artery bypass grafting (CABG) for 2-vessel coronary artery disease (CAD) developed severe LV dysfunction (LVEF ~20%) and heart failure (NYHA class III →IV) refractory to medical therapy. He also had moderate to severe (functional) mitral regurgitation (MR 3-4+). The electrocardiogram (ECG) displayed LBBB. Thus, he had a biventricular pacemaker system implanted in April of 2006 with the LV lead placed at a posterolateral CS branch (**Fig. 1**, thin arrow) at another hospital. However, at this position he suffered from persistent phrenic nerve stimulation (PNS), which could not be remedied by re-programming. He sought a second opinion and was referred to our hospital 2 months later (June 2006).

Indeed, even at threshold levels of pacing output and at all possible lead configurations programmable, there was persistent PNS and re-intervention was recommended.

Procedure

Through the CS and with use of an angioplasty wire technique, all available lead positions, albeit limited due to anatomy, at the lateral CS branches failed to reliably pace while avoiding PNS.

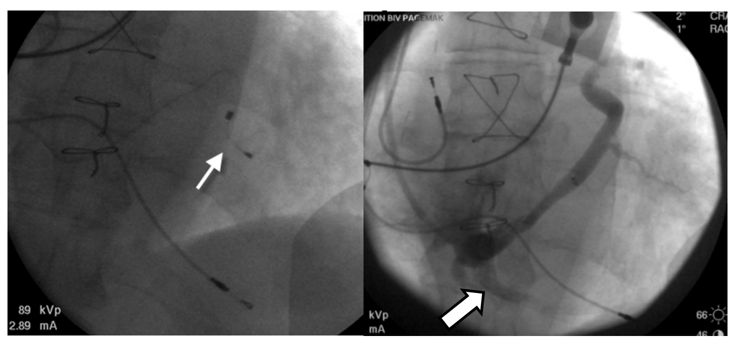

Figure 1

Thus, cannulation was attempted, and finally achieved with some difficulty, of the middle cardiac vein (MCV) originating at the CS os at an acute angle take-off (thick arrow/**Fig. 1**). The pacing lead was placed via the MCV at an apical postero-lateral position (arrow/ **Fig. 1C**). Pace and sense thresholds were excellent.

Patient's course was uncomplicated. Post-

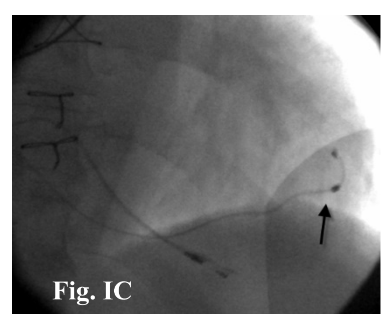

Fig. IC

procedurally, he had an echo-guided optimization of AV and VV intervals and best LV outflow tract velocity time integral (VTI), a surrogate of cardiac output, was obtained with simultaneous RV and LV pacing (VV interval=0) (**Fig. 2**).

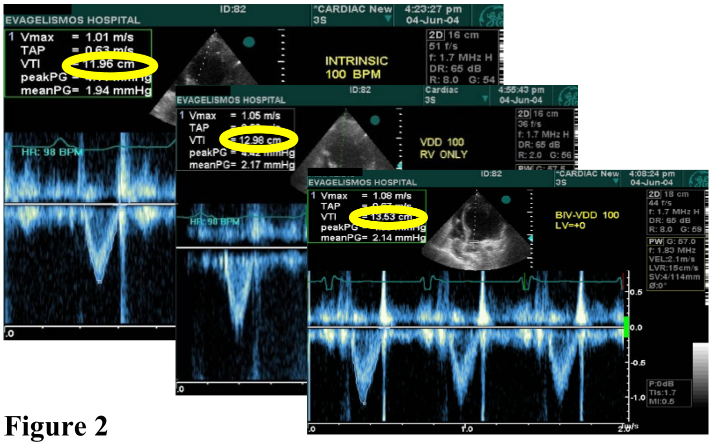

Figure 2

Over the subsequent years he remained without PNS with excellent pace/sense thresholds, considerably improved clinically (from NYHA class III-IV to a class I-II status); MR decreased from severe (3-4+) to moderate (2+).

Mitral Regurgitation

Upgrade from CRT-P to CRT-D at 2 years was performed due to runs of non-sustained ventricular tachycardia (NSVT). At 3 years, he required pulse generator replacement due to battery depletion. Mitral regurgitation (MR) was initially reduced post-CRT, but then gradually increased (**Fig. 3**) with worsening clinical status. At 5 years since the initial implant, the patient was submitted to percutaneous MitraClip insertion which significantly reduced the degree of MR.

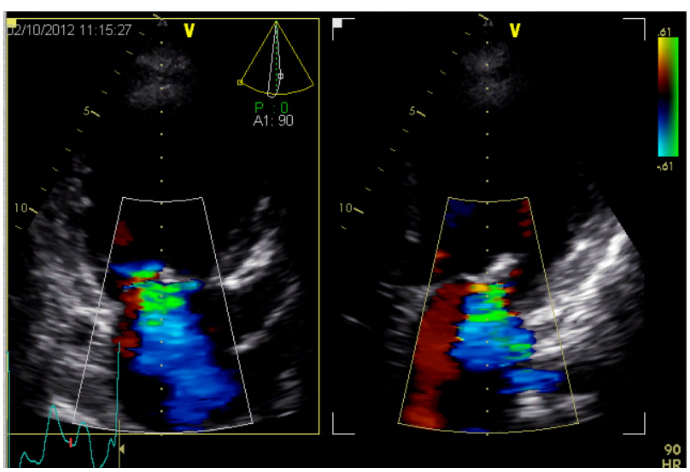

Figure 3

Patient's course post-MitraClip placement was complicated by acute kidney injury (AKI) with worsened renal function. As mentioned, MR was initially reduced from 3^+- 4^+ to 1^+-2^+

Atrial Flutter

Then, atrial flutter (!) developed (**Fig. 4**), which was interfering with CRT leading to worsened clinical status. Thus, conversion was attempted via the noninvasive programmed stimulation (NIPS) function of the CRT-D device with use of overdrive atrial pacing. However, this maneuver led to degeneration of atrial flutter into atrial fibrillation (**Fig. 4D**, arrows), which was subsequently cardioverted electrically with use of a shock at 5 joules delivered by the device (thick arrow, **Fig. 4D**).

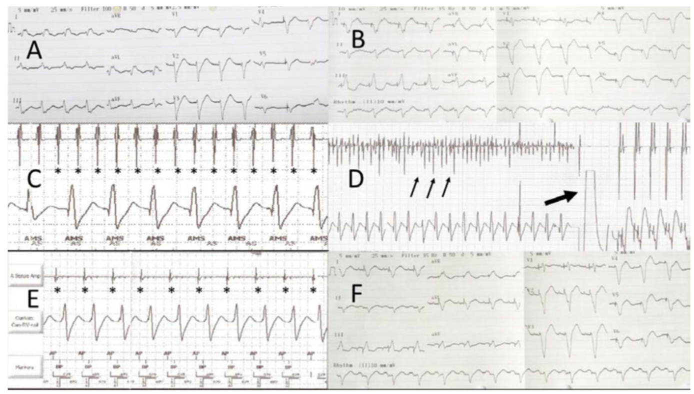

Figure 4 / Manolis AS et al. Hosp Chronicles 2014;9(1): 39–41.[5]

Medical Therapy / Patient's Course

Over the years, the patient was maintained on optimal medical therapy with use of an angiotensin receptor blocker (ARB), a beta-blocker (BB), a diuretic, and a mineralocorticoid receptor antagonist (MRA). During periods of clinical worsening, he also received periodic treatment with 24-hour intravenous (IV) infusion of levosimendan. After stabilization of one of these periods of clinical worsening, the patient was also submitted to coronary angiography which determined the patent status of his saphenous venous grafts.

With use of this combined anticongestive regimen (ARB, BB, diuretic, MRA, periodic levosimendan), the patient fared well for an additional 3 years. Then the angiotensin receptor-neprilysin inhibitor (ARNI), sacubitril-valsartan, became available and the patient was placed on this agent, starting at 24/26 mg-dose, which was gradually uptitrated to the 49/51 mg dose (December 2015). He fared well for an extra 1 year (!); during this time, he received an appropriate ICD shock. Then worsening renal function ensued, leading to worsening heart failure symptoms. He finally succumbed to a low-cardiac-output state at 10.5 years after initial CRT device implantation.

Discussion

Occasionally, for CRT, it is not feasible to place an LV lead in a suitable CS tributary to avoid PNS and/or obtain adequate pace/sense thresholds.[2-4,6] Then, alternate site pacing may be required which is usually inferior to CRT or surgery will be needed, with its attendant risk, for epicardial LV lead placement to effect CRT.[1,2,6,7] MCV pacing avoids PNS, offers optimal CRT and obviates surgery for epicardial lead placement. When LV lead positioning through the CS and into its lateral tributaries is either not feasible or associated with persistent PNS or high thresholds, cannulation of the MCV, albeit technically difficult, and lateral lead positioning via this vein, may offer an excellent alternative for optimal CRT, avoid PNS and obviate need for surgery for epicardial lead placement.

The availability of several modes of HF therapy, applied in a hybrid model that includes optimal medical therapy,[8] comprising a RAS inhibitor (ACEI or ARB), a beta blocker, a diuretic and an MRA,[9, 10] periodic levosimendan infusion,[11] a regimen which was recently enhanced with the availability of an ARNI,[12] combined with CRT with optimal AV/VV interval programming and electrical therapies (cardioversion of arrhythmias) incorporated into the CRT-D device,[5] together with percutaneous correction of severe MR via the MitraClip,[13, 14] all have contributed, as demonstrated in this case, to significantly extending (to 10 years in this case) the life of patients with refractory HF, once considered a highly lethal diagnosis with half of HF patients succumbing to this disease within 2 years. Importantly, additional defibrillator therapy to patients receiving CRT (CRT-D) is associated with a reduced all-cause mortality, particularly in patients with ischemic cardiomyopathy and/or those aged <75 years.[15]

Conclusion

Currently available hybrid therapies (medical/ electrical/interventional) and innovating approaches to CRT prolong the survival in refractory HF patients (NYHA III-IV), as demonstrated in this case of ischemic cardiomyopathy, severe LV dysfunction with very low LVEF (20%). Difficulties in applying CRT with placement of the LV lead in classical posterolateral CS tributaries, can be effected via an alternate route with use of the MCV. This hybrid therapy entails optimization of medical therapy, optimal AV/VV interval programming of the CRT device, percutaneous correction of severe MR amenable to MitraClip, and non-invasive conversion of arrhythmias (e.g., atrial flutter, AF, ventricular arrhythmias) which can compromise CRT. Thus, availing of existing (ARB, BB, diuretic, MRA, levosimendan, CRT-D) and new therapies as they become available (MitraClip, ARNI), the life of our patient with refractory HF and very low LVEF was extended to 10.5 years!

References

1. Manolis AS. Cardiac resynchronization therapy in congestive heart failure: Ready for prime time? *Heart Rhythm* 2004;1:355-63.
2. Manolis AS, Sakellariou D, Andrikopoulos GK. Alternate site pacing in patients at risk for heart failure. *Angiology* 2008;59:97S-102S.
3. Manolis AS, Koulouris S, Tsiachris D. Electrophysiology Catheter-Facilitated coronary sinus cannulation and implantation of cardiac resynchronization therapy systems. *Hellenic J Cardiol* 2018;59:26-33.
4. Pastromas S, Manolis AS. Cardiac resynchronization therapy: Dire need for targeted left ventricular lead placement & optimal device programming. *World J Cardiol* 2014;6:1270-7.
5. Manolis AS, Koumoulidis A, Papadimitriou P, Sakellaris N. ICD device assistance in diagnosis and management of atrial tachyarrhythmia. *Hosp Chronicles* 2014;9:39-41.
6. Manolis AS, Tolis P. Right ventricular septal pacing: In lieu of biventricular pacing for cardiac resynchronization in a patient with right bundle branch block? *Rhythmos* 2015;10:62-63.
7. Manolis AS, Voyiantzakis N, Lazaros G. Improved cardiac output with right ventricular septal pacing in a patient with RBBB and LV dysfunction. *Rhythmos* 2016;11:12-13.
8. Duncker D, Veltmann C. Device therapy in heart failure with reduced ejection fraction-cardiac resynchronization therapy and more. *Herz* 2018;43:415-22.
9. Manolis AA, Manolis TA, Melita H, Manolis AS. Eplerenone vs spironolactone in resistant hypertension: an efficacy &/or cost or just a men's issue? *Curr Hypertens Rep* 2019;21:22.
10. Manolis AA, Manolis TA, Melita H, Manolis AS. Spotlight on spironolactone oral suspension for the treatment of heart failure: Focus on patient selection and perspectives. *Vasc Health Risk Manag* 2019;15:571-79.
11. Thorvaldsen T, Benson L, Hagerman I, et al. Planned repetitive use of levosimendan for heart failure in cardiology and internal medicine in Sweden. *Int J Cardiol* 2014;175:55-61.
12. Manolis AS, Manolis TA, Manolis AA, Melita H. Neprilysin inhibitors: Filling a gap in heart failure management, albeit amidst controversy and at a significant cost. *Am J Cardiovasc Drugs* 2019;19:21-36.
13. Sobajima M, Fukuda N, Ueno H, Kinugawa K. A case report of advanced heart failure refractory to pharmacological therapy who was successfully recovered by combinatory use of CRT, impella and MitraClip. *Eur Heart J Case Rep* 2020;4:1-5.
14. Giaimo VL, Zappulla P, Cirasa A, et al. Long-term clinical and echocardiographic outcomes of Mitraclip therapy in patients nonresponders to cardiac resynchronization. *Pacing Clin Electrophysiol* 2018;41:65-72.
15. Long YX, Hu Y, Cui DY, Hu S, Liu ZZ. The benefits of defibrillator in heart failure patients with cardiac resynchronization therapy: A meta-analysis. *Pacing Clin Electrophysiol* 2020 Dec 29. doi: 10.1111/pace.14150. Online ahead of print.