Roundtable Discussion: Optimal Strategies for Improving CRT Outcomes within the Real-World Practice Setting

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ABSTRACT. Gery Tomassoni, MD, FACC, FHRS (Lexington, KY, USA): In this roundtable discussion portion the Optimal Strategies for Improving CRT Outcomes within the Real-World Practice Setting, we are going to start with several questions. I will start the session by asking Dr. Singh and Dr. Varma how they determine if a patient responds adequately to cardiac resynchronization therapy (CRT).

KEYWORDS. Cardiac resynchronization therapy, non-responsive, response rate, heart failure.

Discussion

Gery Tomassoni, MD, FACC, FHRS (moderator): Welcome to the Roundtable on the Optimal Strategies for Improving CRT Outcomes within the Real-World Practice Setting. In this roundtable, we will discuss the strategies for improving CRT outcomes. I will start the session by asking our experts a very important question: How do you determine if patients respond adequately to cardiac resynchronization therapy (CRT)?

Jagmeet Singh, MD, DPhil: That is an interesting question, because a lot of controversy is attached to it. Most physicians look at anatomical endpoints, such as reverse remodeling, for ascertainment of response. On the other hand, some physicians say that if the patient is not feeling better, if his or her quality of life is not better, and the New York Heart Association (NYHA) class is not better, the patient is a non-responder. Response cannot be classified in a dichotomous fashion as a responder or a non-responder. One needs to look at it as a continuum where someone could be called a mild responder, a moderate responder, a high responder, or a super responder. If you maintain stability in a patient's clinical course and he or she has not had heart failure hospitalizations, which the patient had before, there has been no change in the patient's ejection fraction or quality of life, but at least the patient has not been hospitalized, you could call the patient a limited responder. Depending on whether the patient has improvement in his or her quality of life, in the NYHA class, without any improvement, I would call the patient a mild responder. If the patient has had a significant improvement in quality of life along with improvement in ejection fraction, I call the patient a moderate responder. Obviously, high responders are people who almost normalize their ejection fraction. I look at it as a continuum.

Niraj Varma, MA, MD, PhD, FRCP: I agree with Dr. Singh. We treat patients to treat symptoms and also to improve their outcomes. Outcomes for the heart failure population are heart failure hospitalization and survival. If we reduce heart failure hospitalization, that is a significant response. For improved survival, that is a very significant response. If we make patients feel better, that itself is a therapeutic effect. There is a spectrum of effect, as there is with pharmacological tools. When we treat patients, some people do very well. It is usually a minority. Some people do less well and some do modestly. Still, that is an improvement. One of our roles is to improve the progress...
of patients who are doing modestly well, because there are certain techniques that we can use and that we are beginning to understand, particularly with programming. With interventions for structural heart disease, whether it is valvular regurgitation or intercurrent ischemia, there are several other things, but post-implant monitoring is very important.

Singh: The way we quantify response has a fair amount of subjectivity to it, when we look at quality of life, 6-minute walk test, and the like. These devices have the ability to give us a lot of diagnostic information. For example, the devices can measure physical activity, they can measure heart rate trends, and they can measure transthoracic impedance. In the future, these measures will help us define response because they will be more objective than the conventional measures that we use right now.

Tomassoni: It will be even more amazing if we can use the data to guide individualization of AV optimization and VV optimization to maximize the chance of responding.

Varma: We have that data instantly available with remote monitoring, but managing that data and assessing the signals from that data, which are important to patient intervention, is a current challenge.

Singh: The field is moving in the direction where a lot of the data will be processed, but they will be also used with baseline covariate data depending on sex, age, and other comorbidities. All of that will eventually get integrated, and then we can individually classify response for certain patients. Again, the fact that we classify response as a whole is really interesting. You need to classify it at the individual level, where they were and where they are now, rather than just saying where they fit into the bucket that we are using for response.

Tomassoni: CRT pacemakers versus CRT implantable cardioverter-defibrillators (ICDs): mortality benefit has been shown for both populations. When do you decide about putting in a pacemaker versus a pacemaker with an ICD in a CRT patient?

Varma: We have CRT-P and we have CRT-D. Indications for CRT-D are generally those patients with depressed ejection fraction who otherwise merit ICD implantation. For CRT-P, we have a wide variety of candidates. We have patients with depressed left ventricular (LV) function but probably above 35%. We have patients with non-ischemic cardiomyopathy perhaps related to atrial fibrillation. They are going to have AV nodal ablations or perhaps an increase in recent right ventricular pacing burden from already implanted pacemakers. These are the types of patients in whom I might consider a CRT-P. I also offer this as an option to my patients who are elderly, outlining the benefits of CRT-P versus CRT-D.

Singh: Dr. Varma has touched on all of the different nuances related to when you decide between a CRT-P and CRT-D. The bottom line, however, is a one-on-one discussion with patients, elucidating to them the benefits of one versus the other and the detractors of one versus the other and making them a part of that decision-making process. The bigger part of this decision usually comes in the elderly. With the elderly, there are many other measures, such as physiology or frailty index and the like, that we should be incorporating into our electrophysiological practices, but we are not there yet. Individualizing the decision with a detailed conversation with the patient is often the way I make these decisions.

Tomassoni: A common question that I get asked many times is regarding the time of generator change out. If patients have CRT-D devices and their ejection fraction has somewhat improved, should you downgrade them to CRT-P because of the cost-effective value of this treatment plan?

Singh: That is a burgeoning field of investigation right now. We published a meta-analysis on the long-term impact of an improved ejection fraction in patients who received ICDs. This was published recently in the European Heart Journal. We found that if they have improved above 45%, their incidences of shocks were minimal. Some data from other centers showed that if you are a super responder with complete normalization of your ejection fraction, the risk of ICD therapy is equivalent to a normal population. Again, there are nuances to this. It is not a 100% guarantee. It is an individualized decision with the patient. Rather than call it a downgrade, I call it an upgrade, because they have done so well that you can congratulate them and say, “You do not need the defibrillator anymore. You should be okay with the pacemaker.” It is an evolving question, and there will be some trials to answer this question prospectively.

Varma: It is a difficult choice for a patient who has been committed to a defibrillator for low ejection fraction, and then the question arises about upgrading, as you say, to a pacemaker. In our population, we looked at our group of super responders, at least those who had completely normalized the LV function, and the risk of ventricular rhythm errors was no larger than that of the general population. The survival was equivalent to that of the general population. I would look for complete normalization of the LV function and I would look for lack of ventricular arrhythmia history on the defibrillator platform before I would offer it to them.

Tomassoni: Do you feel that quadripolar technology should be a standard of care? Should all patients now get a quadripolar lead?

Singh: I would have a kneejerk reflex to that and say yes. Not only does it provide many more options for the patient, but it provides a fair amount of solace to somebody like me, who is implanting these leads. I go into the procedure comforted by the fact that I am going to come out successful and not worried about locations, stability, phrenic nerve pacing, and dislodgement because you can put the lead distally as far as you want. It does a lot of good for the patient, but it also does a lot of good for the implanting physician.

Varma: It is my first choice. I will use a quadripolar lead if a vessel is available to accommodate it.

Tomassoni: Let us talk about preprocedural evaluation of patients undergoing CRT. Should it be a standard of care that patients get some type of imaging or coronary
Singh: One area where we do perform imaging now for patient selection is when patients are referred to us as non-responders from other institutions or within our institution. We will perform echocardiographic imaging with speckle tissue tracking to see if there is any residual mechanical dyssynchrony. If there is, we will perform a CT to look at venography and to look at the coronary venous branches that are still available. Then we will decide if we are going to give the patient a second chance with a revision of the LV lead to another location. In the future, the possibility of having endocardial pacing will arise. Once we have endocardial pacing, maybe we will still use imaging, but we will use hemodynamic measures interprocedurally to help guide us also.

Tomassoni: You mentioned CRT non-responders. We know that individually there could be many different factors in a particular patient, but if there was one hard-pressed factor that you think is the most important, which one would it be?

Varma: I would say lead position plus programming. That is technically two things, but I think they are linked.

Singh: I would say lead positioning if I had to choose one. A variety of patients may be potentially non-responders, but if you could position the lead appropriately in those patients, you could have a response. The additional impact of programming compared to lead positioning is less incremental.

Varma: Let me challenge you on that. In certain subgroups, the apex might still be viable, but let us say we avoid the LV apex as a lead position. If we remove the septal segments, you have more than 10 segments that have equal probability of producing the best hemodynamic response.

Singh: That is why I think lead positioning is important, because you are not looking at the apex. What you are trying to do is find the area that has the maximal electrical delay where you potentially have response. Even if it is a non-left bundle or a left bundle, you do not just put it anywhere on the lateral wall and avoid the apex, but you try one or two or three branches. Get the segment of maximal electrical delay, avoid the apex, but use a segment that you think would be most individualized in that particular patient. If you get that segment and you have a significant delay, then the incremental value of AV optimization is relatively less, as it would be in a suboptimal location. I would still hang my hat on lead positioning.

Varma: There is another factor, which is the effect of LV pacing. You can pace from the site of maximal delay, but if your wavefront is jailed, then it is programming.

Tomassoni: If there is one technology right now or in the near future to help with non-responders, what do you see that to be? Is MultiPoint™ Pacing (MPP) (St. Jude Medical, Sylmar, CA) one of those possibilities, or should we be looking for something else in the next few years that may revolutionize non-responder rates?

Singh: I think it will be a combination of multisite/MultiPoint™ Pacing (MPP) (St. Jude Medical, Sylmar, CA). Obviously, we are going to have to understand the electrical activation sequence and the mechanical contractility of the heart a little better. A combination of multiple electrodes or multiple sites and integrating the electrical activation sequence in a better individualized fashion may be something that is really exciting. Also, LV endocardial pacing—not initially for conventional patients, but for non-responders—may be a good strategy for the future.

Varma: I think that understanding electrical activation matters if we improve our candidate selection. We can...
have women with non-ischemic cardiomyopathy and wide left bundle branch block. A proportion of those patients do not respond, and we have to understand why. I think that effect is magnified in other groups, particularly as the QRS morphology becomes less specific for left bundle branch block. A vital ingredient here is the effect of LV pacing, and I think we need a mechanism. I completely agree with your point of using pacing sites within the LV that produce the best electrical effect coupled to the best hemodynamic effect, and we have not really assessed that yet. That might involve multielectrode pacing, simultaneous electrode pacing, or endocardial pacing, and I think one of the promises of endocardial pacing to improve response rates is the fact that electrical activation is accelerated across the endocardium as a faster activation time. That really shows that the electrical activation in response to pacing is a vital ingredient to CRT effect.

Singh: One more therapy that I think is exciting is His bundle pacing. There is a small subset of patients who may have a borderline ejection fraction but have AV conduction block and require pacemakers. Rather than going down the CRT path immediately, one might think about His bundle pacing in the near future. This is an evolving strategy getting a fair amount of traction.