- Hi, I am Michael Gold. I am the Michael E. Assey Professor of Medicine and a cardiac electrophysiologist at the Medical University of South Carolina in Charleston. I'm pleased to be here today to talk about the SMART-CRT Trial.

Rationale behind the study

Cardiac resynchronization therapy is a very successful treatment for many patients with a low ejection fraction and heart failure in the presence of QRS prolongation. They've been many attempts to optimise CRT and the one treatment which is most relevant to this study is the idea of AV optimization or changing the intervals between the atrial and ventricular pacing in these devices. And early studies were somewhat disappointing with this, so that AV optimization is no longer routinely recommended. However, newer approaches to AV optimization using electrical measurements to try to fuse pacing from the left ventricle with normal activation in the right ventricle appears to be a more successful approach. The early studies of this showed a signal towards benefit, although they did not reach statistical significance. And this led to some subgroup analysis and the different studies looked at different subgroups suggesting that the benefit may be most apparent in certain groups of patients, such as those with left bundle branch block or some other characteristics. The characteristic that we found to be most useful is in those patients who have electrical delay so that we achieve more electrical resynchronization by pacing. And we measure the electrical delay by looking at the time between the activation on the right ventricular lead and the left ventricular lead with a so-called RV-LV interval. And in those patients with long intraventricular delays, there is a much greater benefit of AV optimization, we found in a retrospective analysis compared to those with just nominal settings. So we decided to test this, prospectively, in the SMART-CRT Trial in which we had patients undergo CRT implantation, and only those who had a more prolonged RV-LV interval greater than 70 milliseconds with them randomised to either have nominal settings or the specific algorithm, the SMART-AV or SmartDelay algorithm, which is a proprietary algorithm in Boston Scientific devices, the sponsor of this study, but somewhat similar algorithms are now in multiple other manufacturers.

Design and Patient population

The primary endpoint for this study was all based, and secondary endpoint were based on reverse remodelling. So it was a PICO-based study in which patients were implanted, they were randomised and there was a baseline echocardiogram performed and then a follow-up echocardiogram at six months. And the primary endpoint was a percentage of patients who were CRT responders as defined by a 15% reduction in left ventricular end-systolic volume. We have pre-specified secondary endpoints of changes in left ventricle end-systolic volume as a continuous variable, as well as changes in left Ventricular ejection fraction.

Key Results

Study was initially powered to have approximately 370 patients based on what we felt would be the benefit of this therapy. Unfortunately, we performed this study in the middle of COVID. Some studies have been more successful than others in COVID. The challenge for this study, in part, was the patients needed to have echocardiogram so they needed to come to the hospital, many patients were not able to come to the hospital. So we ended up with about 20% fewer patients with adequate numbers of pair tests than we had expected. So with that caveat, what we found to our disappointment, was that although there appeared to be an improvement in the percentage of responders, the primary endpoint, this did not reach statistical significance. Looking at this in a little more detail, showed that the algorithm performed just as well as we expected, but maybe somewhat surprisingly, the control group did much better than what was seen in previous studies. So I think this may be a factor that our medical care has improved significantly, or it may have just been some random effect that the control patients did very well, but it didn't reach statistical significance. Importantly, in our mind, that in addition to the percentage of responders, when we look at left ventricle end-systolic volume as a continuous variable, we did see significant improvements with the SmartDelay algorithm turned on. And we also saw a significant improvement in left ventricular ejection fraction. So what we can say is that the algorithm appears in patients with prolonged RV-LV intervals to produce greater reverse remodelling. If we measure responders by a threshold effect of this, it did not reach statistical significance. I should say, in retrospect, that it's always easy to look at things in retrospect. We and many others are now starting to question the idea of how we define responders and whether we should, in fact, be looking at the continuum of response rather than arbitrary cutoffs. So I think these are important findings in terms of how we can improve outcomes for our patients by being able to improve their left ventricular function.

Take-Home Messages

I think the take-home message is that among patients undergoing CRT, who have a prolonged RV-LV interval, increased interventricular delay, which this represents, that using at least this algorithm, and presumably other algorithms that are similar, to achieve fusion pacing, that they will improve the amount of reverse remodelling when used with CRT patients. And it also, take-home message, to me is that there appears to be a benefit in longer RV-LV intervals and therefore we certainly should think about when programming our patients, that we program them in settings that give us the longest RV interval by choosing the appropriate vector for pacing, assuming that we have an adequate pacing threshold in those vectors.

Next-Steps

I think the next steps are going to be a deeper dive to understand better who were the patients within the study who responded best? Were their subgroups of patients who showed a better response? Was there certain program parameters which showed a better response? And we look forward to the other ongoing studies of other devices, again, using a similar type of strategy of fusion-type pacing to see whether we can find consistent results of this approach to CRT being better for patient outcomes.