paper should be that there is no increase in lumen dimensions as seen by IVUS.

In addition to this, the IVUS data reported in the table partially differ from those reported in the text and includes the measurement of intimal hyperplasia in the coronary segment distal to the recanalized CTO, where no stent was implanted and no intimal hyperplasia could therefore be measured (8).

Finally, the authors underestimated the role of the drug-eluting stent (DES)-dependent endothelial dysfunction, which is normally present in the coronary segment distal to a first-generation DES, caused by the downstream elution of the antiproliferative drug and that has disappeared with the introduction of second-generation DES (5). As the vasomotion substudy included only patients with first-generation DESs, the persistence or the worsening of the endothelial dysfunction at follow-up distal to the stent previously implanted could be first-generation DES-related and not deriving from a long-acting endothelial dysfunction of the coronary segment distal the CTO after recanalization.

Based on these concerns, most of the findings of the present study should be taken as hypothesis generating and would need further investigation in a well-designed and powered study.

Salvatore Brugaletta, MD, PhD
Victoria Martin-Yuste, MD, PhD
Monica Masotti, MD, PhD
Josep Gomez-Lara, MD, PhD
Hector M. Garcia-Garcia, MD, PhD
Patrick W. Serruys, MD, PhD
*Manel Sabaté, MD, PhD

*Thorax Institute
Department of Cardiology
Hospital Clinic
University of Barcelona
Barcelona 08036
Spain
E-mail: masbate@clinic.ub.es

http://dx.doi.org/10.1016/j.jacc.2012.03.073

REFERENCES


Reply

We thank Dr. Brugaletta and colleagues for their valuable comments on our paper (1).

First, as they point out, 3-dimensional quantitative coronary angiography (3D-QCA) might overcome several limitations of 2-dimensional (2D-QCA), as previously shown also in our previous experience (2). We concur that it is unusual to select as the primary measurement the reference vessel diameter (RVD) instead of minimal lumen diameter in this kind of investigation. We made this decision because it was unknown at the beginning of the study whether changes in the vessel caliper would be ascribed to coronary vasomotion or to a remodeling phenomenon. Moreover, we disagree that measuring 3 single QCA points might limit the study results. Indeed, with this method, we were able to provide coronary measurements at a certain point and reproduce them at follow-up, further assessing the relationship between vessel diameter measurement and its percentage of variation.

Second, differently from the standards (3), we decided to perform intravascular ultrasound (IVUS) analysis every 5 mm, considering the very long coronary segments assessed. Thus, we were able to limit the bias related to data clustering. Notably, with such analysis, it was easier to reproduce measurements at follow-up. We probably did not observe any changes in IVUS measurements because of the small sample size of the IVUS substudy, which was not sufficiently powered to show any significant difference. In this regard, we would like to emphasize that the primary endpoint of the main analysis was the RVD at angiographic follow-up as assessed by 3D-QCA, and for this evaluation, an appropriate pre-specified sample size was used.

Third, we truly concur with Dr. Brugaletta and colleagues regarding the possibility that because the vasomotion substudy included only patients receiving first-generation drug-eluting stents (DESs), the persistence or worsening of the endothelial dysfunction at follow-up distal to the implanted stent could be first-generation DES related and not caused by a long-acting endothelial dysfunction of the coronary segment distal to the CTO after recanalization. This is a limitation that was discussed in the text.

Fourth, we apologize to the editor and readers for some typing and spelling errors in the Results section, which did not substantially affect the study conclusions.

Finally, we believe that our study clearly shows that recanalization of CTO is followed by a reversible hibernation of the vascular wall at distal coronary segments, which determine an increase in vessel diameter on long-term follow-up due to an increase in shear stress. We hope that using our findings as hypothesis generating, future sufficiently powered investigations will provide a better explanation of this phenomenon.

*Alfredo R. Galassi, MD
Salvatore D. Tomasello, MD
Filippo Crea, MD
Luca Costanzo, MD

478 Fourth, we apologize to the editor and readers for some typing and spelling errors in the Results section, which did not substantially affect the study conclusions.

Finally, we believe that our study clearly shows that recanalization of CTO is followed by a reversible hibernation of the vascular wall at distal coronary segments, which determine an increase in vessel diameter on long-term follow-up due to an increase in shear stress. We hope that using our findings as hypothesis generating, future sufficiently powered investigations will provide a better explanation of this phenomenon.

*Alfredo R. Galassi, MD
Salvatore D. Tomasello, MD
Filippo Crea, MD
Luca Costanzo, MD

QRS Morphology Is Equally Important!

We read with great interest the TARGET (Targeted Left Ventricular Lead Placement to Guide Cardiac Resynchronization Therapy) study by Khan et al. (1), a randomized controlled trial with targeted left ventricular (LV) lead placement to guide cardiac resynchronization therapy. The results of the study are promising and do emphasize the importance of the location of the LV lead in relation to the latest segment of contraction. However, many conventional variables have not been identified in the study, and more data are needed to support the conclusions of the study.

Morphology of the QRS complex (left bundle branch block vs. right bundle branch block vs. nonspecific intraventricular conduction delay) has not been reported in the study. Many previous studies have consistently shown that QRS morphology is one of the most important predictors of response (2). The distribution of left bundle branch block between both groups should be identified as it can potentially influence the results.

It will be interesting to see if there is a correlation between the QRS morphology and axis with the latest segment of contraction in this study. It is postulated that QRS morphology and frontal axis can predict the latest segment of activation; whether it would predict the latest segment of mechanical contraction is unknown (3). Khan et al. (1) do have the unique opportunity to evaluate this concept in their study population. Nearly one-half (47%) of the patients in the control group ended up having a concordant LV lead location in relation to the segment of latest contraction. It would be very helpful to identify the surface electrocardiogram characteristics (QRS morphology and axis) of this subgroup and compare them with those of patients in whom the LV lead was not concordant. If it is possible to predict the area of latest contraction, with reasonable accuracy, using surface electrocardiogram morphology, it would make the concept of "targeting LV lead" much easier and widely acceptable, without the use of the more sophisticated radial strain measurement.

Total scar burden, an important variable in predicting outcomes in cardiac resynchronization therapy (4) has not been reported in this study. Patients with higher scar burden are intuitively more likely to have a scar at the LV lead site and are less likely to have a concordant LV lead (more remote or adjacent location), thereby significantly influencing the results. The mean total scar burden in both groups should be reported in the study to support the conclusions.

We are grateful for the comments and interest shown by Drs. Reddy and Lakireddy with respect to our recent publication of the TARGET (Targeted Left Ventricular Lead Placement to Guide Cardiac Resynchronization Therapy) study (1) regarding targeted left ventricular (LV) lead placement to guide cardiac resynchronization therapy (CRT). We do not believe that there are robust data to justify the title of their letter and have addressed the specific points below.

First, the morphology of the QRS complex is not, as of yet, part of the guidelines for patients who should be recommended CRT even though, as pointed out by the authors, a number of studies have shown that it is an important determinant of response (2). The centers recruiting for the study routinely implant patients with only baseline left bundle branch block (LBBB) morphology. Reflecting this, there were only 2 patients who had non-LBBB morphology, distributed equally in each group. In both patients, the electrocardiogram showed right bundle branch block morphology, the latest segment of activation was in the inferoseptum, the final lead position was remote, and both patients were CRT

REFERENCES


Reply

We are grateful for the comments and interest shown by Drs. Reddy and Lakireddy with respect to our recent publication of the TARGET (Targeted Left Ventricular Lead Placement to Guide Cardiac Resynchronization Therapy) study (1) regarding targeted left ventricular (LV) lead placement to guide cardiac resynchronization therapy (CRT). We do not believe that there are robust data to justify the title of their letter and have addressed the specific points below.

First, the morphology of the QRS complex is not, as of yet, part of the guidelines for patients who should be recommended CRT even though, as pointed out by the authors, a number of studies have shown that it is an important determinant of response (2). The centers recruiting for the study routinely implant patients with only baseline left bundle branch block (LBBB) morphology. Reflecting this, there were only 2 patients who had non-LBBB morphology, distributed equally in each group. In both patients, the electrocardiogram showed right bundle branch block morphology, the latest segment of activation was in the inferoseptum, the final lead position was remote, and both patients were CRT

REFERENCES


http://dx.doi.org/10.1016/j.jacc.2012.05.017

http://dx.doi.org/10.1016/j.jacc.2012.04.041

Maria Barbara Campisano, MD
Francesco Marzá, MD
Corrado Tamburino, MD
*Department of Internal Medicine and Systemic Disease
Catheterization Laboratory and Cardiovascular Interventional Unit
Cannizzaro Hospital
University of Catania
95021 Catania
Italy
E-mail: argalassi@virgilio.it

Yeruva Madhu Reddy, MD
*Dhanunjaya Lakireddy, MD
*Center for Excellence in Atrial Fibrillation/
Complex Arrhythmia Management
Bloch Heart Rhythm Center at University of Kansas Hospital
Electrophysiology Research
KU Cardiovascular Research Institute
3901 Rainbow Boulevard, MS 4023
Kansas City, Kansas 66160-7200
E-mail: dlakireddy@mac.md