Letter to the Editor

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Tissue Doppler and cardiac resynchronisation therapy: a new challenge for the optimal choice of candidates

Dear Editor

With interest, we read the article of Ghio et al.1 and the Editorial of Breithardt et al.2 in which the usefulness of Tissue Doppler (TD) to detect left ventricular (LV) dyssnergy was reported. Ghio et al.1 defined the intraventricular asynchrony as a difference greater than 50 ms among colour TD-derived regional pre-ejection periods (= time to onset of systolic velocity) between at least two of the four basal and middle segments of LV walls (4- and 2-chamber views). Such asynchrony was observed in a great proportion of patients with low ejection fraction and was independent of the QRS duration (ranging <120 to >150 ms). These data confirm that the mechanical unco-ordination is much more important than the electrical delay3 but, as previously reported, leaves a main question unsolved: which patients can benefit from cardiac resynchronisation therapy (CRT)? This issue is crucial since even 30% of patients do not present an advantage from CRT due to technical problems of implantation or, mainly, to erroneous choice of candidates. Due to limitations of standard echocardiography, able to explore the intra-ventricular uncoordination only partially,3 the TD modalities (pulsed TD, colour TD of mean velocities or Tissue-Tracking combined with Strain Rate Imaging) are earning a pre-eminence in the research on dyssynchrony, clinical impact of CRT and choice of candidates.

Since the major advantage of TD corresponds to the possibility of measuring the unco-ordination in each LV segments, efforts should be addressed to quantify the amount of mechanical asynchrony. In this view, Yu et al.,4 by using colour TD but measuring the criticised time to peak systolic velocity (T_s), calculated a asynchrony index (DI), i.e., the standard deviation of T_s in 12 segments (basal and middle LV walls in 4-, 2- and 3-chamber views). All the patients responding to CRT had DI > 32.6 whereas DI was always <32.6 in non-responders. By a sophisticated combination of Tissue-Tracking and Strain Rate, Sogaard et al.5 also quantified the amount of LV asynchrony as the percentage of delayed longitudinal contraction (= number of segments with myocardial contraction after aortic valve closure at LV base/total circumference of LV base × 100). The attempts of Yu and Sogaard highlight an important aspect: the greater the amount of dyssynergic myocardium the greater the clinical benefit of CRT. On these grounds Ghio et al.1 could also address their findings calculating the variability of the time to onset of contraction in multiple LV segments, adding clinical impact to their valuable data. With this perspective, the evidence of the maximal asynchrony at the lateral wall, where the lead is usually applied, should also be taken into account. Of note, Ghio et al.1 demonstrated the most delayed movement at the lateral wall only showed in about 1/3 of patients with QRS duration above 120 ms. It is our opinion that efforts to reduce the number of non-responders to CRT could be improved by preferentially using the various TD modalities.

References


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Tissue Doppler and cardiac resynchronisation therapy: a new challenge for the optimal choice of candidates: Reply

Dear Editor

The identification of responders to cardiac resynchronisation therapy (CRT) is a major clinical issue.1 Many researchers have focused their attention to the identification of echocardiographic parameters which may be predictive of responsiveness.2-6 However, we still lack comparative data and do not know which is the most useful parameter; in particular we do not know whether new, but not widespread, technology such as tissue Doppler imaging really offers substantial advantage over more simple M-Mode or pulsed Doppler parameters. Ongoing trials will give us the answer. At the same time, research is necessary to address many unsolved pathophysiological issues particularly in the field of electro-mechanical coupling. CRT is emerging as a recommended therapy for patients with heart failure and dyssynchrony, but pathophysiology of dyssynchrony is far from being fully understood. This was, in fact, the area of interest of our work. Studying the prevalence of dyssynchrony in heart failure patients, evaluating the mechanical consequences of conduction disturbances and the relationship between inter and intraventricular dysynchrony is obviously of no immediate help in the selection of candidates to CRT. However, we strongly believe that understanding dyssynchrony is, in the near future, one of the most important things we can do to improve treatments of our heart failure patients.

References


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**Long-term clopidogrel therapy in the drug-eluting stent era: beyond CREDO and PCI-CURE**

We agree with the main thrust of the argument in the recent article by Eriksson1 that long-term clopidogrel treatment (8 and 12 months) confers a small, or at most modest, advantage when compared to the standard 1-month treatment in patients undergoing percutaneous coronary intervention. Eriksson should be commended for the critical analysis of the data from PCI-CURE and CREDO. In particular, for pointing out that the small absolute reductions in composite endpoints of death, myocardial infarction, revascularisation in the long-term clopidogrel treatment group compared to the standard 1-month treatment group, could easily be negated by the increased bleeding risk.

However, we wish to highlight that both trials were conducted before the era of drug-eluting stents. In fact, the main reason for prescribing clopidogrel beyond the standard 1-month period is not so much driven by the results of PCI-CURE or CREDO, but by the implantation of drug-eluting stents.

The theoretical concerns of delayed endothelialisation leading to stent thrombosis have not been borne out by trials comparing drug-eluting stents to bare metal stents. Nevertheless, all these trials of drug-eluting stents have used clopidogrel for beyond the standard 1-month period normally applied to bare metal stents.

In RAVEL,2 where short coronary lesions (mean length 9.58 mm) were treated with a single sirolimus-eluting stent, clopidogrel was prescribed for 2 months. The SIRIUS3 and TAXUS IV4 trials involved treating longer lesion lengths (mean length 14.4 and 13.4 mm, respectively) and more complex disease (diabetes, multiple stents and small vessels). The duration of clopidogrel treatment for SIRIUS and TAXUS IV trials was therefore longer, at 3 and 6 months respectively. None of these trials showed an increased risk of stent thrombosis in the drug-eluting stent group when clopidogrel was prescribed for between 2 and 6 months.

In fact, two recent reports of stent thrombosis in drug-eluting stents5,6 in the literature demonstrate a strong link to the discontinuation of anti-platelet therapy within the first month. Lemos et al.,7 has shown that even in unselected “real world” patients outside the strict entry criteria of trials, patients with complex disease such as multi-vessel disease, bifurcation disease requiring multiple stenting can be treated with sirolimus-eluting stents effectively without an excess of stent thrombosis with clopidogrel treatment of 3–6 months duration.

Although the optimal duration of clopidogrel treatment after drug-eluting stent implantation is not known, empirical long-term treatment (3–6 months) is here to stay because of the fear of the dreaded complication of stent thrombosis and its serious consequences. Depending on lesion complexity and adverse patient characteristics such as diabetes, some authorities even recommend 6–12 months treatment with clopidogrel.8 This prolonged use of clopidogrel has economic consequences and should be considered in any cost analysis of the use of drug-eluting stents.

References


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**Long-term clopidogrel therapy in the drug-eluting stent era: beyond CREDO and PCI-CURE: Reply**

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In the trials comparing drug-eluting stents with bare metal stents, clopidogrel (in addition to aspirin) had been administered for 2–6 months, and no increase in the incidence of stent thrombosis has been reported to date.1 However, I share Dr. Koh’s and Dr. Kadr’s concerns about delayed endothelialisation with drug-eluting stents. Although the optimal period of clopidogrel therapy after drug-eluting stent implantation is not known, clopidogrel is prescribed for 6 months after the implantation of a drug-eluting stent in our institution, which probably provides a wide margin of safety. In contrast, anti-platelet therapy was discontinued after the procedure in four out of the seven patients with a stent thrombosis in the study of Jeremias et al.,2 cited by Koh and Kadr. This is evidently not a strong argument for long-term clopidogrel therapy.

The clinical value of long-term therapy with clopidogrel in addition to aspirin has recently been called in question.3,4 Now the Management of ATherothrombosis with Clopidogrel in High-Risk Patients with