Echocardiographic Assessment of Left Ventricular Dyssynchrony and correlation with QRS width in Chronic Heart Failure.

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Evaluation échocardiographique de l'asynchronisme ventriculaire au cours de l'insuffisance cardiaque chronique et sa corrélation avec la durée du QRS.

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RÉSUMÉ

Prérequis : La sélection des patients insuffisants cardiaque pour une resynchronisation sur des critères électrocardiographiques est grevée d'une forte proportion de sujets non répondeurs. L'échocardiographie permet une approche plus mécanique de l'analyse de l'asynchronisme ventriculaire.

But : Comparer la corrélation des différents paramètres d'étude de l'asynchronisme aux données électriques et estimer leur reproductibilité inter et intra-observateur dans la routine d'un laboratoire d'échocardiographie.

Méthodes : L'asynchronisme ventriculaire a été évalué chez vingt patients insuffisants cardiaque chronique par échocardiographie conventionnelle, Doppler tissulaire (DTI) et tissue tracking (TT).

Résultats : Trois patients avaient un asynchronisme atrio-ventriculaire et six avaient un délai mécanique interventriculaire (DMIV) > 40ms. Il n'y avait pas de corrélation statistiquement significative entre la durée de QRS et le DMIV (r=0.35, p=0.4). Le délai moyen séparant les pics de contraction des parois septale et inférieure était de 83 ± 64 ms, il était supérieur à 130 ms chez 7 patients. La différence maximale des délais électro-systoliques entre les parois du ventricule gauche était de 74 ± 42 ms en moyenne. Il n'y avait pas de corrélation significative entre la durée du QRS et les différents paramètres de l'asynchronisme sus-cités ni de concordance entre le résultats du DTI et ceux recueillis au TT (p=0.3 et 0.6 pour l'asynchronisme spatial et temporel respectivement). La reproductibilité intra et inter observateur dans le recueil des paramètres d'asynchronisme inter (r=0.98 et 0.94, respectivement), atrio- (r=0.99 et 0.96, respectivement) et intraventriculaire (r=0.99 et 0.92 respectivement) était excellente. Elle était médiocre (r=0.27, p=0.31) pour la détermination du Pitzalis.

Conclusion : Pris isolément, chaque paramètre d'asynchronisme mécanique ne semble pas corrélé à la durée du QRS, même si la variabilité inter et intra-observateur était bonne pour le recueil des paramètres échocardiographiques d'asynchronisme auriculo, inter et intra ventriculaire longitudinal.

Mots-clés

Ventricular dyssynchrony, Dilated cardiomyopathy, Echocardiography

SUMMARY

Background: Echocardiographic parameters of mechanical dyssynchrony may improve patients selection for cardiac resynchronisation therapy in chronic heart failure.

Aim : This study aimed to define the prevalence of inter, intra and atrio-ventricular dyssynchrony in heart failure patients with different QRS duration and to evaluate inter and intra-observer variability in collecting different echocardiographic dyssynchony parameters.

Methods : Twenty patients with chronic heart failure of any origin, NYHA functional class II-III with LVEF < 40%, were evaluated by complete echocardiographic examination including tissue Doppler imaging (DTI) and Tissue Tracking.

Results: Three patients had an atrio-ventricular dyssynchrony with a mean left ventricular filling time to cardiac cycle of 33 ± 5%. Six patients had an interventricular mechanical delay (IVMD) ≥ 40 milliseconds, all of them had a QRS duration ≥ 120 milliseconds. Overall, no statistically significant correlation was found between IVMD and QRS duration (r=0.35, p=0.4). The mean septal to posterior wall-motion delay (SPWMD) was 83 ± 64 ms. 7 patients had SPWMD ≥ 130 ms. The baseline QRS duration did not correlate with SPWMD (p=0.7). The mean LV dyssynchrony determined by ΔS-peak was 74 ± 42 ms. Seven patients had LV dyssynchrony. Linear regression did not demonstrate a relation between QRS width and intraventricular dyssynchrony (p=0.34). There was no concordance between intra-ventricular spatial or longitudinal dyssynchrony determined by DTI method and by Tissue Tracking (p=0.3 and 0.6 respectively). The intraobserver reproducibility of LVFT/RR, IVMD and ΔS-peak (ICC= 0.99, 0.98 and 0.99, respectively), as well as the interobserver reproducibility (ICC: 0.96, 0.94 and 0.92, respectively), were very high. However, we observed a high variability for SPWMD measure (ICC=0.27, p=0.31).

Conclusion : Mechanical dyssynchrony did not correlate with QRS duration, despite the poor variability in collecting different echocardiographic parameters.

Key-words

Ventricular dyssynchrony, Dilated cardiomyopathy, Echocardiography

التقييم بواسطة التخطيط بالصدى القلبي لغياب التزامن البطيني أثناء القصور القلبي

الباحثون : زخامة. ل - نفاتي. س - بوصباح. أ - بوخريص. ب - سعد. ر - جندوبي. ع - بالنور. أ - بن يوسف. ث.

الكلمات الأساسية : غياب التزامن البطيني - التخطيط القلبي بالصدى.

The incidence and prevalence rate of heart failure are increasing steadily because of the aging of the population. Cardiac resynchronisation therapy (CRT) has emerged as an established therapy for congestive heart failure (CHF) due to severe left ventricular systolic dysfunction. CRT, by means of atrial-biventricular stimulation, improves quality of life and tolerance to exercise; and reduces the number of hospitalizations,(1) mortality due to progression of heart failure and total mortality.(2) Current selection criteria for patients eligible for CRT include: CHF patients who remain symptomatic in New York Heart Association (NYHA) III – IV despite optimal pharmacological treatment with low left ventricular ejection fraction (LVEF≤ 35%), left ventricular dilatation (LV end diastolic diameter > 55mm), normal sinus rhythm and wide QRS complex (≥120 ms).(3,4) Despite these criteria, approximately 30 % of patients fail to respond to this therapy.1 This important number of non-responders led to the development of new parameters predicting response to CRT. In view of the technical complexity, CRT costs and specially the benefits that it can offer to patients with HF, it is important to identify the individuals who are potentially responsive to the therapy in the population of individuals with dilated cardiomyopathy, in whom the evidence of ventricular dyssynchrony is essential. Accordingly, several echocardiographic criteria have been proposed to identify atrioventricular, interventricular and intraventricular mechanical dyssynchrony. Mainly because of their lack of reproducibility and repeatability in practice, a few of these parameters have demonstrated the ability to distinguish CRT responders from nonresponders with a high degree of accuracy in multiple studies. (5,6). The purpose of this study was to evaluate the interobserver and intraobserver variability in collecting selective dyssynchrony parameters measured with traditional echocardiographic techniques and tissue Doppler imaging (DTI) in our daily practice and to define their correlation with QRS duration in patients with dilated cardiomyopathy.

METHODS

Study population: Twenty patients with chronic heart failure of any origin, NYHA functional class II-III with LVEF < 40%, who had been taking optimal drug therapy for at least three months were included in this study. All of them where in sinus rhythm. Electrocardiographic analysis: All patients underwent a standard 12 lead electrocardiograms acquired at a paper speed of 25 mm/s and a scale of 10mm/ Mv. The measurement of QRS duration and the assessment of QRS morphology were performed. Echocardiographic protocol: A complete M–mode, two dimensional and Doppler evaluation was performed using ultrasonographic equipement (VIVID 7, General Electric). Images were obtained using a 4 MHz transducer from the parasternal and apical views (standard long axis and two and four- chamber views). Left ventricular end systolic and diastolic volumes and ejection fraction were calculated using the biplane Simpson's technique. Three consecutive beats were stored and the images were digitized and analyzed off-line to assess systolic synchronicity by two independent observers blinded to the clinical and electrocardiographic status of the patients.

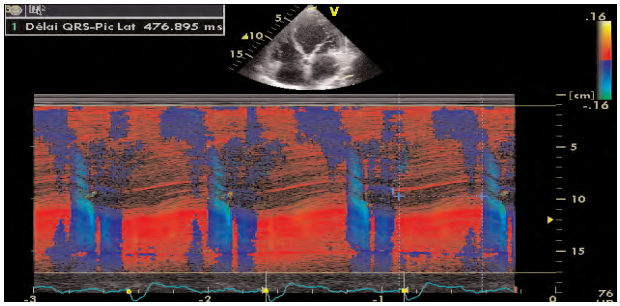
Three types of parameters were evaluated:

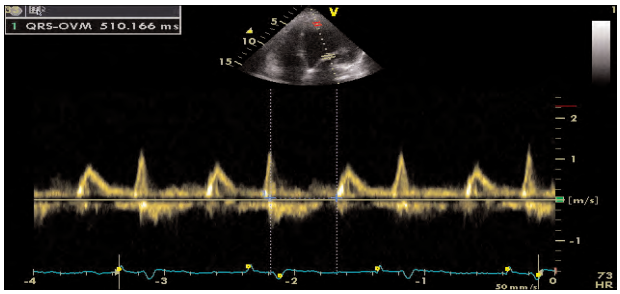
1/ Atrio ventricular dyssynchrony: Defined as a percentage of LV filling time (LVFT) in relation to cardiac cycle length (RR), as measured by trans-mitral Doppler echocardiogram, under 40%.

2/ Inter ventricular dyssynchrony: Pulsed – wave Doppler recordings across the aortic and pulmonary valves were obtained from the apical 5-chamber view and parasternal short axis view respectively. Aortic pre-ejection time was measured from the beginning of QRS complex to the beginning of aortic flow velocity. The pulmonary pre-ejection time was measured from the beginning of QRS complex to the beginning of pulmonary flow velocity curve. The difference between the two values was considered as the interventricular mechanical delay (IVMD); an IVMD > 40 ms was selected as the cut off value for interventricular dyssynchrony.7

3/ Intra-ventricular dyssynchrony: We used color-coded tissue Doppler M-mode to record septal to posterior wall-motion delay (SPWMD) from a parasternal long-axis view. The M-mode cursor was positioned at the midventricular level (papillary muscle level). We measured the time delay from peak inward septal motion to peak inward posterior wall at a sweep speed of 100 mm/s. The cut-off value of greater than or equal to 130 milliseconds was considered a marker of LV dyssynchrony as reported by Pitzalis and al.8 The same mode was used to search an overlap between the end of left lateral wall contraction (LLWC) and onset of LV filling determined by transmitral pulsed Doppler echocardiogram9 (fig 1).

Figure 1 : ISearch of an overlap of left lateral wall contraction and onset of LV filling: A/ time to the end of lateral wall contraction from a color-coded tissue Doppler from an apical 4-chamber view, here at 476 ms, B/ the onset of left ventricular filling from pulsed Doppler transmitral flow, here=510ms: there is no overlap of lateral wall contraction.





Pulsed tissue Doppler imaging was acquired from the apical 4, 2 and 3-chamber views to assess longitudinal LV shortening velocities. The sample volume was placed in the LV basal portions of antero-septal, antero-lateral, inferior, anterior, infero-septal and infero-lateral walls. The time interval between the onset of the QRS complex and the peak systolic velocity was derived (S-peak) (fig 2). Left ventricular dyssynchrony was defined as a maximum difference of time to peak systolic velocities among the six walls within the LV (ΔS-peak) greater than or equal to 65 ms.10,11 On the same images, we measured the maximal difference of time to onset of systolic velocity (S-onset) for the 6 segments at basal level (¢S-onset).

We completed by studying the longitudinal basal displacement (tissue tracking TT) by color-coded tissue Doppler for the six walls from 3 standard apical views on the same cardiac beat. A maximum opposing wall delay more than 65 ms was considered as consistent with significant dyssynchrony.12 (fig 3)

Statistical analysis: The Statistical Package for Social Sciences (SPSS) version 11.5 was used for statistical analysis. Data are presented as means ± SD or total number (percentages). Correlations between variables were assessed using Pearson's linear correlation. Interobserver and intraobserver reproducibilities were evaluated by means of the intraclass correlation coefficient (ICC) with reproducibility being considered almost perfect if the ICC was between 0.81 and 1.0. Statistical significance was defined at $p \leq 0.05$.

RESULTS

Study population: Twenty patients were included. The patient characteristics are summarized in Table 1. Eleven were in NYHA class III. Etiology underlying the cardiomyopathy was ischemic in 25% of patients. Patients had severe LV dysfunction (mean LVEF=29 ±9 %, range 9% to 40%). The QRS duration and PR interval were 118 ± 17 ms (range 80 to 140 ms) and 180 ± 15 ms respectively. 17 patients had QRS duration ≥ 120 ms with left bundle branch block (LBBB). Echocardiographic dyssynchrony parameters and correlation with ECG: The mean LVFT/RR was 46 ± 7%. Only three patients had an atrio-ventricular asynchrony with a mean LVFT/RR of 33 ± 5%. All 3 patients had a PR interval at 20 milliseconds and QRS duration at 120 milliseconds. 7 patients had an aortic pre-ejection time > 150 ms. The mean RV-LV dyssynchrony was 33 ± 22 ms. Six patients had an IVMD ≥ 40 milliseconds (range 44 to 90 ms); all of them had a QRS duration ≥ 120 milliseconds. Overall, no statistically significant correlation was found between IVMD and QRS duration (r=0.35, p=0.4). The mean SPWMD was 83 ± 64 ms (range 12 to 203 ms). 7 patients had SPWMD ≥ 130 ms with QRS duration ≥ 120 ms for 6 of them. The baseline QRS duration did not correlate with SPWMD (p=0.7). Peak of LLWC was determined in only 12 patients because of difficultly to identify the peak of contraction of the anterolatral wall. An overlap of LLWC was seen in 6 patients with a mean QRS duration of 123 ± 18 ms.

Figure 2 : Pulsed tissue Doppler: Measure of S-peak from the beginning of QRS to peak systolic velocity and S-onset from the beginning of QRS to onset of systolic velocity in the lateral wall (A) and the interventricular septal wall (B).

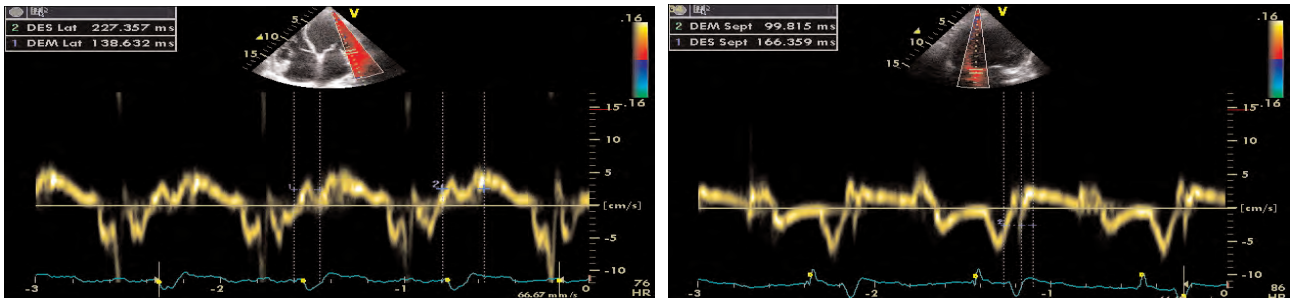
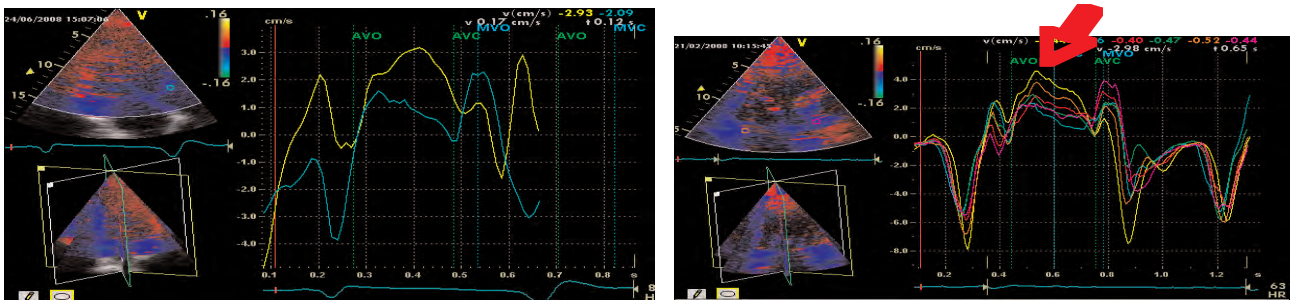
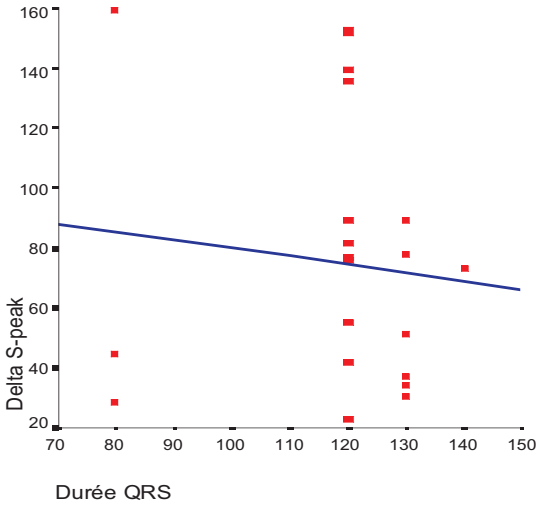


Figure 3 : Tissue Tracking mode. A/ Maximum opposing wall delay of 100 ms between intraventricular septum and posterior wall is seen in apical long axis view, consistent with significant dyssynchrony. B/ Time-velocity curves from representative basal levels show no significant opposing wall delay.



Measure of time to onset and peak systolic velocity was possible in 18 patients. The mean LV dyssynchrony was 74 ± 42 ms (range 23 to 159 ms) considering S-peak and 63 ± 42 ms (range 10 to 143 ms) for S-onset. Seven patients had LV dyssynchrony by the two methods. Six of them had QRS duration ≥ 120 ms. The seventh patient had narrow QRS (=80 ms) contrasting with ΔS-peak and ΔS-onset at 159 and 150 ms respectively. LV dyssynchrony was observed most frequently (four patients) between the interventricular septum and the anterior wall. It was present in 35% of patients with wide QRS (100% of patients with QRS duration ≥ 130ms). Linear regression did not demonstrate a relation between QRS width and intraventricular dyssynchrony (p=0.34). (fig 4)

Figure 4 : Linear regression between maximal ¢S-peak and QRS duration: There was no significant correlation.

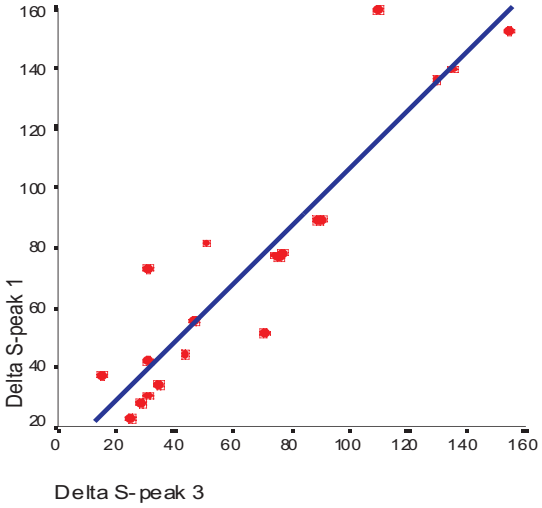


There was no concordance between intra-ventricular spatial or longitudinal dyssynchrony determined by DTI method and by Tissue Tracking (p=0.3 and 0.6 respectively).

Reproducibility of echocardiographic asynchrony parameters: The intraobserver reproducibility for LVFT/RR and IVMD was very high (ICC= 0.99 and 0.98, respectively), as well as the interobserver reproducibility (ICC: 0.96 and 0.94, respectively). At the opposite, we observed a high variability for SPWMD measure: ICC=0.27, p=0.31. Overlap of LLWC, when determined, had a good reproducibility intra and inter observer: ICC= 0.97 (p< 0.001, IC95% = [0.88-0.98]) and 0.85 (p<0.001, C95% = [0.88-0.99]) respectively.

Intraobserver variability of LV dyssynchrony was very low for maximal ΔS-peak and ΔS-onset measure: ICC= 0.99 (p<0.0001, IC95%[0.97-0.98]) and 0.98 (p<0.0001, IC95%[0.97-0.99]), respectively. Interoperator reproducibility was similarly low for ΔS-onset (ICC=0.92, IC95% [0.92-0.99], p<0.0001) and ΔS -peak (ICC= 0.92, IC95% [0.81-0.96], p<0.0001) (fig 5).

Figure 5 : Interobserver variability for the measure of maximal ¢S-peak. ICC=0.92, p<.0001, IC 95%0.81-0.96.



DISCUSSION

Reliability of the ECG as the only tool to define dyssynchrony appears tentative because it may serve as a poor surrogate of mechanical LV function. Many CRT studies indicated that 20 - 30% of patients failed to respond to CRT despite prolonged QRS duration.5,11 More reliable markers of LV dyssynchrony were needed to predict response to CRT to target the most appropriate patients. Despite promising preliminary data from prior single-center studies, echocardiographic measures of dyssynchrony aiming at improving patient selection criteria for CRT do not appear to have a clinically relevant impact on improving response rates when studied in a multicenter setting such as PROSPECT.6

The main result of the present study is the poor relationship between QRS duration and cardiac dyssynchrony observed by conventional and more sophisticated echocardiographic techniques. Even though it was affirmed by Rouleau13 who showed a good correlation between IVMD and QRS width (r=0.86, p<0.01), we failed to show this correlation in our series, this same result has been reported by Ghio14 in a larger series of dilated cardiomyopathy: despite a significant correlation between interventricular delay and QRS duration (r=0.66, p<.01), a wide scattering of the data around the identity line was observed. An explication is that a prolonged right ventricular pre-ejection period (as in the case of right ventricular dysfunction or of pulmonary hypertension) could reduce the difference between aortic and pulmonary pre-ejection periods and therefore impair the correlation between interventricular dyssynchrony and QRS duration. The site of the left bundle branch block (e.g. in the proximal or distal part of the conduction system) might, as well, be an important determinant of the degree of interventricular dyssynchrony.

Unlike Pitzalis,8 we didn't observe a significant correlation between QRS width and SPWMD. PROSPECT6 had shown poor inter and intra reproducibility of this parameter (adjusted coefficient of variation CV=24.3 and 72.1%, respectively) which might explain this poor correlation. The anterior wall was the most delayed segment in our series.

Classically, the lateral wall shows the most delayed movement,10 but this was true in only about one third of patients with QRS duration above 120 ms in Ghio's study.14 These data indicate that in heart failure patients, the sequence of left ventricular activation and wall motion may differ from patient to patient and in about two third of cases the most delayed segment is not the lateral wall. LV dyssynchrony diagnosed with DTI is the most powerful predictor of LV reverse remodeling, even considering more recent echocardiographic techniques such as strain rate imaging.15,16 LV dyssynchrony was present in 35% of patients with QRS duration ≥ 120 ms in our study and in 58% in Haghjoo series.17 We didn't find a significant relation between QRS duration and ΔS-peak. Haghjoo demonstrated a week relation (r=0.35, p<.001) in his study with wide scattering of data around the identity line.17 The QRS duration should be considered as only a generic marker of conduction disturbance, because the fact that left intraventricular asynchrony is often associated with LBBB is not sufficient to presume that the latter is a specific marker of any degree of mechanical asynchrony. Also, LBBB may be the result of abnormalities that do not necessarily cause late contraction of the left free wall (e.g., peripheral conduction defect or global left ventricular dysfunction). Seen in this light, the weak correlation between QRS duration and echocardiographically visualized mechanical asynchrony is not surprising.

In the current study, there was no concordance between TDI and tissue tracking results. TT offers many advantages over the other techniques described for measuring LV dyssynchrony: there is minimal observer bias in measurement, determining timing of peak wall motion is quick and easy from the same heart beat and regional and global longitudinal systolic function can be accurately quantified.12 Nevertheless, because TT quantifies myocardial motion as opposed to velocity (TDI), these 2 techniques can provide different answers with regard to the presence and magnitude of dyssynchrony. This raises the issue of whether differences in timing of peak velocity or differences in timing of peak displacement are more important as measures of LV dyssynchrony. No study had yet, in our knowledge, answers that issue.

Poor reproducibility of echocardiographic measures has been incriminated in PROSPECT trial6 to explain poor ability of these parameters to predict clinical and echocardiographic response to CRT. Similar to our results, interobserver variability was higher for each parameter than intraobserver variability, with high variability for SPWMD (CV= 72.1%) and low variability for IVMD (CV=6.5%)6. In opposition to chung,6 who registered moderate variability for ΔS-peak (CV=31.9%), reproducibility of this parameter was excellent in our study. This can be explained by higher LVEF (29 ±9 % vs 23.6±7 in our series and PROSPECT, respectively) and fewer ischemic cardiomyopathy (25 and 54%, respectively) allowing better DTI images quality, especially for the interventricular septal wall. Overall, the inter-core lab variability in PROSPECT6 was relatively high at 6.5 - 72%, indicating a need for refinement of the methodology. It is likely that dyssynchrony is a dynamic problem and therefore that a single measurement, under one set of physiological circumstances, is not representative of the total disease burden.6

CONCLUSION

The presence of electrical dyssynchrony does not guarantee the presence of mechanical dyssynchrony. Unfortunately, the variability in image acquisition and analysis impair our ability to conclusively assess the potential predictive capacities of echocardiographic parameters in an ideal setting. Thus, current clinical criteria including ECG remain the standard for CRT patient selection. Ultimately, careful consideration of the goals of therapy on an individual patient basis, taking into account co-morbid conditions such as respiratory or renal disease may be more useful in selecting patients than imaging data.

Références

1. Abraham WT, Fisher WG, Smith AL and al. MIRACLE Study Group. Multicenter Insync Randomized Clinical Evaluation. Cardiac resynchronization in chronic heart failure. N Engl J Med 2002; 346:1845-53.
2. Cleland JGF, Daubert JC, Erdmann E and al. The effect of cardiac resynchronization on morbidity and mortality in heart failure (CARE-HF study). N Engl J Med 2005; 352:1539-49.
3. Vardas PE, Auricchio A, Blanc JJ and al. Guidelines for cardiac pacing and cardiac resynchronisation therapy. The task force for the cardiac pacing and cardiac resynchronisation therapy of the European Society of Cardiology developed in collaboration with the European Heart Rhythm Association. Eur Heart J 2007; 28:2256-95.
4. Epstein AE, DiMarco JP, Ellenbogen KA and al. ACC/AHA/HRS 2008 Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines developed in collaboration with the American Association for Thoracic Surgery and Society of Thoracic Surgeons. J Am Coll Cardiol 2008;51:e1-62.
5. Yu CM, Abraham WT, Bax JJ and al. Predictors of response to cardiac resynchronization therapy (PROSPECT)—study design. Am Heart J 2005;149:600-5
6. Chung ES, Angel R, Tavazzi L and al. Results of the predictors of response to cardiac resynchronisation therapy (PROSPECT trial). Circulation 2008; 117: 2608- 2616.
7. Gorcsan J, Abraham T, Agler DA and al. Echocardiography for cardiac resynchronisation therapy: Recommendations for performance and reporting. A report from the American Society of Echocardiography Dyssynchrony Writing Group endorsed by the Heart Rhythm Society. J Am soc echocardiogr 2008; 21:191-213.

8. Pitzalis MV, Lacoviello, Romito R and al. Cardiac resynchronisation therapy tailored by echocardiographic evaluation of ventricular asynchrony. J Am Coll Cardiol 2002; 40:1615-22.
9. Cazeau S, Bordachar P, Jauvert G and al. Echocardiographic modeling of cardiac dyssynchrony before and during multisite stimulation: a prospective study. PACE 2003;26:137-43.
10. Bax JJ, Bleeker GB, Marwick TH and al. Left ventricular dyssynchrony predicts response and prognosis after cardiac resynchronization therapy. J Am Coll Cardiol 2004; 44:1834-40.
11. Laffite S. La stimulation multisite revisitée par échocardiographie. mt cardio 2006; 2:447-457.
12. Bank AJ, Aaron SK. Tissue Doppler imaging and left ventricular dyssynchrony in heart failure. J Cardiac Failure 2006; 12:154-162.
13. Rouleau F, Merheb M, Geffroy S and al. Echocardiographic assessment of the interventricular delay of activation and correlation to the QRS width in dilated cardiomyopathy. PACE 2001; 24:1500-6.
14. Ghio S, Constantin C, Klersy C and al. interventricular and intraventricular dyssynchrony are common in heart failure patients regardless of QRS duration. Eur Heart J 2004; 25:571-78.
15. Yu CM, Fung JW, Zhang Q and al. Tissue Doppler imaging is superior to strain rate imaging and postsystolic shortening on the prediction of reverse remodeling in both ischemic and nonischemic heart failure after cardiac resynchronization therapy. Circulation 2004; 110:66-73.
16. Yu CM, Fung WH, Lin H and al. Predictors of left ventricular reverse remodeling after cardiac resynchronization therapy for heart failure secondary to idiopathic dilated or ischemic cardiomyopathy. Am J Cardiol 2003 ;91:684–88.
17. Haghjoo M, Bagherzadeh A, Fazelifar AF and al. Prevalence of mechanical dyssynchrony in heart failure patients with different QRS durations. PACE 2007; 30: 616-22.