A protocol to screen patients with congestive heart failure for cardiac resynchronisation therapy by a nurse practitioner in an out-patient heart failure clinic

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SUMMARY

- In this article the negative effects and prognosis of a prolonged QRS duration in patients with congestive heart failure are discussed.
- The purpose, criteria for, and effects of cardiac resynchronisation therapy are described.
- A selection protocol for patients with congestive heart failure is outlined, with emphasis on the role of the Heart Failure Nurse Practitioner.
- Results of the selection protocol are presented.

INTRODUCTION

Cardiac resynchronisation therapy (CRT) is a relatively new therapy for patients with severe congestive heart failure (CHF). Since 1998 CRT has been applied in the VU University Medical Center and at that time the VU university medical center was the second hospital in the Netherlands where biventricular pacemakers were implanted.

CRT as a therapy for CHF is described in the guidelines for the diagnoses and treatment for CHF from the European Society of Cardiology in 2005 as a class I-therapy with a scientific evidence level A (see Box 1) (Swedburg, 2005). According to the guidelines, CRT in patients with reduced ejection fraction (EF) and ventricular dyssynchrony [QRS width 120 ms or more and in functional New York Heart Association (NYHA) class III or IV despite medical therapy] is a class I, level of evidence A recommendation to improve symptoms. For mortality CRT is a class I, level of evidence B recommendation.

In this article we describe the negative effects and prognosis of a prolonged QRS duration in patients with CHF, the purpose of CRT as well as the criteria for CRT and the effects of CRT. Also, our selection protocol for patients with CHF is described, with emphasis on the role of the Nurse Practitioner Heart Failure. In addition, we discuss the results of the selection protocol.

HEART FAILURE, INTRA-VENTRICULAR CONDUCTION DELAY AND MECHANICAL ASYNCHRONY

About 30-50% of patients with CHF have an intraventricular conduction disturbance with a QRS duration of > 120 ms. Usually, the conduction disturbance is a left bundle branch block (LBBB) or a conduction delay that mimics a LBBB (Saxon et al., 1999; Abraham, 2000; Abraham & Hayes, 2003) These patients have a high morbidity and mortality (Gottipaty et al., 1999; Silvet at al., 1999). In addition to an intraventricular conduction delay there can be an atrioventricular conduction delay (van Veldhuisen & Voors, 2003).

These intraventricular and atrioventricular conduction delays may result in a decrease of contraction of the myocardium, an increase of mitral regurgitation, a decrease of diastolic filling time and an increase in asynchrony of the contraction pattern of the left ventricle. This results in a decrease of stroke volume and therefore of EF which in turn may lead to apoptosis of the myocytes and a further worsening of CHF (van Veldhuisen & Pit, 2002). Gottipaty et al. (1999) found an increase of one year mortality in relation of the QRS duration (see Figure 1). It is clearly seen that the one year survival decreases when QRS duration increases. The mechanical asynchrony can be made visible using three-dimensional echocardiography (see Figure 2).

Class I-therapy	Evidence and/or general agreement that a given diagnostic procedure/treatment is beneficial, useful, and effective.
Level of evidence A	Data derived from multiple randomised clinical trials or meta-analyses.
Level of evidence B	Data derived from a single randomised clinical trial or large non-randomised studies.

Box 1. European Society of Cardiology classification of evidence for CRT as a therapy for CHF

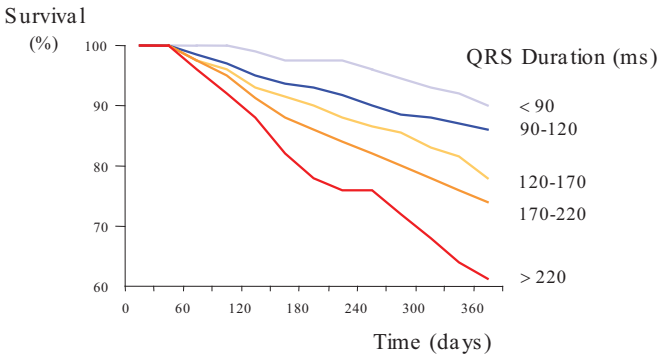

Figure 1. One year survival in patients with CHF in relation to QRS duration.

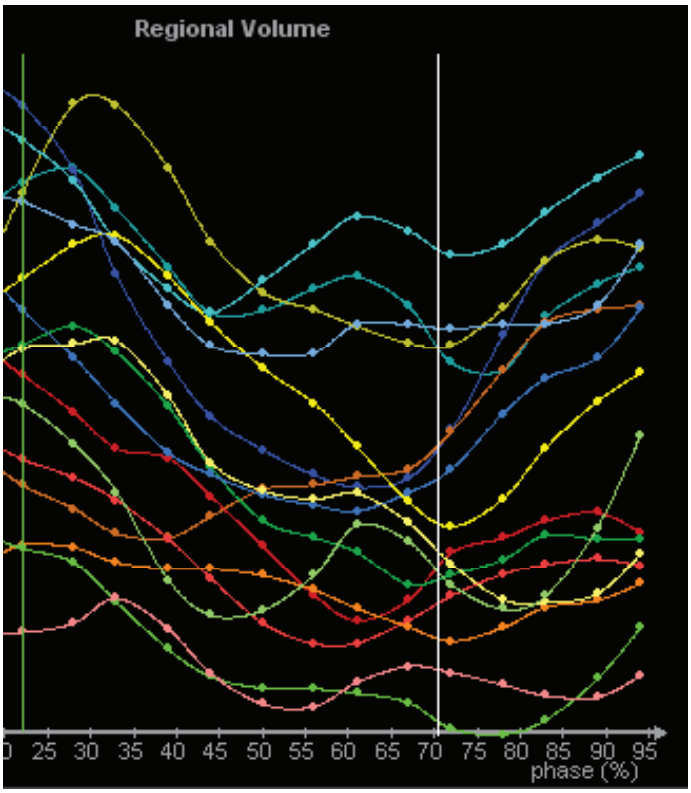

Figure 2. Schematic reproduction of the regional volumes during asynchrony: the lines are not synchronous. Some are going up (more volume = relaxation) while at the same time other lines are going down (less volume = contraction).

The purpose of CRT

The purpose of CRT is to improve the functional class and quality of life of the patient by increasing stroke volume. CRT was also found to reduce mortality (Bakker et al., 2000; van Veldhausen & Voors, 2003; Cleland et al., 2005). To achieve this, electrodes are placed in the right atrium for sensing the atrial depolarisation and in the right ventricle for stimulating the septal part of the left ventricle. In addition, the lateral part of the left ventricle is stimulated by an electrode placed at the lateral epicardium, usually via the coronary sinus in a postero-lateral vein (see Figure 3). Using these three electrodes, atrioventricular and intraventricular delays can be optimised. By optimising the atrioventricular delay the preload will be improved and by optimising the intraventricular delay the asynchrony between the septal wall and the lateral wall will be diminished (see Figure 4). These two factors result in a higher stroke volume and thereby a higher cardiac output and a better functional class of the patient. To achieve an optimal result it is important that the patient will be paced biventricularly continuously.

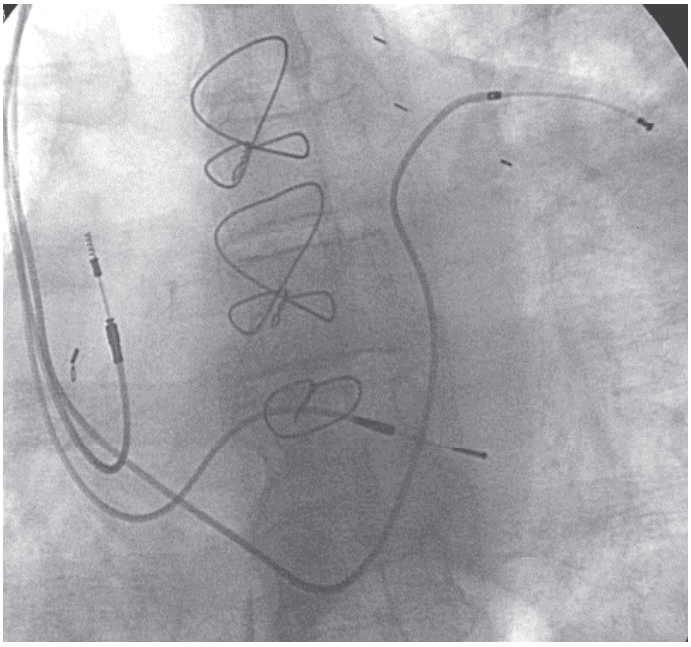

Figure 3. The position of the pacemaker leads during biventricular pacing.

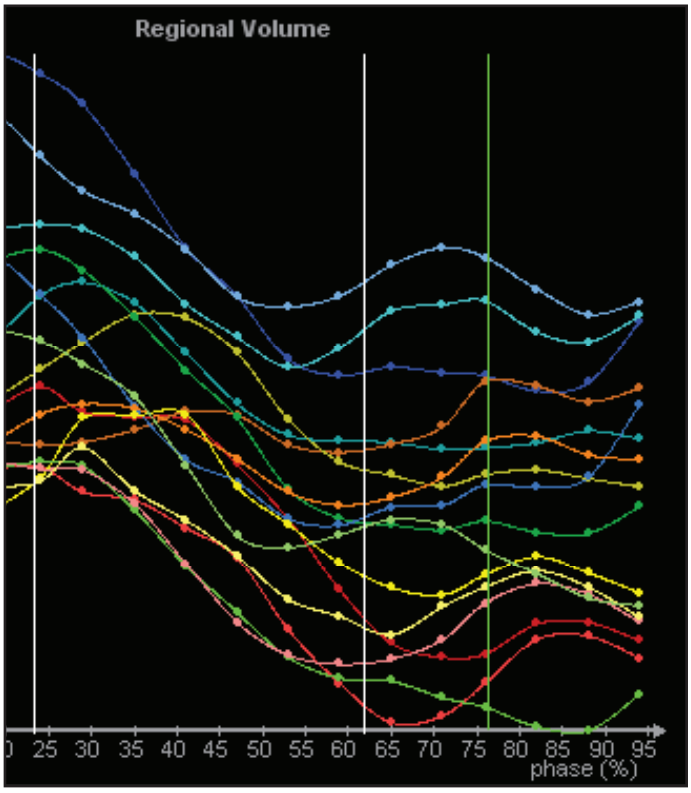

Figure 4. Diagram showing the situation during biventricular pacing. The lines are now more synchronous. There is less asynchrony in the contraction pattern of the left ventricle.

Selection criteria

As mentioned above, patients with advanced heart failure are eligible for CRT treatment. Usual criteria for CRT are: ventricular EF of 35% or less, NYHA functional classification III or IV, QRS duration of 120 ms or more, a stable heart failure medical regime [including an angiotensin-converting enzyme (ACE) inhibitor or substitute and ß-blocker therapy]. The *best*

criteria are given in Box 2. Galizio et al. (2003) showed that in a group of 200 patients only 7.5% met all criteria. (Item scores: NYHA classification 70%, left ventricular diastolic diameter 60%, PR interval > 200 ms 55 %, EF 53.5%, QRS duration of 150 ms 34%.) There is, at this time, still some ongoing discussion about the criteria for CRT. Currently the most common criteria are: NYHA functional classification III or IV, EF of 35% or less and a QRS duration of 120 to 150 ms or more.

Functional NYHA class III or IV
PR interval ≥ 200 ms
QRS duration ≥ 150 ms
Left ventricular diastolic diameter (LVDD) ≥ 60 mm
Left ventricular ejection fraction (LVEF) ≤ 35%

Box 2. Best criteria for CRT (Galizio et al., 2003)

Exclusion criteria are causes of CHF which can be treated otherwise (for example, revascularisation), a medication regime which is not optimal, unstable angina pectoris or an acute myocardial infarction within three months prior to CRT, a cerebrovascular accident within three months prior to CRT, atrial rhythm disturbances one month prior to CRT and terminal diseases other than CHF. (Gras et al., 1998; Abraham et al., 2002; Linde et al., 2002). In the MUSTIC study (Linde et al., 2002) patients were excluded when they were able to walk more that 450 metres in a six-minute walking test.

Clinical effects of CRT

The clinical results of CRT may be amazing from the patient's perspective. Several studies showed an increase in EF, a decrease of mitral regurgitation, an increase of the six minute walking distance and of peak VO_2, an improvement of the NYHA functional class and quality of life, and a decrease of hospitalisation and of mortality (Auricchio et al., 1999; Linde et al., 2002; Achilli et al., 2003; Gaspirini et al., 2003; Linde et al., 2003; Cleland et al., 2005) (see Box 3). Sometimes a decrease in the use of diuretics is observed (Bakker et al., 2000). Using echocardiography a decrease of left ventricular dilatation (reversed remodeling) can be observed (van Veldhausen & Voors, 2003).

Increase in six minute walking distance by 20%
Increase in peak VO2 by 10%
Improving NYHA functional class by 25%
Improving quality of life score by 36%
Increase EF by 5%
Decrease in mitral valve regurgitation by 45-50%
Decrease in hospitalisation rate
Reduction in mortality

Box 3. Clinical effects of CRT

However, not all patients respond as well as described above to CRT. About 30% of the patients receiving a biventricular pacemaker have no advantage of CRT and some deteriorate: these patients are called 'non-responders'. No clinical effects or effects in reversed remodeling are seen in this group of patients. In an attempt to identify this group of patients a special *Temporary Biventricular Pacing Protocol* (TBPP) was developed before a definite biventricular pacemaker is implanted.

THE SCREENING PROTOCOL

In September 2003 the nurse-led out patient heart failure clinic was asked to play a role in screening patients for CRT before TBPP was performed. The reason behind this request was that it had happened more than once that patients who were referred to our hospital for CRT, told the cardiologist that they had walked for 20 kilometers the day before or that they recently played in a game of soccer for more than one hour. This meant that these patients were not in NYHA functional class III or IV. Also, a substantial number of patients had an EF of more than 35% disqualifying them for CRT.

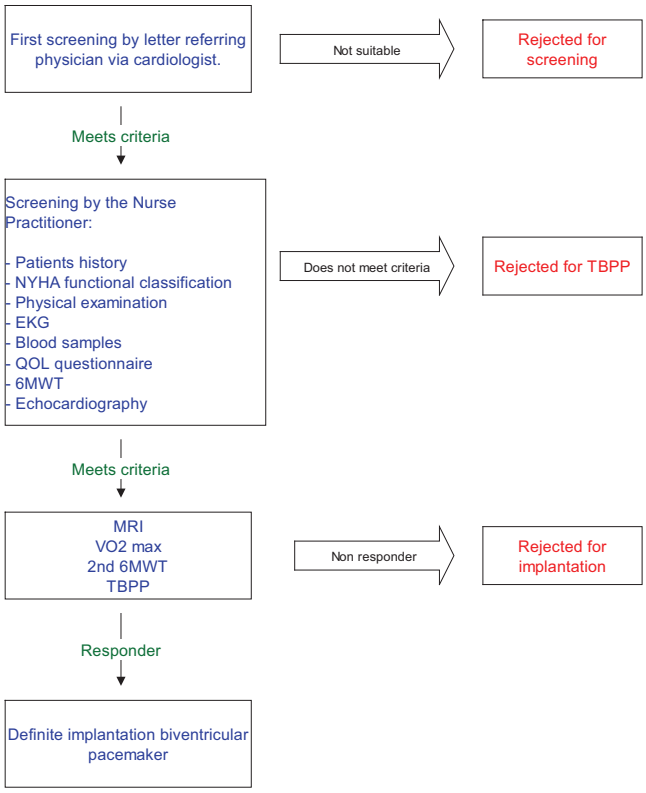

Figure 5. The screening protocol

The screening protocol (see Figure 5) was developed in September 2003 and implemented in October 2003. All patients – including those from our own clinic – are referred by letter to our rhythm team. The rhythm team decides whether a patient is suitable for further screening. These patients will be seen at the out patient heart failure clinic by a Nurse Practitioner. He or she will take the medical history of the patient (including the prescribed medication) and establish the NYHA functional class. In addition, a physical examination, blood samples, an ECG, a six minute walk test and a *Minnesota Living With Heart Failure Quality Of Life Questionnaire* are performed. At the end of the screening session an echocardiographic examination is arranged. During screening the patient is fully informed about the method of action and purpose of a biventricular pacemaker and about the subsequent procedure. In the VU University Medical Center the following criteria for CRT are defined: functional NYHA class III or IV, EF 35% or less and optimal medical treatment without other treatment options.

When, after this screening, the patient still meets the criteria for CRT, he will enter the TBPP. The purpose of the TBPP is to reduce the number of 'non-responders' by a better patient selection. In this protocol – as the name suggests – the heart will be paced using five temporary electrodes: one in the right atrium (for sensing), two at different locations in the right ventricle and two at different locations in the left ventricle via the coronary sinus. Stimulation through all combinations of two electrodes is tested while measuring stroke volume simultaneously. If stroke volume increases by 10% or more the patient is a *responder* and will receive a permanent biventricular pacemaker. Using the TBPP the number of non-responders can be reduced from 30 to 10%.

METHOD AND RESULTS

From October 2003 until October 2006 135 patients were screened. Seventy patients (52%) were rejected for the TBP Procedure. Reasons for rejection are shown in Figure 6.

- NYHA class < III (n = 26, 37%),
- ejection fraction > 35% (n = 17, 24%),
- ischaemia detection and/or treatment (n = 14, 20%),
- other pathology (for example, pulmonary diseases or cardiology problems other than ischemia; n = 14, 20%),
- lack of patient's motivation (n = 11, 16%),
- inadequate medical regime (n = 5, 7%),
- referral for physiotherapy for reactivation (n = 4, 6%)

The six minute walking distance was not used as an exclusion criterion. A first rejection for TBPP did not mean that the same patient was excluded for a second or even a third screening by the Nurse Practitioner after the reason of an earlier rejection was treated (for example, ischaemia detection, optimisation of medication, or otherwise) or patient deterioration. Due to the rejections for TBPP, the waiting list and waiting time for TBPP is also reduced.

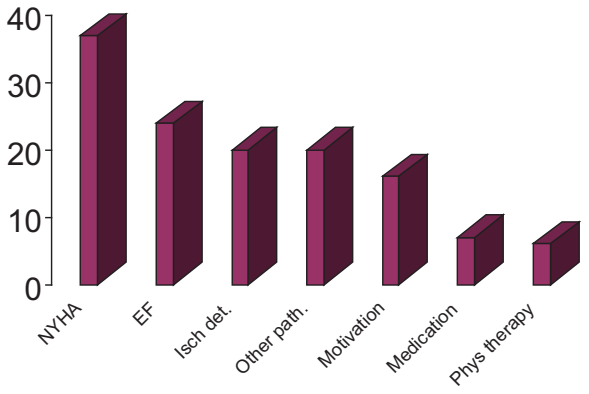

Figure 6. Reasons for rejection (%). (Because a single patient can have more than one reason for rejection, the sum of all is greater than 100%.)

CONCLUSIONS

Treatment with CRT in patients in functional NYHA class III and IV shows a consistent pattern of symptomatic improvement, and the CARE-HF study also shows a positive effect on mortality in a follow up of three years. However, the 30% of the patients receiving a device which do not improve constitute a substantial healthcare problem. In our medical center we can reduce that number to 10% by careful screening and the TBPP.

The screening protocol which was carried out by nurse practitioners revealed several surprising findings. First, it is remarkable that a substantial number of the screened patients are classified in a worse NYHA class by the referring cardiologist, compared to our heart failure team. Without any doubt the lack of a generally accepted standard questionnaire for establishing the NYHA classification plays an important role and the introduction of such a questionnaire will be of great importance for the selection of patients who are referred for CRT. Secondly, the protocol prevents carrying out unnecessary invasive procedures, like the TBPP, in patients referred for CRT. Thirdly, the patients are better informed about the procedure. Finally, the waiting list for TBPP and for implantation of a permanent biventricular pacemaker has been reduced.

Unanswered questions

Despite the developments of recent years, including CRT pacemakers with a cardioverter defibrillator function, not all questions around CRT are answered yet. The effects of CRT in patients in NYHA class I and II are still unclear. Also the question of whether the six minute walking distance has to be used as an inclusion criterion is still open. A common criterion for CRT is a QRS duration of 120 to 150 ms ore more. However, one third of the patients with a QRS duration of less than 120 ms and echocardiographic signs of mechanical asynchrony can benefit from CRT (Achilli et al., 2003; Gasparini et al., 2003).

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