Conclusions and Recommendations

CRT is an effective procedure for treatment of moderate to severe heart failure with LVEF < 35%, sinus rhythm who remains symptomatic despite optimal medical treatment.

QRS duration≥150msec, dilated cardiomyopathy, TAPSE≥15 mm, sinus rhythm, absence of COPD , absence of history of renal disease and optimal LV lead position were the independent predictors of CRT response.

The newly generated CRTscore (in parallel to the current guidelines) may be used to improve patient selection for CRT implantation in order to increase the CRT response rate.

We highly recommend further studies to validated the newly generated CRTscore.

Limitations of the study

1. Small number of patients in NYHA IV included.
2. Small number of patients in AF included, small number of them underwent AV nodal ablation.
3. Small number of patients with narrow QRSd included.
4. Small number of patients with RBBB included.
5. Small number of patients with LV lead position in the anterior, anterolateral, basal and apical regions included.
6. Small number of echocardiographic parameters of mechanical dyssynchrony was assessed and other parameters (especially in TVI, strain and strain rate) were not measured.
7. Automated device based optimization was the only optimization technique used.

Summary

Heart failure is one of the most important causes of morbidity and mortality in the industrialized world.[1] Left ventricular activation delay, as indicated by widening of the QRS complex on a twelve lead electrocardiogram, is present in approximately one-quarter to one-third of heart failure patients. Widening of the QRS complex is a significant predictor of worsened LV systolic dysfunction and poorer outcomes in patients with heart failure.[7] Cardiac resynchronization therapy has been used to improve both the electrical and mechanical dyssynchrony in heart failure patients to improve patient morbidity and mortality.[8] It is generally estimated that 30-40% of patients meeting implantation guidelines fail to respond.[11] Therefore, how to predict who will respond to CRT remains an important and largely unanswered question.[11] Prediction of response to CRT is an important goal in order to derive the desired benefit.[11]

The aim of the study is to assess and identify the best predictors of CRT response.

PATIENTS AND METHODS: Patients with moderate to severe heart failure and LVEF≤35% scheduled for CRT device implantation were subjected to history taking, clinical examination, ECG, echocardiography and coronary angiography in selected patients. CRT was implanted in all patients. CRT response was assessed 6-12 months after implantation. Data were analyzed using SPSS for Windows, version 20.

Results: One hundred and seventy patients were included (mean age 68.8 ± 9.7 years, 38 females and 132 males). Ninety-one patients had dilated cardiomyopathy (DCM) and 79 patients had ischemic cardiomyopathy (ICM). Twenty-three patients presented in NYHA class II dyspnea, 136 NYHY class III and 11 ambulatory NYHA class IV at time of CRT implantation. The mean baseline QRS duration was 145±25 msec, 55.3% of patients had LBBB. During CRT implantation, 147 (86.5%) patients were in sinus rhythm, whereas 23 (13.5%) were in AF. The mean left ventricular internal dimension at end diastole (LVIDd) was 67.6±9 mm, the mean left

ventricular internal dimension at end systole (LVIDs) was 55.7±10 mm, the mean left ventricular end diastolic volume (LVEDV) was 205.7 ± 66 ml and the mean left ventricular end systolic volume (LVESV) was 148.3 ± 56 ml. The mean left ventricular ejection fraction was 28.3±7 %. The mean RV dimension at end diastole (RVd) was 34.15±5.9 mm and the mean tricuspid annular peak systolic excursion (TAPSE) was 18.16±3.8 mm. CRT-P was implanted in 65 patients and CRT-D was implanted in 105 patients. CRT response was achieved in 114 patients (67.1%). CRT implantation was associated with significant improvement in LV dimensions, functions and markers of LV dys-synchrony. CRT implantation was associated with improvement in NYHA class and 6 min walk distance. CRT was also associated with significant improvement in LV diastolic dysfunction and the grade of mitral regurgitation. Compared to non-responders, responders had significantly wider baseline QRS duration, lower BMI, lower baseline serum creatinine level, smaller baseline RV diastolic dimension and significantly greater tricuspid annular peak systolic excursion (TAPSE) value. In univariate analysis, female gender, absence of COPD, absence of history of renal disease, QRS duration ≥ 150 msec, LBBB, sinus rhythm, TAPSE ≥ 15 mm, RVd<35 mm, PAP< 50 mmhg, absence of grade III LV diastolic dysfunction, SPWMD≥130 msec, IVD ≥40msec, Ts-septal-lateral≥60 msec, dilated cardiomyopathy and optimal LV position were significant predictors of CRT response. In multinominal regression analysis to identify the preimplantation predictors of response; QRS duration≥150msec, dilated cardiomyopathy, TAPSE≥15 mm, sinus rhythm, absence of COPD and absence of history of renal disease were the independent predictors of CRT response. We generated a new CRTscore to predict responders to CRT. The score consists of maximum 9 point. The CRT response rate has been markedly different according to the CRTscore. Patients with CRTscore ≥ 6 had CRT response rate of 97.5% vs only 40.7% if CRTscore <6, P<0.001. The CRTscore also did well for predicting CRT response in all classes of recommendations for CRT implantation according to the European guidelines.

Conclusion: CRT is an effective procedure for treatment of moderate to severe heart failure. QRS duration≥150msec, dilated cardiomyopathy,

TAPSE≥15 mm, sinus rhythm, absence of COPD and absence of history of renal disease were the independent preimplantation predictors of CRT response. A new CRTscore may be of benefit to improve the CRT response.

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الملخص العربى

إن فشل القلب هو واحد من أهم أسباب المراضة والوفيات في العالم و يصاحبه فى كثير من الأحيان تباطؤ استحثاث البطين الأيسر الذى يتضح من خلال إطالة مدة إشارة البطين (QRS) فى تخطيط القلب الكهربى و الذى يوجود تقريبا في ربع أو ثلث مرضى فشل القلب. تعتبر إطالة مدة إشارة البطين (QRS) فى تخطيط القلب الكهربي مؤشرا كبيرا على تفاقم الخلل الانقباضي للبطين الأيسر و كما تتنبأ بالنتائج الأكثر سوءا على المدى القريب و البعيد في المرضى الذين يعانون من فشل القلب. وقد استخدم العلاج بزرع جهاز إعادة مزامنة القلب بنجاح لتحسين ضعف التنسيق الكهربائى والميكانيكى في مرضى فشل القلب مما نتج عنه تحسين معدلات الاعتلال والوفيات فى هؤلاء المرضى. ويقدر عموما أن 30-40٪ من المرضى لا يستجيبون للعلاج عن طريق زرع جهاز إعادة مزامنة القلب بالصورة المرجوة برغم مطابقتهم لمتطلبات زرع هذا الجهازالواردة فى المبادئ التوجيهية الأمريكية و الأوربية لعلاج مرضى فشل القلب. لذلك فإن كيفية التنبؤ بالمرضى الذين يستجيبون لزرع جهاز إعادة مزامنة القلب يبقى سؤال مهم ولم يتم الرد عليه إلى حد كبير.

الهدف من هذه الدراسة هو تقييم وتحديد أفضل مؤشرات الاستجابة للعلاج بزرع جهاز إعادة مزامنة القلب.

تمت الدراسة على المرضى الذين يعانون من فشل القلب و ضعف البطين الأيسر بنسبة $\geq$ 35٪ المقرر لهم العلاج بجهاز إعادة مزامنة القلب. وقد خضع المرضى بعد موافقتهم الكتابية للآتى:

أخذ التاريخ المرضى السابق و الفحص الاكلينيكى و رسم تخطيط القلب الكهربى و فحص القلب بموجات صدى الصوت وتصوير الأوعية التاجية في المرضى الذين يشتبه اصابتهم بقصور الاوعية التاجية.

تم تقييم استجابة المرضى للعلاج بجهاز إعادة مزامنة القلب بعد 6-12 شهرا من تركيب الجهاز معتمدا على الاستجابة الاكلينيكية (التحسن فى درجة ضيق التنفس بمقدار درجة او أكثر وفقا لتصنيف جمعية القلب بنيويورك) و فحص القلب باستخدام موجات صدى الصوت (تقليل حجم القلب فى نهاية الإنقباض بمقدار 15% او أكثر) مقارنة بما كان عليه المريض قبل تركيب الجهاز . وقد تم تحليل البيانات باستخدام برنامج SPSS للإحصاء.

النتائج: شملت الدراسة مائة وسبعين مريضا (متوسط أعمارهم 68.8 $\pm$ 9.7 سنوات، 38 من الإناث و 132 من الذكور).

قبل عملية زرع جهاز إعادة مزامنة القلب: كان السبب فى ضعف عضلة القلب هو اعتلال عضلة القلب التوسعى فى 91 مريض و اعتلال عضلة القلب الإقفاري فى 79 مريضا. قبل زرع الجهاز كان المرضى يعانون من ضيق التنفس بحسب تصنيف جمعية القلب بنيويورك من الدرجة الثانية فى 23 مريضا و من الدرجة الثالثة فى مريضا 136 و من الدرجة الرابعة فى 11 مريضا. كان متوسط

مدة إشارة البطين QRS = 145 ± 25 ميللي ثانية. اتضح وجود انسداد بالفرع الضفيرى الأيسر بتخطيط القلب الكهربى فى 55.3٪ من المرضى. أثناء زرع الجهاز كانت ضربات القلب منتظمة وفقا للنظام الجيب أذينى فى 147 مريض (86.5٪) في حين أن 23 مريض (13.5٪) كانوا يعانون من وجود ذبذبة أذينية. وكان متوسط البعد الداخلي للبطين الأيسر في نهاية الانبساط 67.6 ± 9 مم و متوسط البعد الداخلي للبطين الأيسر في نهاية الانقباض كان 55.7 ± 10 مم، وكان متوسط حجم البطين الأيسر في نهاية الانبساط 205.7 ± 66 مل و متوسط حجم البطين الأيسر في نهاية الانقباض 148.3 ± 56 مل. وكان متوسط نسبة طرد البطين الأيسر 28.3 ± 7٪. كان متوسط البعد الداخلى للبطين الايمن في نهاية الانبساط 34.15 ± 5.9 مم وكان متوسط ذروة حركة حلقة الصمام ثلاثي الشرف الانقباضية = 18.16 ± 3.8 مم.

بعد زرع الجهاز: تحققت الاستجابة لزرع جهاز إعادة مزامنة القلب في 114 مريضا (67.1٪). وارتبط زرع جهاز إعادة مزامنة القلب مع تحسن في حجم البطين الأيسر ومهامه وعلامات سوء التزامن فى البطين الأيسر. وارتبط أيضا زرع جهاز إعادة مزامنة القلب مع تحسن في درجة ضيق التنفس و زيادة فى المسافة المقطوعة خلال 6 دقائق سيرا على الأقدام و تحسن في وظيفية انبساط البطين الأيسر وتقليل نسبة أرتجاع الدم بالصمام ثنائى الشرف (المترالى).

مقارنة المستجيبين للجهاز مع غير المستجيبين: مدة إشارة البطين QRS فى تخطيط القلب الكهربى عند بداية الدراسة كانت أطول فى المستجيبين. تميز المستجيبون للجهاز ايضا بالمقارنة بغير المستجيبون عند بداية الدراسة بانخفاض مؤشر كتلة الجسم وانخفاض مستوى الكرياتينين فى الدم و صغر البعد الداخلى للبطين الأيمن و ارتفاع قيمة متوسط ذروة حركة حلقة الصمام ثلاثي الشرف الانقباضية.

مؤشرات الاستجابة لزرع جهاز إعادة مزامنة القلب:

في التحليل وحيد المتغير تبين أن مؤشرات الاستجابة لزرع الجهاز هم كلا مما يلى:

الجنس الأنثوي وعدم وجود مرض الانسداد الرئوى المزمن و عدم وجود تاريخ مرضى لأمراض الكلى و زيادة مدة اشارة البطين QRS فى تخطيط القلب الكهربى بمقدار 150 ميللي ثانية أو أكثر و وجود انسداد بالفرع الضفيرى الأيسر بتخطيط القلب الكهربى و انتظام ضربات القلب وفقا للنظام الجيب أذينى و قيمة متوسط ذروة حركة حلقة الصمام ثلاثي الشرف الانقباضية بمقدار ≤ 15 مم و قيمة البعد الداخلى للبطين الأيمن <35 مم و مقياس ضغط الدم بالشريان الرئوى <50 مم زئبق، عدم وجود اختلال من الدرجة الثالثة بوظيفة البطين الأيسرالانبساطية و وجود تاخير بين الحاجز بين البطينين و الجدار الخلفى للبطين الأيسر بمقدار ≤ 130 ميللي ثانية و وجود تأخير بين البطينين بمقدار ≤ 40 ميللي ثانية و وجود تأخير فى انقباض الجدار الطرفى للبطين الأيسر عن الحاجز بين البطينين بمقدار ≤ 60 ميللي ثانية و الإصابة بمرض اعتلال عضلة القلب التوسعى وأخيرا وجود وصلة البطين الأيسر للجهاز فى مكانها الأمثل.

بينما في التحليل الانحدارى متعدد المتغيرات الإسمية كانت المؤشرات المستقلة للتنبوء المسبق بالإستجابة لزرع جهاز إعادة مزامنة القلب هى كلا مما يلى:

زيادة مدة اشارة البطين QRS فى تخطيط القلب الكهربى بمقدار 150 ميللي ثانية أو أكثر وعدم وجود مرض الانسداد الرئوى المزمن و عدم وجود تاريخ مرضى لأمراض الكلى و انتظام ضربات القلب وفقا للنظام الجيب أذينى و قيمة متوسط ذروة حركة حلقة الصمام ثلاثي الشرف الانقباضية بمقدار $\leq$ 15 مم

و لقد استطعنا انشاء مؤشر متعدد النقاط للتنبؤ باستجابة المرضى لزرع جهاز إعادة مزامنة القلب و يتكون المؤشر من مجموع نقاط معينة لمجموعة المؤشرات المستقلة التى تتنبأ بالاستجابة للجهاز مضاف إليها الجنس الانثوى و انسداد الفرع الضفيرى الأيسر بتخطيط القلب الكهربى على ان تمنح نقطة واحدة لكل مؤشر متوفر لدى المريض قبل زرع الجهاز باستثناء زيادة مدة اشارة البطين QRS فى تخطيط القلب الكهربى بمقدار 150 ميللي ثانية أو أكثر يمنح درجتان حال وجودة و بذلك يكون الحد الأقصى هو 9 نقاط. و قد استجاب للجهاز 97.5 % من المرضى الذين حصلوا على 6 نقاط أو أكثر فى حين استجاب للجهاز 40.7% فقط من المرضى الذين حصلوا على اقل من 6 نقاط.

الاستنتاجات:

العلاج عن طريق زرع جهاز إعادة مزامنة القلب هو إجراء فعال لعلاج حالات فشل القلب الانقباضى. يوجد مجموعة جيدة من المؤشرات التى يمكن استخدامها للتنبؤ باستجابة المرضى لزرع جهاز إعادة مزامنة القلب قبل القيام بزرعه. تجميع المؤشرات فى نظام جديد متعدد النقاط قد يكون طريقة سهلة لإخيار المرضى قبل زرع جهاز إعادة مزامنة القلب لزيادة نسبة الاستجابة له.

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مؤشرات الإستجابة لزرع جهاز تنسيق القلب فى مرضى فشل القلب

رسالة

مقدمة لكلية الطب-جامعة الإسكندرية

إيفاءا جزئيا لشروط الحصول على درجة

دكتوراه فى أمراض القلب

مقدمة من

على احمد على حسن ابو الهدى

ماجستير أمراض القلب و الأوعية الدموية

مدرس مساعد أمراض القلب

كلية الطب جامعة الأسكندرية

كلية الطب

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