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Ehokardiografski parametri probira za kardijalnu resinkronizacijsku terapiju

Echocardiographic Screening Parameters for Cardiac Resynchronization Therapy

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SAŽETAK: *Primjena različitih mogućnosti liječenja kod sve većeg broja pacijenata sa zatajivanjem srca predstavlja značajan pomak u poboljšanju prognoze, kvaliteti življenja i produljenju života. Varijable dobivene temeljem ehokardiografskog pregleda mogu daleko više doprinjeti u postavljanju indikacije za implantaciju biventrikulskog elektrostimulatora nego što je to sada slučaj. U mnoštvu različitih varijabli potrebno je definirati one koji se primjenjuju u probiru pacijenata za implantaciju i za praćenje simptomatskih pacijenata s ugrađenim uređajem, u cilju optimizacije resinkronizacijskog sustava. Cilj ovog članka, nastalog nakon rasprave sudionika 12. hrvatskog simpozija o aritmijama i elektrostimulaciji, je potaknuti daljnju konstruktivnu raspravu.*

KLJUČNE RIJEČI: *ehokardiografija, zatajivanje srca, kardijalna resinkronizacijska terapija.*

SUMMARY: *The application of diverse possibilities of treatment in ever greater number of patients with heart failure represents a significant progress in improvement of prognosis, quality of life and extension of life. Variables obtained on the basis of echocardiography may much more contribute to making indication for the implantation of biventricular pacemaker than what has been the case so far. In many diverse variables, it is necessary to define those applied in screening patients for implantation and monitoring symptomatic patients with implanted device, for the purpose of optimization of resynchronization system. The purpose of this article written following the debate by the participants of the 12th Croatian Symposium on Arrhythmias and Electrostimulation is to stimulate further constructive debate.*

KEYWORDS: *echocardiography, heart failure, cardiac resynchronization therapy.*

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Prevalencija zatajivanja srca (ZS) u Europskim zemljama iznosi u prosijeku 20 oboljelih na 1.000 stanovnika, a u starijih od osamdeset godina prevalencija raste na 10 i više posto[1]. Po nepovoljnoj prognozi ZS je usporedivo s malignim bolestima i sve je veći izazov za liječnike u okružju obilja medikamentnih opcija i biventrikulske resinkronizacijske elektrostimulacije. Na 12. simpoziju u organizaciji Radne skupine za aritmije i elektrostimulaciju srca Hrvatskoga kardiološkog društva održanog u Zagrebu 18. ožujka 2011. godine u diskusiji, u provali emocija protiv, kao i revolta i iznenađenja, stekao se dojam da nedostaju jasni ehokardiografski kriteriji za indikaciju i praćenje kardijalne resinkronizacijske terapije (CRT).

CRT je indicirana kod ambulantnih pacijenata s teškim stupnjem ZS i ventrikulskom asinkronijom u sinusnom ritmu, NYHA razreda III(-IV), trajanjem QRS-kompleksa >120ms, najčvršći dokaz učinkovitosti za tipični potpuni blok lijeve grane, s dilatacijom lijeve klijetke LVEDD >55-60mm, LVEF <35%, dobrim funkcijskim kapacitetom (>4 METS) i očekivanom životnom dobi >1 godine, pod optimalnom medikamentnom terapijom. U NYHA razredu II pacijenata na optimalnoj terapiji i sa širokim QRS-kompleksom >150 ms, LVEF ≤35%[2].

Optimalna terapija implicira primjenu ACE inhibitora, beta-blokatora i antagonista aldosterona za koje postoji dokaz o učinkovitosti i u dozama primjenjenim u kliničkim studijama. Izuzeci s intolerancijom ACEI (ramipril, lisinopril, fosinopril i dr.) i/ili sartana (telmisartan, candesartan,

The prevalence of heart failure (HF) in the European countries is on average 20 diseased per 1000 inhabitants, in persons over 80 years of age, the prevalence rises to 10 per cent and more than that[1]. In case of unfavorable prognosis, HF may be compared to malign diseases and is ever greater challenge for physicians who can choose between different medicamentous options and biventricular resynchronization electrostimulation. At the 12th Symposium organized by the Working Group for Arrhythmias and Electrostimulation of the Croatian Cardiac Society held in Zagreb on 18th March 2011 in debate, outburst of emotions against, revolt and surprise, the author gained an impression that clear echocardiographic criteria for indication and monitoring of cardiac resynchronization therapy (CRT) were missing.

CRT is indicated in outpatients with a serious stage of HF and ventricular asynchrony in the sinus rhythm, NYHA class III(-IV), with QRS-complex duration >120ms, the firmest proof of efficiency for typical complete left bundle branch block, with the left ventricular dilatation LVEDD >55-60mm, LVEF <35%, good functional capacity (>4 METS) and life expectancy of >1 year, on optimum medical therapy. In NYHA class II of patients who are on optimum therapy and with wide QRS-complex >150 ms, LVEF ≤35%[2].

The optimum medical therapy implies the use of ACE inhibitor, beta-blockers and aldosterone antagonists which are proved to be efficient in doses applicable in clinical studies. The exceptions showing ACEI intolerance (ramipril, lisinopril, fosinopril etc.) and/or sartan (telmisartan,

losartan, irbesartan i dr.) su vrlo rijetki. Nešto češće, oko 20%, zastupljena je intolerancija beta-blokatora. Zbog nuspojava spironolakton je moguće zamijeniti eplerenonom. Najčešće ordinirani diuretik furosemid nema pozitivan prognostički učinak i ne produljuje očekivanu životnu dob. Titriranje na više doze treba provoditi kontinuirano i kontrolirano uz elektrokardiogram i po potrebi spirometriju kod kronične opstruktivne bolesti pluća. Beta-blokadom inducirane bradikardije su najčešće prolazne i neopasne. Hrvatska stvarnost još nije optimalna, još uvijek postoji nedostatna potpora liječnika i farmaceuta koji prestrašenim pacijentima kad pročitaju upute za lijek smanjuju doze beta-blokatora (neophodnih u suzbijanju simpatičke aktivacije), kao i ACEI/sartana (nezamjenjivih u temeljnoj terapiji ZS).

Subdozirani pacijenti nemaju indikaciju za resinkronizacijsku terapiju i jasno im se mora istaći da resinkronizacija ne zamjenjuje medikamentnu terapiju, niti broj svakodnevno ordiniranih tableta! Implantacija je posljednja u nizu terapijskih mogućnosti, korisna *ultima ratio* u pomno izabranim slučajevima, a ključna u probiru je ehodoplerkardiografija, neinvazivna, ubikvitarno dostupna, ponovljiva i troškovno učinkovita metoda.

Iako se ehokardiografija ne nalazi u smjernicama za probir CRT, američka ehokardiografski orjentirana društva u najnovijim smjernicama za pravilnu primjenu ehokardiografije, ona ima svoje neupitno mjesto i vrijednost[2]. Prema kliničkim indikacijama[2] ehokardiografija se rangira u evaluaciji prije implantacije i u odabiru adekvatnog uređaja klasom **A** (appropriate) i 9 bodova od mogućih 10. U praćenju i optimiziranju parametara nakon implantacije klasu **U** (uncertain) i 6 bodova. U implantiranih sa simptomima u detekciji komplikacija ili suboptimalnog pacinga klasu A i 8 bodova. Rutinski pregled u razdoblju <1godine kod asimptomatskih pacijenata klasu **I** (inappropriate) 1 bod. Za rutinsko praćenje nakon implantacije >1 godine, kod asimptomatskih pacijenata bez promjene u kliničkoj slici klasu I i 3 boda.

Dostupnom opremom u Republici Hrvatskoj moguća je ehokardiogafska detekcija za CRT, a radi se o opsežnom koji je dugotrajan (time consuming), zahtjeva pregršt varijabli, ali može pomoći i u praćenju i optimiziranju simptomatski resinkroniziranih pacijenata.

U zemljama njemačkog govornog područja koristi se sljedeći protokol[4]:

1. M-Mode i 2D-presjek:

- LVDD enddijastolni promjer lijevog ventrikula
- LVSD endsistolni promjer lijevog ventrikula
- EPSS razmak točke E i septuma
- SPWMD septalno posteriorno kašnjenje gibanja stijenki
- EF biplanom metodom po Simpsonu

2. Dopplerehokardiografski parametri:

- prikaz mitralnog ušća obojenim Dopplerom, obojeni M-mode (PISA i prikaz presistolne MR)
- obojeni Doppler trikuspidnog ušća (color TV)
- mitralni CW-doppler (dp/dt)
- CW Doppler TR (PAP sys.)

candesartan, losartan, irbesartan etc.) are very rare. However, more frequently (around 20%) the beta-blockers intolerance is present. As a consequence of adverse effects, spironolactone may be replaced by eplerenone. The most frequently administered diuretic furosemid has no positive prognostic effect and does not extend life expectancy. Titrating higher doses needs to be conducted continuously and controlled with electrocardiogram including spirometry when required in case of chronic obstructive pulmonary disease. Beta-blocker induced bradycardia are usually transient and harmless. The Croatian reality is not yet optimal, there is still insufficient physicians' and pharmacists' support who reduce the beta-blocker doses when they read the instructions for medicine to upset patients (however, they are necessary for combating sympathetic activation), as well as ACEI/sartan (irreplaceable in the basic HF therapy).

Subdosed patients have no indication of resychronization therapy and they must be warned that resynchronization neither replaces medicamentous therapy nor the number of daily administered tablets. The implantation is the last in the series of therapeutic options, useful ultima ratio in carefully selected cases, echodopplercardiography is crucial in screening and it is a non-invasive, ubiquitously accessible, a repeatable and cost-effective method.

Although echocardiography is not included in the guidelines for screening CRT, the American echocardiography-oriented societies in the most recent guidelines for proper application of echocardiography, it has its unquestionable place and value[2]. According to clinical indications[2] echocardiography is in the evaluation prior to implantation and selection of the adequate device ranked with class **A** (appropriate) and is given 9 points from possible 10 points. In monitoring and optimizing parameters following the implantation it is ranked with class **U** (uncertain) and is given 6 points. In the implanted with symptoms in detecting complications or suboptimal pacing it is ranked with the class A and is given 8 points. The routine examination during the period of <1 year in asymptomatic patients, it is ranked with the class **I** (inappropriate) and if given 1 point. For routine monitoring following the implantation of >1 year in asymptomatic patients without changes to clinical manifestations it is ranked with class I and is given 3 points.

The available equipment in the Republic of Croatia enables the echocardiographic detection for CRT which is extensive and time consuming, it requires a series of variables, but it can help in monitoring and optimizing symptomatic resynchronized patients.

In the German speaking countries, the following protocol is used[4]:

1. M-Mode and 2D-section:

- LVDD left ventricular end-diastolic diameter
- LVSD left ventricular end-systolic diameter
- EPSS E point to septal separation
- SPWMD Septal-to-posterior wall motion delay
- EF by using biplane Simpson's method

2. Doppler echocardiographic parameters:

- Image of mitral orifice by Color Doppler, colored M-mode (PISA and image of pre-systolic MR)
- Color Doppler of tricuspid orifice (Color TV)
- Mitral CW-Doppler (dp/dt)
- CW Doppler TR (PAP sys.)

• PW Doppler mitralnog utoka (E/A relacija, DFT dijastolno vrijeme punjenja)

• PW Doppler LVOT istisnog trakta lijevog ventrikula (udarni volumen i LV-PEP = preejekcijski interval, vrijeme od početka QRS- a do početka VTI)

• PW doppler PA (udarni volumen desnog ventrikula i RV-PEP = analogno lijevom preejekcijskom intervalu)

• fakultativno tkivni Doppler sa septalnog i lateralnog mitralnog prstena (ili ako je dostupan strain) mjerenje kašnjenja apikoanularnog skraćenja u sistoli u odnosu na početak QRS-kompleksa.

• PW Doppler of mitral inflow (E/A relation, DFT diastolic filling time)

• PW Doppler LVOT left ventricular outflow tract (stroke volume and LV-PEP = pre-ejection interval, time from the start of QRS to the start of VTI)

• PW Doppler PA (right ventricular stroke volume and RV-PEP = analogous to left pre-ejection interval)

• Optional tissue Doppler from the septal and lateral ring (or strain, if accessible) measuring the delay of apicoanular shortening in the systole compared to the start of QRS-complex.

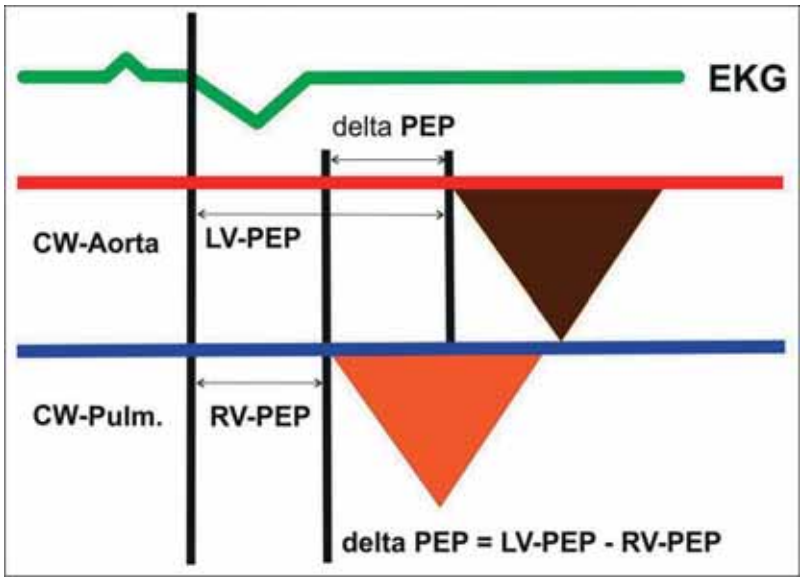

Figure 1. Delta PEP defined as difference between aortic and pulmonary pre-ejection times provides a measure of interventricular mechanical delay and is considered prolonged when greater than 40ms.

Kako smo čuli na simpoziju, bez ehokardiografije ne možemo. I sami smo svjesni velike intra- i interobserverske varijabilnosti, pa je potrebno definirati varijable, ujednačiti kvalitetu prikaza i pouzdanost mjerenja u svim ehokardiografskim laboratorijima i ustanovama diljem Hrvatske, odnosno potrebno je pripremiti nacionalne smjernice.

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As we heard at the symposium, we cannot do anything without echocardiography. You are well aware of great intra- and interobserving variety of variables, so it is necessary to define variables, unify the quality of imaging and reliability of measurement in all echocardiography laboratories and institutions all over Croatia, or it is necessary to prepare national guidelines.

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