KRT'ye «süper-yanıtlı» olgular - Ne yapalım ? 2017

Özgür Aslan

DEÜ Tıp Fak. Kardiyoloji A.D

KRT'ye «süper-yanıtlı» olgular- Ne yapalım ?

- ✓ **KRT'den en çok kim yararlanıyor ?**
- ✓ **KRT'ye «YANIT» tanımları**
  - ✓ **«Süper Yanıt»**
- ✓ **KRT'ye «YANIT»**
  - ✓ **... için belli bir süre var mı ?**
  - ✓ **... ne kadar sürüyor ?**

- ✓ **«Süper yanıtlı» olanlar**
  - ✓ **Ne yapalım ?**
    - ✓ **EF düzelince ICD'yi kapatalım mı ?**

KRT - En çok kim yararlanır ?

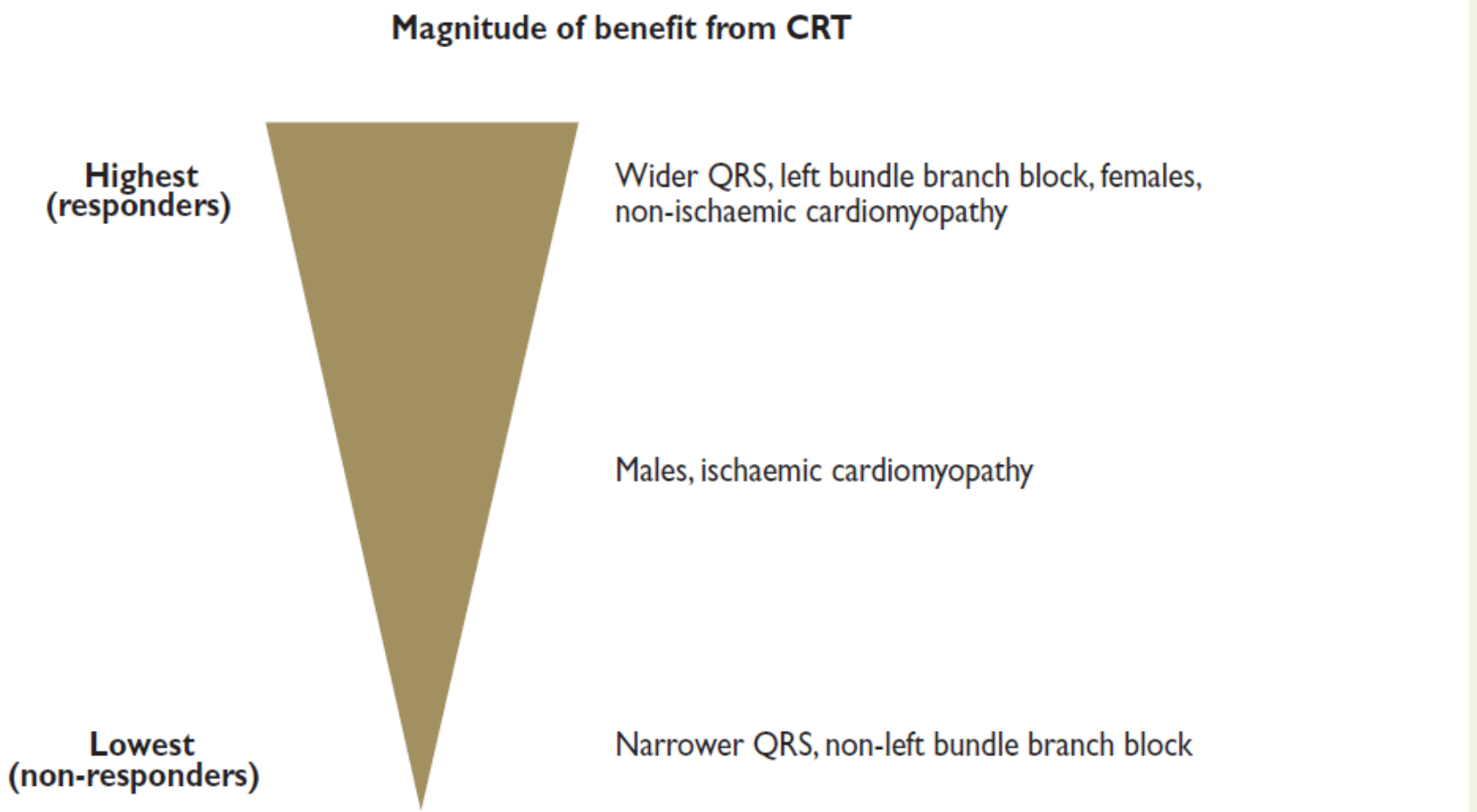

Figure 8 Clinical factors influencing the likelihood to respond to CRT.

2013 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy

KRT'ye «YANIT» tanımları
- «Süper Yanıt»

Yanıt ?

... hastanın tedaviyle daha iyi olması ... ?
... tedavinin hastanın yakınmalarını ve hastalığın muhtemel seyrini anlamlı biçimde etkilemesi ... ?

✓ «Sonlanım» ölçütü («***outcome***») ?
- KY'nin dalgalı ve heterojen seyri ?
- Bir kısım yakınma devam ederken hemodinamik kararlılık olması ?
- EF iyileşmeden fonksiyonel sınıfın düzelmesi ?
- Mortalite için izlem süresi ?....
- ……..

✓ «Yanıt»ı tanımlayan eşik («***response***») ?
- Beklentiler !
  - Yaşam süresi ?
  - Nefes alabilmek ?
  - Yorulmadan yürüyebilmek ?
  - Yapısal iyileşme ?
- Yararlanma hedeflerinin zaman içinde değişimi !

KRT'ye «YANIT» tanımları
- «Süper Yanıt»

«**Sonlanım**» («*outcome*») için «**Yanıt**» («*response*») **ölçütleri** ?

- ✓ **Mortalite / Yaşam süresinin uzaması** ?
  - MADIT-CRT ve REVERSE çalışmalarında **hafif KY** olguları için
    - tüm nedenlere bağlı ölüm oranı düşük
    - mortalite için anlamlı fark yok !
  - COMPANION ve and CARE-HF çalışmalarında **ileri evre KY** olguları için
    - mortalitede anlamlı azalma !
  - *ancak **ileri evre KY** olgularında **KRT'ye yanıt için ölçüt** olabilir !*

- ✓ **Nefes darlığının azaltılması / Fonksiyonel sınıfın iyileşmesi** ?
  - *ancak **semptomatik / ileri evre KY** olgularında **KRT'ye yanıt için ölçüt** olabilir !*

- ✓ **Ventrikülün yeniden biçimlenmesi (küçülmesi ?) / Hastaneye yatışın azaltılması ?**
  - ***KY'nin bütün evrelerinde KRT'ye yanıt için ölçüt** olabilir !*

KRT'ye «YANIT» tanımları
- «Süper Yanıt»

«**Sonlanım**» («*outcome*») için «**Yanıt**» («*response*») **ölçütleri** ?

- **Ventrikülün yeniden biçimlenmesi (küçülmesi ?) ?**
  - Ölçümde teknik sorunlar !
    - LV Volüm ve EF ölçümlerinde «gözlemciler-arası değişkenlik» ! (PROSPECT çalışması)
  - EKO ile ölçümlerde «endpoint» farklılıkları !
    - Çoğu çalışmada **LVESV (>%15 de azalma !)**
    - MADIT-CRT'de LVEDV
  - Hastalık etiyolojisine göre farklı sonuçlar !
    - İskemik KMP'de LV volümlerinde daha az değişiklik

KRT:
- «Süper-Yanıt»

Ortalama 6-24 ayda %10-39

«**Süper-Yanıt**» derken…

✓ Ejeksiyon Fraksiyonu

- EF'de > 2 kat iyileşme
- EF'de > % 20 absolü iyileşme
- EF'de > % 14,5 iyileşme
- EF > % 45 olma
- **EF > % 50 olma**
- **EF 'de %30 iyileşme**

✓ Fonksiyonel iyileşme

- **NYHA Sınıf >1 iyileşme**
- NYHA I-II olma

✓ «Reverse remodelling»

- LVESV > %15 azalma
- **LVESV > %30 azalma**

KRT:
- «Süper-Yanıt»

- Sıklık %7-40
  - Medyan zaman 12 ay

- Öngördürücüler:
  - *NIDKMP*
  - *Başlangıç QRS 144-186*
  - *QRS'de > 40 ms daralma*
  - *LBBB*
  - *Semptom < 12 ay*
  - *LVEDV < 180 ml*
  - *LVEF %30-35*
  - *Kadın cinsiyet*
  - *LAV < 55 ml*
  - *LVESD < 48 mm*
  - *LVEDD < 58 mm*
  - *BMİ < 30 kg/m2*
  - *Küçük LAV İnd*

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Table 2 Studies Assessing Predictors of Hyper- or Super-Responders to CRT

First Author/ Trial (Ref. #)	n	Inclusion Criteria: NYHA Functional Class	Inclusion Criteria: EF, %	Inclusion Criteria: QRS, ms	Inclusion Criteria: Other	Definition of CRT—Super-/Hyper-Response	% Super-Response	Echo Follow-Up	Results—Predictors of CRT Super-Response
Antonio (17)	87	III–IV	35	120	<120 ms + LVMD	Twofold or more increase or >45% in LVEF, improvement >1 NYHA class, LVESV reduction >15%	12%	6 months	Symptoms <12 months was only independent predictor
Castellant (18)	84	III–IV	35	140	LBBB, LVEDD ≥60 mm	LVEF ≥50% and functional recovery (NYHA I–II)	13%	6, 12, and 24 months	NICM
Gasparini (19)	517	II–IV	35	120	HF within 12 months	NYHA class ≤II and LVEF ≥50%	26%	Every 3–6 months	NICM, LVEDV <180 ml, LVEF 30%–35%; super-response median time 12 months
Castellant (27)	51	III–IV	35	140	NICM, LBBB, LVEDD ≥60 mm	LVEF ≥50% and functional recovery (NYHA I–II)	21.5%	6, 12, and 24 months	None
PROSPECT (28)	286	III–IV	35	130		LVESV reduction ≥30%	37.8%	6 months	Female, NYHA class, NICM, LVMD, QRS width (univariate analysis)
Reant (29)	186	III–IV	35	120		Improvement >1 NYHA class, LVEF ≥50% and LVESV reduction ≥15%	9.7%	6 months	LAV <55 ml and global longitudinal strain ≤−12%
Rickard (8)	233	II–IV	40	120		Absolute LVEF increase by ≥20%	13.7%	>2 months (11.6 ± 9)	LBBB
Adelstein (9)	51	III–IV	35	RV pacing >90%, NICM		LVEF ≥50%	29%	≥6 months	LVESD <48 mm, LVEDD <58 mm, CM <24 months (univariate analysis)
Qing (30)	76	III–IV	35	120	LVEDD ≥55 mm	No CV death/transplant, HF admission, improvement >1 NYHA class, LVEF ≥50%	21%	3 months	Pre-implant LVEDV <68 mm
Serdoz (16)	75	III–IV	35	120	Dx >1 year	NYHA class I and LVEF ≥50% without significant MR at 1-year follow-up	17%	Every 6 months (17 ± 9)	NICM, baseline QRS 144–186 ms, QRS narrowing >40 ms
MADIT-CRT (12)	752	I–II	30	130	ICM class I–II, NICM class II	Top quartile of LVEF change (LVEF increase ≥14.5%)	25%	12 months	Female, no prior MI, QRS >150 ms, LBBB, BMI <30 kg/m^2, smaller LAVI

BMI = body mass index; CV = cardiovascular; Dx = diagnosis before implantation; LAVI = left atrial volume index; LVMD = left ventricular mechanical dyssynchrony; MI = myocardial infarction; other abbreviations as in Table 1.

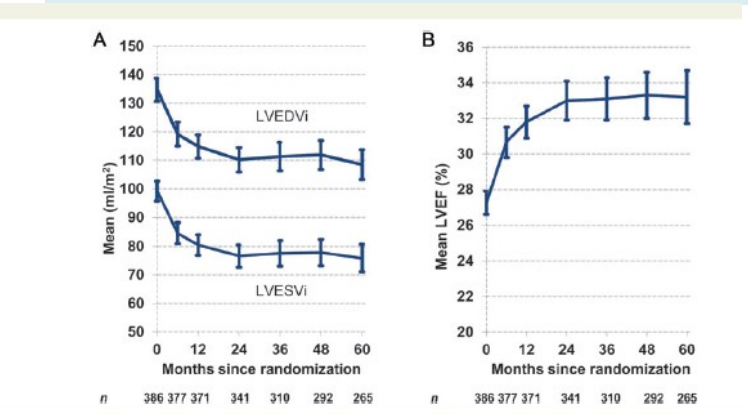
KRT – Yanıt ne kadar sürüyor ?

- ✓ **12. -24. Aydan sonra anlamlı değişiklik olmuyor**
- ✓ **Uzun sürede kötüleşme de olmuyor gibi…**

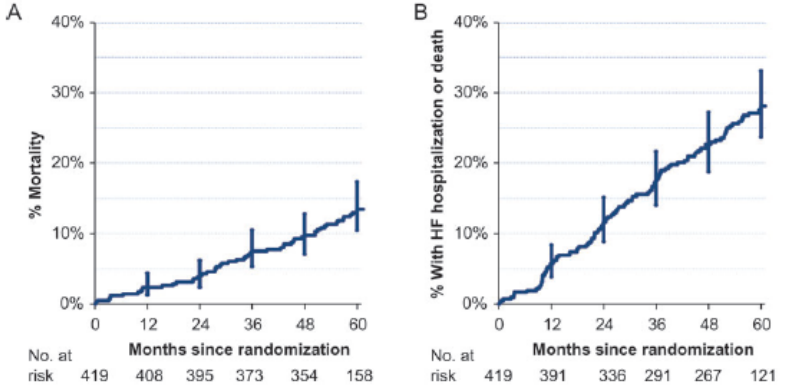
Table 2 Echocardiographic changes over time

From	To	n	Change in LVESVi (mL/m²)	Change in LVEDVi (mL/m²)	Change in LVEF (%)
Baseline	6 months	353	−14.9 ± 27.5, $P < 0.0001$	−15.8 ± 32.4, $P < 0.0001$	3.6 ± 8.3, $P < 0.0001$
6 months	12 months	347	−3.5 ± 18.3, $P = 0.0004$	−3.8 ± 22.2, $P = 0.002$	0.9 ± 6.9, $P = 0.01$
12 months	24 months	322	−5.2 ± 18.8, $P < 0.0001$	−6.3 ± 21.6, $P < 0.0001$	1.3 ± 8.1, $P = 0.005$
24 months	36 months	286	2.7 ± 18.2, $P = 0.01$	3.4 ± 21.6, $P = 0.008$	0.1 ± 8.1, $P = 0.82$
36 months	48 months	260	1.4 ± 20.7, $P = 0.29$	1.0 ± 24.5, $P = 0.52$	−0.7 ± 7.9, $P = 0.17$
48 months	60 months	246	1.0 ± 20.0, $P = 0.43$	−0.7 ± 24.5, $P = 0.65$	−0.9 ± 9.7, $P = 0.15$

The one-sample *t*-test is used to compare changes with 0.



Evolution of left ventricular end-systolic volume index, left ventricular end-diastolic volume index (*A*), and left over time.



Mortality rate (*A*) and time to first heart failure hospitalization or death (*B*) in all patients. Error bars represent 95% cor

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CLINICAL RESEARCH
Heart failure/cardiomyopathy

Long-term impact of cardiac resynchronization therapy in mild heart failure: 5-year results from the REsynchronization reVErses Remodeling in Systolic left vEntricular dysfunction (REVERSE) study

Cecilia Linde[1]*, Michael R. Gold[2], William T. Abraham[3], Martin St John Sutton[4], Stefano Ghio[5], Jeff Cerkvenik[6], and Claude Daubert[7], on behalf of the REsynchronization reVErses Remodeling in Systolic left vEntricular dysfunction (REVERSE) Study Group

[1]Department of Cardiology, Karolinska University Hospital, S-17176, Stockholm, Sweden; [2]Division of Cardiology, Medical University of South Carolina, Charleston, SC, USA; [3]Division of Cardiovascular Medicine and the Davis Heart and Lung Research Institute, The Ohio State University, Columbus, OH, USA; [4]University of Pennsylvania Medical Center, Philadelphia, PA, USA; [5]Fondazione IRCCS Policlinico San Matteo, Pavia, Italy; [6]Medtronic, Inc, Minneapolis, MN, USA; and [7]Département de Cardiologie, CHU, INCERM, CIC_IT 804 Rennes, France

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See page 2582 for the editorial comment on this article (doi:10.1093/eurheartj/eht238)

Background The benefit of cardiac resynchronization therapy (CRT) among patients with mild heart failure (HF), reduced left ventricular (LV) function and wide QRS is well established. We studied the long-term stability of CRT.

Methods REVERSE was a randomized, double-blind study on CRT in NYHA Class I and II HF patients with QRS ≥120 ms and left ventricular ejection fraction (LVEF) ≤40%. After the randomized phase, all were programmed to CRT ON and prospectively followed through 5 years for functional capacity, echocardiography, HF hospitalizations, mortality, and adverse events. We report the results of the 419 patients initially assigned to CRT ON.

Findings The mean follow-up time was 54.8 ± 13.0 months. After 2 years, the functional and LV remodelling improvements were maximal. The 6-min hall walk increased by 18.8 ± 102.3 m and the Minnesota and Kansas City scores improved by 8.2 ± 17.8 and 8.2 ± 17.2 units, respectively. The mean decrease in left ventricular end-systolic volume index and left ventricular end-diastolic volume index was 23.5 ± 34.1 mL/m² ($P < 0.0001$) and 25.4 ± 37.0 mL/m² ($P < 0.0001$) and the mean increase in LVEF 6.0 ± 10.8% ($P < 0.0001$) with sustained improvement thereafter. The annualized and 5-year mortality was 2.9 and 13.5% and the annualized and 5-year rate of death or first HF hospitalization 6.4, and 28.1%. The 5-year LV lead-related complication rate was 12.5%.

Conclusion In patients with mild HF, CRT produced reverse LV remodelling accompanied by very low mortality and need for heart failure hospitalization. These effects were sustained over 5 years. Cardiac resynchronization therapy in addition to optimal medical therapy produces long-standing clinical benefits in mild heart failure.

Clinical Trial Registration: Clinicaltrials.gov identifier NCT00271154.

Keywords Cardiac resynchronization therapy • Heart failure • Electrical dyssynchrony • Mortality

KRT – Yanıt ne kadar sürüyor ?

Yapısal değişikliklere karşın 1. yıldan sonra klinik ölçütlerde değişme olmuyor !

Table 3 Six-minute hall walk and quality of life at baseline and changes from baseline over time. NYHA class distribution over time

	Six-minute hall walk (m)	Minnesota Living with HF QoL score	Kansas City Cardiomyopathy QoL score	NYHA classification		
Baseline	399.2 ± 125.3 387.1–411.3 (416)	27.0 ± 20.1 25.0–28.9 (402)	73.7 ± 19.0 71.7–75.6 (356)	Baseline	I II III IV	75 (18%) 344 (82%) 0 (0%) 0 (0%)
Change from baseline to 12 months	18.6 ± 98.8 8.8–28.4 (393)	−8.4 ± 17.1 −10.1 to −6.7 (386)	8.7 ± 17.8 6.8–10.6 (343)	12 months	I II III IV	177 (44%) 207 (51%) 21 (5%) 0 (0%)
Change from baseline to 24 months	18.8 ± 102.3 8.3–29.2 (370)	−8.2 ± 17.8 −10.1 to −6.4 (369)	8.2 ± 17.2 6.3–10.1 (327)	24 months	I II III IV	162 (42%) 195 (50%) 33 (8%) 0 (0%)
Change from baseline to 36 months	18.6 ± 113.6 6.6–30.7 (345)	−7.9 ± 18.3 −9.8 to −6.0 (350)	7.9 ± 19.6 5.7–10.0 (311)	36 months	I II III IV	152 (41%) 186 (50%) 30 (8%) 2 (1%)
Change from baseline to 48 months	11.3 ± 116.8 −1.8 to 24.4 (308)	−6.4 ± 18.9 −8.4 to −4.3 (323)	6.7 ± 19.7 4.4–9.0 (283)	48 months	I II III IV	117 (35%) 187 (55%) 33 (10%) 1 (<1%)
Change from baseline to 60 months	1.3 ± 119.1 −12.6 to 15.1 (286)	−7.1 ± 18.7 −9.3 to −5.0 (297)	7.2 ± 19.5 4.8–9.6 (261)	60 months	I II III IV	107 (34%) 177 (56%) 28 (9%) 2 (1%)

Cells have mean ± SD, the 95% confidence interval for the mean, and *n* in parentheses or *n* (%). A decrease in the Minnesota QoL score indicates benefit. An increase in the Kansas City Cardiomyopathy QoL score indicates a benefit.

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KRT – Yanıt ne kadar sürüyor ?

- ✓ Verilerin çoğu 12-24 aylık izlem sürelerinden
  - ✓ "6-12 aylık dönemlerde AV ve VV "re-optimizasyonu" gereksinimi?
    - ✓ Reverse remodelling" süreci
    - ✓ Elektromekanik eşleşmede iyileşme
    - ✓ Bölgesel duvar stresinin dağılımda değişiklik
    - ✓ "Reversed – dyssynchrony" olasılığı

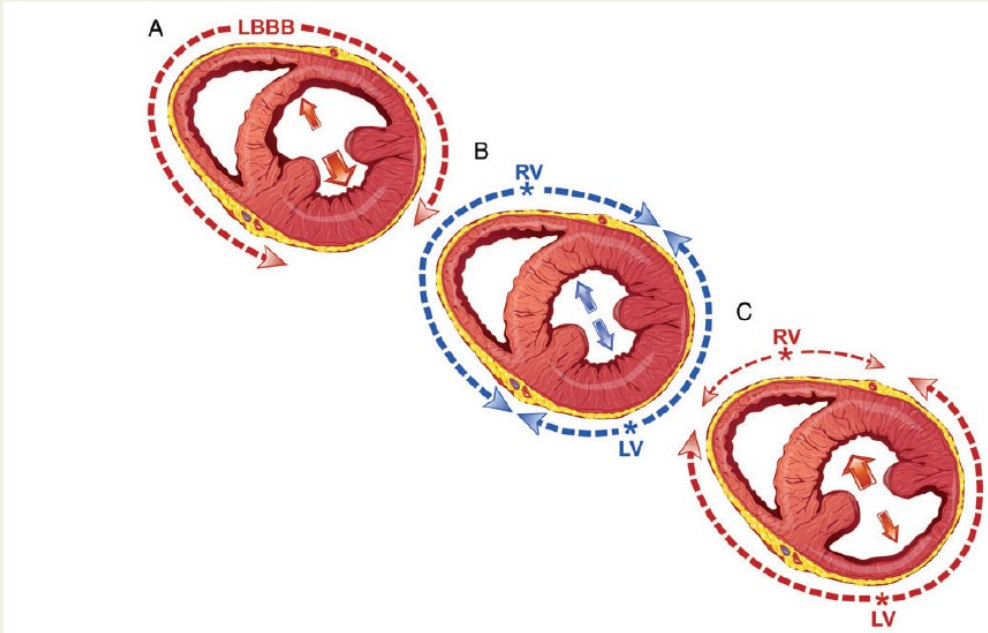

Figure 1 Long-term impact of different ventricular activation patterns on regional load and hypertrophy. A, delayed LV activation in LBBB unloads the septum and increases the regional load in the delayed activated postero-lateral wall resulting in compensatory hypertrophy.[8] B, Optimized CRT may normalize these pathologic relationships by simultaneous and more rapid ventricular activation. C, Hypothetical (and probably exaggerated) result of suboptimal CRT with early LV activation (reverse dyssynchrony). The early activated posterolateral wall is exposed to a lower regional load and the late activated opposing wall (i.e. the septum) responds with regional hypertrophy.

- ✓ 24 aydan uzun izlemlerde optimizasyonun / etiyolojinin rolü ?

OE Breithard. European Heart Journal (2013) 34, 2582–2584

KRT – «Süper-Yanıt» / pacing ?

‘Düzelme’ mi ‘Remisyon’ mu ?

- Tanımdan bağımsız olarak uzun-dönem prognoz mükemmel !
    - Sağ-kalım
    - Ventrikül aritmileri
    - Yaşam kalitesi ve egzersiz toleransı
- ‘Süper-yanıt’lı bireylerin %78’I KRT’nin uyarısı kapatıldığında 12 ayın sonunda kötüleşiyorlar ! (*Cay S, Ozeke O, Ozcan F, et al. Mid-term clinical and echocardiographic evaluation of super responders with and without pacing: the preliminary results of a prospective, randomized, single-centre study. Europace 2015*)
- **Yararın devam etmesi için KRT-pacing in devam etmesi gerekiyor !**

Proclemer A, Muser D, Facchin D. What We Can Learn from “Super-responders”. Heart Failure Clin 13 (2017) 225–232. Card Electrophysiol Clin 7 (2015) 781–788

KRT:
- «Süper-Yanıt»

EF iyileşince ICD'yi kapatalım mı ?

- ✓ Mükemmel uzun dönem sonuçlar
  - ✓ Ani ölüm / hastaneye yatış daha az
  - ✓ Uygun şok daha az
- ✓ EF >%50 olsa da «uygun şok» alan bir grup var
  - ✓ Bu grubun tanımlanması olanağı henüz yok
- ✓ ***KRT-D olarak kalsın !***

Europace (2014) **16**, 363–371
doi:10.1093/europace/eut339

Long-term outcome of 'super-responder' patients to cardiac resynchronization therapy

Massimo Zecchin[1]*, Alberto Proclemer[1], Silvia Magnani[1], Laura Vitali-Serdoz[1], Domenico Facchin[2], Daniele Muser[2], Andrea Nordio[1], Giulia Barbati[1], Ilaria Puggia[1], Gianfranco Sinagra[1], and Alessandro Proclemer[2]

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Aims To evaluate the long-term changes of clinical and echocardiographic parameters, the incidence of cardiac events and parameters associated with late cardiac events in 'super-responders' to cardiac resynchronization therapy (CRT) with [CRT defibrillator (CRT-D)] or without defibrillator back-up.

Methods and results In all consecutive patients treated with CRT in two Italian centres (Trieste and Udine) with left ventricular ejection fraction (LVEF) $\leq$0.35 at implantation (T_{imp}) and LVEF $>$ 0.50 1 and/or 2 years (T_{norm}) after implantation, the long-term outcome and the evolution of echocardiographic parameters were assessed; factors associated with a higher risk of cardiac events, defined as hospitalization or death for heart failure (HF), sudden death, or CRT-D appropriate interventions, were also analysed. Among the 259 patients evaluated, 62 (24%) had LVEF $\geq$ 0.50 at T_{norm} ($n = 44$ with at 1 year, $n = 18$ at 2 years). During a mean follow-up of 68 $\pm$ 30 months, one cardiac death (for HF) and eight cardiovascular events (two hospitalization for HF and six appropriate CRT-D interventions) occurred. At the last echo evaluation (T_{fup}) performed 51 $\pm$ 26 months after T_{imp}, LVEF was $<$0.50 in five patients ($>$0.45 in four of them). At univariable analysis, only LV end-systolic volume evaluated at T_{fup} was associated with a higher risk of cardiac events during follow-up.

Conclusion In 'super-responders' to CRT long-term outcome is excellent. However, cardiac events, mainly CRT-D appropriate interventions, can occur despite the persistence of LVEF $>$ 0.50. Early identification of these patients is still an unsolved issue.

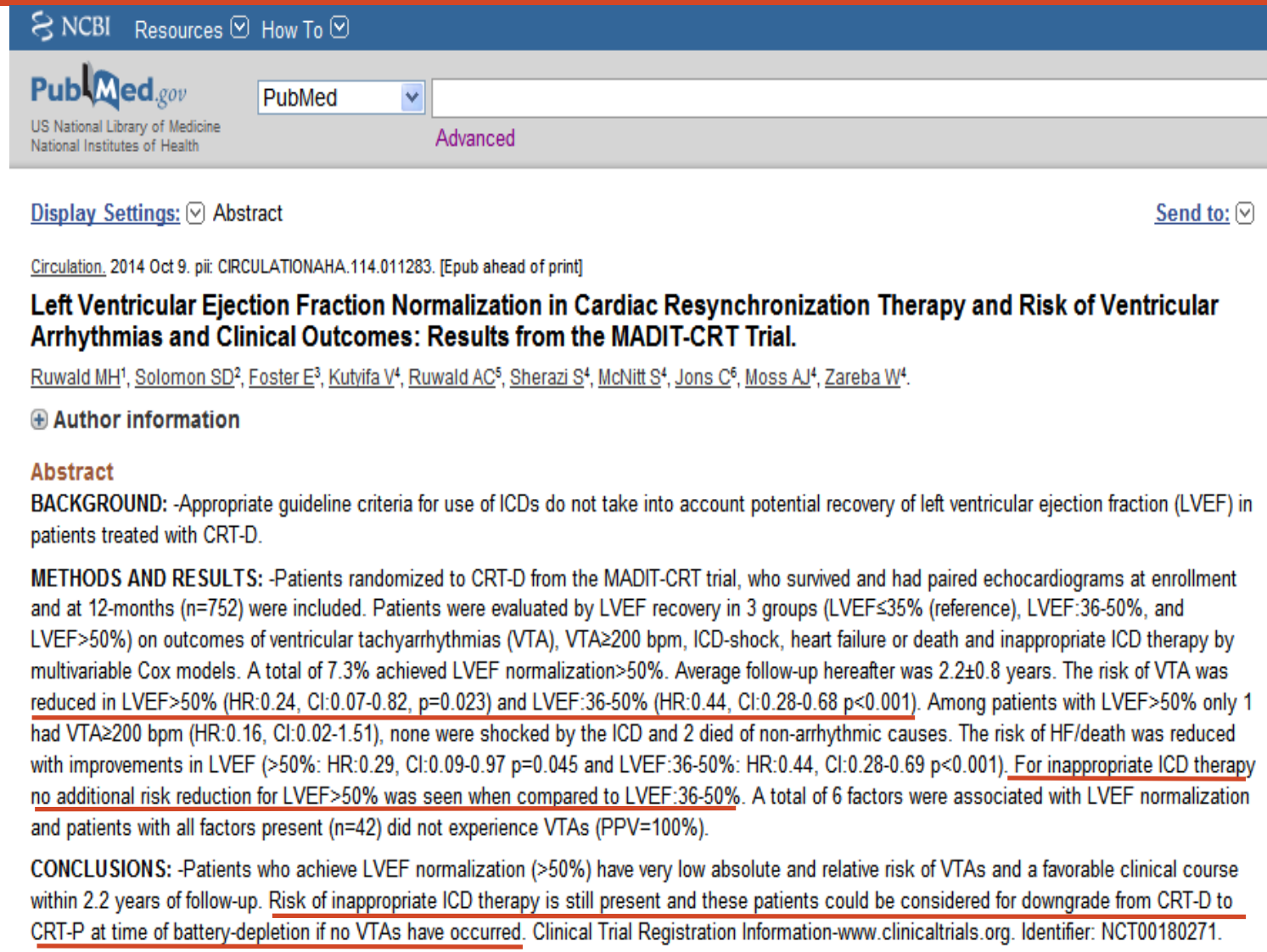
Keywords Outcome • Super-responders • Cardiac resynchronization therapy • Heart failure

KRT:
- «Süper-Yanıt»

EF iyileşince ICD'yi kapatalım mı?

- ✓ EF >%50 olma oranı %7.3
- ✓ İzlem süresi 2.2+-0.8 yıl
- ✓ VT oranı EF > %36 olunca azalıyor !
- ✓ Uygunsuz şok oranında azalma olmuyor !!!
- ✓ ***VT yoksa pil ömrü bittiğinde***

KRT-pacing yapılabilir !



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Left Ventricular Ejection Fraction Normalization in Cardiac Resynchronization Therapy and Risk of Ventricular Arrhythmias and Clinical Outcomes: Results from the MADIT-CRT Trial.

Ruwald MH[1], Solomon SD[2], Foster E[3], Kutyifa V[4], Ruwald AC[5], Sherazi S[4], McNitt S[4], Jons C[5], Moss AJ[4], Zareba W[4].

Author information

Abstract

BACKGROUND: -Appropriate guideline criteria for use of ICDs do not take into account potential recovery of left ventricular ejection fraction (LVEF) in patients treated with CRT-D.

METHODS AND RESULTS: -Patients randomized to CRT-D from the MADIT-CRT trial, who survived and had paired echocardiograms at enrollment and at 12-months (n=752) were included. Patients were evaluated by LVEF recovery in 3 groups (LVEF≤35% (reference), LVEF:36-50%, and LVEF>50%) on outcomes of ventricular tachyarrhythmias (VTA), VTA≥200 bpm, ICD-shock, heart failure or death and inappropriate ICD therapy by multivariable Cox models. A total of 7.3% achieved LVEF normalization>50%. Average follow-up hereafter was 2.2±0.8 years. The risk of VTA was reduced in LVEF>50% (HR:0.24, CI:0.07-0.82, p=0.023) and LVEF:36-50% (HR:0.44, CI:0.28-0.68 p<0.001). Among patients with LVEF>50% only 1 had VTA≥200 bpm (HR:0.16, CI:0.02-1.51), none were shocked by the ICD and 2 died of non-arrhythmic causes. The risk of HF/death was reduced with improvements in LVEF (>50%: HR:0.29, CI:0.09-0.97 p=0.045 and LVEF:36-50%: HR:0.44, CI:0.28-0.69 p<0.001). For inappropriate ICD therapy no additional risk reduction for LVEF>50% was seen when compared to LVEF:36-50%. A total of 6 factors were associated with LVEF normalization and patients with all factors present (n=42) did not experience VTAs (PPV=100%).

CONCLUSIONS: -Patients who achieve LVEF normalization (>50%) have very low absolute and relative risk of VTAs and a favorable clinical course within 2.2 years of follow-up. Risk of inappropriate ICD therapy is still present and these patients could be considered for downgrade from CRT-D to CRT-P at time of battery-depletion if no VTAs have occurred. Clinical Trial Registration Information-www.clinicaltrials.org. Identifier: NCT00180271.

KRT:
- «Süper-Yanıt»

EF iyileşince ICD'yi kapatalım mı ?

- ✓ «Süper-Yanıt» = LVESV'de >%30 düşme
- ✓ «Süper yanıt»lıların %23'ünde yaşamı tehdit edebilecek aritmi
- ✓ «Uygun şok» oranı ilk yıl içinde belirgin azalıyor
  - **%3** vs. %12 (p <0.001)
- ✓ İlk yıldan sonra «uygun şok» oranında azalma yok !
  - 5 yılda toplam **%27** vs. %34 (p=0.13)
- ✓ ***ICD'den hala yararlanıyorlar – değiştirmemeli !***

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Super-responders to cardiac resynchronization therapy remain at risk for ventricular arrhythmias and benefit from defibrillator treatment

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Aims	Mortality and ventricular arrhythmias are reduced in patients responding to cardiac resynchronization therapy (CRT). This response is accompanied by improvement in LVEF, and some patients even outgrow original eligibility criteria for implantable cardioverter-defibrillator (ICD) implantation. It is however unclear if these patients still benefit from ICD treatment. The current study aimed to evaluate if the incidence of ICD therapy is related to the extent of CRT response.
Methods and results	All patients who underwent primary prevention CRT-defibrillator implantation were included. They were divided into subgroups according to the reduction in LV end-systolic volume (LVESV) 6 months after implantation. Pre-defined subgroups were: negative responders (increased LVESV), non-responders (decreased LVESV 0–14%), responders (decreased LVESV 15–29%), and super-responders (decreased LVESV ≥30%). During a median follow-up of 57 months (25th–75th percentile 39–84), 512 patients were studied [101 (20%) negative responders, 101 (20%) non-responders, 149 (29%) responders, and 161 (31%) super-responders]. In the first year of follow-up super-responders received significantly less appropriate ICD therapy (3% vs. 12%; $P < 0.001$). The 5-year cumulative incidence of appropriate ICD therapy was 31% [95% confidence interval (CI) 19–43] in negative responders, 39% (95% CI 25–53) in non-responders, 34% (95% CI 25–43) in responders, and 27% (95% CI 18–35) in super-responders, respectively ($p = 0.13$).
Conclusions	The extent of CRT response was associated with a parallel reduction of appropriate device therapy during the first year of follow-up. Thereafter, no association was observed. Furthermore, 23% of super-responders were treated for potentially life-threatening arrhythmias and benefit from ICD treatment.
Keywords	Cardiac resynchronization therapy • Left ventricular reverse remodelling • Ventricular arrythmias • Implantable cardioverter-defibrillator

KRT:
- «Süper-Yanıt»

- ✓ LVEF'de iyileşme VTA riskinde belirgin bir azalma ile ilişkili
- ✓ **VTA için en düşük risk grubu !**
  - ✓ LVEF ≥%45 olanlar
  - ✓ Primer korunma için ICD takılmış olanlarda LVEF iyileşmesi

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CLINICAL RESEARCH
Arrhythmia/electrophysiology

Reduced appropriate implantable cardioverter-defibrillator therapy after cardiac resynchronization therapy-induced left ventricular function recovery: a meta-analysis and systematic review

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Aims For patients undergoing cardiac resynchronization therapy (CRT) with implantable cardioverter-defibrillator (ICD; CRT-D), the effect of an improvement in left ventricular ejection fraction (LVEF) on appropriate ICD therapy may have significant implications regarding management at the time of ICD generator replacement.

Methods and results We conducted a meta-analysis to determine the effect of LVEF recovery following CRT on the incidence of appropriate ICD therapy. A search of multiple electronic databases identified 709 reports, of which 6 retrospective cohort studies were included ($n = 1740$). In patients with post-CRT LVEF ≥35% (study $n = 4$), the pooled estimated rate of ICD therapy (5.5/100 person-years) was significantly lower than patients with post-CRT LVEF <35% [incidence rate difference (IRD): −6.5/100 person-years, 95% confidence interval (95% CI): −8.8 to −4.2, $P < 0.001$]. Similarly, patients with post-CRT LVEF ≥45% (study $n = 4$) demonstrated lower estimated rates of ICD therapy (2.3/100 person-years) compared with patients without such recovery (IRD: −5.8/100 person-years, 95% CI: −7.6 to −4.0, $P < 0.001$). Restricting analysis to studies discounting ICD therapies during LVEF recovery (study $n = 3$), patients with LVEF recovery (≥35 or ≥45%) had significantly lower rates of ICD therapy compared with patients without such recovery (P for both <0.001). Patients with primary prevention indication for ICD, regardless of LVEF recovery definition, had very low rates of ICD therapy (0.4 to 0.8/100-person years).

Conclusion Recovery of LVEF post-CRT is associated with significantly reduced appropriate ICD therapy. Patients with improvement of LVEF ≥45% and those with primary prevention indication for ICD appear to be at lowest risk.

Keywords Resynchronization • Ventricular tachyarrhythmia • Meta-analysis

KRT:
- «Süper-Yanıt»

EF iyileşince ICD'yi kapatalım mı ?

- ✓ **EF > %35 olanlar**
  - ✓ %21'inde «uygun şok»
  - ✓ 5 yıllık kümülatif «uygun ted.» oranı %20 (%8-32)
  - ✓ LBBB/NLBBB ve iskemik/noniskemik farkı yok !
- ✓ **EF > %40 olanlar**
  - ✓ %27'sinde «uygun şok»
  - ✓ 5 yıllık kümülatif «uygun ted.» oranı %23 (%14-32)
- ✓ ***ICD'den hala yararlanıyorlar – karar dikkatli verilmeli !***

Long-Term Echocardiographic Outcome in Super-Responders to Cardiac Resynchronization Therapy and the Association With Mortality and Defibrillator Therapy

Aafke C. van der Heijden, MD[a], Ulas Höke, MD[a], Joep Thijssen, MD, PhD[a], C. Jan Willem Borleffs, MD, PhD[a], Ron Wolterbeek, MD[b], Martin J. Schalij, MD, PhD[a], and Lieselot van Erven, MD, PhD[a,*]

Super-response to cardiac resynchronization therapy (CRT) is associated with significant left ventricular (LV) reverse remodeling and improved clinical outcome. The study aimed to: (1) evaluate whether LV reverse remodeling remains sustained during long-term follow-up in super-responders and (2) analyze the association between the course of LV reverse remodeling and ventricular arrhythmias. Of all, primary prevention super-responders to CRT were selected. Super-response was defined as LV end-systolic volume reduction of ≥30% 6 months after device implantation. Cox regression analysis was performed to investigate the association of LV ejection fraction (LVEF) as time-dependent variable with implantable-cardioverter defibrillator (ICD) therapy and mortality. A total of 171 super-responders to CRT-defibrillator were included (mean age 67 ± 9 years; 66% men; 37% ischemic heart disease). Here of 129 patients received at least 1 echocardiographic evaluation after a median follow-up of 62 months (25th to 75th percentile, 38 to 87). LV end-diastolic volume, LV end-systolic volume, and LVEF after 6-month follow-up were comparable with those after 62-month follow-up ($p = 0.90$, $p = 0.37$, and $p = 0.55$, respectively). Changes in LVEF during follow-up in super-responders were independently associated with appropriate ICD therapy (hazard ratio 0.94, 95% CI 0.90 to 0.98; $p = 0.005$) and all-cause mortality (hazard ratio 0.95, 95% CI 0.91 to 1.00; $p = 0.04$). A 5% increase in LVEF was associated with a 1.37 times lower risk of appropriate ICD therapy and a 1.30 times lower risk of mortality. In conclusion, LV reverse remodeling in super-responders to CRT remains sustained during long-term follow-up. Changes in LVEF during follow-up were associated with mortality and ICD therapy. (Am J Cardiol 2016;118:1217–1224)

KRT:
- «Süper-Yanıt»

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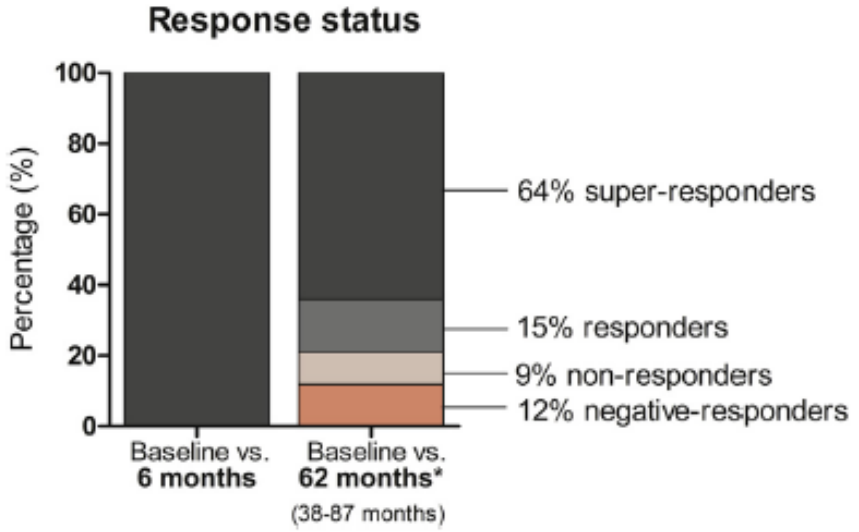
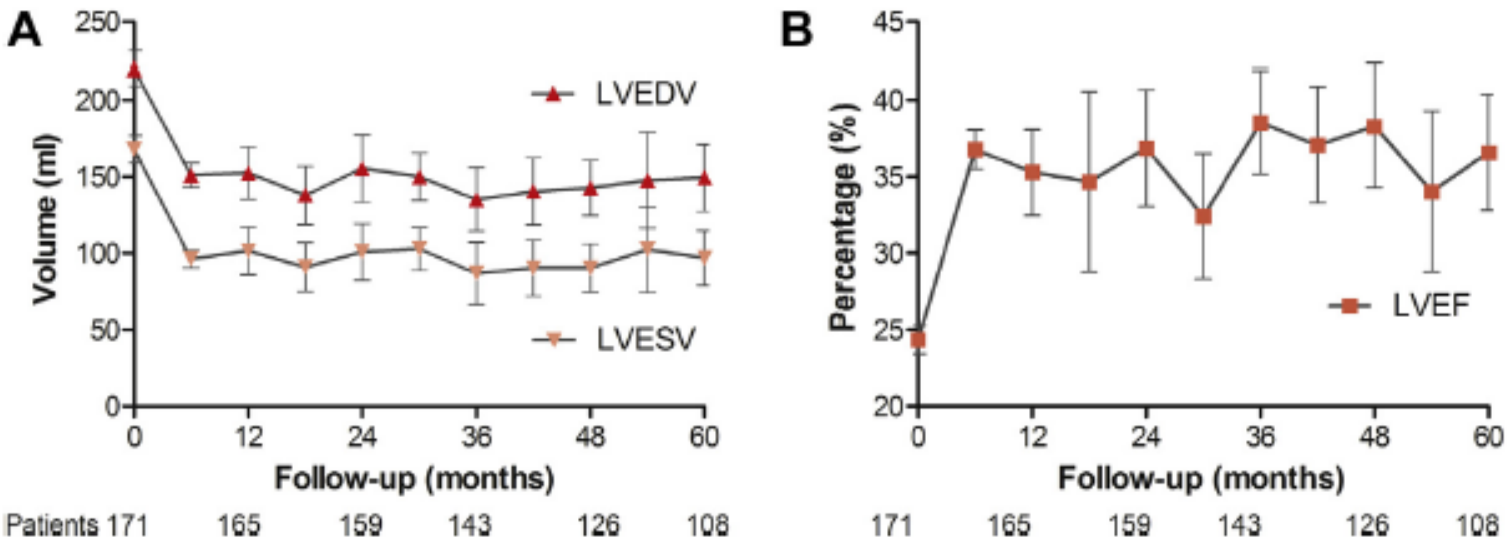


Figure 3. Echocardiographic response status after long-term follow-up. The *left column* depicts the echocardiographic response status at 6 months after CRT-D implantation. The *right column* depicts echocardiographic response status after long-term follow-up. *Results of the last final echocardiographic evaluation, after a median follow-up 62 months (25th-75th percentile, 38 to 87) are compared with baseline.



Long-term echocardiographic outcome in super-responders to cardiac resynchronization therapy

	Baseline	6 months	62 months (38–87 months)	Estimated mean difference (95% CI)	p-value
All (N=171)					
Left ventricular end diastolic volume (ml)	220±72	151±53	150±63	0.58 (-8.80–9.96)	0.90
Left ventricular end systolic volume (ml)	168±61	96±38	99±55	3.86 (-4.66–12.39)	0.37
Left ventricular ejection fraction (%)	24±6	37±9	36±11	-0.63 (-2.88–1.61)	0.55

KRT:
- «Süper-Yanıt» / ICD'yi kapatalım mı? : *Durum net değil!*

- ✓ KRT implantasyonunun birincil nedeni prognozu iyileştirmek ise yarar kanıtlarının çoğunluğu …
  - ✓ NYHA – Sınıf II olguları için KRT-D 'den
  - ✓ NYHA – Sınıf III-IV olguları için KRT-P'den
- ✓ KRT ile ICD gereksinimi azalıyor mu ?
  - ✓ Aritmi yükünü azaltır !
- ✓ KRT ile ICD yararı artıyor mu ?
  - ✓ KY kötüleşmesinden kaynaklanan mortaliteyi azaltarak aritmi riskine maruz kalınan süreyi uzatır !

2016 ESC Guidelines for diagnosis and treatment of acute and chronic heart failure.
European Heart Journal (2016) 37, 2129–2200

Teşekkürler!...